Effects of Opium Addiction and Cigarette Smoking on Hematological Parameters

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Abstract

Original Article

Background: The aim of the present study was to investigate the effects of opium addiction and cigarette smoking on the complete blood count (CBC).

Methods: Eighty-six male subjects, including 31 opium-addicted cigarette smokers (OACS), 19 opium-addicted non-cigarette smokers (OANCS), 17 non-opium-addicted cigarette smokers (NOACS), and 19 non-opium-addicted non-cigarette smokers (NOANCS) participated in this study. The CBC test was measured in all individuals.

Findings: The OACS had significantly higher white blood cell (WBC), lymphocyte, and red blood cell (RBC) count but lower in mean corpuscular volume (MCV) compared to NOANCS. The OANCS had significantly higher lymphocyte in comparison with NOACS. Our results demonstrated that the number of WBC, lymphocytes, and RBC were significantly higher, while, MCV was lower in OANCS subjects when compared to NOACS. The OACS had significantly higher level of lymphocyte in comparison with NOACS. The mean number of lymphocyte in OANCS was found significantly higher than NOACS. The smokers were shown to have significantly higher levels of WBC compared to NOANCS.

Conclusion: Our results showed that opium-addiction, especially when associated with cigarette smoking, has intensive effects on hematological factors and these alteration might leads to greater risk for developing atherosclerosis, cardiovascular diseases, and imbalance in immune system.

Keywords: Cigarette smoking; Addiction; Opium; Complete blood count

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Introduction

Cigarette smoking is considered as a major leading causes of health problem in word over.1 There are more than 4000 chemicals found in cigarette smoke, and a cigarette smoker is exposed to a number of harmful substances including nicotine, free radicals, carbon monoxide and other gaseous products.1,2 In a number of studies, it has been found that smokers have higher white blood cell (WBC) counts than nonsmokers.² Tarazi et al. have reported increased red blood cell (RBC), several RBC-related parameters, and hemoglobin (Hb) concentration in cigarette smokers.3 It is suggested that increase in hemoglobin level in blood of smokers may be a compensatory mechanism. However, all smokers does not show increase in hemoglobin level and this relates to smoker situation.⁴ The effects of opium addiction on the number of RBC, the levels of some RBC-related parameters, and total and differential of peripheral WBC have shown counts elsewhere.⁵ Opium can be used to synthesize some medications such as morphine, codeine, noscapine, and papaverine.6 There are many reports regarding the effects of opium derivatives on biological systems. The presence of specific morphine receptors on lymphocytes has been reported. It is suggested that opioid receptor acts in both autocrine and paracrine fashion.7 Although it is proposed that morphine affects some immune cells indirectly, but morphine can macrophages also directly affect and polymorphonuclear (PMN) leukocytes functions, and regulate expression of some type of T-cell surface markers.8 Some researcher reported that the endogenous opioid peptides, including β -endorphin and the dynorphin peptides, and exogenous alkaloids such as morphine plays an important role in the lymphocytes and other immune cells function.9 Although heroin induced increase in circulating leukocytes, but it decrease the number of splenic leukocytes by induction of leukocytes apoptosis.¹⁰ Ke et al.,¹¹ have reported that noscapine plays key antitumor activity without the interference of immune responses. Moreover noscapine down-regulates proliferation cell lines¹² and it induces of leukemia chromosomal loss, hyperdiploidy and hypodiploid in human lymphocytes in in vivo

conditions.¹³ Obviously these effects can directly influence the lymphocytes function, and thereby affecting cytokine networks and therefore, impact immune cells differentiation and proliferation. Papaverine, other opium alkaloids, induced apoptosis in different cell lines.¹⁴ Patently, these events can influx metabolism and function of lymphocytes. It is also reported that papaverine, by stimulation of production of transforming growth factor- β (TGF- β) which has potent immunosuppression effects, inserts a highly fatal constrictive bronchiolitis.15 syndrome as However, opium contains more than 20 alkaloids, and more than 70 ingredients.¹⁶ Thus, its effect is clearly different from morphine, noscapine, codeine and papaverine. Our previous studies on the effects of opium on apoptosis,17 immune functions,¹⁸ hematological parameters⁵ and also the influence of cigarette smoking on cell functions, led us to evaluate the biological effects of opium and cigarette on peripheral blood cells of opium-addicted, cigarette smokers opiumaddicted, and cigarette smokers non-opiumaddicted individuals.

