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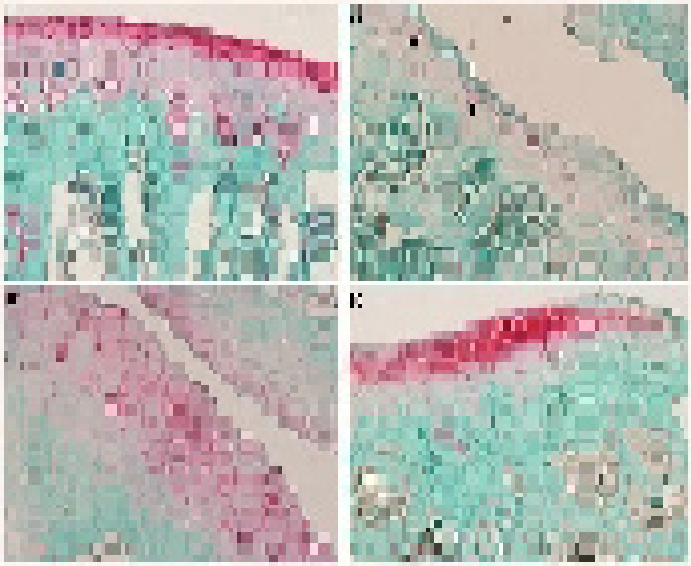

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Editorial

J. Exp. Clin. Med., 2017; 34(3):159
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A new issue of Journal of Experimental and Clinical Medicine

Dear Readers

The editorial team of Journal of Experimental and Clinical Medicine prepared a new issue with the contribution of very distinguished authors.
Kızıltepe et al. investigated the attitude of emergency nurses toward death and get very interesting results. According to these results, authors also made important recommendations about the subject. Aksan et al. presented very important data about the association of red cell distribution width and coronary plaque burden in type 2 diabetes mellitus patients. They showed that RDW values have significant correlation with total plaque burden, and the number of non-calcified and mixed plaques.
Deşer and Demirağ shared us their carotid endarterectomy series and their mean 17 months follow up results. Similarly Ünal et al. presented the clinical data of patients who were operated by the same surgeon due to parotid mass. Nar and Avcı investigated the relationship between glucose levels in different sample types with simultaneous measurements. Kayacan et al. examined a sports team for the level of physiological and psychological stress generated by a handball competition via non-invasive saliva analysis. Baki et al. investigated the effects of oral propolis treatment in terms of cartilage tissue protection on an experimental osteoarthritis model in rats.
Additionaly, very interesting case reports are presented in this issue.
I hope you enjoy this new issue and I look forward to hear your comments and feed backs regarding this issue.

Dr. Serkan Yüksel
Editor in Chief
Samsun, Turkey

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Clinical Research

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Can we trust the positivity of semi-quantitative glucose measurement in the urine?

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ABSTRACT

As known, when the blood glucose level exceeds the renal threshold value of 180-200 mg/dL it begins to be excreted with urine. Spot urine analysis is easy to perform and an important test, with false positive or negative test results incompatible with the clinic. Our aim in this study is to investigate the relationship between glucose levels in different sample types with simultaneous measurements.Material and Simultaneous fasting serum glucose, HbA1c levels and urine glucose of 2375 patients were screened retrospectively from the hospital information system between June 1, 2015 and November 30, 2015. Fasting serum glucose was measured by enzymatic hexokinase method in biochemical autoanalyzer, HbA1c was measured by chromatographic method on HPLC and urine glucose was measured semi-quantitatively by urine autoanalyzer by strip glucose oxidase method. It was found that there was a medium-strong relationship between all three results. There was significant; correlation;between; fasting serum glucose and HbA1c (r: 0.787, $p < 0.001$) and the correlation between urinary glucose and fasting serum glucose and HbA1c were (r: 635, $p < 0.001$) and (r: 533, $p < 0.001$), respectively. In our study, we indicated that there is a strong correlation between the glucose results of different types of samples that we use in our laboratory. The patient's concurrently measured HbA1c and fasting serum glucose results may be helpful to the laboratory specialist to avoid both false positives and false negatives.

1. Introductıon

The tests used to measure glucose in the blood were developed about 100 years ago, and they became the only criteria for the diagnosis of diabetes and hyperglycemia. The most widely accepted glucose-based criteria for the diagnosis of diabetes are fasting plasma glucose (FPG) ≥ 126 mg/dL or 2 hours plasma glucose ≥ 200 mg/dL during the 75 g oral glucose tolerance test (OGTT). In addition, a patient with classic diabetes symptoms, having a single measured random plasma glucose ≥ 200 mg/dL is considered diagnostic (Sacks, 2011; Sacks et al., 2011; ADA, 2016). HbA1c is a marker that is formed by nonenzymatic glycosylation of hemoglobin, indicating glucose regulation and glucose tolerance (Koenig et al, 1976). HbA1c levels of 6.5% or above is also among the diagnostic criteria for diabetes (Sacks, 2011; ADA, 2016) and it is accepted that HbA1c in diabetic patients reflects the risk of developing diabetic complications and the quality of diabetic care (Herman and Fajans, 2010, Karatoprak et al., 2012).

Routine urine screening is a strip test method that includes chemical tests for, pH, protein, glucose, ketone, erythrocyte, bilirubin, urobilinogen, nitrite, leucocyte esterase and specific gravity. Urine analysis results may change depending on the type of strip, the autoanalyzer or the evaluation method used in the laboratories and provides qualitative (positive or negative) or semiquantitative (eg, negative - 4+ positive) measurement results (Simerville et al., 2005; Mundt and Shanahan, 2010).

There is no glucose in the urine of a healthy person or it can be detected in small quantities (2-20 mg/ dl) (Mundt and Shanahan, 2010). The amount of glucose in the urine depends on the blood glucose level, the glomerular filtration rate and the degree of reabsorption from the tubules. Generally, glucose starts to be detected in urine after a blood level of about 180-200 mg/dL, which is the normal renal threshold for glucose (Simerville et al., 2005; Cersosimo et al., 2014). Glycosuria occurs when the blood glucose exceeds the renal threshold since the tubules can not reabsorb all filtered glucose (Mundt and Shanahan, 2010). Diabetes mellitus, Cushing's syndrome, diseases of the liver and pancreas, and

Fanconi syndrome are included in the etiology of glucosuria (Simerville et al., 2005). Urinalysis for glucose can be used to detect diabetic hyperglycemia, including ketoacidosis, but false positives and negatives can occur (Mitchell et al., 2013). It has been reported that urinary glucose level varies depending on the time after the meal which may hence affect the validity of urinary glucose test as a screening test for diabetes (Shinozaki et al., 1999).

Currently, blood and urinary glucose measurement results are routinely used in evaluating the glucose level. However, the reliability of the relationship between existing methods creates a question mark in the minds of physicians. Especially in spot urine analysis, false positive or negative test results incompatible with the clinic are frequently observed. In this study, it was aimed to evaluate the relationship between measured glucose results using different methods in three different sample types and the location of urine glucose in diabetes screening.

2. Materıals And Methods

Simultaneous serum glucose, HbA1c levels and urine glucose were scanned retrospectively from the hospital information system of 2375 patients who applied to Ahi Evran University Training and Research Hospital between June 1, 2015 and November 30, 2015. Fasting serum glucose was measured by enzymatic hexokinase method in biochemical autoanalyzer, HbA1c was measured by chromatographic method on HPLC and urine glucose was measured semi-quantitatively by urine autoanalyzer by strip glucose oxidase method. HbA1c levels were converted to estimated glucose values using the formula EG (mg / dL) = (28.7 x HbA1c) - 46.7 (Nathan et al., 2008). Semiquantitative urine results were converted to quantitative results using the values given in the kit brochure (± (90 mg / dl), 1+ (252 mg / dl), 2+ (504 mg / dl), 3+ (1980 mg / dl)). Subjects with HbA1c <6.5%, HbA1c ≥ 6.5%, serum glucose <126 mg / dl, serum glucose ≥126 mg / dl, serum glucose ≥180 mg / dl and serum glucose ≥200 mg / dl were divided into groups. The mean glucose value, mean HbA1c value and glucose positivity counts in the urine were evaluated in the groups.

Statistical analysis of the data was performed using the SPSS analysis program. SPSS version 17.0 software (SPSS Inc., Chicago, Illinois, USA) and Microsoft Office Excel 2007 programs were used for statistical evaluations. The relationship between sample types was evaluated by Pearson correlation coefficient. P <0.05 was considered statistically significant. The results of the groups were expressed as mean ± standard deviation.

3. Results

In the analysis of correlation, it was seen that there was a medium-strong relationship between all three results. Correlation between serum glucose and HbA1c was r: 0.787, p <0.001, correlation between urine glucose and serum glucose was r: 0.635, p <0.001 and correlation between urine glucose and HbA1c was r: 0.533, p <0.001 (Table 1).

Table 1: Correlation between serum glucose, urine glucose and HbA1c

Variables	r value	p value
Serum glucose-HbA1c	0.787	<0.001
Serum glucose - Urine glucose	0.635	<0.001
HbA1c-Urine Glucose	0.533	<0.001

878 patients with an HbA1c value <6.5% had a mean serum glucose of 104.8 mg/dl and urine glucose positivity (1+) was detected in only one patient with serum glucose 130 mg/dl and HbA1c value 6.4%. This group had a mean serum glucose of 180.7 mg/dl and urine glucose positivity was detected in 242 of these persons. Urine glucose positivity was found in persons with an HbA1c level of 6.6% or above (Table 2).

Table 2: Mean glucose and HbA1c values of the groups and the number of urine glucose positivity

Groups	Number of subject	Mean glucose value	Mean HbA1c value	Urine glucose positivity
HbA1c value less than 6.5 (%)	878	104.8 ± 17.83	5.82 ± 0.38	1 (0.11%)
HbA1c value of 6.5 and above (%)	1497	180.7 ± 72.46	8.53 ± 1.79	242 (16.2%)
Serum glucose values below 126 (mg/dl)	1084	102.8 ± 13.38	6.2 ± 1.01	7 (0.64%)
Serum glucose values 126 and above (mg/dl)	1291	194.6 ± 69.1	8.62 ± 1.88	236 (18.2%)
Serum glucose values 180 and above (mg/dl)	600	248.7 ± 67.5	9.83 ±1.82	218 (36.3) %
Serum glucose values 200 and above (mg/dl)	442	270.2 ± 66.56	10.27 ±1.80	210 (47.5%)

When 1084 subjects with serum glucose <126 mg/dL were analyzed, the mean HbA1c value was found as 6.2% and urine glucose positivity was found in 7 persons. In 1291 subjects with serum glucose ≥126 mg/dl, the mean HbA1c value was found as 8.62% and urine glucose positivity was found in 236 persons. Urine glucose positivity was found in 218 (36.3%) of 600 subjects with a renal threshold value of 180 mg/dl and above serum glucose values and negative in 382

Table 2: Mean glucose and HbA1c values of the groups and the number of urine glucose positivity

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4. Discussion

All of the urine strips used for the semiquantitative measurement of urine glucose use glucose oxidase, a glucose-specific enzyme in a chromogenic assay. There is no glucose in

the urine of a healthy person or it can be detected in small quantities (2-20 mg/dl) (Mundt and Shanahan, 2010). Usually, glucose will not be present in the urine until the blood level exceeds 180–200 mg/dL, which is the normal renal threshold for glucose (Mundt and Shanahan, 2010; Simerville et al., 2005; Cersosimo et al., 2014). In routine examinations, the negative result of the strip test is usually interpreted as the absence of glucose in the urine specimen (Altınısık, 2010). However, there are factors that affect the urine test and lead to misjudgment of the result. The increased amount of ketones and the use of levodopa may lead to false positives of the glucose result in the urine, while elevated specific gravity, uric acid and vitamin C can lead to false negativity in the urine (Simerville et al., 2005; Mundt and Shanahan, 2010).
The benefit of glucose screening in the urine and the relationship between urinary glucose and diabetes have been shown in various studies (Davies et al. 1993; Yokota et al., 2004; Urakami et al., 2005; Ogawa et al., 2012). The school health law of Japan was passed in 1974 mandating urine screening of elementary and junior high-school students for the detection of renal disease, in 1994 urine glucose screening was also made compulsory (Yokota et al., 2004).

Ogawa E. et al. performed urine glucose screening in Tokyo between 1988 and 2009 and glucosuria was detected in 298 school children. As a result of the application of the oral glucose tolerance test to these children, they detected renal glucosuria in 146 students, diabetes mellitus in 133 students, and impaired glucose tolerance in 19 students (Ogawa et al., 2012).

Urakami T et al. investigated 8,812,356 school-aged children for glucosuria from 1974 to 2002 in Tokyo, when the urine was positive for glucose, an oral glucose tolerance test was carried out to confirm diabetes. In all, 232 students were identified to have type 2 diabetes. Low cost urine glucose screening has been shown to be useful for school children in the detection of diabetes in the early stages of the disease (Urakami et al., 2005).

However, the usefulness of urinary glucose as a screening test for unrecognized diabetes is limited because the urine test was found with specificity of > 98% and low sensitivities (21-64%) (Englelgau et al., 2000). Davies MJ at al. performed OGTT on 330 subjects, who were screened for postprandial glucosuria and detected positive glucose in urine. 99 of these subjects had newly diagnosed diabetes, 56 had impaired glucose tolerance. The test had a sensitivity of 43% and specificity of 98% (Davies et al., 1993). Friderichsen et al. evaluated the urine glucose test by randomly selected 106 test-negative participants and they detected 3 DM and 4 impaired glucose tolerance. They reported that the test had a sensitivity of 21% and specificity of 99% (Friderichsen and Maunsbach, 1997).

Considering the renal threshold value, we found glucose positivity in urine only 36.3% in the group with serum glucose value of 180 mg/dl and above. A randomly measured plasma glucose of ≥ 200 mg/dL is a diagnostic criteria for diabetes. In our study, glucose positivity was detected in the urine of 210 patients (47.5%) in this group, but we observed negativity more than half. This is consistent with the literature and may depend on the timing of the urine sample collection, the difference between the individuals at the renal threshold value, and the low sensitivity of urine glucose sc-Glycosuria test may give false-negative results in the diagnosis of diabetes mellitus, as age-related increases in renal threshold (Friderichsen and Maunsbach, 1997). The urine sample collection timing for urine glucose screening test should be carefully examined and its performance is usually better with random, postprandial, or glucose-loaded measurements than fasting measurements (Shinozaki et al., 1999; Englelgau et al.,2000).

Glucose measurement in fasting plasma is widely used as a diabetes diagnostic criteria (ADA, 2016). Easily and cost-effectively analysis with automated devices in the laboratories all around the world are the advantages of this test, however, there are some limitations. Fasting glucose concentrations vary significantly from day to day in a single individual. Individual changes in a healthy person are reported between 5.7% and 8.3% (Lacher et al., 2005). Fasting plasma glucose (FPG) can range from 112 to 140 mg/dL in an individual with an FPG of 126 mg/dL, depending on a CV (coefficient of variation) of 5.7%. Plasma glucose concentration can be altered by preanalytical factors such as drugs, foods, long-term fasting, exercise, sample handling (Young and Bermes, 2006; Sacks, 2011).

HbA1c is formed by non-enzymatic binding of N-terminal valine glucose in the β-chain of hemoglobin. HbA1c reflects the long-term mean plasma glucose, representing the mean glucose concentration over the previous 2-3 months. Compared with OGTT, HbA1c measurement is faster and more useful. Many factors that alter fasting blood sugar do not significantly affect HbA1c concentrations. Short-term lifestyle changes such as acute illness, exercise, recent food consumption and sampling conditions do not significantly change HbA1c levels. In non-diabetic individuals, intraindividual variation of HbA1c is minimal with 1% CV (Hu et al., 2003; Sacks, 2011).

Hillman N. et al. reported a correlation between mean blood glucose values and HbA1c values of 146 DM patients (r: 0.620, p <0.001) (Hillman et al., 2004). Ogawa E. et al. reported a high correlation between fasting plasma glucose and HbA1c values (r: 0.86, p <0.0001) (Ogawa et al., 2012). Motor S. et al. observed a correlation between HbA1c levels and mean blood glucose levels in 131 DM patients with chronic renal failure (r: 0.755, p <0.001) (Motor et al., 2013). In our study, there was a significant correlation between serum glucose and HbA1c levels (r: 0,787, p <0.001) and it was found consistent with the previous studies.

The remarkable point in our study is the significant correlation between urinary glucose and serum glucose and HbA1c (p<0.001). As stated by the World Health Organization, semiquantitative urine glucose screening test for diabetes mellitus is not appropriate due to its low sensitivity (WHO,2003; Wei and Teece, 2006; Altınısık, 2010). However, we believe that when there is no blood sample, without ignoring the false-negative results, urine glucose results can be used in diabetes mellitus screening.

5. Conclusion

In our study, we found a strong correlation between the results of different methods that we used in three different sample types of glucose analysis in our laboratory. While reporting urine glucose results, we think that evaluating concurrently analyzed HbA1c and fasting serum glucose results

may help the laboratory specialist in avoiding both false positives and false negatives. In addition, if there is no evidence of blood glucose and positive urine glucose results are encountered, it is necessary to perform further examination for diabetes and also with urine glucose negativity clinician physicians should not exclude diabetes risk.

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The effect of status and frequency of confronting death in emergency nurses on attitude towards death

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ABSTRACT

Perception and attitude towards death is influenced from various factors such as religion, culture, social value judgments, beliefs and traditions. People may develop negative or positive attitude towards death according to the experiences they live about death of individuals in their environment. In this study, mean score of Attitude to Death Scale was determined as 123, mean score of "Neutral Acceptance and Approach Acceptance" among sub-dimensions of scale is 68, mean score of sub-dimension of "Escape Acceptance" is 20.235.98, mean score of sub-dimension of "Fear and Avoidance of Death" is 35.9810.06. It was determined that score of Attitude to Death Scale does not differ according to socio-demographic or occupational characteristics such as age, education, marital status, receiving education during or after occupational education yet; mean score of nurses who have experienced the loss of a close relative recently was higher than those who have not.

1.Introduction

Death is a universal incident. Death is the truth and part of life (Öz, 2004). The concept of death in people's mind has effect on people's behaviours and life styles in religious, philosophical, moral and legal sense; people who are always closely related with death can develop attitude towards death through thinking of it (Bilge et al.,2013). Perception and attitude of death can be influenced from various factors such as religion, culture, social value judgment, beliefs and perceiving death (Özdemir and Ekinci, 2014). People may develop negative or positive attitude according to the experience they had about death of people around them (İnci and Öz, 2009) and attitudes and reactions developed towards death may vary from individual to individual (Özdemir and Ekinci, 2014). Although the attitude developed towards death is a reaction on against experience of death, this reaction is defined as the sense of threat, fear and discomfort (Rooda et al., 1999). Personality, emotions and behaviours of a nurse who is taught the responsibility of sustaining life throughout her occupational life may influence her attitude towards death; a nurse who adopts care and treatment of a patient may experience fear, anxiety, rejection, anger, guilt, depression, despair and sorrow against the loss of patient (Öz, 2004; Karakurt, 2013). When the nurse lives misconception about death and cannot develop a positive attitude, it becomes difficult to work with a deadly patient (Tanhan and Arı, 2006), the attitude she has developed towards death influences the quality of care negatively and prevent the peaceful and easy death which the patient deserves (Ay and Öz, 2013). In this sense, it is quite

important that a nurse is conscious of her feelings towards death, manage these feelings correctly and develop suitable attitude. One of the departments in which many critical patients are given care and treatment in hospital and the incident of death is frequently experienced is the emergency unit. Although the incident of death is frequently experienced in the department of hospital, each loss of patient is unique and quite sorrowful for nurses (Öz, 2004; Karakurt, 2013). In this study which was carried out in order to determine the effect of status and frequency of confronting death in emergency nurses on attitude towards death, answers were sought for these questions:

- What are the socio-demographic and occupational characteristics of nurses working at emergency unit?
- Do the socio-demographic characteristics, thoughts about death and status of confronting death of emergency nurses influence their attitude to death?

2. Material and Methods

Design

This is a descriptive and cross-sectional study which was carried out in order to determine the effect of status and frequency of confronting death in emergency nurses on attitude towards death. The study was carried out between 15 April-20 May 2016 with the participation of 122 nurses who accepted to participate in the study and who have been working at emergency unit for at least 6 months out of 136 nurses working at 5 state hospitals and one university hospital in Samsun city center. 14 nurses who were off or who received report during the days when the survey form was applied were excluded from the scope of study. Respondency rate of survey form is 89.7%. In this study data were collected by using introductory information form for nurses and "Attitude to Death Scale". Introductory information form for nurses is composed of 20 questions which aim to determine socio-demographic and occupational characteristics of nurses and their attitude and tendency towards death. Attitude to Death Scale is a scale which was developed by Wong et al. (1994) in order to evaluate attitude of individuals towards death and adapted into Turkish by Işık et al. (2009). Attitude to Death Scale is seven-grade Likert type scale which is composed of 26 items based on the view that death exists. The scale is composed of three sub-dimensions namely "Neutral Acceptance and Approach Acceptance" (items no. 4, 6, 8, 12, 13, 14, 15, 19, 21, 22, 23, 25), "Escape Acceptance" (items no. 5, 9, 11, 20, 24.) and "Fear and Avoidance of Death" (items no. 1, 2, 3, 7, 10, 16, 17, 18, 26.) and measures attitude of individuals towards death. Score can be obtained from each one of the sub-dimensions and also total score of scale can be obtained as well. Total high score to be obtained from the scale is evaluated as developing negative attitude towards death (Işık et al., 2009)."Neutral Acceptance" is to believe that death is a part of life. In this way a person is neither afraid of death or accepts it. The person only accepts it as one of the irrevocable truths of life. He tries to get the most out of restricted life. "Approach Acceptance" is to think that death is a passage to other life and to believe in a happy afterlife. "Escape Acceptance" is to believe that death provides relief from physical and psychological pain of death and problems of life. It is to believe that life is full of suffering and misery and pain and death is a fine alternative that can be embraced. "Fear of death" is the feeling of fear which is felt when one comes face to face with death. "Avoidance of death" is to avoid from thinking and speaking of death with the hope of decreasing the anxiety of death. Therefore, avoidance of death is a defence mechanism a person uses while keeping death away from themselves (Wong et al., 1994).

The survey form was tested with a pre-application with a group of 5 people before it was applied on nurses and nurses who were included in the pilot study were excluded from the sampling. Nurses who participated in the study were informed about the study and data were collected by the researcher after their informed consent was obtained. Data collection lasted nearly for 8-10 minutes. Nurses were explained that it is totally their decision to take part in the study or not, that their names would not be written on the survey form and data to be obtained from this study will only be used within the scope of this study. The study started after taking the consent of Ondokuz Mayıs University Medical Faculty Ethical Committee (issue no. 14.04.2016/; B.30.2.ODM.020.08/236). In order to collect data, written consent was obtained from hospital managers and university hospital management and informed consent was obtained from nurses in the scope of research. In this study, Attitude to Death Scale Cronbach Alpha coefficient was .078, Neutral Acceptance and Approach Acceptance among sub-dimensions of scale, Escape Acceptance, Fear and Avoidance of Death Cronbach Alpha coefficients were .079, .066 and .073.

Statistical analysis

Data obtained from the study were analyzed in computer environment by using SPSS 15.0 package program. Normality test of quantitative data were analyzed with Shapiro Wilk. Mann Whitney U and Kruskal Wallis tests were used in the analysis of non-normally distributed data, one-way analysis of variance test technique, independent sample t test were used in the analysis of normally distributed data. Cronbach Alpha analysis was used in determination of reliability of scales used. Results were provided in frequency, percentile, average, Standard deviation; mean (min-max.). Significance level was taken as $p<0.05$.

