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The relationship between smoking dependence, exposure to cigarette smoke, carboxyhemoglobin and perioperative complications in patients who underwent laparoscopic cholecystectomy under general anesthesia

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ABSTRACT

Objectives: The aim of this study; to determine the effects of preoperative smoking dependence and noninvasively measured carboxyhemoglobin (COHb) levels on perioperative complications in patients who underwent elective laparoscopic cholecystectomy.

Methods: Ninety patients (Group I: smoker, Group II: non-smoker, and Group III: passive smoker) who underwent laparoscopic cholecystectomy under general anesthesia were studied. The level of dependence of smokers was evaluated with the Fagerstrom Test for Nicotine Dependence (FNBT). Preoperative COHb level was determined with a pulse CO-oximeter by placing a sensor on the fingertip. Respiratory complications in the perioperative and recovery room and Modified Aldrete Score (MAS) in the recovery room were recorded as 5^{th}, 10^{th} and 15^{th} min.

Results: Female gender was significantly higher in Groups II and III. Significant increases were noted in Group I in terms of increased perioperative secretion and incidence of bronchospasm. In the recovery room, the increase in MAS 5^{th} min in Group I and MAS 10^{th} min and 15^{th} min in Group III was significantly lower. In Group I, positive correlations between the COHb level and the number of cigarettes smoked and the FNBT level, and a negative correlation between MAS and the number of hours past after the last cigarette smoked were determined. In Group II, the COHb level correlated positively with the number of cigarette smokers at home and negatively with MAS. All these correlations were statistically significant.

Conclusions: It was demonstrated that cigarette smoking increased the incidence of perioperative respiratory complications under general anesthesia. Preoperative COHb level estimated by the pulse CO-oximeter can be used as an indicant of the potential risk of perioperative repiratory complications.

Keywords: Smoking, carboxyhaemoglobin, noninvasive pulse CO-oximetry, perioperative respiratory complications, laparoscopic cholecystectomy

Smoking, which threatens health, is a preventable cause of perioperative respiratory complications, wound infection, myocardial infarction, stroke and mortality [1, 2]. It has been reported that there may be increased reactivity in the respiratory system, such as narrowing of the small airways, insufficient clearance

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of pulmonary secretion, and increased mucus secretion in patients who smoke /exposed to cigarette smoke and are to be anesthetized [3]. Lung function may be affected by stimulation of the intra-abdominal organs during laparoscopic cholecystectomy and gallbladder traction, and this may be exacerbated in the lung exposed to cigarette smoke [4].

Clinical studies on smoking have mostly focused on the postoperative period, and complications during the operation and in the recovery room have been neglected [5-8].

In many studies cigarette smoking have relied on self-reporting [9, 10]. Carbon monoxide (CO) is found in tobacco smoke as an exogenous source and is absorbed from the lung to form COHb. Measurable COHb levels can be used to investigate inhalation in passive smokers as well as the accuracy of direct self-reporting. There is a weak but statistically significant relationship between the COHb level and self reported smoking [11]. COHb levels are typically less than 2% in non-smokers and 5-9% in smokers [12]. In this way, the relationship between COHb change and perioperative complications can be revealed in smokers, non-smokers and passive smokers. COHb level that can be measured with a Pulse CO-o0ximeter; It is a simple, non-invasive and rapid method to help confirm the non-smoking interval. In addition, there are publications stating that there is a high positive correlation between COHb pulse and COHb blood test [13, 14].

In this study we determined the effect of preoperative cigarette smoking dependence and the noninvasively measured COHb level on perioperative respiratory complications seen in patients undergoing elective laparoscopic cholecystectomy under general anesthesia.

METHODS

This study was carried out in University of Health Sciences Bursa Yuksek Ihtisas Training and Research Hospital between January 2020 and July 2020, in accordance with the principles of the Declaration of Helsinki, after informed consent of the patients and the approval of the local Ethics Committee (2011-KAEK-25 2019/12-22).