Methods

Subject selection

Subjects participated in this study consisted of 86 males, including 31 opium-addicted cigarette smokers (OACS), 19 opium-addicted noncigarette smokers (OANCS), 17 non-opiumaddicted cigarette smokers (NOACS), and 19 nonopium-addicted non-cigarette smokers (NOANCS) individuals. All subjects were aged from 19 to 56 years. Exclusion criteria included any kind of disease (either symptoms or diagnosis), consumption of any medication that might interfere with assessed parameters, consumption of other component of opium (heroin, morphine etc.) and withdrawal drugs such as methadone or other withdrawal regimes. Opium addicted subjects had been using opium at least 500 mg per day for more than 1 year prior to sample preparation. The method that was used by all subjects was smoking opium using opium pipe (Bafur). A cigarette smoker was defined as one who smoked at least 5 cigarettes per day for more than 1 year but did not use any other kind of tobacco. Each individual in the control group were selected with similar attributes regarding age, residency and BMI with no addiction to opioids or cigarette in case group. This study was approved by the ethical committee of the Rafsanjan University of Medical Sciences, Iran, and written informed consent was filled out by the participants, prior to sample collection.

Blood cells counting

Peripheral blood samples were collected from the subjects at 8-9 A.M., before consuming opium or cigarette and CBC was tested immediately. The total cell count was made using a hematology analyzer (Sysmex KX-21N) and Gimsa's stain and a light microscope were used for differential WBC counts (lymphocytes, monocytes, neutrophils, basophils and eosinophils per 100 WBC), which were based on morphological characteristics of the cells.

Results are presented in mean \pm standard errors (SE). To compare the mean values between groups, the one-way analysis of variance (ANOVA) was used. Statistical analysis was performed by SPSS software (version 18, SPSS Inc., Chicago, IL, USA) for Windows. P < 0.05 was considered statistically significant.

Results

Mean number of total WBC were significantly higher in OACS, OANCS and NOACS than NOANCS (P < 0.001).

The mean percent of lymphocytes in OACS and OANCS was significantly higher when compared with NOACS and NOANCS (P < 0.001). The numbers of RBC were also significantly increased in OACS and OANCS when compared with NOANCS (P = 0.018).

MCV was also significantly different among the enrolled groups (P = 0.001). MCV was significantly decreased in OACS and OANCS when compared with NOANCS.

The mean of neutrophils count (P = 0.168), Hct (P = 0.925), Hb (P = 0.913), and platelets count (P = 0.084) was not different among the studied groups. The results are shown in details in table 1.

Discussion

Our result revealed the profound effects of opium and cigarette on the total and differential counts of peripheral WBC, lymphocytes, RBC, and MCV (as a RBC-related parameter).

We have showed that the mean number of total WBC in opium and cigarette consumers was significantly higher than NOANCS groups. The precise mechanisms by which opium and cigarette could strongly elevate WBC counts and also can alter the differential WBC counts have yet to be identified. It may be hypothesized that opium and cigarette lead to liberation of WBC from bone morrow in indirect format by induction of pro-inflammatory cytokines which have been reported by our previous investigations.19 Additionally, the number of peripheral WBCs was influenced by the modification of the expression of adhesion molecules on the endothelial cells and the differentiation of leukocytes from bone marrow stem cells.20

 Table 1. Comparison of hematological indices between participants groups with and without opium addiction or smoking

Variable	OACS	OANCS	NOACS	NOANCS	Р
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	
WBC (Number/dl)*	7077 ± 261	7595 ± 443	7247 ± 551	5326 ± 152	< 0.001
Lymphocytes (Percent)**	45.70 ± 1.74	43.90 ± 1.68	35.90 ± 2.63	35.40 ± 1.09	< 0.001
Neutrophils (Percent)	49.00 ± 1.15	48.60 ± 2.09	56.60 ± 5.37	52.00 ± 1.01	0.168
RBC (Million/dl) [†]	5.70 ± 0.12	5.70 ± 0.16	5.40 ± 0.12	5.20 ± 0.12	0.018
$MCV^{\dagger\dagger}$	80.30 ± 1.41	78.70 ± 1.47	83.20 ± 1.67	87.00 ± 0.93	0.001
Hb	14.90 ± 0.24	14.80 ± 0.40	14.60 ± 0.31	14.80 ± 0.24	0.913
Hct	45.50 ± 0.76	44.90 ± 1.17	45.00 ± 0.74	44.90 ± 0.71	0.925
Plt	267.00 ± 17.90	240.00 ± 16.90	235.00 ± 12.30	211.00 ± 9.39	0.084