3. Results

According to the findings obtained from the study, it was determined that 63.1% (n=77) of the nurses are married, 37.7% (n=46) have associate degree, 34.7% (n=41) received education about process and management of death and 21.2% (n=25) received education after graduation, 80.5% (n=91) want to have information about communication skills required to be used in approach to dying patient, 41.3% (n=50) have confronted with death risk and 67.3% (n=35) have experienced traffic accident. In this study, it was determined that 34.5% (n=41) have experienced the loss of family member who are first degree relatives, status of confronting death influenced perspective towards occupation of 43.3% (n=52) of nurses, comparing with the individuals who are dying or already dead 71.1% (n=86) felt sorrow and 52.9% (n=64) tried to behave cold-blooded, in order to cope with the emotions they felt against the incident of death 85.6% (n=101) prayed, 39.8% (n=47) shared with their friends and family, 21.2% (n=25) cried and 16.9% (n=20) moved away

from the environment, 50% (n=61) abstained from coming across with the relatives of the deceased and 79.7% (n=94) did not want to inform about the death to the relatives of patient. In this study, mean score of Attitude to Death Scale was determined as 123, mean score of "Neutral Acceptance and Approach Acceptance" among sub-dimensions of scale is 68, mean score of sub-dimension of "Escape Acceptance" is 20.235.98, mean score of sub-dimension of "Fear and Avoidance of Death" is 35.9810.06 (Table 1).

Table 1. Mean and median score values of total and sub-dimensions of Attitude to Death Scale

Sub-dimension of Scale	Med (Min - Max) A.O ± S.S
Neutral Acceptance and Approach Acceptance	68 (11-83)
Escape Acceptance	20.235.98
Fear and Avoidance of Death	35.98 10.06
Attitude to Death Scale	123 (24 -179)

A.O: Arithmetic average

Some of the socio-demographic and occupational characteristics of nurses and scores obtained from Attitude to Death Scale were compared in Table 2,3. According to the findings, it was determined that score of nurses obtained from Attitude to Death Scale do not differ according to their age group (p=0.975, X2=0.051), educational status (p=0.051, X2=7.779), marital status (p=0.312, U=1521.5), receiving education about death during their occupational education (p=0.487, U=1419.0) or after graduation (p=0.683, U=1055.5), receiving education about death, status of losing relatives at first degree (p=0.176, U=1339.5), status of confronting with death risk (p=0.281, U=1547.5), status of confronting with death influencing their perspective towards occupation (p=0.075, U=1432.0), avoidance of facing the relatives of the deceased (p=0.828, X2=0,378) status of wanting to inform about the death to the relatives of patient (p= 0,748, U=1068.5), while mean score of nurses who have experienced a close relative recently (127) was higher than those who have not (120) (p=0.001, U=1114.5) (Table 2,3).

Table 2. Comparison of socio-demographic characteristics of nurses and scores of Attitude to Death Scale

Characteristics		Neutral Acceptance and Approach Acceptance Med (Min-Max) A.OSS	Escape Acceptance Med (Min-Max) A.OSS	Fear and Avoidance of Death Med (Min-Max) A.OSS	Attitude to Death Scale Total
Age Groups	18-28 age	68 (28-82)	20.28 6.21	36.42 10.83	122 (40-164)
	29-39 age	67 (11-83)	19.87 6.08	36.49 9.86	123 (24-179)
	40 and above	68 (46-79)	21.56 5.18	33.22 9.31	124 (90-149)
Test statistics, p value		**p=0.935, =0.134**	**p=0.591, F=0.528**	**p=0.455, F=0.793**	**p=0.975, =0.051**
Marital status	Married	68 (11-83)	20.36 5.84	36.6610.10	125 (24-179)
	Single	68 (28-82)	20.00 6.27	34.829.99	121 (40-164)
Test statistics, p value		**p=0.936, U=1695.0**	**p=0.747, t=0.268**	**p=0.693, t=0.156**	**p=0.312, U=1521.5**
Educational status	VocationalSchool of Health	68 (40-82)	22 (11-35)	39.72 11.22	126 (84-179)
	Associate degree	68 (11-83)	20 (0-29)	33.59 9.79	123 (24-147)
	Undergraduate	68 (44-80)	20 (11-32)	36.58 9.40	124 (84-158)
	Postgraduate	66 (43-70)	15 (14-21)	32.865.98	115 (85-121)
Test statistics, p value		**p=0.367, ==3.165**	**p=0.102, ==6.200**	**p=0.057, F =2.573**	**p=0.051, =7.779**

A.O: Arithmetic average, U: Mann Whitney U test statistics,: Kruskal Wallis test statistics, F:One way analysis of variance test statistics, t: Independent sampling t test statistics

It was observed that mean score of Attitude to Death Scale "Neutral Acceptance and Approach Acceptance" sub-dimension varies according to the status of nurses' losing a close relative recently (p=0.014, U=1249.5), mean score of "Escape Acceptance" sub-dimension varies according to the status of wanting to inform about the death to the relatives of patient (p=0.002, F=0.285), mean score of "Fear and Avoidance of Death" sub-dimension varies according to status of confronting with death influencing their perspective towards occupation (p=0.025, U=1365.0) (Table 3).

4. Discussion

It is quite important to develop positive attitude towards death both in the sense of health care professionals and the patient and his family. Positive attitude of health care professionals towards death would decrease fear and worry of patients about death and provide a care environment where the satisfaction level is high (Frommelt, 2003; Eues, 2007). In this study, only one third of the nurses who participated in the study (34.7%) have received information about process and management of death during their occupational education, few nurses have received education about this subject in the institution they work after graduation

(21.2%) and nearly four fifth of nurses want to have information about communication skills required to be used in approach to dying patient. Supporting the findings of this study, it was stated in some of the studies carried out on this issue that great majority of the nurses have not received education about process and management of death, great majority of nurses who have received education do not think that it is sufficient, they find themselves insufficient in fulfilling emo-

Table 3. Comparison of vocational characteristics of nurses and scores of Attitude to Death Scale

Characteristics		Neutral Acceptance and Approach Acceptance Med (Min-Max) Med (Min-Max) Escape Acceptance Med (Min-Max) A.OSS	Escape Acceptance Med (Min-Max) A.OSS	Fear and Avoidance of Death Med (Min-Max) A.OSS	Attitude to Death Scale Total
Having education about death in vocational education period	Yes	70 (49-82)	20.73 5.21	35.24 8.89	124 (87-158)
	No	66 (11-83)	19.75 6.14	35.8210.35	122 (24-164)
Test statistics, p value		**P=0.076,U =1232.0**	**P=0.387,t =0.291**	**p=0.764, t =0.600**	**P=0.487,U =1419**
Having education about death after graduation	Yes	70 (49-82)	20.08 5.30	32.72 9.15	124 (87-143)
	No	66 (11-83)	20.16 6.14	36.6710.24	124 (24-179)
Test statistics, p value		**p=0.122,U=887**	**p=0.952, t =0.370**	**p=0.083, t=0.129**	**p=0.683, U=1055.5**
Having experienced the loss of relative at first degree	Yes	68 (28-83)	20 (0-30)	35.3910.45	127 (40-158)
	No	66 (11-82)	20 (1-35)	35.949.89	123 (24-179)
Test statistics, p value		**p=0.281, U=1388**	**p=0.201, U=1371**	**p=0.780, t =0.457**	**p=0.176, U=1339.5**
Having experienced loss of a relative recently	Yes	69 (44-83)	21.54 5.94	35.7510.74	127 (84-164)
	No	66 (11-82)	19.405.90	34.759.44	120 (24-179)
Test statistics, p value		**p=0.014, U=1249.5**	**p=0.055, t =0.965**	**p=0.109, t=1.808**	**p=0.001, U=1114.5**
Confronting the risk of death	Yes	68 (43-79)	20 (12-32)	35.50 (19-61)	125 (84-164)
	No	67 (11-83)	20 (0-35)	37.00 (12-62)	122 (24-179)
Test statistics, p value		**p=0.641, U=1662.5**	**p=0.103, U=1466**	**p=0.778, U=1721.5**	**p=0.281, U=1547.5**
Influence of confronting death on occupational perspective	Yes	68 (28-83)	20.33 6.06	39 (12-61)	125 (40-164)
	No	67 (11-82)	20.265.94	33 (12-62)	122 (24-179)
Test statistics, p value		**p=0.443, U=1623.5**	**p=0.952, t =0.011**	**p=0.025, U=1365.0**	**p=0.075, U=1432.0**
Avoiding to confront the relative of the deceased	Yes	68 (11-83)	19.266.25	35.11 9.68	123 (24-158)
	No	67 (40-82)	21.605.86	36.62 10.12	123 (84-179)
Test statistics, p value	No matter	66 (43-78) **p=0.709, x^2x^2 =0.687**	20,324,93 **p=0.202, F =1.449**	37,3711,39 **p=0.616, F=0.487**	119 (85-149) **p=0.828, x^2=0.378**
Wanting to inform the relative about the death of patient	Yes	68 (11-83)	19.715.43	36.45 9.43	123 (24-164)
	No	68 (40-82)	23.67 5.79	34.38 11.66	123 (84-179)
Test statistics, p value		**p=0.655, U=1050**	**p=0.002, t =0.285**	**p=0.362, t=2.498**	**p=0.748, U=1068.5**

A.O: Arithmetic average, U: Mann Whitney U test statistics,: Kruskal Wallis test statistics, F:One way analysis of variance test statistics, t: Independent sampling t test statistics

tional and spiritual requirements of dying patient and his relatives (Mallory, 2003; Menekli and Fadıloğlu, 2014; Yılmaz and Vermişli, 2015). According to the findings it is thought that the education of death given during undergraduate education is not sufficient in preparing nurses to give care to a dying patient and therefore education on this issue should be sustained periodically through in-service training/continuing education programs. Education given about process and management of death would increase awareness of nurses and provide information, psychosocial skills and cultural sensitiveness which is required to develop positive attitude towards death (Dunn et al., 2005).

Nurses who come across to individuals that are about to die or who are dying may live different emotion-status changes. In this study it was determined that most of the nurses feel sorrow (71.1%) and behave cold-blooded (52.9%) when they see an individual who is close to death or who is dying. In accordance with the findings of this study, in some of the studies carried out on this issue, it is stated that when they come across to individuals who are close to death or who are dying, most of the nurses feel anger, sorrow, grief, despair, react normally and think it as the fact of life, cry, think their pain ended, feel sorry, feel afraid, feel discomfort and they do not want to give care to a deadly patient (Ünsal and Sabuncu, 2008; Çevik and Kav,2010; Acehan and Eker, 2013; Önsöz and Çam, 2013;Yılmaz and Vermişli, 2015), prefer to work in services where there is not deadly patient since they are afraid of being insufficient and unsuccessful in patient care (Öz, 2004; Üstün et al., 2005; Özcan, 2007).

In addition to this, as a result of the study which was carried out in order to determine how nurses prepare themselves for the care of deadly patients and which coping methods they used, Iranmanesh et al. (2008) stated that nurses have complicated feeling towards their patients who are close to death and nurses who are new in their occupation feel pain and sorrow for days. In fact in literature it was reported that reactions of nurses against death are influenced from many factors such as age, gender, marital status, occupational experience, belief and coping methods (Acehan and Eker, 2013). It was determined that nurses working at emergency unit respectively prefer praying, sharing with their friends and family, crying and moving away from the environment in order to cope with the feelings they experience against the incident of death.

When reactions and coping methods used against death are analyzed, it is seen that although elements specific to our culture are prominent, no matter how much cold-blooded nurses try to behave against the incident of death according to the professional principles of their occupation, they prefer to receive support by praying, sharing with their friends and family. Parallel to the findings of research, in other studies, it was expressed that nurses make use of coping methods such as thinking that death is a natural incident, praying, talking to friends/family, focusing on other issues (Çevik and Kav, 2010; Acehan and Eker, 2013), nurses who encounter with dying patients exhibit more positive attitudes (Dunn et al., 2005), compared with the nurses who have less experience, nurses who have more experience show more neutral and positive attitude against death (Lange et al., 2008). Moreover, in their study which was carried out in order to compare anxiety of death and coping methods of hospice and emergency nurses, Payne et al. (1998) stated that compared with hospice nurses, emergency nurses avoid from talking about death more and experience the fear of death more, positive attitude of emergency nurses towards death is lower than those of hospice nurses.

In this study it was determined that nearly half of the nurses avoid from confronting relatives of the deceased patient and do not want to inform relatives about the death of patient. Supporting the findings of this study, in other studies carried out on this issue, it was stated that nurses cannot talk the concept of death with the patient and their relatives (Çevik and Kav, 2010), when it is the duty of nurse to inform about the death of patient "they have difficulty in how to explain it to the family", "it is more suitable for the doctor to inform relatives about the death of patient" (Önsöz and Çam, 2013). In this study, mean score of Attitude to Death Scale was determined as 123, mean score of "Neutral Acceptance and Approach Acceptance" among sub-dimensions of scale is 68, mean score of sub-dimension of "Escape Acceptance" is 20.23±5.98, mean score of sub-dimension of "Fear and Avoidance of Death" is 35.98±10.06. Zaybak and Erzincanlı (2016) stated total mean score of Attitude to Death Scale as 116.9±13.4, sub-dimension mean scores of "Neutral Acceptance and Approach Acceptance", "Escape Acceptance" and "Death and Avoidance to Death" as 65.7±7.3, 15.9±5.2, 35.2±7.8 respectively. In the study of Yılmaz and Vermişli (2015), it was determined that the highest score of nurses in Attitude to Death scale was obtained from the sub-dimension of Denial of Death (4.44±1.85), the lowest score was obtained from Neutral Acceptance sub-dimension (2.67±0.95), in the study of Maysui and Braun (2015), it was determined that the highest score of nurses in Attitude to Death scale was obtained from the sub-dimension of Neutral Acceptance (3.24±0.99), the lowest score was obtained from Denial of Death sub-dimension (2.10±0.84), in the study of Gama et al. (2012), it was determined that the highest score of nurses in Attitude to Death scale was obtained from the sub-dimension of Neutral Acceptance (5.35), the lowest score was obtained from Denial of Death sub-dimension (3.50). Although scores obtained from Attitude to Death Scale and its sub-dimensions differ according to researches, it is thought that this difference might result from social and cultural characteristics of nurses such as religious belief, cultural, social value judgments, belief.

In this study it was determined that score of Attitude to Death Scale does not differ according to socio-demographic or occupational characteristics such as age, education, marital status, receiving education during or after occupational education yet; mean score of nurses who have experienced a close relative recently was higher than those who have not. In accordance with the research findings, in other studies carried out on this issue it was stated that age, educational status, the place they live, income, working years, receiving education about death and losing a relative at first degree do not influence score of Attitude to Death Scale (Kara and Işıl, 2002; Önsöz and Çam, 2013; Yılmaz and Vermişli, 2015; Zaybak and Erzincanlı, 2016;), also in spite of this research findings, in other studies it was stated that gender, marital status, thinking that the education received about death as insufficient and being satisfied from the service they work influence score of Attitude to Death Scale (Lange et., 2008; İnci and Öz, 2009;Çevik and Kav 2010;Abu-Hasheesh et al., 2013; Önsöz and Çam, 2013; Ayhan and Pekyardımcı, 2013). In addition to this, total high score obtained from Attitude to Death Scale is evaluated as developing negative attitude towards death and attitude of nurses towards death who experienced loss of someone they love recently is more negative, status of losing a relative influences attitude towards death considerably. It was observed that Attitude to Death Scale mean scores of "Neutral Acceptance and Approach Acceptance" sub-dimension differs according to status of losing someone nurses over recently, mean score of "Escape Acceptance" sub-dimension differs according to status of informing relatives about death of patient, mean score of "Fear and Avoidance of Death" sub-dimension differs according to confronting with the incident of death having influence on their occupational perspective. In spite of research findings, in other studies carried out on this issue, it was stated that when Attitude to Death Scale, mean score of "Neutral Acceptance" sub-dimension is compared with the nurses in 20-29 age group, it was higher among nurses who are 40 and above (Abu Hasheesh et al., 2013); status of wanting to inform the family about the death of patient increase Acceptance" sub-dimension of Attitude to Death Scale (Önsöz and Çam, 2013), nurses who have 11 years or more working experience have higher mean score of "Fear and Avoidance of Death" sub-dimension (Lange et al., 2008)

Occupational education of health care professionals influences their attitude towards death. Like the definition of death, attitudes developed towards death vary according to personal characteristics, society, religion, cultural characteristics. Based on the experience of others about death, people develop an attitude towards death. In this sense, in order to provide a qualified care for the healthy/ill people and their family, it is quite important to determine the meaning assigned for the illness and death by nurses. Restrictions of this study are that information obtained about the attitude of nurses towards death is based on their expressions and no observation was done on this issue, emergency nurses vary in the sense of education, experience, knowledge and skill.

5. Result and Suggestions

It was determined in this study that only one third of the nurses (34.7%) who participated in the study have informa tion about the process and management of death during their

education, nearly four fifth of them want to have information about communication skills to be used while interacting with a dying patient, they feel sorrow when they encounter a dying or deceased person (71.1%) and try to behave cold-blooded (52.9%), in order to cope with the feelings they experienced against the incident of death, they respectively do praying, share with their family and friends, abstain from confronting the relatives of the deceased and do not want to inform them about the death of patient. In this study it was determined that score of Attitude to Death Scale does not differ according to socio-demographic or occupational characteristics such as age, education, marital status, receiving education during or after occupational education.

According to the findings obtained, it is suggested to:

- Give importance to education programs about death process and management in nursing education curriculum,
- Organize continuing education programs in order to increase awareness of nurses about positive or negative attitudes of nurses exhibited to dying patients,
- Encourage nurses to talk about their feeling about death,
- Give education and consulting services which would enhance their communication and coping methods,
- Since death is a concept which is influenced from various variables, it is suggested to use qualitative methods that would reveal deeper information about the concept of death.

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Association of red cell distribution width with coronary plaque burden and sub-types in patients with type-2 diabetes mellitus

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ABSTRACT

Red cell distribution width (RDW) is an inflammatory marker that is associated with CAD presence and prognosis.We aimed to evaluate the relationship between RDW value, coronary atherosclerosis, coronary plaque burden and morphology in diabetic patients.147 DM patients who were evaluated with 128-slice dual-source coronary computed tomography angiography (CCTA) for suspected CAD were included in the study. The study population was divided into two groups [a CAD group (Group I) and non-CAD group (Group II)]. The plaque characteristics were analyzed on a per-segment. RDW values were obtained from the automated complete blood count.RDW values were found to be significantly higher among diabetic patients with CAD compared to those without CAD (14.6±1.4% vs 13.3±1.6%, p<0.001). In the correlation analysis, RDW value showed significant positive correlation with hs-CRP (r=0.523, p<0.001), total plaque burden (r=0.379, p<0.001), mixed plaques (r=0.253, p=0.018) and non calcified plaques (r=0.413, p<0.001). Also, multivariate logistic regression analysis revealed RDW as a significant and independent predictor of the presence of CAD in patients with DM .(OR=1.659, 95% CI:1.257-2.190; p<0.001).In our study we have determined that RDW value is an independent predictor among diabetic patients for the presence of CAD. Moreover, RDW values showed significant correlation with total plaque burden, and the number of non-calcified and mixed plaques.

1. Introduction

Diabetes mellitus (DM) is an important cardiovascular risk factor. Cardiovascular disease is responsible for 70-80% of mortality among diabetic patients, and 3 out of 4 deaths among them is cause by coronary artery disease (CAD) (Johnstone and Nesto, 2005; Özgen, 2004). ´National Cholesterol Education Program Adult Treatment Panel III´ (NCEP ATP III) has listed diabetes among cardiovascular risk factors as equivalent to CAD. (Expert Panel, 2001). DM is the strongest risk factor among unmodifiable risk factors for atherosclerosis. Key players in the pathogenesis of atherosclerotic diseases, chronic inflammation and oxidative stress levels are high in diabetic patients (King and Loeken, 2004; Wellen and Hotamisligil, 2005). High morbidity and mortality in DM patients due to CAD has prompted researchers to search for new markers that can predict and aid in the prognosis of CAD.

Red cell distribution width (RDW) is indication of variation in size of the circulating erythrocytes which is get from a standart automated complete blood count. Increased RDW is sign of the presence of anisocytosis, that is related to impaired erythropoiesis and erythrocyte degradation, reflecting chronic inflammation and a high level of oxidative stres (Evans and Jehle, 1991; Weiss and Goodnough, 2005; Ferrucci et al., 2005). Studies have shown that high RDW values are associated with unfavorable prognosis in acute myocardial infarction (Dabbah et al., 2010; Uyarel et al., 2011), heart failure (Felker et al., 2007, Al-Najjar et al., 2009), stable angina (Tonelli et al., 2008), peripheric artery disease (Ye et al., 2011), and stroke (Ani and Ovbiagele, 2009). It has also been reported that higher RDW values are associated with CAD presence, extent and complexity among patients with stable angina and ST-elevation myocardial infarction (STEMI) (Isık et al., 2012, Akın et al., 2013).

A study by Malandrino et al that evaluated the association of RDW and macro- and microvascular complications in diabetic patients demonstrated that higher RDW values were associated with cardiovascular disease (myocardial disease, heart failure, stroke) and nephropathy, and RDW was implicated as an important clinic marker for vascular complications (Malandrino et al., 2012).

The use of coronary computed tomography angiography (CCTA) is as a sensitive and specific tool not only for the demonstration of significant coronary stenosis, but also for detecting plaque morphology and plaque outward expansion (Achenbach et al., 2004; Leber et al., 2005; Miller et al., 2008). Plaque morphology and vulnerability evaluated by CCTA can provide additional information about possible future acute coronary events (Leber et al., 2003; Motoyama et al., 2009). Although the relationship between RDW and cardiovascular diseases is well documented, there are no data concerning the relationship between RDW and CCTA findings in diabetic patients. Therefore, we have aimed to evaluate the association between RDW values and coronary atherosclerosis, coronary plaque burden and plaque morphology.

2. Material and method

Study population

This retrospective analysis was performed in a subset of 681 patients, who were admitted to our Cardiology departmant for cardiovascular evaluation between January 2010 and March 2015 and in whom CCTA was performed for suspicion of CAD after clinical assessment. Among these patients, 147 diabetic patients were included in this study. The indications for CCTA were atypical chest pain with an intermediate risk for CAD, inconclusive stress test result, suspected coronary anomalies and exclusion of CAD among patients undergoing noncoronary cardiac surgery. After an assessment of the CCTA images, the study population was divided into two groups [a CAD group (Group I) and non-CAD group (Group II)] on the basis of the presence of coronary atherosclerosis. Missing demographic, clinical and medication information about the patients was completed from patient files.

Patients with history of documented CAD, percutaneous coronary intervention, acute coronary syndrome (ACS), heart failure, coronary bypass surgery, renal disease, hepatic dysfunction, myeloproliferative disease, malignancy, anemia, pregnancy, active or chronic inflammatory or autoimmune diseases were excluded from the study.

Diabetes mellitus was defined as fasting plasma glucose levels >126 mg/dl or hemoglobin A1c (HbA1c) >6.5%, or current treatment with insulin or oral hypoglycemic agents. Hypertension (HT) was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg, or treatment with antihypertensive drugs. Anemia was defined as a hemoglobin level <12.0 gr/dl in women and <13.0 gr/dl in men, based on the World Health Organization definition (World Health Organ., 1968)

Laboratory measurements

Venous blood samples were obtained by the venipuncture of the large antecubital veins of the patients. Blood values that were determined at the time of cardiovascular evaluation (before CCTA) were recorded from medical reports. RDW, hemoglobin, platelet values and white blood cell count were obtained from the automated CBC using a Sysmex XE-2100 Automated Hematology Blood Analyzer System (Sysmex, Kobe, Japan). Biochemical parameters were measured in Cobas 8000 Modular Analyzer (Roche Diagnostics, Indianapolis, USA) using commercially available assay kits. High sensitive C-reactive protein (hs-CRP) was quantitatively measured by BN II System Nephelometer (Global Siemens Healthcare, Erlangen, Germany) by immunonephelometric method from patients' serum and the results were reported in mg/L.