In this prospective and single-blind study, elective laparoscopic cholecystectomy operation was planned, patients aged 18-70 years, with American Society of Anesthesiologists physical condition classification (ASA) I-II-III, smokers, non-smokers and passive smokers (who had not previously used tobacco products but exposed to tobacco smoke at home and/or place of work) were included. Patients with a history of allergy to drugs to be used, known psychiatric disorders, pregnant women, those who were breastfeeding, those who had a respiratory system infection in the last one month, those with drug and alcohol addiction, those with difficult intubation prediction, and those with a body mass index of ≥ 30 kg were excluded from the study.

The patients included in the study were grouped as smokers (Group I, n = 30), non-smokers (Group II, n = 30) and passive smokers (Group III, n = 30). Demographic characteristics of the patients and smoking habits of smokers were learned on the day of the operation (self-reporting). Whether smokers smoked in the last 12 hours and how many cigarettes they smoked, and the number of smokers in the exposed areas (home, workplace, etc.) in passive smokers were questioned and recorded. Nicotine dependence was assessed on the day of surgery by the FTND. Before induction of anesthesia, the COHb level was determined by placing a fingertip sensor with a pulse CO-Oximeter (Rad-57 Masimo Corporation, Irvine, CA).

Anesthesia was administered by an anesthesiologist who did not know the COHb value and FTND level of the patients and who was blind to the study. Routine monitoring was applied to all patients. After the vascular access was established, intravenous (IV) 0.01-0.02 mg/kg midazolam (Zolamid®, Defarma Ankara, Turkey) was given for premedication. For anesthesia induction, 2mg/kg propofol (Pofol®, İlsan-İltaş Kocaeli, Turkey), 0.6mg/kg rocuronium (Jecron® Tüm Ekip İlaç AS. Istanbul, Turkey) and 1-2mcg/kg fentanyl (Talinat®, Vem, Istanbul, Turkey) was applied. In the maintenance of anesthesia, inhalation anesthetic sevoflurane (Sevorane®, Abbvie, Istanbul, Turkey) was used with a mixture of O_2 + air, with a MAC 1.0. Near the end of the surgery, 10 mg metoclopramide HCl (Metpamid®, Sifar İlaç AŞ, Istanbul, Turkey) and 2g paracetamol (Parol®, Atabay, Istanbul, Turkey) IV were administered for postoperative pain. Following spontaneous respiration, 100% O_2 was given and 0.03-0.05 mg/kg neostigmine (Neostigmine®, Adeka, İstanbul, Türkiye) and 0.01 mg/kg atropine (Atropin sülfat®, Osel, İstanbul, Türkiye) were given i.v. for reversal of neuormuscular blockage, followed with extubation under clinical observation.

Primary Outcomes

All patients were followed up routinely. Perioperative peripheral oxygen saturation (SpO_2), hypoxia, apnea, laryngospasm, bronchospasm, use of bronchodilator therapy, increased secretion, nausea, vomiting; In the recovery room, hypoxia, apnea, bronchospasm, use of bronchodilator therapy, increased secretion, nausea and vomiting were recorded. $SpO_2 < 95$ for more than one minute was considered as hypoxia, breath-holding for more than 15 seconds apnea, and the need to remove secretions with an aspirator were considered as increased secretion.

Secondary Outcomes

The duration of general anesthesia and operation from induction to extubation, and the length of stay in the recovery room for recovery after extubation were recorded. MAS was evaluated at the 5^{th}, 10^{th} and 15^{th} minutes after admission to the recovery room. The MAS score was recorded upon completion of the postoperative recovery.

Statistical Analysis

SPSS 21.0 for Windows program (Statistical Package for the Social Sciences, NY, USA) was used for statistical analysis. The Shapiro wilk test was used to determine whether the variables were normally distributed. Continuous variables were defined as mean ± standard deviation, and categorical data were expressed as n (%). Pearson chi-square test was used to detect differences between groups on the basis of categorical variables. The Indipendent Samples T test was used to compare the mean values of age, anesthesia time, surgery time, recovery time, COHb level, Aldarete 5^{th}, 10^{th} and 15^{th} minutes between the groups. The Mann-Whitney U test was used to compare the difference between the 5^{th} minute MAS scores and the 15^{th} minute and the 5^{th} minute MAS scores and the 10^{th} minute and 5^{th} minute MAS scores. The Spearman rho test was used to determine the correlations between the COHb level and the FTND result, the number of cigerettes smoked before the operation, the time of the last cigarette smoked and the MAS score in Group I, MAS score and the number of cigarette smokers present in the area of exposure in Group III. The p values of < 0.05 and < 0.01were accepted to express statistical significance.