^{*}The post hoc (Tukey) test showed that the number of total WBC and lymphocytes were significantly increased in OACS, and NOACS in comparison to NOANCS, ^{**}The post hoc (Tukey) test showed that the percent of lymphocytes in OACS and OANCS were significantly increased when compared with NOACS and NOANCS, [†]The post hoc (Tukey) test revealed that the number of RBC were significantly increased in OACS and OANCS when compared with NOANCS, ^{††}The post hoc (Tukey) test demonstrated that MCV were significantly decreased in OACS and OANCS when compared with NOANCS.

WBC: White blood cell; RBC: Red blood cell; MCV: Mean corpuscular volume; Hb: Hemoglobin; Hct: Hematocrit; Plt: Platelet; OACS: Opium-addicted cigarette smokers; OANCS: Opium-addicted non-cigarette smokers; NOACS: Non-opium-addicted non-cigarette smokers; SE: Standard error

Moreover, some opium side effects on the number of WBCs may be mediated through infection.5 The release of catecholamines which are important factor to elevate the leukocyte count are induced by morphine.²¹ Opium components change some multi-functional cytokines, such as Interleukin-6 (IL-6), which induces inflammatory process that leads to elevations in the peripheral blood leukocyte count.22 Consistent with our results, Asakura et al.23 showed that the risk of acute infection is higher in heroin addicted patients. As we know clearly today, the hematopoiesis is affected by a complex network of cytokines.²⁴ The serious effects of opium on the secretion of some cytokines such as TGF-B, IL-4, IL-5, IL-10 and IFN-y has been shown.¹⁸ Hence, the opium or some of its components interfere network and consequently with cytokine influence the production of WBC and lymphocytes. These findings indicated that the opium addiction have deep adverse effects on WBC and lymphocytes counts. Moreover, the opium or some of its derivatives may affect lymphopoiesis via interference with cytokines which are the responsible factors for differentiation of lymphocytes from bone marrow stem cells.²⁵ On the other hand cigarette smoking suppresses the immune response which may contribute to an increased risks of periodontal disease in smokers.²⁶ Our results showed significant differences in hematological parameters of subjects, as the OACS and OANCS participants had significantly higher lymphocyte compared to NOACSs. Our results demonstrated that the number of lymphocytes and WBC were significantly higher in OANCS subjects when compared to NOANCS. The cigarette smokers had significantly higher levels of WBC in comparison with NOANCS. We found that regular smokers had significantly higher WBC count compared to non-smokers. The high WBC count in male smokers in this study is consistent with other published reports.27 Vulser et al.28 observed that median total leukocyte count was 36% higher in current smokers as compared to non-smokers. Although, it is reported that inflammatory stimulation of the bronchial tract induces an increase in inflammatory markers in blood. but the mechanism the for smoking-induced increase in WBC count is not clear yet.²⁹ In addition, inducing effect of nicotine

on blood lymphocyte counts has also been suggested. While leukocytosis may simply be a marker of smoking-induced tissue damage, the high count can promote cardiovascular diseases through multiple pathologic mechanisms that mediate inflammation, plug the microvasculature, induce hypercoagulability, and promote infarct expansion.³⁰ Seinen et al. found that the greater the number of cigarettes smoked, the lower the hypoxanthine-guanine phosphoribosyltransferase (HGPRT) activity, and that HGPRT activity was higher in smokers who had started smoking later. On the other hand, it was demonstrated that HGPRT activity was inversely related to the WBC.31 In fact, several studies have shown that WBC count is an independent predictor of cardiovascular diseases and its related complications.³² The high WBC count in our male smoking subjects may also suggest that they might be at greater risk for developing atherosclerosis and cardiovascular diseases. We observed that RBC values were significantly higher in OACS in comparison to NOANCS, that is consistent with other investigations.33 It is reported that high level of RBC, WBC and hematocrit are associated with blood viscosity and clotting in the individuals.³⁴ Interestingly, our results also demonstrated that the numbers of RBCs were significantly increased in the opium and cigarette addicted individuals.