Coronary computed tomography angiography: image acquisition

All the scans were obtained using 128-slice dual source computed tomography system. (Somatom Definition AS; Siemens Healthcare, Forchheim, Germany). Patients with an initial heart rate of ≥65 beats/min were taken β blocker therapy according to the local protocols. Every participant received 0.4 mg of sublingual nitroglycerin 1 minute prior to contrast administration for coronary arteries dilatation. The coronary angiographic scan was obtained with injection of 70-80 ml nonionic contrast medium (350 mg I/ml iomeprol; Bracco Omnipaque, Milano, Italy) at flow rate of 5 mL/s followed by 50 mL of saline solution and contrast administration was controlled with bolus tracking. The acquisition parameters were 2x64x0.6 mm detector collimation, resulting in 2x128x0.6 mm sections by means of the z-axis flying focal spot technique, 280 ms gantry rotation time, 75 ms temporal resolution, 100 to 120 kV tube voltage depending on body mass index (no greater than 30 kg/m2 BMI 100 kV; greater than 30 kg/m2 BMI 120 Kv), 330 mAs per rotation tube current and 0.2-0.47 pitch adapted to the heart rate. ECG-gated helical mode scan was performed with the full radiation dose window set at 68-78% of the R-R interval in patients with heart rates ≤70 bpm or 200-400 ms after the R peak in patients with heart rate of >70 bpm. The minimum tube current with 4% of the full radiation dose (MinDose; Siemens Healthcare, Forchheim, Germany) was applied to the remainder of the R-R interval to minimise radiation dose. Images were reconstructed with a slice thickness of 0.6 mm, a reconstruction increment of 0.4 mm and using a soft-tissue convolution kernel (B26f).

Coronary computed tomography angiography: image analysis

All scans were performed independently by two experienced radiologists who were blinded to the clinical information using a 3D workstation (Syngo; Siemens Healthcare, Erlangen, Germany) After making independent evaluations, a consensus interpretation was concluded at to obtain a final CCTA diagnosis. Each identified lesion was examined using maximum intensity projection and multiplanar reconstruction techniques on short axis and along multiple longitudinal axis. The radiologists analyzed the plaque characteristics on a per-segment basis according to the modified American Heart Association classification (Austen et al., 1975). Plaques were defined as structures >1 mm2 within and/or adjacent to the vessel lumen, which could be clearly distinguished from the lumen and surrounding pericardial tissue. Coronary plaques were classified as non calcified, calcified and mixed according to their morphology.

Plaques without any calcification were defined as non calcified plaques, plaques with more than 50% of the plaque area occupied by calcified tissue (density ≥130 HU in native scans) were defined as calcified and plaques with less than 50% calcified tissue were defined as mixed type (Leber et al., 2006). All plaque components were assessed on a per-segment basis. The number of any plaques (total plaque burden), as well as plaques with different features was calculated per patient. Additionaly, as an indicator of vulnerable plaques, the ratio between non calcified plaques and total plaque burden was calculated. Inter-observer agreement for the detection of any plaque/patient and plaque/segment were excellent (Cohen's κ=0.94 and 0.82, respectively).

Statistical analysis

Statistical evaluation was performed using SPSS 15.0 (Statistical package for the social sciences, Chicago, IL, USA). Categorical variables were presented as frequencies and percentages and were compared with the $\chi 2$ test. Continuous variables were expressed as means and SD. The normal distribution of continuous variables was tested with Kolmogorov-Smirnov test. Differences in continuous variables between groups were examined using the nonparametric Mann-Whitney U test. Correlation analysis was performed using Spearman's coefficient of correlation. Multivariate logistic regression analysis was also performed and the model included potential confounders (age, body mass index [BMI], serum creatinine, low density lipoprotein cholesterol [LDL-C], high density lipoprotein cholesterol [HDL-C], HbA1c, hypertension, RDW, high sensitive C-reactive protein [hs-CRP]) for CAD. $p< 0.05$ was considered statistically significant.

3. Results

Baseline clinical characteristics

Eighty eight diabetic patients with CAD (Group I, 43 males; mean age 56.7±9.1) and 59 diabetic patients without CAD (Group II, 24 males; mean age 52.5±9.2) were included in the study. Demographic, clinical and laboratory parameters of the patients are presented in Table 1. No significant difference was detected between the groups regarding BMI, hypertension, smoking, white blood cell count, hemoglobin, platelet count, serum glucose, serum creatinine, HbA1c, triglyceride, total cholesterol, LDL-C values and medications ($p>0.05$). In the CAD group, hs-CRP values were significantly higher ($p=0.004$) while HDL-C levels were significantly lower ($p=0.019$) compared to the non-CAD group. RDW values were also significantly higher in the CAD group (14.6±1.4% vs 13.3±1.6%, $p<0.001$) (Figure 1). Number of plaques were detected as 4.81±2.1 in the CAD group. Among the 424 plaques evaluated for plaque subtypes, calcified type was the most frequent (n=187, 44.2%), followed by mixed type (n=124, 29.2%) and non-calcified type (n=113, 26.6%). Non-calcified/Total plaque burden ratio was 0.37±0.42 in the CAD group. (Table 1)

Association of RDW levels with clinical characteristics, laboratory findings and coronary plaque burden and sub-types

In the correlation analysis, RDW showed significant positive correlation with HbA1c ($r=0.212$, $p=0.047$), hs-CRP ($r=0.523$, $p<0.001$) (Figure 2), total plaque burden ($r=0.379$, $p<0.001$), number of mixed plaques ($r=0.253$, $p=0.018$), and non calcified plaques ($r=0.413$, $p<0.001$) (Figure 3) in the CAD group (Table 2). In addition, RDW was also positively correlated with non-calcified plaque/total plaque burden ratio ($r=0.307$, $p=0.004$) (Figure 4).

Association of RDW levels with the presence of coronary artery disease.

Simple logistic regression analysis revealed that age (OR=1.051, %95 CI:1.012-1.092; p=0.010), serum creatinine (OR=5.306, %95 CI:1.099-25.611; p=0.038), HDL-C (OR=0.954, %95 CI:0.924-0.985; p=0.004), RDW (OR=1.851, %95 CI:1.420-2.413; p<0.001) and hs-CRP (OR=1.535, %95 CI:1.207-1.952; p<0.001) showed an association with the presence of CAD in all patients. These variables were entered into a backward stepwise multivariate logistic regression model. Multivariate logistic regression analysis demonstrated that HDL-C, RDW and hs-CRP levels were significant and independent predictors for the predicting the presence of CAD in patients with DM (OR=0.953, %95 CI:0.921-0.988; p=0.008, OR=1.659, %95 CI: 1.257-2.190; p<0.001, OR=1.380, %95 CI:1.058-1.800; p=0.018 respectively) (Table 3).

To investigate the predictive value of RDW for CAD in patients with DM, a receiver operator characteristic (ROC) curve was generated for sensitivity and specificity using the respective areas under the curve (AUC). The analysis indicated that RDW values of more than 16.05% had a 94.9% sensitivity and a 86.4% specificity for predicting CAD in the DM patients (AUC=0.722; 95% confidence interval, 0.637–0.807; P<0.001) (Figure 5).

4. Discussion

In the present study, we determined higher RDW values in diabetic patients with CAD than non-CAD patients. Moreover, RDW was associated with plaque morphology, and significantly correlated with total plaque burden and number of mixed plaques, and non-calcified plaques in diabetic patients. Diabetes is an important risk factor for cardiovascular diseases. Approximately 60% of diabetic patients have cardiovascular disease. Overall rate of cardiovascular mortality is twice as high in these patients compared to non-diabetic patients. (Seshasai et al., 2011). Evaluation of cardiovascular risk and detection of CAD is very important in managing treatment. Accordingly, new biomarkers that can contribute to detection of CAD in its early stages is enthusiastically awaited by researchers.

Red blood cell distribution width is an indicator of the heterogeneity in the size of circulating erythrocytes. RDW can be measured as part of daily automated CBC. In recent years, studies have focused on RDW and its association with CAD and adverse cardiovascular outcomes. In a study by Dabbah et al. in acute coronary syndrome patients, high RDW values were associated with long-term adverse clinical outcomes (Dabbah et al., 2010). Tonelli et al reported an association between high RDW values with death and cardiovascular events in CAD patients under long-term follow-up (Tonelli et al., 2008). In another study, higher RDW values were revealed as an independent predictor for in-hospital and long-term cardiovascular mortality among STEMI patients undergoing primary

percutaneous coronary intervention (PCI) (Uyarel et al., 2011). In a long-term prospective follow-up study among non-ST elevation myocardial infarction patients, high RDW values were associated with cardiovascular mortality, hospitalization for heart failure and reinfarction (Gül et al., 2012). Additionally, high RDW values were associated with angiographically detected CAD presence and complexity (Isık et al., 2012). Another study in hypertensive patients has shown an independent and strong association of RDW with carotis intima media thickness which is accepted as an early phase of atherosclerosis (Wen et al., 2010).

In general, patients with DM have oxidative stress and high levels of chronic inflammation which play key roles in the progression of atherosclerosis diseases (King and Loeken, 2004; Wellen and Hotamisligil, 2005). Consequently, recent studies have been designed to establish the relationship between RDW levels and CAD in diabetic patients. In a study by Tsuboi et al. increased RDW was significantly associated with long-term all-cause mortality in diabetic patients with stable angina undergoing PCI (Tsuboi et al., 2013). In a metaanalysis presented by Patel et al. an association between RDW and all-cause mortality was shown in the subgroup of diabetic patients. (Patel et al., 2010). Malandrino et al. reported a relationship between RDW and micro- and macrovascular complications in diabetic populations in the United States with the Third National Health and Nutrition Examination Survey (NHANES III). In that study, higher RDW levels are related with increased adjusted odds of myocardial infarction, nephropathy, heart failure and stroke. Also, RDW was underlined as an important clinical marker for vascular complications (Malandrino et al., 2012). A study presented by Heba et al reported similar findings and showed that higher RDW values were associated with increased macrovascular complication (CAD, peripheral vascular disease, cerebrovascular disease) risk (Sherif et al., 2013). Similar to these studies, we have shown higher RDW values in diabetic patients with CAD compared to those without CAD. Furthermore, we demonstrated that high RDW values were an independent predictor for presence of CAD in diabetic patients. There are reports supporting that inflammation increases RDW by inhibiting erythropoietin-induced erythrocyte maturation and iron metabolism (Weiss and Goodnough, 2005; Patel et al., 2009). A study by Pascual-Figal et al. revealed that inflammatory cytokines increase erythrocyte heterogeneity by suppressing erythrocyte maturation and releasing juvenile erythrocytes into circulation (Pascual-Figal et al., 2009). Considering the role inflammation plays in the development of atherosclerosis (Libby et al., 2002; Hansson, 2005), an inflammatory process may be the underlying cause of high RDW values observed in the CAD group in our study. Accordingly, we have also detected higher levels of hs-CRP in the CAD group.

Red blood cells have a huge antioxidant capacity and they are prone to oxidative damage, which decreases cell survival and induces the release of juvenile erythrocytes into circulation (Kiefer and Snyder, 2000). Oxidative stress plays a role in the pathogenesis of atherosclerosis by causing endothelial dysfunction and increasing expression of proinflammatory mediators (Dzau et al., 2006). İn our study, oxidative stress may be a contributing factor for the high RDW values in the CAD group. Studies by Kato et al (Kato et al., 2005) and Cole et al (Cole et al., 2000) have illustrated that neurohormonal system activation influences red blood cell maturation through direct stimulation of endothelial progenitor cells and upregulation of erythropoietin. Several studies demonstrated an essential part of renin-angiotensin system (RAS) in pathophysiology of heart and vascular system, including atherosclerotic disease (Pacurari et al., 2014; Wu et al., 2014). In our study, higher RDW values observed in the CAD group compared to the non-CAD group might be caused by increased neurohormonal activation. In conclusion, the increase in RDW values in our study might be the combined result of increased inflammation, oxidative stress and neurohormonal activation among CAD patients with diabetes.

Besides revealing the severity of coronary stenosis, coronary computed tomography angiography can provide additional information on vessel walls and plaque composition (Miller et al., 2008). Coronary plaque composition is an important factor of clinical progression and outcomes in CAD (Greenland et al., 2003). Plaques with lipid rich core and proinflammatory immun cells are more vulnerable to rupture and are often non calcified plaques with low attenuation of CCTA (Motoyama et al., 2007). In a study by Pundziute et al. (Pundziute et al., 2008) demonstrated that non-calcified and mixed plaques were more extensive in ACS patients compared to stable CAD patients. In another study by Russo et al. (Russo et al., 2010) on suspected CAD patients reported that patients with non-calcified and mixed plaques suffered cardiac events more frequently than patients with calcified plaques. CCTA studies that assessed plaque subtypes in diabetic patients revealed a higher ratio of calcified plaques among these patients (Pundziute et al., 2007; Pundziute et al., 2009). Similarly, we have detected a higher ratio of calcified plaques than non-calcified and mixed plaque distribution.

Some studies report an association between non-calcified and mixed plaques and inflammatory markers. Hausleiter et al. detected a higher CRP level in patients with non-calcified plaques compared to those with calcified plaques, and associated it with increased inflammatory activity (Hausleiter et al., 2006). Similar results were reported in a study conducted by Bamberg et al. on patients with low cardiovascular risk profile, and higher CRP levels were observed in patients with non-calcified plaques (Bamberg et al., 2012). In another presented study, thin-cap fibroatheromas (TCFA) that play a key role in plaque vulnerability were more extensive in ACS patients, and observed more frequently in mixed plaques (Pundziute et al., 2008). A post-mortem study that analysed the association of CRP levels and TCFA demonstrated that increased CRP is significantly correlated with the number of TCFAs and associated with plaque vulnerability (Burke et al., 2002). Research investigating the relationship between inflammation and RDW detected an association between increased RDW and hs-CRP along with various other inflammatory markers (Patel et al., 2009; Lippi et al., 2009). Accordingly, RDW showed a significant correlation with hs-CRP in our study. This finding seems to support the role of inflammation in increased RDW.

Furthermore, we have detected significant correlations between RDW values and total plaque burden, non-calcified plaque and mixed plaque, along with non-calcified/total plaque burden ratio. Our study is the first study to assess the

relationship between RDW and coronary plaque subtypes. In light of the aforementioned studies, we believe that the significant correlation between RDW and the number of non-calcified and mixed plaques might be associated with the increased inflammatory activity observed in these plaque subtypes.

Study Limitations

Our study had some limitations. First, this was a retrospective study with a relatively small number of patients. Second, RDW levels may affected in conditions of ineffective red blood cell production (such as folate, iron or B12 deficiency and hemoglobinopathies), erythropoietin levels, increased red cell destruction (such as hemolysis), and after blood transfusion. Only Hb levels were measured in this study, and other factors including iron, folate and vitamin B12 were not measured. Third, the study could have provided more accurate information if the relationship between RDW levels and plaque morphology had been evaluated with intravascular ultrasound.

5.Conclusion

We have detected that RDW is an independent predictor for CAD among diabetic patients. Moreover, RDW was significantly correlated with total plaque burden, and the number of non-calcified, and mixed plaques. RDW can be a potential and cheap marker in the evaluation of diabetic patients for CAD, and contribute to risk assessment for coronary events and identification of suitable treatment strategies in diabetic patients.

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Is the incidence of clostridium difficile in nosocomial diarrhoea underestimated?

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ABSTRACT

Clostridium difficile (C. difficile) is a Gram-positive, obligatory anaerobe, spore-forming microorganism and is highly associated with the nosocomial infections. The incidince of nosocomial diarrhoea and C. difficile-associated nosocomial diarrhoea rates are not clear in our country. To determine the C. difficile-associated nosocomial diarrhoea incidence, to review the current resistance status of C. difficile, and to evaluate diagnostic and therapeutic approaches for this pathogen were the aims of the present study. This prospective clinical study included 100 diarrhoea samples from hospitalized patients in İstanbul University Cerrahpaşa Medical Faculty of. The diarrhoea samples were investigated by culture, card test and ELISA methods and bacterial resistance profiles were shown with the E-test method. Toxin A/B was found positive at 30/100 patients (30%) by ELISA. The duration of hospitalization and diarrhoea period were significantly longer in Toxin A/B positive patients than negative patients ($p<0.05$). Recurrences detected in 41% of Toxin A/B positive patients (statistically not significant but clinically may be important). When ELISA was accepted as the main test, the sensitivity and specificity of culture and card test methods were found as 56%, 75% and 76%, 80%, respectively. The C. difficile resistance rates were determined for metronidazole as 29.4%, for vancomycin and teikopilanin as 2.9%. Our results support that the C. difficile is still an important factor in nosocomial diarrhoea. Furthermore, highness of antibiotic resistance for metronidazole may be caused by difficulties in treatment. The results indicate the necessity of further studies to develop control measures and effective treatment options for patients.

1.Introduction

Clostridium difficile (C. difficile) is the most common cause of healthcare associated infectious diarrhoea (Kelly and Lamont,2008). The spectrum of the Clostridium difficile-associated diseases ranges from diarrhoea to pseudomembranous colitis, and is frequently termed as C. difficile-associated diarrhoea (CDAD)(Khanna and Pardi, 2010). All around the world, the incidence and severity of CDAD has increased (Cartman et al., 2010). This increase appears to be caused by a number of factors such as large outbreaks of CDAD in hospitals, inappropriate antibiotic usage and performing inadequate hygiene techniques (Stuart and Marshall, 2011). C. difficile is highly responsible for developing pseudomembranous colitis, antibiotic-associated colitis and antibiotic-associated diarrhoea with approximate rates in 90%, 75% and 33%, respectively (Barbut et al., 2007). In Turkey, the incidence rates of C. difficile in nosocomial infections are not clear. However, C. difficile has become an important

pathogen in last years, because of the treatment failure detection in many hospitilazed patients, increasing mortality rates, diffuculties to control the hospital outbreaks and changing antibiotic resistance profile of C. difficile. Despite the sensitive diagnostic techniques, effective antibiotic treatments and healthcare infection control practices, C. difficile is still an important agent in nosocomial infections (Aygun et al., 2005; Cohen et al., 2010). The aim of the present study was to determine the incidence of nosocomial diarrhoea in our hospital and to determine the role of C. difficile. Additionally, diagnostic techniques and antibiotic susceptibility for CDAD were investigated.

2. Materials and Methods

Study Design

We prospectively examined stool samples from hospitalized patients over a 13-months period. The samples were firstly examined macroscopically to ensure that they were loose, watery, and the patients were questioned to confirm that had a minimum three-days hospitalized period and also older than 18 years old. One-hundred samples meeting these criteria from 100 patients were included in our study.

Methods

Firstly, all samples were lightly inoculated on Clostridium difficile selective agar (Oxoid, United Kingdom) and incubated at 37^{O}C for 72 hours in Anaerobic Jar with an Anaerobic Gas Generating Kit (Oxoid, United Kingdom) to determine the anaerobic and fastidious C. difficile colonies. After 72 hours, plates were evaluated in terms of the existence C. difficile colonies, and C. difficile positive samples were transferring on Iso-Sensitest Agar (Oxoid, United Kingdom) to determine the on-scale Minimum Inhibitory Concentration (MIC) of metronidazole, vancomycin, and teikoplanin with the E-test strips (bioMérieux, France) by the recommendation of Clinical and Laboratory Standards Institute (CLSI). Enzyme-linked immunosorbent assay (Generic Assays, Germany) and immunochromatographic card test (Veda Lab, France) were used for detection of C. difficile toxins A and B.

Statistical Analyses

All statistical analyses were performed by using SPSS (Version 17.0 for windows) software by applying Student's t-test to determine the differences, Chi-square and Kappa values to determine the potential false-positivity and false-negativity. A p value of <0.05 was accepted as statistically significant.

Ethics

Permission to conduct this study was obtained from the local ethics committee of Istanbul University Cerrahpaşa Medical Faculty. Informed consents were obtained from all patients. Additionally, our study was performed according to principles of Helsinki Declaration.

3. Results

One-hundred patients were included in this study. Forty-eight of these patients were men and 52 were women. The average age and hospitalization time at the time of study of the 100 patients was 55 years (range 24 to 94 years) and 21 days (range 3 to 108 days), respectively. There was no significant correlation in terms of genders and years of included patients C. difficile toxin A or B was detected in 30 (30%) samples by ELISA method, and the hospitalization time was significantly long in C. difficile toxin A or B positive group than the negative group ($p<0.05$). Addition, recurrences were detected in 41% of C. difficile toxin A or B positive patients ($p>0.05$, this is statistically not significant but clinically might be important).Conventional anaerobic culture, immunochromatographic card test and ELISA were used as diagnostic methods to determine the existence of C. difficile in diarrhoea samples. When ELISA accepted as the gold-standard test, sensitivity and specificity rates of culture and card test methods were found as 56%-75% and 76%-80%, respectively. Thirty-four C. difficile strains were grown in Clostridium difficile selective agar. The C. difficile resistance rates were determined for metronidazole as 29.4%, for vancomycin and teikopilanin as 2.9%.

4. Discussion

The incidence of C. difficile infections continues to rise and infection is associated with increased morbidity and mortality in the elderly. In the United States, the incidence of C. difficile infection has doubled in the past 10 years (Tschudin-Sutter et al., 2012). Loo et al. analyzed a dozen of hospitals in Canada, and determined an incidence of 22.5 cases per 100,000 hospital admissions (Loo et al., 2005). In the present study, detected 30% positivity rate for C. difficile toxin A or B was found parallel with these findings, and also support that the incidence of CDAD continues to rise. The main causes of this rising might be connected with increase antibiotic resistance and lack of applying the infection control measures.

The main risk factors associated to C. difficile are age older than 65, use of laxatives, proton pump inhibitors, chemotherapy, renal failure, gastrointestinal surgery, nasogastric tube, mechanical ventilation, prolonged hospital stay and previous antibiotic therapy (Blondeau,2009). Predisposing factors to C. difficile infection include inappropriate antibiotic use; which is thought to alter the colonic flora, allowing C. difficile to proliferate. Many case reports would suggest that previous antibiotic use is also related with C. difficile-associated diarrhoea (Lundeen et al., 2007; Lavallée et al., 2009; Dineen et al., 2013). In our study, there were no correlation detected between the patients with previous antibiotic usage and C. difficile toxin A or B positivity.

Different methods are used to diagnosis of C. difficile infections, such as cell culture, stool culture, ELISA and card tests. Stool culture is not used due to its cost, to being labor intensive, and to the fact that the results take long to be obtained. Cell culture is the gold-standard method for diagnosis of CDAD (Musher and Aslam, 2008). In the diagnosis of CDAD, enzyme immune assays are the most used laboratory methods, with results in up to 2 hours. Nevertheless, depending on the exam methodology, sensitivity may vary between 50 and 99%, and specificity from 70 to 100% (Peterson et al., 2007). In the present study, card test and ELISA methods were used for the diagnosis of CDAD, and ELISA was preferred to detection the toxin A or B positivity of C. difficile strains with its high sensitivity and specifity rates.

The rising incidence of CDAD since 2000 and the related extreme increases in severity, morbidity, and mortality have caused to the improve of new agents to aid in disease prevention and treatment. These include new antibiotics for CDAD and also probiotic agents, bacteriotherapy, passive immunotherapy, and vaccine development (Higa and Kelly, 2013). In Israel, 49 patients with CDAD examined and metronidazole resistance rates found as 2% (Bishara et al., 2006). Moreover, Huang et al. reported that many C. difficile isolates are

still susceptible to vancomycin and metronidazole, however transient and heteroresistance to MTZ and decreased sensivity have been determined. Resistance to antimicrobials in C. difficile varies widely between countries (Huang et al., 2009). In our prospective study, C. difficile resistance rate to metronidazole was 29.4%, much higher than previously suggested in the literature. Our findings corroborate the alarming reports about the increasing metronidazole resistance rates of C. difficile.

In conclusion, C. difficile is one of the major complications related to healthcare and is easily spread at hospitals with its spore formation. The rising incidence and increased metro nidazole resistance of C. difficile are alarming findings for hospitalized patients, especially in the elderly populations. Patients with severe disease and/or treated in the intensive care units remain at high risk for this pathogen, and preventive measures, such as fastidious contact precautions, hand antisepsis, environmental disinfection, and, most importantly, antibiotic stewardship, are the cornerstones of the management C. difficile-associated infections.

