Medical Sciences
ISSN: 1308-7312
Article ID: 1B0109

Status : Research Article
Received: 12.01.2021
Accepted: 25.04.2021

Gürkan Çıkım
Adıyaman University, drgurkanc@hotmail.com, Adıyaman-Turkey
Ülkü Veranyurt
Health Sciences University, ulkuveranyurt@gmail.com, İstanbul-Turkey

DOI	http://dx.doi.org/10.12739/NWSA.2021.16.2.1B0109	
ORCID ID	0000-0002-7572-3962	0000-0003-4838-3373
Corresponding Author	Ülkü Veranyurt	

EVALUATION OF HOMOCYSTEINE AND VITAMIN D LEVELS IN OSTEOARTHRITIS PATIENTS

ABSTRACT

In this study, we aimed to investigate whether there is a change in the levels of vitamin D, vitamin B12, folic acid, which are important for metabolism, and homocysteine levels, which are considered to be an indicator of oxidative stress, in women with osteoarthritis. This study was conducted on 30 women with osteoarthritis (Group I) and 30 healthy women (Group II) who applied to the orthopedic outpatient clinic in Kahramanmaraş Necip Fazıl City Hospital between January and December 2020. Plasma homocysteine, serum folic acid, vitamin B12 and vitamin D levels were evaluated in the study. In homocysteine levels; a statistically significant increase was found in the group with osteoarthritis (Group I) ($p<0.05$). In folic acid, vitamin B12, vitamin D levels; a statistically significant decrease was detected in the group with osteoarthritis (Group I) ($p<0.05$). In conclusion, we think that folic acid, which provide homocysteine excretion; vitamin B12 and vitamin D levels that contribute to the development of OA should be followed up and added to the diet in case of deficiency in patients with OA or joint disease that reduce the quality of life.

Keywords: Osteoarthritis, Homocysteine, Vitamin D, Vitamin B12, Folic Acid

1. INTRODUCTION

Osteoarthritis (OA) is a common term for progressive, inflammatory degenerative joint involving more frequent presentation in load-bearing joints, cartilage damage, bone hypertrophy, subchondral sclerosis, synovial membrane and joint disorders [1]. It is the most important cause of chronic musculoskeletal pain and most commonly affects the knee and hip joints in women [2]. In several studies conducted around the World, it was observed that in people over 65 years of age, knee and hip OA prevalence of 10-40% were observed whereas in Turkey these ratios were determined between 8%-22.5% [3, 4 and 5]. Although the cause of OA is not known exactly; age, obesity, genetics, increasing uncompensated chondrocyte apoptosis, extracellular matrix synthesis disorders, trauma and environmental factors are the main factors [6, 7 and 8]. In people with OA, one can observe an increase in morbidity and mortality due to the limitation of movement and a decrease in the quality of life. For Patients with OA, We can also observe an increase in the rates of diseases such as cardiovascular system and diabetes [9 and 10]. Homocysteine is a metabolized amino acid which is composed methionine. It is transsulfyrated in the presence of vitamin B6 with beta synthase enzyme and then remethylated to vitamin B12 and methylene

How to Cite:
Çıkım, G. and Veranyurt, Ü., (2021). Evaluation of Homocysteine and Vitamin D Levels in Osteoarthritis Patients, Medical Sciences, 16(2):68-73,
DOI: 10.12739/NWSA.2021.16.2.1B0109.