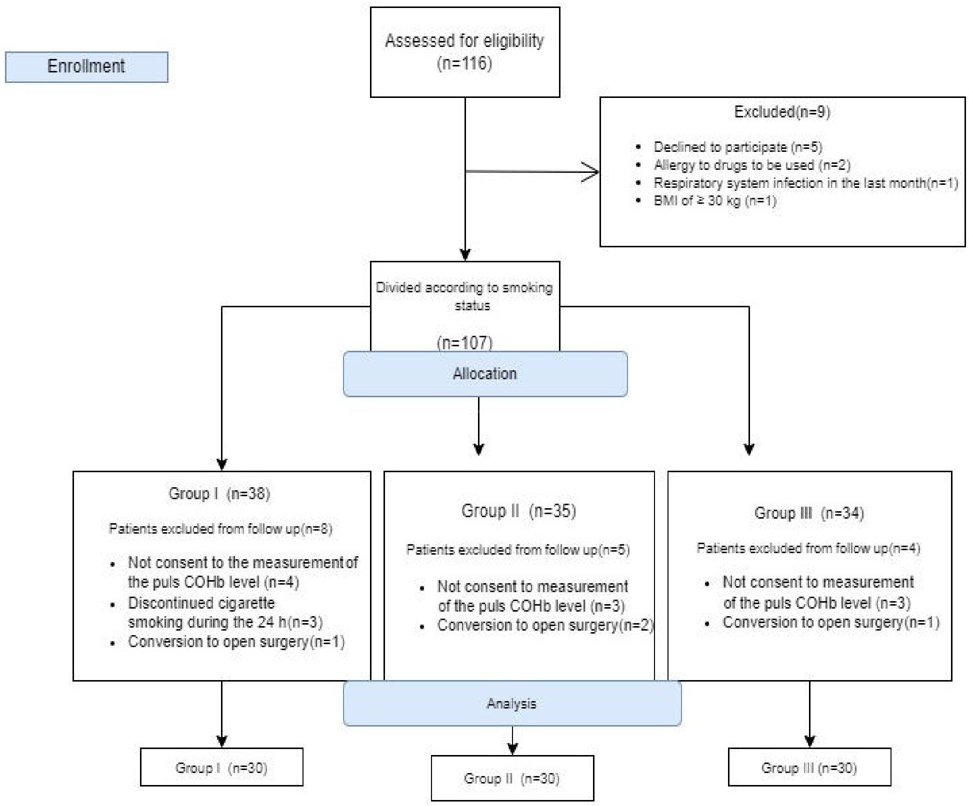

Fig. 1. Flow chart.

RESULTS

Data obtained from 90 patients out of 116 patients who underwent laparoscopic cholecystectomy were included in the study analysis. A total of 9 patients, 5 who did not want to participate in the study, 2 with a history of allergy, 1 with a respiratory tract infection, and 1 with a BMI > 30, were not accepted into the study because they did not meet the criteria. 4 patients in Group I, 3 patients in Group II and 3 patients in Group III who did not approve the measurement of COHb level with Pulse CO-oximeter; 3 patients in Group I who quit smoking 24 hours before surgery; 1 patient in Group I, 2 patients in Group II and 1 patient in Group III who underwent open cholecystectomy were excluded from the study (Fig. 1).

In demographic data of the patients, there was no difference between the groups in terms of age, ASA, comorbidities, duration of anesthesia, operation time, and time spent in the recovery room. Female gender was significantly higher in Groups II and III ($p < 0.001$, Table 1 and 2).