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Salıvary cortisol levels in elite male handball players during a match*

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ABSTRACT

Cortisol is a corticosteroid hormone produced by the adrenal cortex and it is associated with the stress response of the body. It is an important marker for determining the level of stress during or after exercise. The purpose of this study was to examine a sports team for the level of physiological and psychological stress generated by a handball competition via non-invasive saliva analysis. Fourteen athletes aged 20.7 ± 2.5 years who were members of the Ondokuz Mayıs University male handball team participated in the study. A total of three saliva samples were taken, one before, one during half-time and one immediately after an important match for the team in terms of the group standpoint. and were analyzed by ELISA. Data were analysed by repeated measures test and Mauchly's test of sphericity; also $p<0.05$ denoted statistical significance. As a result of the analysis, salivary cortisol levels were found to be significant in the three different samples taken from the athletes ($p = 0.018$) At the onset of the ıy defferent competition, cortisol levels were also seen to increase in parallel with the rise in the stress levels of the athletes. The highest cortisol levels of the athletes were found in the samples taken between halves during the match. It was found that submaximal exercise used in the team sport of handball had a significant effect on salivary cortisol levels. In samples taken during an event with a high level of importance for the team, significantly variable levels of cortisol as a stress hormone were expressed in the athletes. Therefore, saliva cortisol measurement appears to be an important parameter that can be used to develop stress-management and other necessary strategies in sport branches such as handball where the mental and physical stress is intense.

1. Introduction

Exercise brings about endocrinological changes to balance homeostasis during challenging coordinative movements, thus leading to physiological and psychological stress. It triggers a coordinated series of physiological responses which influence systems like the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic nervous system in particular, two of the basic stress activation systems (Soria et al., 2015; Furtado et al., 2016).

Cortisol is considered a stress hormone. It is released when the body is exposed to any threat or danger which stimulates the sympathetic nervous system by activating energy sources, thus enabling the body to cope with possible dangerous situations (Triviño-Paredes et al., 2016). Cortisol is a corticosteroid hormone produced by the adrenal cortex and it is associated with the stress response of the body. It regulates the level of energy use by activating amino acids in the skeletal muscles, thus promoting glycogenic activity (Öztürk, 2008; Wingfield et al., 2015). It is an important marker for determining the level of stress during or after exercise (Yazdanparast et al., 2009). Sufficiently intense exercise has an effect that can trigger cortisol release. Circadian and diurnal rhythm, nutrition, sleep, previous exercise and body composition are other important factors that can affect cortisol release (Kanaley et al. 2001).

When there is a high amount of cortisol in the body, the positive effect of the defense mechanism is reversed and the organism is driven to utilize its own defensive measures. Therefore, it is important to keep cortisol release constantly in balance. Athletes perform in a very stressful environment, especially when they need to make quick decisions during a competition. The organism can develop responses against

this situation in different ways. In this sense, regular training and good preparation are positive ways that can help to avoid this stress (Dinçer, 2011).

Many studies have shown that in different species, exercise increases the level of cortisol (Kindermann et al., 1982; Farrell, 1989; Soria et al., 2015; Wingfield et al., 2015; Kayacan et al., 2016; Klentrou et al., 2016; Koutsandréou et al., 2016). However, data in the literature suggest that cortisol release varies with physiological activation parameters such as exercise intensity and duration and physical conditions (Filaire et al., 1996; Yazdanparast, 2009). One study reported that in mild-intensity exercises, no increase in cortisol release was observed, while in high-intensity exercise, there was a significant increase in cortisol levels as a response against stress (Günay, 2013).

There are several different methods for cortisol analysis. Saliva cortisol analysis has been widely used recently (Takagi et al., 2013; Cobb et al., 2016; Soroko et al., 2016), because it is non-invasive, does not require venipuncture and makes the sample collection phase easier and faster for subjects of different age groups.

Handball is a popular global sport played by more than 30 million athletes throughout the world. As an intermittently intense physical activity lasting over an extended time period, it requires both aerobic and anaerobic strength and durability. Despite this fact, not many studies have been done to date dealing with the influence of handball on the hormonal composition (Nedić et al., 2016).

The purpose of this study was to examine a sports team for the level of physiological and psychological stress generated by a handball competition via non-invasive saliva analysis.

2. Methods

Fourteen athletes aged 20.7 ± 2.5 years who were members of the Ondokuz Mayıs University male handball team participated in the study. A total of three saliva samples were taken, one before, one during half-time and one immediately after an important match for the team in terms of the group standpoint. Under the supervision of the team coach, saliva samples were taken by means of an Ependorf tube using the passive drool method. For the samples, the saliva spontaneously filling the mouth was collected in the saliva tube while the chin was tilted forward toward the chest. The collected saliva samples were then stored at -20 °C in the Inonu University Medical Faculty Physiology Laboratory and were later analyzed using the ELISA method.

ELISA cortisol procedure

The steps of the cortisol ELISA test are briefly described as follows. A 96-well ELISA plate was coated with Cortisol: BSA at the determined concentration. A 1% bovine serum albumin (BSA) solution was used to block the uncoated areas of the wells. Standard sample quantities of the cortisol antibody in the established concentration were then pipetted into the wells. The plate was incubated for 45 min at 37 °C. Following incubation, the plate was washed four times to remove unbound cortisol and antibodies and then dried by lightly wiping with a paper towel. Anti-Rabbit IgG antibodies labeled with the biotin concentration capable of binding to the cortisol antibody were pipetted into all the wells and the plate was incubated for 30 min at 37 °C. After incubation, the washing was repeated in the same manner. Streptavidin peroxidase at the determined concentration to bind biotinylated antibody was then pipetted into all the wells. The plate was incubated at + 4 °C for 15 min and following incubation, washing was repeated again in the same manner. Substrate solutions containing tetramethylbenzidine were then pipetted into all the wells and the plate was incubated at room temperature for 15 min to complete the color formation. Without delay, a stop solution containing H2SO4 was pipetted into all the wells and the resultant yellow color was read on a plate-reader spectrophotometer (Biotek, Synergy HT, USA) at 450 nm. Standard curves were generated with the Gen 5 computer program and the concentrations were determined according to these standard curves. The sensitivity of the test was 1-1000 ng/ml. The intra-assay coefficient of variation (CV) was 10.4% for the low-concentration samples and 8.1% for the high-concentration samples; the inter-assay CV was 13.3% for the low-concentration samples and 12.2% for the high-concentration samples.

Determination of match difficulty

In order to determine the difficulty level of the match, a 10-point Likert-type scale was used for the sportsmen. The rating ranged from 1 (very easy) to 10 (very difficult). The scale was also applied to other group matches and the difficulty levels of the matches were calculated. An easy match was rated as 1-4 points, a moderate one as 4.1-7 points and a difficult competition as 7.1-10 points. According to this classification, the difficulty level of the match for which the saliva samples were taken was found to be high (Nazem et al., 2011).

Statistical analysis

The IBM SPSS v.21 software package was used for statistical analysis. Mean and standard deviation values were given as descriptive statistics for data with normal distribution. In order to investigate the differences between the averages of pre-match, half-time and post-match replicated measurements, the ANOVA test was used to analyze the data for the replicated measurements from the parametric tests. The validity of the sphericity assumption was tested using Mauchly's test of sphericity. The sphericity assumption results were used in the comparison of the replicated measurements when the sphericity assumption of $p > 0.05$ was met, while the Greenhouse-Geisser result was used when the assumption was violated. Fisher's least significant difference (LSD) test was used to perform binary comparisons to determine which time interval caused the difference between the measurements that were found. Statistically, the alpha value was accepted as $p < 0.05$.

3. Results

First, to determine whether the assumption of sphericity had been achieved, the Mauchly sphericity test was applied to the normally distributed data. According to the findings of this test, the sphericity assumption values were examined to obtain the assumption of sphericity ($p = 0.478$) and the alpha value was found as $p = 0.042$. Moreover, the magnitude of the effect was determined to be 0.216. As a result of the analysis, salivary cortisol levels were found to be significant in the three different samples taken from the athletes ($p = 0.018$) (Table 2). At the onset of the competition, cortisol levels were also seen to increase in parallel with the rise in

the stress levels of the athletes. Mean cortisol levels were 41.4 ng/ml before the match, 65.2 ng/ml during the match and 54.8 ng/ml after the match (Table 1).

Table 2. Comparison of samples according to the phases of the match

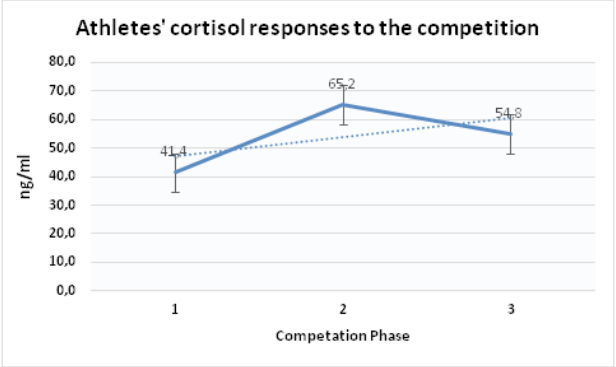
Phase*	Phase*	Mean Difference	SD	P
1	2	-23,821	7,245	,018
	3	-13,429	9,636	,560
2	1	23,821	7,245	,018
	3	10,393	9,660	,905
3	1	13,429	9,636	,560
	2	-10,393	9,660	,905

*** 1. Pre-game, 2. Half-time, 3. After game**

Table 1 shows the arithmetic means and standard deviations of the salivary cortisol levels of the 14 athletes participating in the study according to the phases of the match.

Table 1. Descriptive statistical data for the athletes according to the phases of the match

	n	$\bar{x}$	Sd
Pre-game	14	41,41	31,904
Half-time	14	65,23	37,909
After game	14	54,84	26,392



1. Pre-game, 2. Half-time, 3. After game

Figure 1. Athletes' cortisol responses to the competition

When the cortisol competition responses of the athletes are examined, it can be seen that the highest levels were reached in samples taken during the match between the halves (Fig. 1). Directly after the match, the level of cortisol in the athletes decreased.

4. Discussion

In the present research, the aim was to investigate the stress level of athletes via non-invasive methods during a handball game, where the aerobic energy structure is used more intensely, although it is recognized that this type of activity affects both aerobic and anaerobic metabolism (Ascensao et al., 2008). The stress response has complex molecular, cellular, physiological and behavioral effects on the organism. Physical stress can occur as a result of heat, cold, radiation, trauma and infective or toxic agents. Emotional causes can also be a factor. The stress response system is tonically active and is in fact necessary for the continuance of any organism. The HPA components CRH, ACTH and cortisol (the classic stress-related neurohormones of the stress system) have been reported in the literature as having a significant effect on stress response [Türsen, 2011]. However, this effect may vary according to the energy metabolism used during physical activity. For example, Filaire et al. (1996) conducted a study to investigate the effect of physical exercise and training on salivary cortisol concentration in women. They collected a total of six saliva samples throughout the day from a total of 31 adult women divided into three groups which included seven sedentary controls, 14 handball players and 10 swimmers (with both latter groups at the national level).

There was no significant difference between the swimming and sedentary groups for any of the samples collected during the day, whereas a significant increase was detected in the handball players after training (18.00-19.30, $p < 0.05$). In another study, cortisol concentrations were found to be significantly high in samples taken from 13 male athletes after inter-university competitions held in the Southern University Football Division, when aerobic energy was heavily used (Edwards et al., 2006). These results demonstrate that the type of sport is effective on the saliva cortisol concentration and stress level and support the results found in the present study.

It has been reported in the literature that stress due to high-intensity aerobic exercise causes significant increases in ACTH and cortisol levels (Raynaud et al., 1997; Skoluda et al., 2012; Moghadasi and Najafi, 2017). For example, Hill et al. (2008) found that for 30 min of intensive forms of exercise at 40%, 60%, and 80% maximal oxygen consumption (VO2max), there was a parallel between the increase in cortisol levels and the increase in oxygen consumption, i.e., the stress level increased as the exercise became more strenuous (Hill et al., 2008). Tsai et al. (2014) determined that the cortisol level of athletes increased during acute endurance exercises (Tsai et al., 2008). Minetto et al. (2008) put 15 footballers through intensive exercise programs and found a statistically significant increase in cortisol after the exercise program compared with before, in terms of the awakening response and daytime cortisol levels (Minetto et al., 2008). The release of cortisol is the result of activating the energy stores that help by intervening in emergency situations. Changes in the parameters mentioned above can be interpreted as signs of the activation of these stress pathways (Jayasinghe et al., 2014). It has been stated that stress symptoms emerge physiologically (physically), psychologically or behaviorally, and that the magnitude of these stress types influences the individual's physiological state (Tilbrook and Clarke, 2006). Before a match, athletes become anxious, fearful and excited, and they express these feelings physiologically, mentally and socially. This may cause the athlete to become nervous before a match. This state of anxiety can also manifest itself in a crucial situation during the competition. A critical game strategy applied by handball coaches is to attempt to break the player exchange or concentration of the opposing team, but such applied strategies and moves can also be a stress factor in their own players as well. This is because sports branches such as handball, in which the physiological burden constantly increases during the competition, are different from the steady-state branches of exercise. The sport of handball is a significant source of stress on the aerobic metabolism of an athlete (Buchheit et al., 2009). In addition, handball includes many anaerobic actions that

require body contact, sepeated acceleration, sprinting, throwing, blocking, pushing, and quick about-turns. Among the most important factors that increase stress in sportsmen are the risk of muscle damage-based injury, performance decline and fatigue resulting from the necessity of participating twice a week during a handball season, where the competition is intense (Baker et al., 2004; Margonis et al., 2007).

In this context, given the physiological and physical requirements of the sport of handball, the hypothesis that athletes may be exposed to a stressful situation is logical. Filaire et al. (1999) collected samples from 20 top women athletes 5 min before and after a handball and a volleyball match and measured saliva cortisol, androstenedion and dehydropyandrosterone (DHEA) via radioimmunological assay. Three different psychometric scales (the Trait Anxiety Inventory, Bortner Scale, and Personality Questionnaire for Sport Participation) were used to measure the psychological levels of the participants. The results showed that although the cortisol levels after the competition had increased significantly from before in both groups, the degree of anxiety the handball players. These findings indicated that the adrenocortical changes during the handball and volleyball competitions had increased the level of anxiety related to losing or winning by affecting their personal characteristics.

As a consequence; It was found that submaximal exercise used in the team sport of handball had a significant effect on salivary cortisol levels. In samples taken during an event with a high level of importance for the team, significantly variable levels of cortisol as a stress hormone were expressed in the athletes. It is thought that cortisol may affect the performance either positively or negatively, depending on the orientation of the psychological stress of the athletes.

According to the findings, the salivary cortisol levels started to increase before the match, rose during the match and started to fall at the end of the match. Therefore, saliva cortisol measurement appears to be an important parameter that can be used to develop stress-management and other necessary strategies in sport branches such as handball where the mental and physical stress is intense.

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Oral propolis treatment decelerates experimentally induced osteoarthritis in rats.

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ABSTRACT

Propolis has antioxidant, anti-inflammatory and immunomodulatory features. It also has protective effects in human chondrocyte cultures. These effects of propolis are associated to its constituents like pinocembrin, and caffeic acid phenethyl ester. The aim of this study was to expose the effects of propolis in terms of cartilage tissue protection on an experimental osteoarthritis model in rats. Twenty-eight Sprague Dawley rats divided into four equal groups (Arthrotomy: A, Surgical control: SC, Propolis 100: P1, and Propolis 200: P2). Following right knee arthrotomy the medial meniscus was removed in groups SC, P1 and P2. The surgical procedure was concluded after arthrotomy in Group A. A solution prepared from propolis extract was administered from the first day for five weeks orally in doses of 100 mg/kg/day to the rats in the P1 group and 200 mg/kg/day to the rats in the P2 group. At the end of the study, specimens taken from the medial tibial joints were assessed histologically based on the Mankin scoring system. Compared to the SC group the histological results from both of the groups receiving propolis treatment were significantly better ($p<0.001$ for both). However, there was no significant difference between the P1 and P2 groups ($p=0.506$). In conclusion, propolis was observed to reduce cartilage degeneration in an experimental model of OA. We attribute this to the effect to the components that contained in propolis, such as pinocembrin and caffeic acid phenethyl ester.

1. Introduction

Osteoarthritis (OA) is the most common joint disease, which affect more than half of the population aged over 65. It affects load bearing joints such as the hip and knee. It is characterized by progressive joint cartilage degeneration and subchondral bone changes (Bove et al., 2006; Teeple et al., 2013).

Overproduction of inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, IL-17 and IL-18) plays an important role in the pathophysiology of OA. These cytokines, especially TNF-α, exacerbate cartilage destruction by increasing the release of matrix metalloproteinases (MMPs), various aggregants and catabolic enzymes. Cytokines such as TNF-α, IL-1, IL-17 and IL-18 also reduce MMP inhibitors and extracellular matrix components which results an imbalance in the anabolic and catabolic process of the cartilage tissue (Bramono et al., 2004; Lorenz and Richter, 2006; Pasternak and Aspenberg, 2009; Ma et al., 2015; Zhang et al., 2015). Therefore, functional and structural loss in joint cartilage become progressive.

The main objectives in the treatment of OA are reducing pain, restoring the joint function and decelerating the progression of the disease (Teeple et al., 2013). There is intensive research on drugs which are altering the course of the disease. Such drugs particularly intend to alter the course of the disease by affecting the inflammatory cytokines that play an important role in the pathophysiology.

Propolis is a natural resin produced by honey bees. It is obtained through collection from various plants, and used as an adhesive (Khalil, 2006). Various studies have referred to its anti-inflammatory, antioxidant, antimicrobial and antitumor properties by reducing the secretion of various MMPs (MMP-1, MMP-3 and MMP-13), prostoglandine E2 (PGE2), nitric oxide (NO), IL-6, IL-1 and TNF-α (Hu et al., 2005;

Khalil, 2006; Gao et al., 2010; Guney et al., 2011; Soromou et al., 2014; Zhang et al., 2015). These effects of propolis are also associated to its constituents like pinocembrin (PB), and caffeic acid phenethyl ester (CAPE) (Borrelli et al., 2002; Cardile et al., 2003; Hu et al., 2005; Yüce et al., 2015; Armutcu et al., 2015; Zhang et al., 2015).

The purpose of this study was to determine the effects of propolis in terms of cartilage tissue protection on an experimental OA model in rats.

2. Experimental Procedure

This study was performed in the Karadeniz Technical University surgical research laboratory following approval from the institutional ethical committee. Twenty-eight Sprague-Dawley rats with a mean weight of 275 gr (250-300 gr) and aged 20 weeks were used. All rats were placed into separate cages. Room temperature was set at 20-24°C and the light: dark cycle was adjusted to a rhythm of 12 hours of light and 12 hours of dark. Standard rat chow and water were provided. Following observation for 1 week, the rats were randomly assigned into one of four groups (Arthrotomy: A, Surgical control: SC, Propolis 100: P1, and Propolis 200: P2).

Surgical procedure

Following a 4-hour fasting, anesthesia was achieved with the intraperitoneally injection of 10 mg/kg xylazine hydrochloride (Rompun: Bayer, Leverkusen, Germany) and 50 mg/kg ketamine hydrochloride (Ketalar: Pfizer, Istanbul, Turkey). Anesthesia was extended when necessary with additional administration of ketamine. The right leg of the rat was shaved and prepared with povidone-iodine solution. Arthrotomy was performed with a medial parapatellar incision to the right knee. In Group A the surgical procedure was concluded after the arthrotomy stage. In order to obtain an experimental OA model in groups SC,P1 and P2 patella was displaced laterally, the medial collateral ligament was severed and the medial meniscus was removed (Bendele, 2001; Janusz et al., 2002). After the operation, all rats were placed into separate cages and permitted unrestricted weight-bearing as soon as they recovered from anesthesia. No antibiotic was used for infection prophylaxis.

Propolis preparation and application

Propolis specimens collected from various regions of Turkey were powdered and mixed. 100 gr propolis was dissolved with distilled water and left to incubate for 24 h. At the end of 24 h, the extract was removed from the stirring incubator and filtered through filter paper. It was then prepared for use by being passed through a 0.22-μm sterile filter. Study solutions of desired concentrations were prepared from stock propolis extract at a concentration of 100mg/ml. One day after the surgical intervention, this solution was administered by oral gavage to the rats in P1 group at a dose of 100 mg/kg/day and to P2 group at a dose of 200 mg/kg/day. This application was repeated every day for 5 weeks. At the end of the 5th week all rats were sacrificed by cervical dislocation.

Histological analysis

The right knee joints were removed. Muscles and soft tissues were removed without damaging the knee joint. The knee joints were fixed in 10% formalin solution for 24 hours then they were kept in 10% formic acid for decalcification. Hydration was performed with ethanol. All specimens were cut in the exact midline in the sagittal plane. The medial sections were then taken and fixed in paraffin blocks in such a way as to remain on the top surface. Serial sections of 5 micrometers in thickness were taken with a microtome in order to obtain the medial tibial joint surface planned for histological analysis. Specimens were taken from the load bearing region of the medial tibial joint. These sections were stained with Safranin-O/FastGreen and examined blindly on the basis of the Mankin scoring system (Pearson et al., 2011) under a light microscope by a histologist (Olympus BX51).

Statistical analysis

The statistical analyses were performed using the IBM SPSS statistics 22. The compliance of the quantitative data with normal distribution was evaluated by Kolmogorov-Smirnov test. Comparison of groups were performed with Mann-Whitney U test. Bonferroni correction was calculated for comparison of the groups and p values less than 0.016 was considered statistically significant.

3. Results

Limping observed on the first postoperative day and gradually improved in the following days. No infection was observed in the surgical wound site. No contracture or patella dislocation was observed in any knee joints taken for evaluation. All rats survived the study period.

The degree of the cartilage tissue injury of the medial tibial joint surface was examined microscopically in terms of cartilage surface integrity, chondrocyte status, amount of matrix staining with Safranin O and the structure of tidemark.

In Group A, the cartilage structure was generally regular, and cells were normal in terms of shape, numbers and morphology. Staining with Safranin O was mildly decreased in three joints and normal in the others. No tissue loss occurred in the joints (Figure 1).

In the SC group, clefts were observed in the cartilage structure toward the middle layer in five rats and toward the calcified layer in two. Hypocellularity was observed in five rats and cloning in two. Staining with Safranin O decreased moderately in six joints and intensely in one joint. Structurally, the tidemark was not crossed in three joints but was crossed in four (Figure 1).

In the P1 group, superficial irregularity in medial tibial cartilage was seen in six joints. Superficial irregularity and a pannus appearance were seen in one joint. In terms of cell structure, cloning was observed in four joints and intense hypercellularity in three. A mild decrease in staining with Safranin O was observed in two joints and a moderate decrease in five. Tidemark integrity was determined in four joints, while vasculature crossed the tidemark in three (Figure 1).

In the P2 group, in terms of cartilage structure, superficial irregularity was observed in three joints. Superficial irregularity and pannus were seen in three and clefts extending to the middle layer in one. In terms of cell structure, cloning was observed in four joints and hypocellularity in three. A mild decrease in Safranin O staining was observed in three joints and a moderate decrease in four. The tidemark was found intact in three joints while vasculature crossed the tidemark in four (Figure 1).

The full histological values obtained from the groups are shown in Table 1. At statistical analysis, all groups differed significantly from Group A ($p<0.001$). In addition, the P1 and P2 groups differed significantly from the SC group ($p<0.001$ for both). However, no significant difference was observed between the P1 and P2 groups ($p=0.506$).

The Mankin scoring values obtained from Group A were almost normal. However, marked worsening was observed in the SC group (total score: 63). The histological scores of P1 and P2 groups decreased markedly when compared to the SC group (total score in the P1 group: 34, total score in the P2 group: 39).

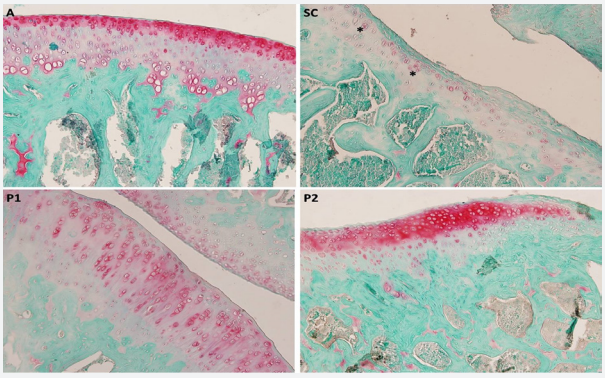

Fig. 1.