tetrahydrofolate reductase (MTHFR). MTHFR is a form of folic acid formed by enzyme N5 methl tetrahydrofolic acid. It is metabolized again with methionine synthase enzyme [11]. Homocysteine levels have been shown an increase in vitamin B12 and folic acid deficiency [12]. Studies have shown that hyperhomocysteinemia plays a role in many diseases such as cardiovascular, cerebrovascular, and renal disorders [13 and 14]. In another study, it was found that homocysteine caused osteoarthritis by causing mitochondrial malfunction [15]. Vitamin D is a steroid-based hormone that regulates the body's calcium (Ca) and phosphorus (P) balance, provides bone development, contributes to the formation of the immune system, prevents cancer development, and has physiological apoptosis and anti-inflammatory properties [16 and 17]. Vitamin D levels in humans vary according to various parameters such as age, gender, ethnicity and season [18]. Vitamin D deficiency has been shown to contribute to the development of diseases such as rickets, osteomalacia, hashimoto, cancer, autoimmune diseases, heart diseases, reactive arthritis, and diabetes [19 and 20]. In the scope of this study, we targeted to analyze if there was a change in the amounts of vitamin D, vitamin B12, folic acid, which had significant functions for metabolism, and homocysteine levels. These levels considered as indicators of oxidative stress, in women with osteoarthritis.

2. RESEARCH SIGNIFICANCE

Osteoarthritis (OA) is a progressive, inflammatory degenerative joint disease, which is more common in load-bearing joints, including cartilage damage, bone hypertrophy, subchondral sclerosis, synovial membrane and joint capsule disorders (1). It is the most important cause of chronic musculoskeletal pain and affects women and knee and hip joints more (2). In several studies conducted around the world in people over 65 years of knee and hip OA prevalence of 10-40%, while in Turkey, 8% - 22.5% has been determined that (3, 4, 5). In this study, we aimed to investigate whether there is a change in the levels of vitamin D, vitamin B12, folic acid and homocysteine, which are important functions for metabolism in women with osteoarthritis, which are considered to be an indicator of oxidative stress.

3. MATERIALS AND METHODS

Our study was conducted by scanning the data in Kahramanmaraş Necip Fazıl City Hospital, and 30 female osteoarthritis patients with knee and hip joint pain (Group I) who were admitted to the orthopedics department between January and December 2020. This group consisted of non-smokers. The second group included 30 healthy individuals (Group II) who did not have any complaints in the similar age group. Plasma homocysteine, serum folic acid, vitamin B12 and vitamin D levels were evaluated in the study. Cobas e 602 autoanalyzer device (Roche Diagnostics, F. Hoffmann-La Roche Ltd., Kaiseraugst, Switzerland) and electrochemiluminescence immunoassay method were used in the analysis of homocysteine, vitamin B12, folic acid and vitamin D levels. Statistical Analysis: Data were analyzed using the SPSS 20.0 program for Windows (SPSS, Inc. Chicago, IL, USA. Normal distribution of continuous and discontinuous data was analyzed by Kolmogorov and Smirnov, and homogeneity of variances was analyzed by Levene test. Descriptive variables were expressed as mean ± standard deviation (SD). In comparison of parameters between groups, Student T Test was used for those with normal distribution, Mann-Whitney U test for those who did not, and Spearman's rho method for correlation.

4. RESULTS

The study was conducted in female patients with hip and knee osteoarthritis. The mean age of the groups was: Group I: 49.6±4.05, Group II: 48.3±3.10. There was no statistically significant difference between ages (p=0.210). Homocysteine levels (µmol/L):Group I:18.04±8.44, Group II:11.19±4.03; vitamin B12 levels (ng/L):Group I:324.5±95.87, Group II:416.11±90.76; folic acid levels (µg/L):Group I:7.33±3.46, Group II:10.26±2.71; vitamin D levels (ng/ml) Group I:10.09±4.56, Group II:19.81±8.96. In the homocysteine levels; a statistically significant increase was found in the group with osteoarthritis (Group I, p<0.05). As shown in Table 1, in folic acid, vitamin B12, vitamin D levels; a statistically significant decrease was found in the group with osteoarthritis (Group I, p<0.05).