The mean FNBT values were determined as of low dependence (3.67). Preoperative COHb pulse level was found to be statistically significantly higher in Group I compared to Groups II and III (3.23 ± 1.43, 0.63 ± 0.81, and 2.27 ± 1.05; $p < 0.001$, respectively). Comparing the MAS at the 5th, 10th and 15th minutes; The increase in the change in MAS (10-5th min) and MAS (15-5th min) was found to be significantly lower in Group III at MAS 5th min Group I ($p = 0.041$, $p = 0.002$, and $p = 0.005$, respectively) (Table 1).

Table 1. Demographic data

	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	*p* value
Age (years), (mean ± SD)	50.10 ± 10.32	49.53 ± 16.04	47.27 ± 12.17	0.625
Gender, n (%)				**< 0.001**
Female	13 (43.3)	26 (86.7)	27 (90.0)	
Male	17 (56.7)	4 (13.3)	3 (10.0)	
ASA, n (%)				0.158
I	2 (6.7)	8 (26.7)	8 (26.79	
II	26 (86.7)	21 (70)	22 (73.3)	
III	2 (6.7)	1 (3.3)	0 (0.0)	
Comorbidities, n (%)				0.731
Yes	16 (53.3)	15 (50.0)	18 (60,0)	
No	14 (46.7)	15 (50.0)	12 (40.0)	
COHb level (%), (mean ± SD)	3.23 ± 1.43	0.63 ± .81	2.27 ± 1.05	**< 0.001** [b]
Duration of anesthesia (min), (mean ± SD)	63.33 ± 18.16	63.67 ± 21.73	58.60 ± 8.95	0.943 [a]
Duration of surgery (min), (mean ± SD)	52.0 ± 14.54	51.50 ± 21.78	48.33 ± 8.13	0.710 [a]
Time required for recovery (min), (mean ± SD)	28.20 ± 6.36	27.13 ± 6.08	27.0 ± 3.85	0.822 [a]
MAS (5th min), (mean ± SD)	7.20 ± .81	7.23 ± 1.01	7.73 ± .64	**0.041** [a]
MAS (10-5th min), (mean ± SD)	1.10 ± .31	1.43 ± .73	0.97 ± .32	**0.002** [a]
MAS (15-5th min), (mean ± SD)	2.43 ± .73	2.40 ± .86	1.93 ± .37	**0.005** [a]

Data are presented as mean ± standard deviation or n (%). ASA = American Society of Anesthesiologists score, MAS = The Modified Aldrete Score, COHb = Carboxyhemoglobin level in the pulse CO-oximeter, 10-5th = difference score of MAS measurement between 10th and 5th minutes; 15-5th = difference score of MAS measurement between 15th and 5th minutes.

[a] Mann-Whitney U test, [b] Independent samples t-test.

Table 2. Distribution of comorbidities by groups

	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	*p* value
HT	8 (26.7)	6 (20.0)	14 (46.7)	0.067
DM	6 (20.0)	5 (16.7)	7 (23.3)	0.812
Thyroid diseases	3 (10.0)	3 (10.0)	3 (10.0)	1.00
Heart diseases	3 (10.0)	4 (13.3)	2 (6.7)	0.690
Obesity	1 (3.3)	2 (6.7)	1 (3.3)	0.770
Asthma	1 (3.3)	1 (3.3)	2 (6.7)	0.770
COPD	0 (0.0)	0 (0.0)	1 (3.3)	0.364
Kidney diseases	0 (0.0)	1 (3.3)	1 (3.3)	0.600

Data are presented as n (%). HT = Hypertension, DM = Diabetes Mellitus, COPD = Chronic Obtructive Pulmonary Disease. Pearson chi-square test

Table 3. Comparison of the incidence of perioperative complications between groups