Table 1. Mankin scores of the groups.

Group/ Rat	Structure	Cells	Safranin O	Tidemark	Total
A-1	0	0	1	0	1
A-2	0	0	0	0	0
A-3	0	0	1	0	1
A-4	0	0	0	0	0
A-5	0	0	1	0	1
A -6	0	0	0	0	0
A -7	0	0	0	0	0
SC-1	3	3	2	0	8
SC-2	3	2	2	1	8
SC-3	5	2	2	1	10
SC-4	3	3	2	1	9
SC-5	3	3	2	0	8
SC-6	5	3	3	1	12
SC-7	3	3	2	0	8
P1-1	1	2	2	0	5
P1-2	1	2	1	0	4
P1-3	1	1	1	1	4
P1-4	1	2	2	1	6
P1-5	1	1	2	0	4
P1-6	2	1	2	0	5
P1-7	1	2	2	1	6
P2-1	3	1	1	1	6
P2-2	1	0	2	1	4
P2-3	2	2	2	1	7
P2-4	2	2	2	1	7
P2-5	1	3	1	0	5
P2-6	2	2	1	0	5
P2-7	1	2	2	0	5

A: Arthrotomy group
SC: Surgical control
P1:Propolis 100
P2 Propolis 200

4. Discussion

OA is a common degenerative disorder. It affects millions of people worldwide and usually causes workforce losses and decrease in the quality of life. The searches on the therapeutic treatment methods for OA aim at changing the course of the disease and decreasing the progression of cartilage degradation. MMPs and MMP inhibitors control the turnover and the function of the extracellular matrix. Therefore, they play a dominant role in the pathophysiology of OA (Pasternak and Aspenberg, 2009; Zhang et al., 2015).

Propolis is a substance that derived from plant resins by honeybees. It contains more than 300 different chemical compounds (Cardile et al., 2003; Guney et al., 2011). It has been shown in various studies that propolis has antioxidant, anti-inflammatory, immunomodulatory, antitumor and neuro-protective features. Also it has time dependent beneficial effects on fracture healing (Guney et al., 2011; Yüce et al., 2015).

PB is a flavonoid component of propolis (Zhang et al., 2015). PB inhibits the release of MMP-1 (Collagenase 1), MMP-3 and MMP-13 (Collagenase 3) from human chondrocytes. Thus, it reduces the facilitating effect of MMPs in the pathophysiology of OA. In addition to the inhibitory effect of PB on MMPs, it has also been reported to reduce inducible nitric oxide synthase (INOS), TNF-α, IL-1β and IL-6 release (Gao et al., 2010; Soromou et al., 2014; Zhang et al., 2015). This may contribute to the anti- inflammatory effect of propolis.

IL-1β is an important cytokine in cartilage tissue degradation. IL-1β increases the levels of INOS and Cyclooxygenase 2 (COX-2) with consequent increase of NO and arachidonic acid metabolites in chondrocytes. In particular, NO increases the release of MMPs from chondrocytes and inhibits the proteoglycan synthesis (Lyons-Giordano et al., 1993; Cipolletta et al., 1998; Cardile et al., 2003). CAPE is another flavonoid component of propolis. It reduces the deleterious effects of IL-1β and inhibits Xanthine oxidase activity on chondrocytes in cartilage tissue cultures (Cardile et al., 2003; Armutcu et al., 2015). Therefore, this significant effect of CAPE on IL-1β decrease the formation of free radicals and can explain the antioxidant properties of propolis. In addition, CAPE is a potent inhibitor of receptors that stimulate the activation of T cells that play a key role in inflammatory diseases. CAPE significantly inhibits IL-2 gene transcription that stimulates IL-2 and T cells (Marquez et al., 2004).

There were few studies that have been presented the protective action of propolis in human cartilage cultures (Cardile et al., 2003; Armutcu et al., 2015). On the contrary, to the best of our knowledge, this is the first study to report the protective effects of propolis in an experimental osteoarthritis model in rats. Rat medial meniscectomy model was chosen for achieving the progressive cartilage degeneration because an appropriate cartilage degeneration can be obtained as in human knee osteoarthritis in a period of four weeks (Bendele, 2001; Janusz et al., 2002).

The histological scores of both groups receiving propolis therapy in this study were significantly better compared to the SC group in terms of cartilage structure, chondrocyte status, amount of matrix staining with Safranin O and the integrity of tidemark. In other words, less experimentally induced cartilage degeneration occurred in the groups receiving

propolis compared to the control group. Also there were no statistically significant histological score difference between the P1 and P2 groups.

This study suggest that propolis has a decelerating effect on experimentally induced OA. The result exhibited by propolis under this experimental study can be explained by the effects of its active ingredients such as CAPE and PB on interleukins, TNF-α and MMPs. The fact that the findings are not supported by biochemical data is a weakness of this study.

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Our experience with Carotid Endarterectomy

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ABSTRACT

Stroke is the second most common cause of cardiovascular mortality. Atherosclerosis is the most common cause of carotid artery stenosis. The most common site is carotid bifurcation where the carotid baroreceptors and internal carotid artery exist. The primary objective of carotid surgery is to protect the brain from an ischemic damage. In this study, we evaluated early and mid term result of 24 patients who had undergone unilateral carotid endarterectomy surgery.A total of patients (17 males, 7 females; mean age 68.62 years; ranges from 55 to 91 years) who underwent CEA operations between January 2015 and january 2017 were retrospectively analyzed. Postoperative complications (neurological and non-neurological) and mortality were the primary outcome points in the study. Clinical findings and risk factors were evaluated. Among the seven of the 24 NIRS monitored patients (5 males, 2 females; mean age 65.8 years; range 60 to 75 years), a significant decrease in cerebral SO2 was observed during clamping of the common carotid artery. For this reason we decided to use intracarotid shunt. We observed that the cerebral oximetry values were increased after the use of a shunt in these seven cases. Discussion NIRS monitoring is a precious tool which provides vital information and is used to determine whether a shunt is needed during CEA surgery. The present study showed that carotid endarterectomy under general anesthesia accompanying NIRS, measurement of the stump pressure and usage of dacron patch material can be performed with acceptable mortality and morbidity.

1. Introduction

Stroke is the second most common cause of cardiovascular mortality. Atherosclerosis is the most common cause of carotid artery stenosis. The most common site is carotid bifurcation where the carotid baroreceptors and internal carotid artery exist. Baroreceptors play an effective role in the autoregulation of the blood pressure. A carotid endarterectomy (CEA) is an effective treatment modality for patients with carotid stenosis of greater than 70% (De Bakey ME, 1975) Perioperative stroke risk ranges from 2 to7.5%. Different techniques of carotid endarterectomy (CEA) have considerable affect on the results and the need for restenosis. The primary objective of carotid surgery is to protect the brain from an ischemic damage. The blood flow is directed from common carotid artery (CCA) to the ICA via a shunt. Shunt is generally used in patients with contralateral carotid artery stenosis or failure of Willis. A number of techniques for monitoring are used to define the need for peroperative shunt placement. Observation of stump bleeding from the internal carotid artery (ICA), measurement of carotid artery stump pressure (CASP), jugular venous oxygen saturation (SO2), transcranial Doppler (TCD), electroencephalography (EEG), the bispectral index (BIS), and cerebral oximetry [near-infrared spectroscopy (NIRS)] are used to determine the lack of cerebral perfusion and a need for shunt placement during surgery (Aksun M et al., 2013). Cerebral NIRS monitoring is an easy and noninvasive method for measuring cerebral oxygen saturation (rSO2) and provides the direct measurement of SO2. NIRS detect the reflections from a deep pool area at the intersection of the anterior cerebral artery and the middle cerebral artery in the brain. This device shows mixing of arterial and venous blood at a ratio of 30/70. NIRS monitoring Carotid endarterectomy (CEA) surgery reduces the incidence of stroke in patients with critical carotid artery stenosis (Ballotta E, 2002)

2. Patients, materails and methods

A total of 24 patients (17 males, 7 females; mean age 68.62 years; ranges from 55 to 91 years) who underwent CEA operations between January 2015 and january 2017 were retrospectively analyzed (Table 1). Stenosis of the carotid arteries according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. The initial examination was performed by color Doppler ultrasonography, whilst the definitive diagnosis was made by computed tomography angiography. A written informed consent was obtained from each patient. Five of the symptomatic patients had transient ischemic attack (TIA), six had hemiparesis, three had amaurosis fugax. 70 to 95% carotid artery stenosis was confirmed by computed tomography angiography. Ten patients were operated for the left side and fourteen patients for the right side. All patients were operated by a single surgeon. All patients were operated under the general anesthesia. All patients received low molecular weight heparin before and after the operation and acetylsalicylate 100 mg/day or clopidogrel 75 mg/day after the operation. Postoperative neurological evaluation was performed according to the presence of clinical findings. Postoperative complications (neurological and non-neurological) and mortality were the primary outcome points in the study. Clinical findings (grade of stenosis grades, symptoms, stroke), risk factors (coronary artery disease, previous coronary artery bypass surgery, preoperative myocardial infarction, hyperlipidemia, diabetes mellitus, smoking, hypertension, peripheral arterial disease, chronic obstructive, postoperative neurological complications (Paralysis, stroke, monoplegia, hemiplegia, hemiparesis, TIA) and non neurological complications (Bleeding, rupture, infection and thrombosis), renal insufficiency, gastrointestinal complications, arrhythmias, heart failure and mortality were recorded.

3. Results

Twenty one patients (87%) had right internal carotid artery stenosis ranges between 30% and 100%. Seventy patients (70%) had left internal carotid artery stenosis ranges between 30% and 99%. Ten patients (41%) had underwent left carotid endarterectomy and fourteen patients (59%) had underwent right carotid endarterectomy surgery. One patient (4.15%) had a history of chronic renal insufficiency, thirteen (54%) patients had a history of HT and thirteen (54%) had a history of DM. The mean body mass index was 27.65 kg/m2. Among the seven of the 24 NIRS monitored patients (5 males, 2 females; mean age 65.8 years; range 60 to 75 years), a significant decrease in cerebral SO2 was observed during clamping of the common carotid artery. For this reason we decided to use intracarotid shunt. We observed that the cerebral oximetry values were increased after the use of a shunt in these seven cases. There was no infection, pseudoaneurysm, or patch rupture. Four patients (16%) had minor incisional hematoma and required revision. Ten patients (41%) had coronary stenting or underwent coronary artery bypass grafting. Two deaths (8.3%) and one major stroke (4.15%) were seen among the patients. Twenty two (91%) patients were recovered uneventfully and were discharged with oral anticoagulation or antiagregan therapy. The mean time to discharge was 3.83±2.64 (range, 3 to 27) days except two deaths and major stroke. Within the follow-up period, none of the patients had neurologic events, residual stenosis, restenosis, occlusion or pseudoaneurysm. The mean follow-up after CEA operation was 17±6.4 (range, 11 to 24) months. No restenosis or residual stenosis were detected on follow up by computed tomography angiography.

4. Discussion

More than 70% stenosis in diameter for asymptomatic and more than 50% stenosis in diameter for symptomatic patients were the indications for carotid endarterectomy (Brott TG et al., 2011). Carotid endarterectomy is recommended to patients who are asymptomatic under the age of 75 years old, more than 70% stenosis with a 3% surgical risk (Grego F et al., 2005). The risk of stroke and death is five years and stroke development are 3% and 12% respectively (Liapis CD et al., 2009; Hidiroglu M et al., 2010). The postoperative cranial nerve damage was found 8.6% in NASCET study and in ECST study 5.1%. Only one (4.15%) patient was oberserved with temporary cranial nerve damage in our study. North American Symptomatic Carotid Endarterectomy Trial; NASCET) suggest that surgey should be postpone 4-6 weeks after cerebrovascular event. 40-50% patients who are diagnosed with carotid artery stenonis are associated with coronary artery stenonis (Yildirim T et al., 2004). Shunt placement has a 1-3% risk of an emboli or dissection (North American, 1991). It is postulated that the most sensitive monitoring for cerebral perfusion takes placein patients who are awake, for this reason many CEA operations are performed under general anesthesia. Intracarotid shunt can be used to ensure adequate cerebral perfusion. NIRS monitoring is a precious tool which provides vital information and is used to determine whether a shunt is needed during CEA surgery. Syntetic patch materials prevent incision related morbidities (i.e. bleeding, hematoma, edema, infections) in diabetic and obese patients (Ozdemir N et al., 1995). The main limitation of our study is the absence of long-term follow-up data. In addition, another limitation was the absence of the comparison of the CEA with medical or carotid artery stenting. This small sample study may have affected the results and the retrospective design of the study.

In conclusion, carotid endarterectomy under general anesthesia is an easy, effective and quick technique. It provides an adequate surgical exposure. Our study demonstrates that carotid endarterectomy under general anesthesia accompanying NIRS, measurement of the stump pressure and usage of dacron patch material can be performed with acceptable mortality and morbidity. Our clinical experience and early results of surgery are compatible with the literature and support carotid endarterectomy as a safe procedure with low morbidity and mortality rates.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Tables

Table 1: Demographic features of the patients.

	Age	sex	endarterectomy	CRI	DM	HT	right ICA	left ICA
1	72	M	left			+	0	80
2	83	M	right		+		80	0
3	71	M	left			+	0	70
4	73	M	right		+		75	0
5	74	F	left			+	50	90
6	59	F	left		+		70	0
7	91	M	right			+	90	60
8	72	M	left		+		90	60
9	65	M	right		+		90	0
10	69	M	right			+	85	45
11	82	F	right				95	0
12	66	M	right			+	80	0
13	62	M	right		+	+	80	80
14	48	M	left				60	60
15	59	M	left				100	99
16	74	M	right		+	+	80	30
17	75	F	right	+	+	+	85	65
18	61	M	left				0	75
19	65	F	left		+	+	30	75
20	55	F	left				30	80
21	65	M	right		+	+	90	0
22	66	M	right		+		99	30
23	67	M	right		+	+	60	60
24	73	F	right		+	+	80	90

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Retrospective analysis of the results of parotid surgery performed by the same surgeon

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ABSTRACT

Objective: The aim of this study was to examine retrospectively the clinical data of patients who were operated by the same surgeon due to parotid mass. Material and Method: The clinical data of 110 patients who had parotidectomy due to parotid mass between the years 2009 and 2014 were examined retrospectively. Results: 45 of the patients were female while 65 were male. The average age of female patients was 45, while the average age of male patients was 48.9. The most common lesion observed in female patients was pleomorphic adenoma (71,1%), while the second most common lesion was whartin tumor (4,4%) and benign cystic lesion (4,4%). The most common lesion in male patients was pleomorphic adenoma with a frequency of 38.5%, the second most common lesion was whartin tumor with a frequency of 27.7%. When the distribution of benign and malignant lesions was analyzed in terms of gender, it was found that 93,3% of the female patients had benign lesion while 6,7% had malignant lesion and 83,1% of the male patients had benign lesion while 16,9% had malignant lesion. Overall, 87,3% of the patients were found to have benign lesion while 12,7% were found to have malignant lesion. As a conclusion, while the most commonly observed lesion in our study was pleomorphic adenoma, followed by Warthin tumor, which was in parallel with the literature, it was remarkable that lipoma was seen in 4 patients and unlike the literature, the most common malignant tumor was squamous carcinoma and none of the patients under 40 years of age had malignant tumor and Warthin tumor.
Keywords: Pleomorphic adenom, Warthin, Parotid, Parotidectomy

1.Introduction

Salivary gland tumors make up 3-6% of all head-neck tumors. 80% of salivary gland tumors are seen in parotid (Cıncık et al., 2004). Of these, 80% are benign, 70-75% are pleomorphic adenoma, 15-20% are Warthin tumor and 10-15% are other benign tumors.Salivary gland tumors are more common in women, and they are seen in between second to fourth decades most frequently (Suen and Hanna, 1998). In parotid masses, fine-needle aspiration biopsy (FNAB), ultrasonography, computerized tomography and magnetic resonance imaging methods are used with physical examination in order to get more detailed information and to make a treatment plan (Topak et al., 2013). In parotid gland tumors, surgical resection forms the basis of the treatment. The most conservative approach in benign tumors which involve the superficial part of parotid is superficial parotidectomy; in tumors which involve the deep lobe, total parotidectomy is performed (Eisele et al, 2001; Guintinas et al., 2006).

2.Material And Method

In our study, the surgery data and pathological diagnoses of 110 patients, 45 women and 65 men, who were operated by the same surgeon in the Otorhinolaryngology Clinics of Samsun Training and Research Hospital and Ondokuz Mayıs University Faculty of Medicine between the years 2009 and 2014 were examined retrospectively. Our study received approval from the ethics committee of Samsun Training and Research Hospital. The treatment that the patients received, histopathological diagnosis, age, and tumor type were assessed. All the patients who had neo-plastic and non-neoplastic

pathologies were included in the study. Parotidectomy was performed as superficial parotidectomy by protecting facial nerve in pathologies which involved parotid superficial lobe, and as total parotidectomy by protecting facial nerve in pathologies which involved deep lobe or expanded to deep lobe from superficial lobe. In surgeries, intraoperative facial nerve monitorization was performed and nerve stimulator was used when facial nerves and branches had to be determined.

3.Results

When the age distributions of the patients were analyzed, it was found that women had an average age of 45±2,325(min 16-max 86) while men had an average age of 48.9±2.128(min 13-max 80). While 71,1 %(32 patienQts) of the women had pleomorphic adenoma, Warthin tumor and benign cystic lesion were seen in 4,4% (2 patients each) of the patients.

The most commonly seen lesion in men was pleomorphic adenoma which was seen in 38,5% (25) of the patients and Warthin tumor the second most frequently seen with a rate of 27.7% (18 patients). When all the patients were taken into consideration, the most commonly seen lesion was pleomorphic adenoma which was seen in 51,8% (57) of the patients, while Warthin tumor was the second most common which was seen in 18,2% (20) of the patients. These were followed by chronic lymphadenitis with a rate of 5,5% (6 patients) and lipoma and squamous cell carcinoma with a rate of 3,6% (4 patients each). When malign tumors were assessed, squamous cell carcinoma was found to be the most frequent one with a rate of 3,6% (4 patients), while the second most frequent one was lymphoma with a rate of 1,8% (2 patients).

Table 1: Pathological Distribution Of All Patients

	GENDER				Total	
	FEMALE		MALE			
	Count	%GENDER	Count	%GENDER	Count	%GENDER
Pleomorphic adenoma	32	71,1%	25	38,5%	57	51,8%
whartin tumor	2	4,4%	18	27,7%	20	18,2%
monomorphyic adenoma	1	2,2%	2	3,1%	3	2,7%
lipoma	1	2,2%	3	4,6%	4	3,6%
benign cystic lesion	2	4,4%	0	0,0%	2	1,8%
chronic lymphadenitis	1	2,2%	5	7,7%	6	5,5%
mucoepidermoid carcinoma	0	0,0%	1	1,5%	1	0,9%
mucoepidermoid carcinoma	0	0,0%	1	1,5%	1	0,9%
acinic cell carcinoma	0	0,0%	1	1,5%	1	0,9%
ADENO CARCINOMA	0	0,0%	1	1,5%	1	0,9%
LYMPHOMA	1	2,2%	1	1,5%	2	1,8%
DUCTAL CARCINOMA	0	0,0%	1	1,5%	1	0,9%
CHRONIC SIALOADENIT	1	2,2%	0	0,0%	1	0,9%

When the benign-malign distribution was analyzed in terms of gender, benign lesions were seen in 93,3% (42) of the female patients, while malign lesions were seen in 6,7% (3) of the female patients and benign lesions were seen in 83,1% (54) of the male patients, while malign lesions were seen in 16,9% (11) of the male patients. In total, while benign lesions were seen in 87,3% (96) of the patients, malign lesions were seen in 12,7% (14) of the patients. However, the difference between genders was not statistically significant (p>0,05).

Table 2: Distribution Of Patient benign/malign

			BENIGN	MALIGN	
GENDER	**FEMALE**	**Count**	42	3	45
		% within GENDER	93,3%	6,7%	100,0%
	MALE	**Count**	54	11	65
		% within GENDER	83,1%	16,9%	100,0%
Total		**Count**	96	14	110
		% within GENDER	87,3%	87,3%	100,0%

In patients younger than 40, pleomorphic adenoma was found to be the most common lesion in 78,9% (15) of the female patients and 70% (14) of the male patients. As a who le,74,4% (29) of the patients had a diagnosis of pleomorphic adenoma. Warthin tumor was not seen in younger than 40. Malign lesion was not found in any of the patients younger than 40.

In female patients older than 40, the most common lesion was pleomorphic adenoma with a rate of 65,4 % (17 patients) in female patients, while it was Warthin tumor with a rate of 40% (18 patients). In men, the second most common lesion was pleomorphic adenoma with a rate of 24,4% (11 patients). Overall, 39,4% (28) of the patients were found to have pleomorphic adenoma while 28,2% (20) of the patients were found to have Warthin tumor.

Malign tumor was seen in 11,5% (3) of women older than 40, in 24,4% (11 patients) of men older than 40 and in 19,7 (14 patients) of the patients in total. Of the patients younger than 40, 35% (89,7) had superficial parotidectomy while

Table 3: Pathological Distribution of Patients younger 40 Years

			PATHOLOGICAL DIAGNOSIS						
			PLEOMORPHIC ADENOMA	BENIGN CYSTIC LESION	CHRONIC LYMPHADENITIS	PLEXIFORM SCHWANNOMA	LYMPHANGIOMA	BENIGN LYMPHOEPITHELIAL LESION	Total
GENDER	FEMALE	Count	15	2	0	1	1	0	19
		% within GENDER	78,9%	10,5%	,0%	5,3%	5,3%	,0%	100,0%
	MALE	Count	14	0	5	0	0	1	20
		% within GENDER	70,0%	,0%	25,0%	,0%	,0%	5,0%	100,0%
Total		Count	29	2	5	1	1	1	39
		% within GENDER	74,4%	5,1%	12,8%	2,6%	2,6%	2,6%	100,0%

Table 4: Pathological Distribution of Patients older 40 Years

	GENDER				Total	
	FEMALE		MALE			
	Count	%GENDER	Count	%GENDER	Count	%GENDER
PLEOMORPHIC ADENOMA	17	65,4%	11	24,4%	28	39,4%
WHARTIN TUMOR	2	7,7%	18	40,0%	20	28,2%
MONOMORPHYIC ADENOMA	1	3,8%	2	4,4%	3	4,2%
LIPOMA	1	3,8%	3	6,7%	4	5,6%
CHRONIC LYMPHADENITIS	1	3,8%	0	,0%	1	1,4%
MUCOEPIDERMOID CARCINOMA	0	,0%	1	2,2%	1	1,4%
ADENOID CYSTIC CARCINOMA	0	,0%	1	2,2%	1	1,4%
ACINIC CELL CARCINOMA	0	,0%	1	2,2%	1	1,4%
ADENO CARCINOMA	0	,0%	1	2,2%	1	1,4%
LYMPHOMA	1	3,8%	1	2,2%	2	2,8%
DUCTAL CARCINOMA	0	,0%	1	2,2%	1	1,4%
CHRONIC SIALOADENIT	1	3,8%	0	,0%	1	1,4%
SQUAMOUS CELL CARCINOMA	1	3,8%	3	6,7%	4	5,6%
BASAL CELL CARCINOMA	0	,0%	1	2,2%	1	1,4%
UNDIFFERENTIATED CARCINOMA	1	3,8%	0	,0%	1	1,4%
METASTATIC TUMOR	0	,0%	1	2,2%	1	1,4%
TOTAL	26	100,0%	45	100,0%	71	100,0%

total parotidectomy was performed on 4 patients (103%). Of the patients older than 40, superficial parotidectomy was performed on 62 (87,3%) patients while total parotidectomy was performed on 9 (12,7%) patients. Overall, superficial parotidectomy was performed on 97 (88,2%) patients while total parotidectomy was performed on 13 (11,8%) patients.