It has been established that fibrinogen levels are higher in smokers than in non-smokers, and it has been estimated that the increasing risk of cardiac disease in smokers may be associated with higher fibrinogen levels through arterial wall infiltration and its effects on blood viscosity, platelet aggregation, and fibrin formation. This elevation may lead to congenital heart disease, pulmonary fibrosis and elevated erythropoietin level and, therefore, polycythemia.⁴ Cigarette smoking developed a combined polycythemia to chronic hypoxia, leading to increased RBC production, with concomitant plasma volume reduction.35 During cigarette smoking, carbon monoxide (CO) is produced by the imperfect ignition of its material. CO displaces oxygen from hemoglobin in RBCs, which decreases the release of oxygen to tissues.³⁶ Thus, the oxygen content of blood in the presence of carbon monoxide is much lower than normal. Obviously, this event leads to polycythemia. MCV, MCH and MCHC are important RBC indices that represent average size and hemoglobin composition of the RBCs.37 We found that MCV level in OACS and OANCS groups was significantly decreased compared with NOANCS. MCV indicates the size of a RBCs and presence of red cells smaller or larger than normal size means the person has anemia. A lowered level of MCV in our study indicates that subjects might suffer from macrocytic anemia that usually caused by iron and folic acid deficiencies. Furthermore, we demonstrated that in opiumaddicted group the RBC counts was significantly increased when compared with control group. The reasons for these differences are remained to be cleared. According to the results of the present study the RBC indices are markedly decreased. It may be due to the either direct or indirect impact of opium derivatives on both bone marrow and RBC progenitor cells and theses are in parallel with the results of Chan et al.38 Further studies should be conducted in order to obtain a better understanding of the mechanisms that induce

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these alterations in peripheral blood cells of opium-addicted subjects.

Conclusion

Our findings showed that opium-addiction, especially when associated with cigarette smoking, induced serious adverse effects on hematological factors and these alterations might lead to imbalance in immune system and acute infection. On the whole, based on the findings of the present study and the results from similar research, opium may have a serious influx on the bone marrow including stem cells and progenitor cells of RBC.

Conflict of Interests

The Authors have no conflict of interest.

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اثرات اعتیاد به تریاک و مصرف سیگار بر شاخصهای خونی

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مقاله يژوهشي

چكىدە

مقدمه: هدف از انجام مطالعه حاضر، ارزیابی اثرات اعتیاد به تریاک و سیگار بر شمارش کامل سلولهای خونی (Complete blood count یا CBC) بود.

روشها: ۸۶ مرد شامل ۳۱ فرد معتاد سیگاری، ۱۹ فرد معتاد غیر سیگاری، ۱۷ فرد سیگاری غیر معتاد و ۱۹ فرد بدون اعتیاد به تریاک و سیگار در مطالعه حاضر شرکت کردند و آزمایش CBC بر روی خون تمام افراد انجام گرفت.

يافتهها: ميزان White blood cell) WBC)، لنفوسيتها و Red blood cell (RBC) در افراد معتاد سيگاري بالاتر، اما ميزان MCV (Mean corpuscular volume) در مقایسه با گروه شاهد (غیر معتاد و غیر سیگاری) کمتر بود. میزان لنفوسیتها در افراد معتاد سیگاری در مقایسه با افراد سیگاری غیر معتاد، بیشتر به دست آمد. تعداد WBC، لنفوسیتها و RBC در افراد معتاد سیگاری و افراد سیگاری غیر معتاد به طور معنیداری بالاتر، اما میزان MCV در مقایسه با افراد سیگاری غیر معتاد پایینتر مشاهده شد. افراد معتاد سیگاری میزان بالاتری از لنفوسیتها در مقایسه با افراد سیگاری غیر معتاد داشتند. میانگین تعداد لنفوسیتها در افراد معتاد سیگاری نسبت به افراد سیگاری غیر معتاد بیشتر بود. میزان WCB در افراد سیگاری نسبت به گروه شاهد (غیر معتاد و غیر سیگاری) افزایش بیشتری را نشان داد.

نتیجه گیری: نتایج مطالعه حاضر نشان داد که اعتیاد به تریاک به ویژه وقتی با مصرف سیگار همراه باشد، اثرات مخربی بر شاخصهای خونی اعمال می کند. این تغییرات می تواند منجر به افزایش خطر ابتلا به آترواسکلروز، بیماریهای قلبی- عروقی و عدم تعادل سیستم ایمنی گردد.

واژگان کلیدی: مصرف سیگار، اعتیاد، تریاک، CBC

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