Table 1. Demographic and biochemical results of the study groups

	Group I (n=30)	Group II (n=30)	P value
Homocysteine (µmol/L)	18.04±8.44	11.19±4.03	0.005
Folik Asid (µg/L)	7.33±3.46	10.26±2.71	0.003
Vitamin B12 (ng/L)	324.50±95.87	416.11±90.76	0.002
Vitamin D	10.09±4.56	19.81±8.96	0.000
Age (Years)	49.60±4.05	48.30±3.10	0.210

5. DISCUSSION

OA is the most common musculoskeletal disease. It reduces the quality of life and body functions. Clinically, joint pain, tenderness, stiffness, limitation of movement, sometimes effusion, inflammation, and redness are observed [2]. The most affected joints are the knee and hip joints. The pain experience in OA causes limitation of activity, which leads to the emergence of chronic diseases such as coronary heart disease and diabetes [21]. Although the cause of OA cannot be determined exactly, trauma, obesity, genetic, biological and environmental effects, are suggested as possible factors [22]. Considering the studies conducted all over the world, OA occurs in 18% in women and 9.6% in men over the age of 60 [23]. Homocysteine is an amino acid consisting of methionine, which is excreted by conversion to cystathione or methionine in the presence of vitamin B6 and B12 [11]. Homocysteine levels have been shown to increase in vitamin B12 and folic acid deficiency [12]. Homocysteine affects many systems such as cardiovascular, cerebral, vascular, and renal tissues [13 and 14]. Homocysteine is linked to proteins via the lysine amino acid (N-homocysteine protein, N-homocysteinelation) or via disulfide bond with the cysteine amino acid (S-homocysteine protein, S-homocysteinelation) [24]. Histone proteins are proteins that ensure proper folding of DNA and chromosome formation. Histone proteins are rich in lysine and arginine. Homocysteine inhibits acetylation by binding to the lysine amino acid of histone proteins by N-homocysteinelation, thus inhibiting protein synthesis [15]. It has been shown that homocysteine levels increase in patients with OA, and homocysteine causes loss of cartilage chondrocytes and joint degeneration [15]. On the other hand, it is known that the adenosine molecule formed by the 5-nucleotidase enzyme is cytotoxic for many cells including chondrocytes and triggers chondrocyte apoptosis [25]. It has been shown that 5 'nucleotidase enzyme activity increases in joints with OA [26]. In our study, homocysteine levels were found to be high in the group with OA, consistent with the studies. We believe that homocysteine, by converting to homocysteine-thiolactan, also increases the formation of free radicals and its effects, while on the other hand, it damages the joint tissue by providing more adenosine

synthesis, thus contributing to the development of OA. Vitamin D is a steroid molecule that regulates the body's Ca and P balance, and in its deficiency, diseases such as rickets, osteomalacia, hashimoto, cancer, autoimmune diseases, heart diseases, reactive arthritis, and diabetes are seen [19 and 20]. It has been shown that vitamin D increases the phagocytosis and antimicrobial activity of macrophages, monocytes and natural killer cells in the immune system, and also increases anti-inflammatory cytokines such as IL-4, IL-5, and decreases the synthesis of pro-inflammatory cytokines such as IL-2 and IL-3 [27]. In a study, it has been shown that patients with OA have vitamin D deficiency and vitamin D deficiency causes pain, and pain decreases with vitamin D supplements [28 and 29]. In our study, vitamin D levels were found to be low in the group with OA, which was consistent with the studies. We think that in vitamin D deficiency, calcium levels decrease, the structures of tissues such as cartilage and bone deteriorate, and anti-inflammatory cytokines decrease and proinflammatory cytokines increase, and all these reasons cause OA to occur.

As a result, we think that folic acid, vitamin B12 and low vitamin D levels that contribute to the development of OA should be followed up and added to the diet in case of deficiency in patients with OA or joint diseases that reduce the quality of life, in order to prevent the disease and to stop the progression of the disease.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

FINANCIAL DISCLOSURE

The authors declare that this study has received no financial support.

ETHICAL COMMITTEE APPROVAL

Study Preliminary Permit Certificate was obtained from Necip Fazıl City Hospital on 04.01.2021. Verbal and written informed consent were obtained from the participants.

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