4.Discussion

Sixty to eigthy five percent of the salivary gland tumors result from parotid gland. It should be considered that a mass found here may be neoplastic (Taş et al., 2009). In a study of 937 cases, 52,5% of the patients were female while 47,5% of the patients were male; in another study, 42%were female and 58% of the patients were male (Upton et al., 2007). In our study, 40% of the patients were women, while 60% were men.

Parotid gland is the biggest of the salivary glands with the most pathologies. The most common benign in parotid glands are benign tumor pleomorphic adenoma (Lin et al., 2008). While pleomorphic adenoma made up 62,4% of parotid benign tumors according to Pinkstone and Cole, Özeri et al. found this rate as 90%, Gök et al. found this rate as 78,8% and Yılmaz et al. found this rate as 61%(Özeri et al., 1990; Pinkston and Cole, 1999; Yılmaz et al., 2000; Gök et al., 2001). In our study, the most frequent benign tumor in parotid gland was pleomorphic adenoma. In our study, pleomorphic adenoma was seen with a rate of 51,8%. This rate was 71,1% in female patients and 38,5 in male patients.

Warthin tumor is the second most common benign tumor of the parotid gland. They make up 6-10% of all the parotid tumors. In their study, Gök et al. reported the frequency of Warthin tumor in parotid gland as 9%, while Yılmaz et al.'s study reported this frequency as 11,8%. (Yılmaz et al., 2000; Gök et al., 2001) There are also studies which report the frequency as higher (23%) when compared with other studies in literature (Lin et al., 2008). In our study, the second Warthin tumor. Warthin tumor was found with a rate of 18,2% in our study. The second most common tumors in women was Warthin tumor and benign cystic lesion with a rate of 4,4%. In men, Warthin tumor was the second most frequent lesion with a high rate of 27,7%. In patients younger than 40, Warthin tumor was not found. In patients older than 40, Warthin tumor was the most frequent second lesion with a rate of 28,2%. In male patients older than 40, Warthin tumor was seen with a rate of 40% as the most common lesion.

The most common malign tumor of the parotid was mucoepidermoid carcinoma. In their study, while Lima et al. stated the frequency of mucoepidermoid carcinoma as 31,7% Yılmaz et al. reported this rate as 29,7%. (Yılmaz et al., 2000; Lima et al., 2005) Özbay et al. reported most common malign tumor in the parotid glands was adenoid cystic tumor (Özbay et al., 2016). In our study, just one patient with mucoepidermoid carcinoma and one patient adenoid cystic tumor were found. Unlike literature, the most common lesion in our study was squamous cell carcinoma and the second most frequent one was lymphoma.

In salivary gland tumors, treatment is shaped according to the size of the tumor, its local expansion, histopathology, lymph node involvement and stage of the illness. In benign tumors of the parotid, since the tumor is located at the parotid tail most of the time, superficial parotidectomy is the most used technique. In cases where tumor involves deep lobe, total parotidectomy is the preferred treatment modality (Aydın et al., 2008). 88,2% of our patients underwent superficial parotidectomy due to their superficially located tumor and 11,8% of the patients underwent total parotidectomy due to deep located tumor.

As a conclusion, while pleomorphic adenoma was the most frequent lesion and Warthin tumor was the second most frequent lesion, the facts that 4 patients had lipoma, the most frequent malign tumor was squamous cell carcinoma and none of the patients under 40 having malign tumor or Warthin tumor were found to be remarkable

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Case Report

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Clinical management of metformin overdose: A case report

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ABSTRACT

Metformin is first-line therapy in diabetes mellitus treatment. Metformin intoxication may cause lactic acidosis. A 29-year-old woman presented to our emergency department with loss of consciousness. Arterial blood gas revealed severely increased anion gap lactic acidosis. Continuous venovenous hemofiltration was performed for 39 h. After extracorporeal treatment, the acidosis resolved and the patient became conscious. There is no specific treatment for metformin intoxication; current treatment is supportive only. Our aim is to highlight the diagnosis, chromatographic measurement of the drug blood level, and management of metformin overdose.

1. Introduction

Metformin is in the biguanide drug class and is less likely to cause lactic acidosis than phenformin. Therapeutic doses of metformin do not cause hypoglycemia and patient compliance is better with this drug (Misbin,1977; Luft et al.,1983). The incidence of metformin-associated lactic acidosis (MALA) is 5-9 cases per 100,000 patients (Stang et al., 1999; Von Mach et al., 2004). Lactic acidosis is described as a blood la ctate level greater than 5 mmol/L and a blood pH below 7.35 (Misbin,1977). MALA has a mortality up to 50% and has been reported in the settings of chronic use and acute overdose (Luft et al., 1983; Stang et al., 1999; Von Mach et al., 2004). Here, we report an acute metformin toxicity associated with hypoglycemia and wide anion gap metabolic acidosis.

2. Case Report

A 29-year-old woman presented to our emergency department with loss of consciousness. She had no history of intoxication or medical illness. On arrival, the patient's Glasgow Coma Scale score was 4 (E1M2V1). The vital signs were: blood pressure 70/50 mmHg, pulse rate 60 beats per minute, and respiratory rate 20 breaths per minute. Capillary blood glucose level was 24 mg/dL. It was learned that the patient had no oral feeding problem. Her liver function tests were within normal limits. Initial arterial blood gas testing revealed a pH of 6.90. The anion gap was 20.9 mmol/L and lactate was 16.55 mmol/L (Table 1). Arterial blood gas testing showed severely increased anion gap lactic acidosis. Intravenous (IV) dextrose was started to correct hypoglycemia. Additionally, IV sodium bicarbonate was administered.

Drug particles were seen during gastric lavage; therefore, activated charcoal was administrated. Toxicology tests including opioids, barbiturates, benzodiazepines, ethyl alcohol, acetaminophen, salicylates, and tricyclic antidepressants were negative. Metformin was analyzed by high-performance liquid chromatography (Fig. 1). Severe metabolic acidosis was treated with IV 30 mEq/h sodium bicarbonate; hypoglycemia was treated with IV 10% dextrose. Because of refractory hypotension, IV 10 µg.kg−1.min−1 dopamine and 10 µg.kg−1.min−1 norepinephrine were administered. After 2 h, hemodialysis was started. In the seventh hour, hemodialysis was stopped because of worsening hemodynamic instability and increasing lactic acidosis level (Table 1). Continuous venovenous hemofiltration (CVVHDF) was started after confirmation of metformin overdose; the serum metformin level was 169.35 µg/mL (Figure 1). CVVHDF was performed for 39 h. After CVVHDF treatment, pH was 7.38 and lactate was 2.25 mmol/L (Table 1). The patient's Glasgow Coma Scale score improved to 15 (E4V5M6) after 12 h of CVVHDF. The patient said she had attempted suicide by ingesting 70 metformin tablets (70 g). She was discharged on the ninth day of admission.

Table 1. Acid base disorders on admission, after hemodialysis and CVVHD

	Admission	Hemodialysis	CVVHDF	Reference values
pH	6.9	7.06	7.38	(7.35-7.45)
pCO2 (mmHg)	38.2	12.4	22.9	(35-45)
pO2 (mmHg)	99	136	71	(75-100)
Anion Gap	31	32.6	7	(8-16)
HCO3 (mmol/L)	8	3.4	13.4	(21-25)
Na (mEq/L)	139.9	140	135.4	(132-152)
K (mEq/L)	3.8	3.5	3.6	(3.3-4.8)
Cl (mEq/L)	111	115	115	93-110
Lactate (mg/dL)	16.55	20.6	2.25	0.9-1.7
Glucose (mg/dL)	5	110	112	(74-110)
BUN (mg/dL)	12	7	7	(10-50)
Creatinine(mg/dL)	1.62	0.7	0.8	(0.5-1.4)

Chromatographic Method

A 10 mL blood sample was collected from subject; the sample was centrifuged at 2500 rpm for 10 min. The serum obtained was separated and frozen at -20 °C until the time of analysis. To a 0.5 mL aliquot of serum sample 0.5 mL acetonitrile were added to precipitate protein and the mixture was vortexed for one minute, than centrifuged at 3500 rpm for 10 min. The liquid phase was transferred to another tube and then the sample was diluted 1:20 by volume with acetonitrile. The injection volume into the HPLC-DAD system ranged from 5-40 µL. Chromatographic experiments were performed using an Agilent 1100 series system (Agilent Technologies, Waldbronn, Germany), which included a G1311A gradient delivery pump, a G1329B robotic autosampler, a G1315A diode-array detector, a G1322A vacuum degasser and a G1316A thermostatted column compartment. A Kromasil 100-5C18 analytical column (4.6 × 150 mm, 5 µm particle size, Hichrom, UK), protected by a guard column filled with the same material, was used. The HPLC analysis was performed using an adaptation of the method with some modifications of Moore et al. A standard calibration curve consisted of five concentration points of 12.5, 25, 50, 75 and 100 ng of metformin (Moore et al., 2003). Each concentration point was performed for three times. Working Standard solution (2.5 ng/mL), was prepared on the day of assay. The calibration curve was constructed using a series of metformin dilutions. As expected, a very high metformin concentration (169.35 µg/mL) was measured in the serum sample (Figure 1).

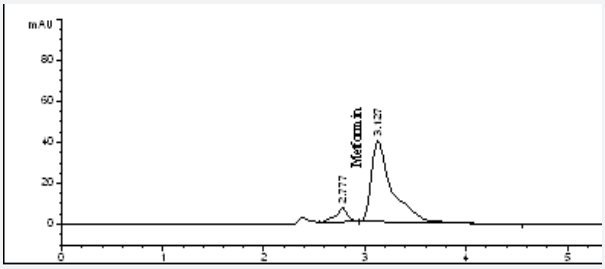

Fig. 1.

3. Discussion

Wide anion gap metabolic acidosis in a drug overdose should alert clinicians to metformin intoxication (Perrone et al., 2011). MALA can present with anorexia, lethargy, nausea, vomiting, epigastric pain, hypotension, hypothermia, respiratory failure, and cardiac dysrhythmia (Gan et al., 1992; Spiller, 1998; Von Mach et al., 2004). Our patient presented with profound hypoglycemia. Hypoglycemia may occur in the setting of MALA (Cullen et al., 2004). Hemodialysis and CVVHDF are useful in acid–base disorders and to remove causes of lactic acidosis (Spiller, 1998). Sodium bicarbonate should be considered in patients with normal respiratory functions if their blood pH is lower than 7.0 (Yang et al., 2009). This approach has no significant effect on mortality and may cause detrimental effects, including decreased cardiac output, decreased intracellular pH, and paradoxical increased lactate production (Luft et al., 1978). Other complications may include volume overload, hypernatremia, and left shift of the oxyhemoglobin dissociation curve (Gan et al., 1992). A large cohort study of patients treated for MALA failed to show a significant benefit for bicarbonate infusion, and in our patient, sodium bicarbonate infusion did not increase blood pH despite her lactate level increasing to 24 mmol/L (Bruijstens et al., 2008) (Table 1). Hemodialysis with a bicarbonate buffer is successful in MALA treatment (Lalau et al., 1987; Soyoral et al., 2011).

In addition to drug removal, bicarbonate dialysis can rapidly correct acid–base disorders (Lalau et al., 1987; Spiller, 1998). Because of the drug's low molecular weight and lack of protein-binding, metformin has a high plasma clearance with conventional dialysis modalities (Lalau et al., 1987; Soyoral et al., 2011). Our patient could not tolerate hemodialysis for the required time. After 7 h of hemodialysis, she was hemodynamically unstable; therefore, CVVHDF was the treatment of choice in this case (Davenport et al., 1993). Wide distribution of metformin allows continuous hemodialysis or hemoperfusion to maximize metformin remo-

val (Yang et al., 2009). In this case, CVVHDF was performed for 39 h. After CVVDHF, the patient's pH improved to 7.38 and her lactate level decreased to 2.25 mmol/L. Early diagnosis and treatment of hypoglycemia and lactic acidosis may provide complete recovery in metformin intoxication. The treatment for metformin intoxication is usually supportive only. Vasopressors can be used if there is refractory hypotension. Accurate and prompt diagnosis is mandatory in metformin overdose. In hemodynamically unstable patients, hemodialysis with bicarbonate buffer may be inadequate, and CVVHDF should be considered for prompt metformin removal.

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Conflict Of Interest
The authors declare they have no conflict of interest.

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Case Report

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Conservative treatment with tracheal montgomery® T-tube in anastomotic leak due to total pharyngolaryngeal esophagectomy

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ABSTRACT

Following total pharyngolaryngeal esophagectomy and gastric pull up, anastomotic leaks are the most important complications that increase the postoperative morbidity and mortality. In this study, we would like to present a patient who underwent Montgomery® (Boston Medical Products) tracheal T-tube placement due to anastomotic leak after gastric pull-up and laryngectomy performed for a cervical esophageal tumor.

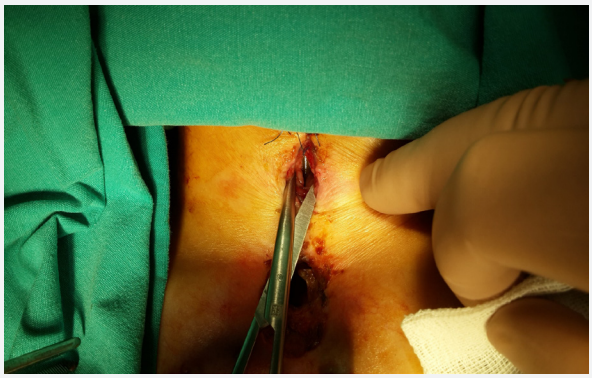
1. Introduction

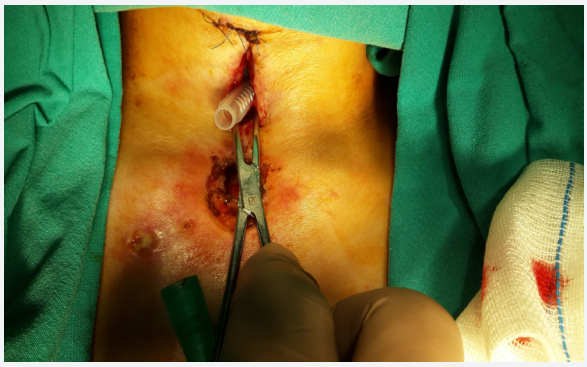
Cervical esophageal cancers are highly aggressive tumors. They often exhibit multifocal mucosal and submucosal lymphatic invasion. Total pharyngolaryngeal esophagectomy and gastric pull up are the most common treatment options (Erişken, 2003). In this study, we would like to introduce you a patient who underwent gastric pull-up and laryngectomy because of a cervical esophageal tumor.

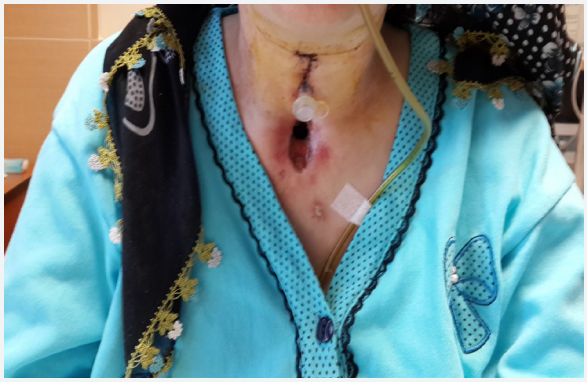
Case

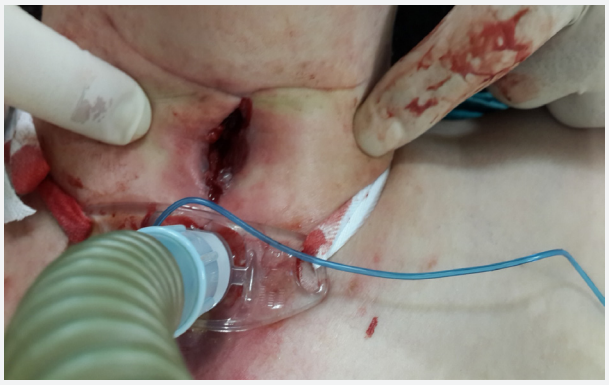
Three months ago, a 45-year-old female patient presented with the complaints of dysphagia and pain while eating solid food. Computerized thorax tomography (CTT) revealed a concentric esophageal wall thickening, starting from the thoracic entrance at about 3 cm distal to the epiglottis and continuing down for about 25 mm. It was about 12 mm at the thickest point. In the neck and thorax magnetic resonance imaging (MRI), it was detected that there was a tumoral mass at the esophageal upper end, continuing for about 4 cm, having irregular margins and close neighboring to the back wall of the trachea. Pharyngoesophageal graphy revealed a tumoral lesion in the cervical esophagus. It was about 5-6 cm inferior to the priformis and was causing a concentric stenosis in a 3-mm area at lumen. In PET CT, 18 fluorodeoxyglucose (FDG) uptake SUV-max value of the lesion was 21.6. Endoscopy revealed a concentric stenosis in the lumen and an irregularity and color change in the mucosa at the 15th cm of the esophagus. The biopsy samples taken from these lesions were reported to be epidermoid carcinoma. A tumoral mass originating from cervical esophagus, invading the postcricoid region and the posterior wall of the trachea and continuing down to the 4th tracheal ring was observed in the exploration. Total laryngectomy, including the 6th tracheal ring, was performed. Cervical esophagus was freed by dissecting the posterior part. The stomach was freed and tubelized. Esophagus was freed with blunt dissection by using transhiatal method. Esophagectomy and gastric pull-up were performed. Anastomosis was performed by hand at the cervical area. An anastomotic leak developed on the postoperative 11th day. Oral feeding was ceased. A new cervical exploration was performed. In the exploration, it was observed that the front wall of the anastomosis line was open, and the stomach wall was necrotic (Fig.1). After the debridement of the tissues, a 10-mm silicon Montgomery® tracheal T-tube was placed at the anastomosis line through the fistula tract (Fig. 2a-b). Nutrition was started on the postoperative 3rd day. No additional problems were encountered during the follow-up. T-tube was removed after the 4-week follow-up.

It was observed that the regeneration tissue created a new lumen along the T-tube, and that the defect on the anastomosis line healed completely except the defective area caused by the T-tube at the anterior (Fig.3). The defect was closed primarily with 3-0 vicryl by using skin support. Postoperatively, water and liquid food were started gradually. On the 7th day of the tube withdrawal, the patient was discharged although her dysphagia score was +1 when receiving soft foods. Along 6 month follow-up period, neither complication nor stenosis was observed.









2. Discussion

Cervical esophageal tumors are the ones that have the worst prognosis of all the head and neck tumors. These tumors characteristically have high multifocal mucosal involvement and exhibit submucosal lymphatic invasion, and they often display no symptoms until the advanced stage (Chu and Chang, 2009). So, in the treatment of these tumors, reconstruction with total pharyngolaryngeal esophagectomy and gastric pull-up can be performed in addition to hypopharynx (Sreehariprasad, 2012).

Pulmonary complications and anastomotic leaks are the most serious complications after total pharyngolaryngectomies (TPL), and they are the most important factors increasing the postoperative morbidity and mortality. Accordingly, hospital costs and length of hospital stay are affected significantly (Yenigün, 2013). In the literature, the rate of anastomotic leak has been reported to be between 9-14% after TFL (Orringer, 2007; Lindenmann, 2008). Shuangba et al. (Shuangba, 2011) reported that in the study they evaluated 208 patients with cervical and hypopharyngeal tumors, 9.1% of the patients had anastomotic leak. Of these patients, 15 healed spontaneously, and 4 underwent reconstruction with the use of pectoralis major muscle.

The frequency of anastomotic leak after esophagectomy varies depending on the organ used for anastomosis, localization of the anastomosis and the nutritional status of the patient. If the anastomosis is not too stretched, blood supply is good, the quality of the tissue is adequate and the surgeon is experienced enough, the risk of leak will be minimized (Yenigün, 2013). Levy et al. (Levy, 2010) reported in their study that the patients who underwent Mckeown esophagectomy had higher anastomotic leak rate than the patients who underwent İvor-Lewis esophagectomy. The likely cause is considered to be the poorer blood supply to the anastomosis in the cervical area on which the Mckeown esophagectomy is performed.

In cervical anastomotic leak; erythema at the incision site, high temperature and leukocytosis related to the crepitation are observed (Iannetoni, 1995). In our patient, the first symptom was erythema around the wound site.There was also food outcome through the tracheostomy stoma after food ingestion. Cervical esophagogastric anastomotic leaks are usually small. Drainage is often enough for treatment. Cases requiring anastomotic revision occur rarely. Gastric necrosis, esophagocutaneous fistula and vertebral osteomyelitis, epidural abscess resulting in paraplegia, pulmonary microabs-

cesses related to the internal jugular vein abscess and fistula of the tracheaesophagogastric anastomosis are some of these cases (Iannetoni, 1995). There was also food outcome through the tracheostomy stoma after food ingestion.
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In the literature, T-tube placement has usually been reported in the series of patients treated for esophageal perforation (Linden, 2007; Yenigün 2013). No study reporting a tracheal T-tube placement due to anastomosis leak after TPL has been encountered in the literature.T-tube placement can be suggested particularly in patients whose diagnoses have been made after the first 24 hours, and/or when the surgical repair is not possible. The aim of T-tube placement is to create a controlled esophagocutaneous fistula. It has been reported that the morbidity and mortality rates were lower in patients who were admitted with delayed esophageal perforation and underwent T-tube placement, although their hospital stays were longer (Linden, 2007; McMahon, 2009). T-tube is withdrawn in about 4-6 weeks after the placement. During this period, while the drainage of the content is performed, the regeneration of the esophagus around the T-tube occurs through epithelialisation (Linden, 2007; Fonseca, 2009). Enteral nutrition could safely be continued in this period. Our patient started to receive food orally on the 3rd day following T-tube placement. When the T-tube was removed in the 5th week, it observed that the front wall of the esophagus had regenerated on top of the T-tube and formed a new front wall. Thanks to the design of t tube, it was prevented migration of tube and development of a new esophageal stricture.

The mortality rate after TPLs has been reported to be 15%. The most significant factors reducing this rate are the advances in the surgical techniques, advanced intensive care follow-up and the efficient nutritional support (Homma, 2014).
The reoperation rate has been reported to be 30% in patients treated with T-tube placement, and the mortality rate in these patients is 9% (Linden, 2007). In our patient, we managed to start a high-calorie and protein-rich oral enteral nutrition just on the 2nd day following the T-tube placement. Thus, new mucosal healing around the T-tube was achieved in the 4th week, and feeding continued without any additional problem after the removal of T-tube. Total pharyngolaryngeal esophagectomy and gastric pull-up resections are safe and effective treatment methods for the local control in cervical esophageal tumors. When other treatment alternatives are not effective enough in patients that developed postoperative anastomotic leak, T-tube placement can be considered as a suitable conservative treatment option.

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Case Report

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Acute cholecystitis developing as a result of verapamil intoxication

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ABSTRACT

Calcium channel blockers are the drugs with the highest poisoning-related mortality. The most commonly seen finding in verapamil intoxication is hypotension, with other frequently encountered findings being bradycardia and atrioventricular block. It may also lead to potentially fatal complications such as non-cardiogenic pulmonary edema. Gastrointestinal symptoms such as nausea and vomiting are uncommon. This report describes a case brought to the emergency department with abdominal pain, in which cholecystitis was determined following tests performed when hypotension and bradycardia could not be explained, and in which it was learned that the patient had taken a high dose of verapamil with the aim of committing suicide.Cholecystitis as a result of verapamil intoxication has never previously been reported in the literature.