Recorded complications	Stages of the surgery	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	*p* value
Nausea					
	Perioperative	6(20,0)	1 (3.3)	4 (13.3)	0.140
	Recovery room	1 (3.3)	0 (00.0)	4 (13.3)	0.064
Vomiting					
	Perioperative	1 (3.3)	0 (00.0)	0 (00.0)	0.364
	Recovery room	0 (00.0)	0 (00.0)	0 (00.0)	-
Increased secretion					
	Perioperative	14(46.7)	2 (6.7)	8 (26.7)	**0.002**
	Recovery room	0 (00.0)	0 (00.0)	0 (00.0)	
Apnea					
	Perioperative	3(10.0)	0(00.0)	1(3.3)	0.160
	Recovery room	4(13.3)	0(00.0)	2(6.7)	0.117
Laryngospasm					
	Perioperative	4 (13.3)	0 (00.0)	0 (00.0)	**0.015**
	Recovery room	0 (00.0)	0 (00.0)	0 (00.0)	**-**
Bronchospasm					
	Perioperative	0 (00.0)	1 (3.3)	0 (00.0)	0.364
	Recovery room	0 (00.0)	0 (00.0)	0 (00.0)	-
Need for bronchodilators					
	Perioperative	4 (13.3)	1 (3.3)	3 (10.0)	0.383
	Recovery room	0 (00.0)	0 (00.0)	0 (00.0)	
SpO_2 < 95%					
	Perioperative	4 (13.3)	2 (6.7)	2 (6.7)	0.578
	Recovery room	3 (10.0)	0 (00.0)	1 (3.3)	0.160

Data are presented as n (%). Pearson chi-square test

There was no statistical difference between the groups in terms of the incidence of hypoxia, apnea, bronchospasm, bronchodilator therapy, nausea and vomiting in the perioperative and recovery room; however, perioperative laryngospasm and increased secretion were significantly higher in Group I compared to the others ($p = 0.015$ and $p = 0.002$, respectively) (Table 3).

In Group I, there was a positive correlation between COHb pulse level and how many cigarettes smoked and FNBT ($p < 0.05$ and $p < 0.001$, respectively), and a negative correlation between how many hours ago he smoked and MAS ($p < 0.05$); In Group III, there was a positive correlation between the COHb pulse level and the number of people smoking at home, and a negative correlation between the 5*th* and 10*th* minutes of MAS ($p < 0.001$ and $p < 0.05$, respectively) (Table 4). The results were statistically significant.

DISCUSSION

The relationship between preoperative COHb pulse levels and the effects of smoking and/or passive smoking on perioperative respiratory complications was the focus of this study. In our study, the incidence of perioperative laryngospasm and increased secretion was significantly higher in Group I patients. When the recovery room first 15 min MAS recovery was compared; the increase in the change in MAS 5th min Group I, MAS 10th min and 15th min measurement was significantly lower in Group III.

It has been reported that especially the pulmonary mechanics are affected by abdominal organ stimulation and bladder traction during laparoscopic cholecystectomy surgery [4]. In cigarette smoking patients undergoing general anesthesia, hyperactivy in the respiratory system, decreased clearance of pulmonary secretion, increased mucus secretion, coughing and apnea incidences are increased [3, 9, 10]. The respiratory complications of laryngospam and increased secretion observed in our investigation are in agreement with the literature.

Most of the studies evaluating perioperative complications of passive smoking have been performed in children, reporting significantly increased perioperative complication incidences and longer post-anesthesia care unit (PACU) stay [15, 16]. In less number of studies made on adults, Tütüncü *et al*. [17] had only noted significantly increased coughing and excessive secretion in passive smokers. Şimşek *et al*. [18] reported increased incidences of peri- and post-operative respiratory complications due to passive exposure to cigarette smoke that significantly correlated with longer PACU stay and increased risk of coughing, desaturation and hypersecretion in relation to the duration of the exposure. In our study, incidences of secretion increase were 46.7% in smokers, 6.7% in non-smokers and 26.7% among the passive smokers, but the patients of the three groups had similar durations of stay in the recovery room.

Anesthesia and surgery duration and especially upper abdominal surgical procedures are important parameters affecting the risk of respiratory complications [19]. It has been reported that laparoscopic cholecys-

Table 4. In Group I correlation between COHb with how hours ago last cigarette smoked, how many cigarettes smoked, FNBT and MAS. In Group III correlation between COHb with MAS and the number of people smoking at home

	How hours ago last cigarette smoked	how many cigarettes smoked	FNBT	MAS (5th min)	MAS (10-5th min.)	MAS (15-5th min.)	number of people smoking at home
Group I							
COHb level	**- 0.387***	**0.429***	**0.466****	**- 0.437***	**- 0.412***	**- 0.402***	-
Group III							
COHb level	-	-	-	**0.470****	**- 0.395***	- 0.353	**0.629****