1. Introduction

Verapamil, a powerful calcium channel blocker (CCB), inhibits the L-type voltage gated calcium channel. This leads to vascular smooth muscle relaxation and negative inotropic and chronotropic effects in the heart (1). Verapamil is frequently used in the treatment of ischemic heart disease, arrhythmias, hypertension and hypertrophic cardiomyopathy. Potential fatal complications such as hypotension, bradycardia and non-cardiogenic pulmonary edema may develop as a result of verapamil intoxication. Other reported complications include sinus arrest, atrioventricular block, decreased cardiac output and hyperglycemia2). This case report describes acute cholecystitis as a complication that has not previously been reported in the literature. On arrival he was lucid, with a Glasgow Coma Scale score of 15. Blood pressure was 60/40 mm/Hg, temperature of 36 C° and pulse rate 40/min. Electrocardiography was compatible with sinus bradycardia. At physical examination, the skin was pale and cold. There was widespread sensitivity at abdominal examination. Laboratory findings were leukocyte 15,200/mm3 and creatinine 1.8 mg/dl, other biochemical markers were normal. Ejection fraction at echocardiography was 65%, and no findings for coronary insufficiency were determined. Pronounced hypotension, leukocytosis and widespread abdominal sensitivity suggested the presence of a surgical pathology in the abdomen. Abdominal tomography

revealed elevated thickness in the bile duct wall and fluid around the duct (Figure 1). The patient's examination findings, leukocyte values and abdominal tomography findings were interpreted in favor of acute cholecystitis. But the patient had unexplained hypotension and bradycardia, he was questioned again. It was then established that he had taken some 30 verapamil tablets for the purpose of suicide. The patient was transferred to the intensive care unit. He received 20 ml/kg crystalloid over 20 min. Although appropriate volume resuscitation he had hypotension and bradycardia. Then admininstered dopamine 10 microgram/min. His blood pressure and heart rate resolved on the fourth day. The previous pathological appearance in the bile duct was observed to have contracted at ultrasound on the fourth day. The patient was discharged in a healthy condition following psychiatric evaluation.

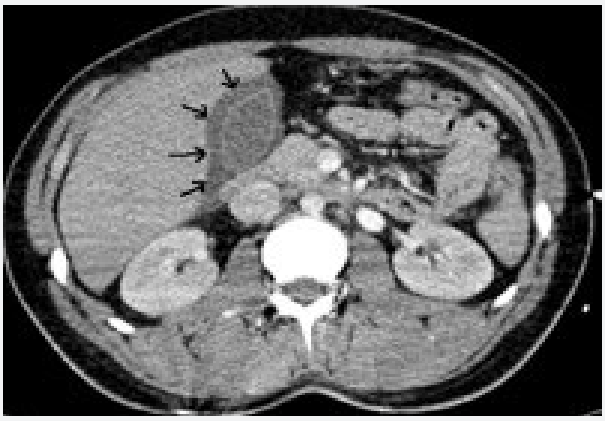

Fig. 1.

3. Discussion

Verapamil is a potent CCB used in the treatment of hypertension, ischemic heart diseases and supraventricular tachycardia. It exhibits a negative inotropic and chronotropic effect by relaxing the smooth muscles. It causes dilatation in the peripheral and coronary arteries. Taken in high doses it inhibits insulin secretion in the pancreatic β cells, resulting in hyperglycemia (1,2). The most significant complications in verapamil overdose are congestive heart failure, cardiac arrest, deep hypotension and atrioventricular block. It can also cause reddening in the face edema, confusion, nausea and constipation (3).

Aggressive decontamination may be life-saving in verapamil overdose. It is recommended that patients be given 50-100 g activated charcoal by oral or nasogastric tube. In addition, digestive system irrigation should be performed with balanced saline solution. Airway management may be performed to ensure a safe respiratory tract. Decontamination performed in this way is most effective within 1 h of ingestion. Since the drug binds powerfully to protein and has a wide tissue distribution, enhanced elimination techniques such as hemodialysis and hemoperfusion are not recommended. 'ABC' should be evaluated as a priority in emergency treatment. A venous path should be opened and patients started on 0.9% normal saline solution infusion without delay. Patients require close monitoring. Standard support treatments such as atropine in bradycardia and vasopressor in hypotension must be administered at once. Agents that have a direct effect in hypotension and bradycardia,to play a role in the cholecystitis development mechanism. such as norepinephrine and epinephrine, should be preferred over dopamine. Calcium, and particularly calcium chloride, should be given in antidotal treatment (4). The aim in this treatment is to prevent potential bradycardia, dysrhythmia and hypotension. Calcium chloride is recommended in poisoning since it contains three times more calcium than calcium gluconate.

One gram intravenous calcium chloride may be given in 5 min or so a maximum 3-4 times every 10-20 min. If calcium does not correct the hypotension, glucagon, an agent of questionable effectiveness, may be given (5). Glucagon 0.15 mg/ kg (approximately 5 mg) may be given every 5 min in IV bolus form, repeated 3 times until response is achieved. If there is no response after a 15 mg dose, other dosages will be of no clinical benefit. But if there is a significant rise in the patient's blood pressure, IV glucagon can be commenced. Glucagon frequently leads to vomiting and hyperglycemia. In addition to these, insulin and glucose are used to achieve hyperinsulemia/euglycemia in the treatment of severe intoxication. Carbohydrate absorption to the heart is thought to be impaired as a result of hypoinsulinemia developing following CCB ingestion (6). While the exact mechanism is unclear, insulin/glucose therapy may cause a dramatic improvement in blood pressure. The initial insulin dose is 0.5-1 U/kg, and infusion at 0.5-1 U/kg/hour may be started. An additional 25 g or 50 ml 50% dextrose (0.5 g/kg 25% dextrose in children) bolus may be given. Blood glucose level should be kept at a 100-200 mg/dL level. Among the side-effects of this treatment are hypoglycemia and hypocalcemia. Series glucose and potassium follow-up must be performed together with insulin therapy. In the event of resistance to all treatments then ventricular pacing may be tried in order to regulate heart rate. In this situation it is recommended that heart rate should not exceed 60/min (7).

No cases of verapamil overdose-associated cholecystitis have been reported in the literature. The mechanism by which cholecystitis develops is unclear, but it is thought perhaps to bear a similarity to the non-cardiogenic pulmonary edema mechanism developing in association with verapamil intoxication. Cholecystitis may have developed in association with peripheral edema resulting from prostacyclin inhibition, capillary leakage syndrome and precapillary vasodilatation (3). CCBs, including verapamil, are known to affect the immune system. CCBs have been observed to suppress macrophages, mast cells and T cells in several in vitro studies (8,9). Although CCBs are thought of as immune suppressants, drugs such as amlodipine and verapamil have been found to activate BP interleukin IL-1 and IL-6-associated transcription factor and nuclear factor KB (10). The relationship between verapamil and inflammatory cytokines is fo be conudered.

4. Conclusions

There has been an increasing rise in drug intoxication in recent years. Drug intoxication may be confused with several life-threatening diseases. Verapamil may complicate the clinical findings of a case of intoxication resulting in acute cholecystitis. Good anamnesis and physical examination are therefore very important. This will permit early diagnosis and thus reduce mortality and morbidity.

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Case Report

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Invisible double-J after kidney transplantation

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ABSTRACT

Ureteral catheterization is widely used in patient after kidney transplantation. The catheters are radiopaque in order to check by radiography. A 52-year-old man underwent kidney transplantation presented a radiolucent ureteral catheter during follow-up. The forgotten double-J catheter complicated with stone encrustation. Further surgical treatment for removal of this catheter was also presented.

1. Introduction

Kidney transplantation is one of the treatments for end-stage renal disease (ESRD). Ureteral double-J catheterization is generally used in patients underwent kidney transplantation. Prophylactic ureteric stenting reduces the incidence of major urological complications significantly in patients underwent kidney transplantation (Mangus and Haag, 2004; Wilson et al., 2005). Complications including stone encrustation, migration, fragmentation and even death may occur with forgotten double-J stent (Singh, 2005). The catheters are usually made radiopaque for further follow-up. There was no cases describing a radiolucent ureteral catheter have been reported. Here we present a radiological invisible double-J catheter in a case of 52-year-old man received kidney transplantation.

2. Case Report

This 52-year-old man received kidney transplantation one year ago in China. After surgery, he turned to visit our out-patient department for post-transplantation care. Elevated serum creatinine level to 2.18 mg/dl was noted in recent check-up. Abdominal ultrasound showed hydronephrosis of graft kidney, ureteral and graft kidney with hyperechoic spots with acoustic shadow. Graft renal stone and ureteral stone were impressed initially. Kidney-ureter-bladder plain film (KUB) was checked but no urolithiasis or retained catheter was found (Fig.1). We speculated these lesions to be radiolucent stones. However the following computed tomography (CT) showed a ureteral stent with stones in graft ureter (Fig.2). Cystoscopy was arranged for removal of the stent but failed due to stone encrustation. Then the operation of endoscopic cystalitholapaxy for encrusted double-J stent was performed. Radiologist was consulted for antegrade removal of double J but failed again. Graft percutaneous nephrostomy drainage (PCND) was done for the hydronephrosis

therefore. The operation of graft ureteroscopic lithotripsy (URSL) for encrusted stone over double-J stent (Fig.3) and double-J stent removal (Fig.4) were smoothly undergone 2 days later. A radiopaque double-J stent was inserted due to swelling and mucosa tear during ureterosopic lithotripsy. Patient serum creatinine level returned to 1.05 mg/dl 3 days after URSL. The double J stent was removed 2 weeks later. The patient is being regularly followed up at our outpatient department with uneventful condition.

3. Discussion

The prevalence rate of ESRD in Taiwan is about 2500 per million populations. The high dialysis prevalence and incidence result in large medical expenditures. More and more patients choose kidney transplantation as a treatment instead of hemodialysis. Placement of ureteral stent in the construction of an ureteroneocystostomy reduces obstruction or urinary leak in the early post-transplant period (Mangus and Haag, 2004; Wilson et al., 2005).

Ureteral stents have become an integral part of urologic practice nowadays. History of the catheters can be traced back to the 19th century. The early catheters were constructed from fabric coated with varnish, and then vulcanized rubber, finally polyvinylchloride (PVC), polyuerethane and polysi loxanes (silicone). Evaluations of the presence and locationare usually performed with fluoroscopy because it is quickly and easy available. The materials of the catheter are always radiopaque. Some stents even contain fillers to enhance ra diopacity. Barium sulfate (BaSO4), bismuth compounds and tungsten (W) are used as common radiopacifiers and are added in polymer formulations contemporary (Mottu et al., 1999). Considerations of the compound depend on various factors. Barium sulfate, the first radiopaque material widely compounded in medical formulations, is the most common filler used with medical-grade polymers. It is inexpensive but might not appear as bright on newer X-ray machines which operate at higher energy levels than older ones. Bismuth compounds are twice as dense, but ten times more expensive than barium. Cheapness, poor quality, lower loading or even lack of radiopacifiers might be the most possible reason why the catheter became invisible in our case.

In spite of the various advantages, loss to follow-up of the catheter, so-called forgotten double-J, may lead to several complications such as migration, stone encrustation, fragmentation, chronic renal failure(Aron et al., 2006), and finally even death(Singh et al., 2005). Forgotten stents is not rare in urologic practice, but relatively rare in kidney transplanted patients. Only 16 cases in 14 reports were in the literature

Table I: Reported forgotten ureteral stents in renal transplant patients (1989-Present).

Case	Year	Author	Patient age	Presenting complaint	Duration of stent	Pre-operative imaging	Operative procedure
1	1989	Gedroyc et al.	3	UTI	17 months	KUB	PCNL, extraction
2	1999	Gustacchini et al.	45	Recurrent UTI	3 years	Ultrasound, KUB	Cystoscopy, PCNL
3		Henderson et al.	52	Not reported	5 months	Unreported	PCNL, URS, Ho:YAG laser
4	2002	Henderson et al.	59	Not reported	6 months	Unreported	PCNL, URS, Ho:YAG laser
5	2004	Yenicesu et al.	34	Hematuria, Dysuria	7 years	Ultrasound, KUB	Cystoscopy, Removal under fluoroscopy
6	2005	Romanowsky et al.	48	Recurrent UTI	4 years	KUB, CT	PCNL, Ultrasonic lithotripsy
7	2005	Singh et al.	Unknown	Hematuria, UTI	1 year	Ultrasound, KUB	Retrograde approach
8	2006	Veltman et al.	47	UTI	5 months	KUB, CT	PCNL, URS, Ho:YAG laser, Cstoscopy, Lithotripsy
9	2009	Bhuva et al.	32	Nocturia, Weak stream	10 years	KUB, CT	Cystoscopy, PCNL
10	2012	Lai et al.	47	Hematuria, UTI	5 years	Ultrasound, KUB, CT	URS
11	2013	Lasaponara et al.	39	Severe UTI	8 years	CT	ureteroureteral anastomosis
12	2014	Bardapure et al.(3 cases)	34-55	Recurrent UTI	3 -5 years	Ultrasound, KUB	ESWL, Cystoscopy
13	2014	Wu et al.	Unknown	Recurrent UTI	19 years	KUB	ESWL, URS, Ho:YAG laser
14	2015	Karabıcak et al.	55	Recurrent UTI	5 years	KUB	Cystoscopy
15	2015	our case	52	Elevated creatinine	7 months	Ultrasound, KUB (invisible), CT	URS, lithoclast lithotripsy

Our case presented with the unique characteristic of invisible stent. The serious morbidity and mortality are associated with increased financial burden for health services (Sancaktutar et al., 2012), and sometimes legal problems. Many approaches for treating encrusted forgotten ureteral stents had been reported including extracorporeal (shock wave lithotripsy), endoscopic (transurethral lithotripsy, percutaneous nephrolithotripsy, or holmium laser) and open procedures (nephrolithotomy or cystolithotomy) (Rabani, 2012). In addition to the polyurethane and silicone stents, a novel biodegradable stent was also documented (Chew et al., 2013). Although the material of the stent in our case is still undetermined, the stent was removed successfully despite its long indwelling time. Advanced ureteral stent register and reminder system are always helpful for avoiding forgotten ureteral stent (Lynch et Al., 2007; Sancaktutar et al., 2012)

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Case Report

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Giant abdominal mass originating from the ovary.

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right ovary and ovarian cancer

ABSTRACT

Adnexial masses are commonly seen in gynecologic practice. Distinguishing malign from benign masses should be done for these patients. Mucinous cystadenoma is among the most common benign ovarian neoplasms. It may grow to an enormous size. Here, we report a case of mucinous cystadenoma originating from the right ovary in a 57-year-old woman.

1. Introduction

In women, adnexial mass is a common gynecologic problem. Differential diagnosis is the principal goal of the evaluation of an adnexial mass. For women with a suspicious mass after an initial evaluation, surgical exploration is required. There is no noninvasive techniques for the diagnosis of ovarian cancer (Buys SS , 2005). The most important finding used to determine the presence of malignancy in an adnexal mass is the appearance of the mass by transvaginal ultrasound. Many adnexal masses are asymptomatic and it is discovered as an incidental finding on pelvic imaging. (Myers, 2006). The degree of clinical suspicion of ovarian cancer is significantly higher for postmenopausal compared to premenopausal women; therefore, surgical exploration may be required for many postmenopausal women. The incidence of ovarian cancer increases with age (seer.cancer.gov, 2012).

Size of the mass is an important factor. Surgical exploration is essential for postmenopausal women with a $\geq$ 5 cm mass who also have symptoms suggestive of ovarian cancer (Curtin JP. 1994).Other factors for ovarian cancer, such as menopausal status, elevated tumor marker, symptoms, or risk factors may increase the degree of suspicion. CA 125 isa tumor marker used most commonly for the detection of epithelial ovarian cancer (CA 125 >35) (Im SS, 2005). referral to a gynecologic oncologist is advised for masses that are highly suspicious for ovarian cancer,. Long term Survival in patients with early stage disease, could be possible if an optimal staging could be performed by the sugeon. (ACOG, 2011).

We present a case of delayed development of aggressive, treatment-resistant abdominal mass with unusual gross features.

2. Case Report

A 57-year-old woman was admitted to the hospital. The woman was, gravida 6, abortus 0, and parity 6. She had a long-standing history of constipation, and pelvic pain. , She was treated with nonsteroidal anti-Inflammatory drugs which were ineffective. On pelvic examination her uterus was found to be slightly enlarged. Abdominal examination showed a mass with 200x200 mm in diameters. The rest of her physical examination was unremarkable. Laboratory data revealed white blood cell count as 9700, hemoglobin as 11.4, hematocrit as 33.6, and platelets as 221.000 . Serum CA 125 level was elevated (CA-125; 132 IU). Chemistry profile and other serum tumor markers was unremarkable.

BUN, creatinine, and blood sugar were normal. Liver profile was unremarkable. Serum FSH (Follicle stimulating hormone) and LH (Luteinizing hormone) concentrations were increased.(FSH: 30 mIU and LH: 20 mIU) No evidence of gastrointestinal pathology (Intestinal mucinous tumors, etc.) was detected by colonoscopy.

Ultrasonography showed a gross mass arising from the right adnex filling the abdomen. The diameters were 200*220 mm. Pelvic ultrasound showed the presence of a large solid, rather than cystic, mass with normal endometrial lining. The gross appearance revealed cystic areas. Blood flow was displayed by color Doppler in mass. It was hypervascular at color Power Doppler evaluation. In computed tomography imaging, right adnexial mass with a maximum diameter of 200*200 mm was detected (cystic right ovarian mass). It was solid with rare cystic spaces. The cyst wall was 2–15 mm in diameters.

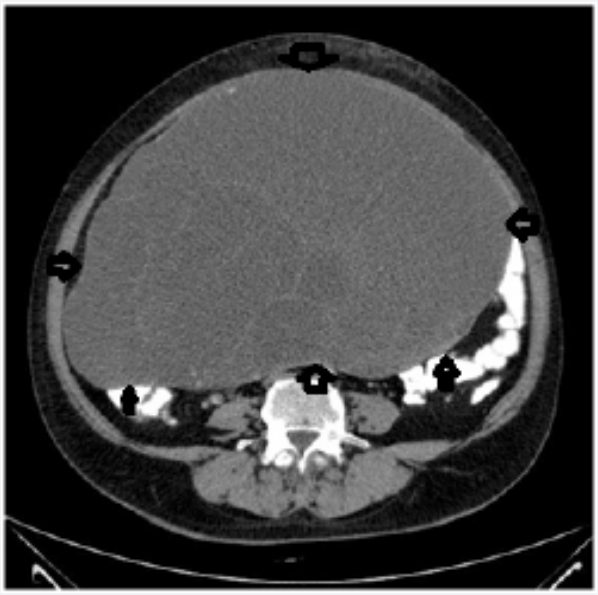

Fig.1. The computed tomography imaging showing the mass (Transverse diameter of the mass was 205 mm).

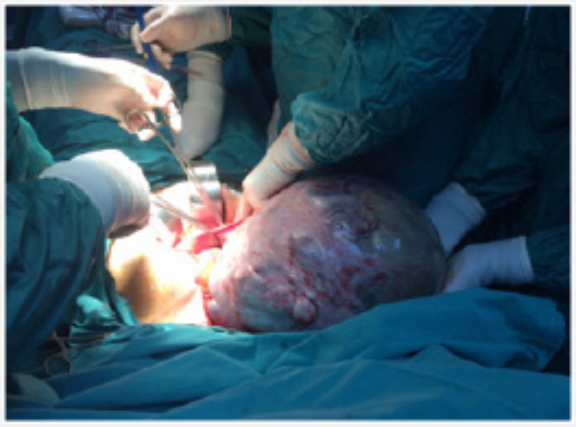

Fig. 2. The operation image of the right ovarian mucinous cystadenom. Bunun yerine patolojiye giden hali konulabilir

Midline incision reaching up to xiphoid process in laparotomy was done . The mass was diagnosed in frozen as an right ovarian mucinous cystadenom . Hysterectomy was performed due to symptomatic uterine adnexial mass. Being a mother at 48 years with menopause, bilateral salpingo-oophorectomy was added to the surgery. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. Intraoperative evaluation revealed a mass measuring 210*240 mm in diameters originating from the right over. (Fıg. 2). Uterus, appendix and left over were normal in appearance.

Histopathological examination of hysterectomy specimen revealed a mass measuring 210x240x250 mm attached to the right ovarian. Cut section of the mass showed compatible with mucinous cyst adenoma according to microscopic examination. Evaluation for uterus and left ovary was unremarkable.

3. Discussion

The degree of clinical suspicion of ovarian cancer is increased for postmenopausal in comparison to premenopausal women. Therefore, surgical exploration is required for many postmenopausal women with an ovarian mass. Size of the mass must also be considered who proceed to surgical exploration for women with a 5 to 10 cm mass with symptoms suggestive of ovarian cancer (Roman LD, 1997). CA 125 is the tumor marker used most commonly for ovarian cancer. Other serum markers are used to evaluate women for less common histologic types, germ cell and sex cord-stromal tumors. Ovarian mucinous carcinoma generally do not express CA125. (Vang R, 2007)

When all types of mucinous neoplasms are taken into consideration, they account for 10 to 15 percent of all ovarian neoplasms. Approximately 80 percent are benign mucinous cystadenomas. In addition the majority of the rest are (20 percent) mucinous borderline neoplasms (Hart WR. 2005). In addition to this, most mucinous carcinomas originate frequently from the gastrointestinal tract (the most common appendix). The ovarian masses are metastases from these sites (Riopel MA, 1999). Mucinous cystadenomas are among the most common benign ovarian neoplasms. Malignant mucinous tumors may be bilateral in 10% to 20% of cases, benign tumors are rarely bilateral Mucinous cystadenomas occur less frequently whichare more likely to be multiloculated, and larger (they can grow to an enormous size). Clinically, mucinous tumors may grow quite large, reaching 30 cm in size and weighing as much as 40 kg (Ozols, 2005). In the differential diagnosis; Other ovarian masses, fallopian tubal cancer, ectopic pregnancy, hydrosalpinx , tuboovarian abscess, paratubal or paraovarian cyst, broad ligament leiomyoma, should always be excluded (Guerriero S, 2002).

Ovarian cysts may cause pain or pressure symptoms. Women who present with acute pain and an ovarian mass should be evaluated without delay and may require urgent intervention. The first step in the evaluation of an adnexal mass is to confirm the presence and anatomic location of the mass with pelvic imaging, usually with ultrasound. Sensitivity of pelvic ultrasound for the diagnosis of ovarian cancer ranges to 86 percent and the specificity ranges to68 percent in a large meta-analysis (Myers ER, 2006)

In a randomized trial , among 570 women who underwent surgical evaluation for suspected ovarian cancer, 20 cases of malignancy were found. If malignancy is suspected based upon these factors, surgical exploration is required to obtain a specimen for histologic diagnosis. Many women undergo surgical procedures to identify the rare cases of malignancy

who have large adnexial masses (SS, 2005) The objective of this report is to identify distinct features of a giant adnexial mass in a woman. In older patients with giant adnexial mass, laparotomy should be performed. A definitive diagnosis of ovarian mucinous cystadenom can only be made from histological examination of laparotomy specimens.

Declaration of interest: The authors report no conflicts of interest.

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Case Report

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Neonatal hypercalcaemia associated with congenital adrenal hyperplasia

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ABSTRACT

Adrenal insufficiency is an important and potentially life-threatening condition, and it is also a rare cause of hypercalcaemia. We report a case of resistant hypercalcaemia (calcium [Ca] 13.8 mg/dL) in an 18-day-old male infant in which normalised serum Ca levels could not be achieved even after treatment with hyperhydration and furosemide. Long term lowering of serum Ca was only achieved after the diagnosis of congenital adrenal hyperplasia (CAH) was made and the initiation of hydrocortisone replacement therapy. Prior to presentation, the patient had only mild scrotal hyperpigmentation, and findings were otherwise unremarkable for CAH. Hypercalcaemia is a rare but well-recognised complication of CAH. The mechanism of this form of hypercalcaemia is unclear, because congenital adrenal insufficiency is a rare cause of hypercalcaemia and patients are treated as soon as the diagnosis is made. Neonatologists should consider CAH in the differential diagnosis of neonatal hypercalcaemia.

1.Introduction

Adrenal insufficiency is an important and potentially life-threatening condition, and is also a rare cause of hypercalcaemia. It was first described in 1932 by Loeb (Loeb, 1932), in an adult patient with Addison's disease. In the majority of published cases, patients with hypercalcaemia and adrenal insufficiency present in adulthood (Walser et al.,1963; Pieters et al., 1990; Diamond and Thornley, 1994; Bhatti and Flynn 2012). However, there is a single case report of a 12 year old who presented with the hypercalcaemic effects of adrenal insufficiency due to idiopathic atrophy of the adrenal glands (Prader et al.,1959). Herein, we report a case of congenital adrenal hyperplasia (CAH) due to 11-beta-hydroxylase deficiency in a new-born presenting with hypercalcaemia.

2.CaseReport

An 18-day-old male infant was born at 36 weeks gestation to a 30-year-old healthy mother by emergency caesarean section for foetal distress and intrauterine growth retardation. His parents were first-degree cousins. At birth the patient weighed 2200 g with a length and head circumference of 46 and 34 cm, respectively. The patient was referred to our paediatric endocrinology clinic due to his resistant hypercalcaemia.

On physical examination, the infant was ill appearing with the following vital signs: heart rate 160 beats/min, respiration rate 68/breaths/min and blood pressure 93/67 mm/Hg (>95th percentile). Genital examination revealed bilateral palpable gonads, a 3.5-cm phallus and mild scrotal hyperpigmentation. The laboratory evaluation revealed the following results: glucose 58 mg/dL; creatinine (Cr) 0.7 mg/dL; calcium (Ca) 13.8 mg/dL; phosphorus (P) 6 mg/dL; sodium 134 mEq/L; potassium 6.8 mEq/L; alkaline phosphatase 1100 U/L; adrenocorticotropic hormone (ACTH) 104 pg/mL (normal range [N]:6-48); morning (8am) cortisol 3.4 µg/dL (N:4-21); 17-hydroxyprogesterone (17-OHP) 1900 ng/dL (N:<2000); dehydroepiandrosterone sulphate (DHEA-S) 1000 µg/dL; total testosterone 506 ng/dL (N:75-400); progesterone 4.05 ng/mL; androstenedione 3.4 ng/mL (N:0.1-0.5); free T4 1.46 ng/dl (N: 0.93-1.7); and TSH 2.7 uIU/mL (N: 0.5-4.2). During a standard-dose ACTH test (Synachten® 0.25 mg) the peak cortisol level was 12 µg/dL, and the peak 17-OHP and 11-deoxycortisol levels were 4800 ng/dL and 37.1 ng/mL, respectively. T treatment with intravenous (IV) he diagnosis of 11-beta-hydroxylase deficiency was established. Further evaluation revealed a serum 25-OH vitamin D level of 10.5 ng/mL and a parathyroid (PTH) level of 4.8 pg/mL. Laboratory evaluation of both parents indicated that their serum Ca, P and PTH levels, as well as their urine Ca/Cr ratio, were all normal. Abdominal ultrasonogram of the patient demonstrated medullary nephrocalcinosis. Interestingly, the patient's serum Ca levels did not normalise after

saline followed by IV furosemide at a dose of 1 mg/kg every 12 h. Oral hydrocortisone treatment at a dose of 20 mg/m2/day was commenced. Hypertension and hypercalcaemia were corrected after 3 days of hydrocortisone replacement therapy. The patient's serum Ca level decreased to 9.1 mg/dL, with a corresponding random urine Ca/Cr ratio of 0.1, and the values remained consistent (Figure 1). During a follow-up appointment, the patient had no evidence of hypercalcaemia or hypertension.

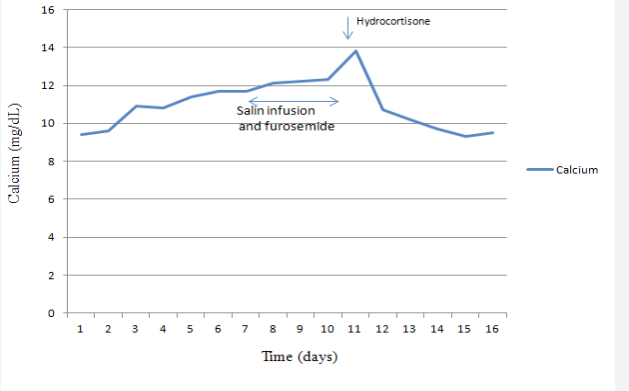

Figure 1. Serum calcium concentration prior to and directly after hydrocortisone replacement therapy.

3. Discussion

The common causes of hypercalcaemia in infants are primary hyperparathyroidism, idiopathic infantile hypercalcaemia, drugs (e.g. thiazide diuretics and vitamin A) and hypophosphatemia. Hypercalcaemia has also been reported in infants given human milk with a very high vitamin D content due to maternal hypoparathyroid treatment with high-dose vitamin D, infants who receive milk with excessive vitamin D fortification due to a processing error, and preterm infants given chronic vitamin D supplementation with a high-Ca and high-P milk formula. Neonates with extensive subcutaneous fat necrosis often have a history of perinatal asphyxia and may develop hypercalcaemia after a period of low or normal serum Ca concentration (Lietman et al.,2010). The data from our patient provide no evidence of primary hyperparathyroidism, because the PTH-vitamin D axis was suppressed. In our patient, there was no history of drug use or vitamin D3 supplementation. Additionally, there was no evidence of excessive maternal use of vitamin D3 or other drugs. Maternal laboratory tests, including Ca, PTH, vitamin D, thyroid function and urinary Ca excretion, were normal. Finally, the patient did not have any of the dysmorphic features of Williams syndrome or the typical skin changes indicating subcutaneous fat necrosis. When an extensive work up excluded the most frequent causes of hypercalcaemia, the patient's hypercalcaemia was attributed to adrenal insufficiency. Adrenal insufficiency is a rare cause of hypercalcaemia and physiological amounts of glucocorticoids may normalise serum Ca levels. Hypercalcaemia has been reported to occur both with primary adrenal insufficiency and secondary adrenal failure (Downie et al.,1977; Miell et al. 1991; Vasikaran et al.,1994; Patel and Clayton, 1994). In the present case, the examination and laboratory work-up excluded the most frequent causes of hypercalcaemia.

The hypercalcaemia observed in our patient was finally attributed to an 11-beta-hydroxylase deficiency, the second most common cause of CAH characterised by adrenal insufficien cy and virilisation of external genitalia, due to the normalisation of the patient's blood pressure following hydrocortisone therapy. Multiple mechanisms for hypercalcaemia have been proposed. It has been suggested that hypovolaemia and a decreased glomerular filtration rate lead to a reduction in Ca filtrate and increased proximal tubular reabsorption of Ca and sodium (Muls et al.,1982; Vasikaran et al.,1994).

These alterations in renal function are secondary to volume depletion and should improve rapidly following rehydration. In the case presented here, urine Ca excretion was increased indicating an increased amount of Ca in the extracellular fluid. Therefore, fluid infusion and furosemide treatment could not fully correct the hypercalcaemia, which persisted irrespective of volume status or glomerular filtration rate indicating the low significance of renal factors in this case. In contrast, complete correction of plasma Ca levels was observed shortly after the initiation of glucocorticoid replacement therapy. Another potential cause of hypercalcaemia is increased bone resorption of Ca. Physiological amounts of glucocorticoids are essential for the preserve of bone structure (Muls et al.,1982). The mechanism by which glucocorticoid deficiency enhances Ca release from bone was described by Montoli et al. (Montoli et al., 1992). The authors found no evidence of increased osteoclastic activity in bone biopsies from patients with Addison's disease, and all cellular activities at the trabecular surfaces appeared to be depressed. Thus, Ca mobilisation from bone was not associated with bone remodelling. Moreover, glucocorticoids appear to play an important role in modulating the metabolism of PTH and its influence on Ca homeostasis (Lee et al., 1978). The levels of PTH and 25-OH vitamin D were low in our patient, indicating a suppressed PTH-vitamin D axis, and these levels returned to normal after corticosteroid replacement therapy similar to previous reports (Muls et al.,1982; Montoli et al., 1992).

In addition, excessive intestinal absorption of Ca has been suggested as a potential cause of the type of hypercalcaemia observed in our patient (Muls et al.,1982). However, since our patient had very poor intake of his mother's milk, intestinal absorption was excluded as a significant source of Ca. While examining the effects of a Ca rich diet, Walser et al. (Walser et al.,1963) demonstrated that hypercalcaemia occurred with comparable frequency in adrenalectomised dogs fed a Ca-rich or Ca-free diet. Overall, these findings indicate that in our patient, the aetiology of hypercalcaemia is likely increased release from bone rather than increased intestinal absorption or decreased renal excretion of Ca. In conclusion, this case report confirms that, though rare, CAH and adrenal insufficiency should be considered in cases of hypercalcaemia that can be corrected by corticosteroid administration. The patient reported herein presented with only mild scrotal hyperpigmentation and no other findings remarkable for CAH. The mechanism of hypercalcaemia in CAH patients is unclear, because congenital adrenal insufficiency is a rare cause of hypercalcaemia and patients are treated as soon as the diagnosis is made.

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Case Report

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The final state of prosthesis and orbita of A patient who has never taken off the anterior segment of the prothesis for eighteen years

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ABSTRACT

A 56 year old woman came to our clinic with complaints of rheum in her eye. It has been understood that eighteen years before her story, the patient underwent an evisceration surgery after the reparation of her penetrating left eye, and after the third month of the operation, she didn't go to the examinations. During the consulation the patient only had complaints about rheum, and it has been understood that the patient had no additional problems, besides the irregularities developing on the surface of the prothesis. We aimed to present the interesting case of this patient, whose prothesis were creating no problems, and were kept on during the eighteen year period.

1. Introduction

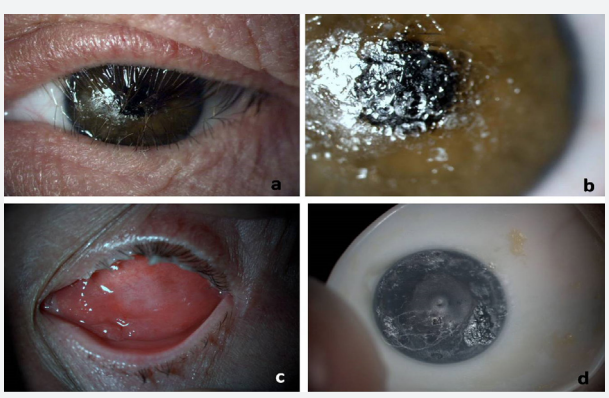
Psychological problems can be seen in a person who has lost one of his eyes for a particular reason. Ocular prosthesis is made to minimize these problems. Eye prosthesis create great physical and cosmetic results for the patient. The purpose of the Ocular prosthesis is to transmute the patient to their normal aspects and living standards. However, the user has to show sensitivity for the prothesis to be long lasting (Berkan, 1982). Complications that can occur due to Ocular Prosthesis; pseudoptosis, ptosis, the lowness of the bottom eyelid, entropion, ectropion, giant papillary conjunctivis not being used for a long period of time, socket contraction secondary to traumas, and infections were notified (Chalin et al., 1971; Beumer et al., 1979; Bozkurt et al., 2007).

2. Case Report

A 56 year old woman patien, came to our clinic with complaints of rheuming in her eye. According to the story of the patient, it was undersood that eighteen years ago, she went through evisceration surgery after her penetrating left eye troubles.The prosthesis was imposed after three months passed from the evisceration, the patient had complaints about rheuming and fainting from time to time due to missing the control checkups. In the examination, the patients right eye degree of vision was 1.0 with the Snellen eye chart, and the examination of the anterior segment and fundus seemed natural. In the examination of the left eye, other than the irregularities developing on the surface of the prothesis, it was seen that the position of the prosthesis was proper. (Figure 1a, 1b)

There was a case of entropion on the bottom left and top eye lids, including some rheuming.

(Figure 1c) After the prosthesis was taken out from the patient, it was seen that the sockets and the conjunctival tissue were normal. Besides the thinness of the Ocular prosthesis, and the secretion deposits on the back side of it, there were no additional abnormalities. (Figure 1d)



3. Discussion

The abnormal and deficient formations in the body from birth are called "Congenital Defect". The substance loss that comes subsequently is known as "Earned Defect." Bulbus Oculi is not developed from birth, but it can be lost after birth, due to traumatic and pathological reasons. In these cases of defect, Ocular prosthesis is called for. The formations of these defects are caused by maligant neoplazm, trauma, congenital or developmental anormaly, and infections (Covillard and Schaff, 1976; Berkan, 2004).

After resection, no surgical operation can emplace the eye back in its place. In these situations, eye prosthesis required. Because these defects create significant psychological problems, the making of the prosthesis should be done as soon as possible. Thus, the patients can proceed in the social activities in their lives, and they would wound up having an acceptable appearance in terms of cosmetics (Parr and ark., 1983; Raizada and Rani, 2007).

In this case report, we aimed to examine a patient who never took off the prosthesis from the day that it was put on after her eyes had been eviscerated due to a trauma. Due to a long use of the prosthesis, ptosis, pseudoptosis, the lowness of the bottom eyelid, socket contractions (postenuclation socket syndrome), entropion, and ectropion, can be seen as shown in literature (Beumer et al., 1979; Chena and Hehera, 2004). In our case, based on literature, we have not observed any additional anomalies, other than the development of entropion.

It has been observed that the socket and conjunctiva tissue were normal. In addition, there have been no obvervations of deformation of the prosthesis, other than the disorder of the front surface. Similar to our patient, patients suffering from rheum, having bacterial colonization in their sockets is one of the things we must keep in mind.

In a microbiotic study where thirty nine cases of socket conjuctivals were evaluated, %73 gram-positive, %27 gram-negative bacterial reproduction was detected. In the same study for people using prothesis for over ten years, we saw the balance shifting towards the gram-negative bacteria (Taner et al., 2003). For patients coming with rheum troubles, the evaluation of the socket and beginning the right healing process is very important for the consistency of using of the prosthesis. Yearly checkups for patients using prosthesis are important in decreasing the complications that can occur due to prosthesis. In addition to protein renewal that is suggested once every ten years, the state of the socket, the relation between the prosthesis and the socket, and the surface of the prosthesis should be examined carefully and regularly. Prosthesis that's been used and hasn't been taken out for a long time period would create socket and conjunctival tissue. In our opinion, it is interesting and for this purpose we decided to report this case.

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Case Report

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An uncommon collateral pathway in a renal artery occlusion due to takayasu's arteritis

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ABSTRACT

Takayasu's Arteritis is a rare vasculitis that affects large vessels. We experienced a case of renal artery occlusion in a 27-year-old woman suffering from Takayasu's Arteritis. On Computed Tomography Angiography, a millimetric outpouching simulating a stub was detected at the level of right renal artery orifice. Feasibility of endovascular intervention was evaluated with Digital Subtraction Angiography. However, no luminal filling could be demonstrated beyond the outpouching. While seeking the collateral circulation, the subphrenic artery trunk was shown to be the source. The subphrenic artery should be kept in mind in case the source of collateral filling could not be detected in a renal artery occlusion.

1.Introduction

Takayasu's Arteritis (TA) is a granulomatous systemic vasculitis causing arterial stenosis, thrombosis, and aneurysms. Although TA principally affects the aorta and its main branches, the renal arteries may also be involved. It may result in renal artery occlusion (Gotway et al.,2005; Chaudhry and Latif, 2013).

Renal artery occlusion does not always result in kidney injury. Collateral circulation frequently reconstructs the occluded artery (Bergqvist et al., 2001). Existance of collaterals indicates a haemodynamic significant stenosis, yet they are not always identified (Henney et al., 1982; Bergqvist et al., 2001). They can be used as an outflow for endovascular interventions (Bergqvist et al., 2001). Hence, determination of the collaterals is favourable for the procedures.

In this study, we aimed to emphasize the efficiency of Digital Subtraction Angiography (DSA) in order to demonstrate collaterals, and to present an uncommon collateral pathway in renal artery occlusion.

2. Case Report

A 27-year-old woman followed-up with the diagnosis of TA had a progressive increase in the serum creatinine levels. Her right kidney was diminished in size, and her left kidney was atrophic on Ultrasound examination. Computed Tomography Angiography (CTA) showed that branches of the aortic arch and abdominal aorta were involved by the disease. The abdominal aorta was narrowed with irregular borders due to calcified plaques. The right renal artery was not visualised entirely. At the level of the orifice, a milimetric outpouching simulating a stub of nearly occluded renal artery was detected. However, the distal part of the artery was normal. . The left renal artery could not be visualised (Figure 1). The patient was consulted by interventional radiology department in order to evaluate the feasibility of endovascular intervention for the right renal artery with this background. The angiographic procedure was performed with a monoplane DSA unit (Artis Zee, Siemens, Munich, Germany). Nonselective angiograms were obtained by using a 5-French (F) diagnostic pigtail catheter (Imager II, Boston Scientific, Marlborough, Massachusetts, USA) located at the 12th thoracic vertebral body level. The angiograms revealed that the abdominal aorta was narrowed with irregular borders. A millimetric out

pouching was detected at the level of the right renal artery orifice (Figure 2). This outpouching was tried to be catheterized gently by a 5FPP Simmons 1 catheter (Tempo Aqua, Cordis, Miami Lakes, Florida, USA) in order to recanalize. However, no luminal filling could be demonstrated beyond it. To identify the feeder of the right kidney, the superior mesenteric artery and the celiac trunk were catheterized. Nevertheless, no collateral circulation was demonstrated. While seeking the other probable pathways, the subphrenic artery trunk was catheterized incidentally. The subphrenic artery angiograms revealed that there were several collaterals reconstructing the renal artery just before the renal hilum. These were associated with the suprarenal artery and the capsular artery of the kidney (Figure 3). Having seen that both of the renal arteries were occluded, and blood flow of the right kidney was provided by collaterals, endovascular intervention was abandoned.

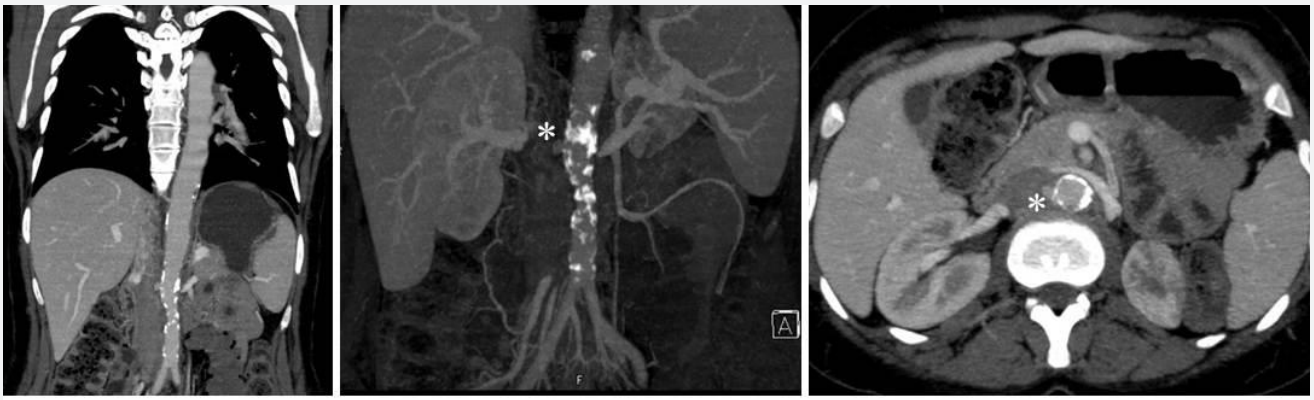

Fig. 1.

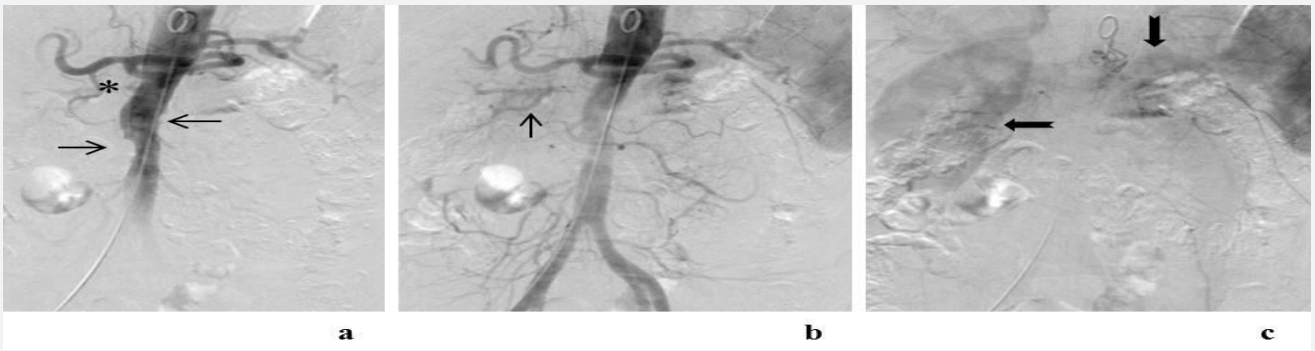

Fig. 2.

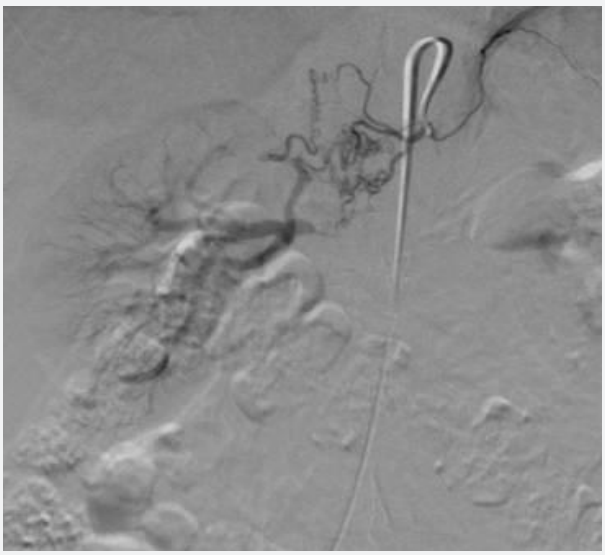

Fig. 3.

3. Discussion

Early and late-phase of TA represent different pathologic features. In the early-phase, great vessel wall thickening is the primary feature. Hence, CTA is helpful for the early diagnosis since it is able to depict wall thickening, as well as luminal narrowing (Park et., 1997). Diagnostic evaluation of TA has been carried out with the assistance of DSA, traditionally (Park et., 1997; Gotway et al.,2005). Long, smooth, tapered stenoses or frank occlusions are well shown on DSA (Park et al., 1989; Gotway et al.,2005). However, DSA is not convenient to distinguish luminal narrowing due to acute mural inflammation from stenosis due to chronic transmural fibrosis since it cannot demonstrate changes in the wall architecture as obviously as CTA (Yamada et al., 1993; Gotway et al.,2005). On the other hand, collateral vessels are well shown because DSA is actually a luminography. The imaging findings of the patient confirmed that knowledge. Collateral pathways secondary to renal artery occlusion were listed by Bergqvist et al. as follows: along the ureter, by the

suprarenal arteries, from the capsular arteries, from the lumbar arteries and rarely by the mesenteric vessels (Bergqvist et al., 2001).

The collateral circulation involving the lumbar arteries was reported to be the most common (Hietala and Kunz, 1979). Duan et al. (Lian et al., 2014) reported a case with collateral circulation originating from the subphrenic artery. To the best of our knowledge, it is the unique report mentioning the pathway. One should look for the subphrenic artery as a source of collateral filling in case routine angiographic examinations fail to show the origin.

Radiological findings suggesting renal artery occlusion does not always mean the kidney will be lost, since collaterals frequently reconsruct the occluded artery. Physicians who are not familiar to this knowledge may worry about the affected kidney. With therefore, they consider that an immediate intervention is compulsory. They should be warned with respect to this fact, and redundant interventional requests should be precluded.

Although predominant findings of TA are stenotic or occlusive changes, fusiform or saccular aneurysms may also be found (Matsumura et al., 1991). Hence, any outpouching could represent a saccular aneurysm. Because of the weakened structure of aneurysm wall, its catheterization requires attention against the risk of rupture.

4. Conclusion

To detect collaterals, DSA is an excellent diagnostic tool of choice. The subphrenic artery should be kept in mind in case the source of collateral filling could not be detected in renal artery occlusion. Findings suggesting renal artery occlusion do not always mean the kidney will be lost. Finally, any outpouching encountered during angiograhic procedure in a patient with TA requires attentive catheterization against the risk of rupture.

The Authors declare that there is no conflict of interest. Informed written consent for patient information and images to be published was provided by the patient.

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