COHb = Carboxyhemoglobin, FNBT = Fagerstrom Test for Nicotine Dependence, MAS = Modified Aldrete Score
Spearman's rho *$p < 0.05$, **$p < 0.001$

tectomy durations changed between 30 and 166 minutes and the duration of anesthesia, on a basis of group comparisons, changed between 3.5-4.5 hours [3, 10, 19-21]. Özgünay *et al*. [22] reported that in laparoscopic cholecysctomy the duration of anesthesia was significantly increased among cigarette smokers. In our study; although there was no difference between the groups in terms of duration of operation, duration of anesthesia and waking up for recovery; while the operation time was consistent with the literature, the anesthesia time was shorter. This advantageous situation may have resulted in fewer perioperative complications in smokers and/or passive smokers in our study.

Although smokers are known to have elevated blood COHb levels due to CO inhalation in cigarette smoke, limited data are available on COHb levels in passive smokers exposed to cigarette smoke. Reddy *et al*. [23] in their study in the outpatient clinic; they found COHb pulse levels to be 5.9%+/-4.45% in smokers, 1.95%+/-1.55% in non-smokers, and 1.94%+/-1.55% in passive smokers. In our study, the COHb pulse level was 3.23%+/-1.43% in smokers, 0.63%+/-0.81% in non-smokers, and 2.27%+/-1.05% in passive smokers. Our result was higher than the literature value in passive smokers, but COHb pulse value was significant in Group I in group comparison. COHb pulse measurement has been used for screening purposes in pediatric patients with preoperative passive smoking exposure in a few studies in the literature [24, 25]. However, perioperative or postoperative respiratory complications have not been investigated. Our study is valuable because it includes the perioperative and recovery room under anesthesia.

FTND score has been used to assess the level of nicotine dependence [5, 21], The mean level of FTND determined in our study was 3.67, indicating low level nicotine dependence. Lee *et al*. [21] reported a mean value of 4.3. Moller *et al*. [5] have observed in most patients a medium level of dependence. However, FTND has not been investigated in most studies involving the effects of smoking on perioperative complications [5, 9, 20, 26].

Only one study reported a relationship between MAS scores and the time required for recovery in adults regarding the effect of smoking on perioperative respiratory complications [22]. Ozgünay *et al.* [22] in smokers; MAS 5.10. they stated that the changes in the 15th min were lower and the time required for recovery was also significantly longer. In our study, our results were similar in terms of MAS changes. However, we did not find any difference between the groups in terms of time to awakening.

Yee *et al*. [24] observed in children exposed to parental cigarette smoking that the COHb levels were higher in comparision to the control children. In our study, the COHb level was directly related to the number of cigarettes smoked and the nicotine dependence level and to the exposure of the passive smokers to the number of the smokers in their dwellings; and high levels affected recovery adversely.

Limitations

Low FNDT scores, and not having data on coughing, headache, throat ache and long term respiratory complications are the limitations of our study.

CONCLUSION

The incidence of perioperative respiratory system complications increases in the first minutes in the recovery room. Specifically, it has been shown that the level of COHb is directly related to the amount of cigarettes smoked and the number of people who smoke, and to affect recovery. It should be remembered that detailed interrogation of the preoperative smoking status of the patients, measuring the COHb value with puls CO-Oximeter a simple and non-invasive technique, especially in passive smokers, will be beneficial for the anesthetists in terms of possible perioperative respiratory complications. More comprehensive studies are needed on this subject. More comprehensive studies are needed on this subject.

Authors' Contribution

Study Conception: ŞE, ŞEÖ; Study Design: ŞE; Supervision: ŞE, ŞEÖ; Funding: ŞE; Materials: ŞE; Data Collection and/or Processing: ŞE, ŞEÖ; Statistical Analysis and/or Data Interpretation: ŞE, ŞEÖ; Literature Review: ŞE, ŞEÖ; Manuscript Preparation: ŞE, ŞEÖ and Critical Review: ŞE, ŞEÖ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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