Effects of Opium Addiction on Some Biochemical Factors in Diabetic Rats

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Abstract

Background: The present study was carried out aiming to investigate the effects of opium on some biochemical factors in diabetic and non-diabetic male and female rats.

Methods: This experimental study was carried out on 28 male and 28 female Wistar rats. The animals were divided into diabetic addicted (DA), diabetic non-addicted (DNA), non-diabetic addicted (NDA), and non-diabetic non-addicted (NDNA) groups of male and female. A double dose of opium was intraperitoneally administered to the addicted groups. Peripheral blood samples were collected to measure the creatinine, uric acid, cholesterol, triglycerides (TG), total protein, and albumin levels. Three-way analysis of variance (ANOVA) was used to compare the mean levels of biofactors among the study groups.

Findings: Cholesterol and total protein were significantly affected by opium and sex, but not diabetes condition, such that there was a decrease of cholesterol and total protein levels in opium-addicted rats compared to non-opium-addicted ones. However, uric acid, TG, albumin, and creatinine were not affected by opium and diabetes conditions.

Conclusion: Opium significantly decreased cholesterol and total protein levels. It could be deduced that the effects of opium on cholesterol and total protein are not sex-dependent, moreover, opium consumption may not have significant effects on biochemical factors in diabetic conditions.

Keywords: Biochemical markers; Cholesterol; Creatinine; Diabetes mellitus; Opium addiction; Total protein

Citation: Asadikaram G, Vakili S, Akbari H, Kheirmand-Parizi M, Sadeghi E, Asiabanha M, et al. Effects of Opium Addiction on Some Biochemical Factors in Diabetic Rats. Addict Health 2018; 10(2): 123-30.

Received: 11.12.2017
Accepted: 14.02.2018

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Introduction

Numerous studies have investigated the effects of opium and its derivatives on various systems of the body. Opium has been used as a recreational and pharmaceutical drug since 5000 BC. Since opium was prescribed as a drug in traditional medicine, some people consumed opium to reduce the effects of the disease, such as cardiovascular diseases (CVDs) and diabetes complications. Thus, the prevalence of opium consumption among patients with diabetes mellitus (DM) is comparatively much higher (11.2%) than among individuals without DM (2.6%).

Overall, opium addiction can cause various functional and physiological conversions in the body. Opium consumption, irrespective of the type of intake, increases the levels of hemoglobin A1C (HbA1C), C-reactive protein (CRP), lipoprotein A (LPA), apolipoprotein B (Apo B), aspartate aminotransferase (AST), alanine aminotransferase (ALT), fibrinogen, and factor VII. Furthermore, the apolipoprotein A (Apo A) and HDL-C levels decreased significantly among other opium consumers. The fasting blood sugar (FBS) level among opium addicts was significantly higher, and the blood insulin level was lower in comparison to the control group. Interestingly, the FBS level among addicts with DM was significantly lower compared to non-addict people with DM. Besides, another study on animal models indicated that the HbA1C levels did not differ between rats treated and untreated with opium.

Interestingly, it has been demonstrated that opium consumption can lead to different effects in diabetic and non-diabetic circumstances. The potassium (K) and ferrous (Fe2+) levels were increased among consumers with DM compared to those without DM. Moreover, the amount of triiodothyronine (T3), an important metabolic hormone, in addicted diabetic rats was significantly lower compared to the non-diabetic rats (Unpublished data). Furthermore, the addiction effect on patients with DM can be gender-dependent. The HbA1C level increased among addicted men with DM, while this increase was not significant among addicted women with DM.

Various studies have been carried out to assess the alterations of biochemical factors in patients with DM. Studies have revealed the decreased levels of albumin in patients with DM and CVDs compared to healthy subjects. Decreased serum levels of creatinine are considered as a risk factor for type 2 diabetes. Moreover, uric acid levels are related to metabolic disorders and mortality and morbidity of diabetes and CVDs. Previous studies on animal models have shown that cholesterol and triglycerides (TG) have significantly higher levels in diabetic animals compared to control ones.

Regarding the importance of opium addiction among patients with DM as well as various effects of its consumption in diabetic and non-diabetic cases, the present study aimed to evaluate the effects of chronic consumption of opium on some biochemical factors, such as creatinine, uric acid, cholesterol, TG, total protein, and albumin in diabetic and non-diabetic male and female rats.

Methods

Animals and drug: Twenty-eight male and 28 female Wistar rats (250-300 g) were divided into 8 groups including diabetic addicted (DA), diabetic non-addicted (DNA), non-diabetic addicted (NDA), and non-diabetic non-addicted (NDNA) in both sexes. Animals were maintained on a 12-hour light-dark cycle and free access to food and water. The present study was approved by the Ethic Committee of Rafsanjan University of Medical Sciences, Rafsanjan, Iran. All processes related to the maintenance of animals were performed based on “Guide for the care and use of laboratory animals” [National Institutes of Health (NIH) Publication, No. 85-23: 1985]. The required opium was supplied from Kerman’s Anti-Narcotics Police (Iran) as described in the previous report.

According to the official information, the origin of opium was Helmand, Afghanistan. The gas chromatography/mass spectrometry (GC/MS) test showed that the opium includes more than 30% alkaloids and the rest consisted of non-alkaloid organic and non-organic substances such as water (13%). Most opium alkaloids were morphine, codeine, thebaine, and papaverine with rates of 16.0%, 5.5%, 4.4%, and 3.2%, respectively.

Induction of diabetes: To induce diabetes, streptozocin (solved in sodium citrate buffer; pH = 4.4) was intravenously administered into the
Opium Effects on Biochemical Factors in Diabetes

Asadikaram et al.

Table 1. Mean serum levels of biochemical factors measured in opium-treated rats under diabetic conditions

| Variable | Groups | Non-diabetes (mean ± SD) | Diabetes (mean ± SD) |
|----------|--------|--------------------------|----------------------|
|          | Opium-addicted | Non-opium-addicted | Opium-addicted | Non-opium-addicted |
| Cr       | Male    | 0.69 ± 0.09              | 0.76 ± 0.10         | 0.79 ± 0.07        | 0.76 ± 0.10       |
|          | Female  | 0.73 ± 0.11              | 0.73 ± 0.13         | 0.70 ± 0.28        | 0.71 ± 0.07       |
| Cholesterol | Male    | 42.99 ± 1.43             | 48.51 ± 4.31        | 44.31 ± 4.14       | 55.11 ± 7.26      |
|          | Female  | 54.74 ± 3.05             | 54.46 ± 8.00        | 54.59 ± 6.63       | 53.56 ± 9.46      |
| TG       | Male    | 67.00 ± 10.26            | 66.14 ± 11.70       | 66.43 ± 13.13      | 91.57 ± 32.57     |
|          | Female  | 86.57 ± 22.95            | 84.57 ± 22.66       | 98.43 ± 37.42      | 78.71 ± 26.61     |
| Total protein | Male    | 5.26 ± 0.52             | 5.70 ± 0.67         | 5.47 ± 0.52        | 5.70 ± 0.67       |
|          | Female  | 6.49 ± 0.70             | 7.16 ± 0.76         | 6.56 ± 0.50        | 6.70 ± 0.42       |
| Alb      | Male    | 2.60 ± 0.16              | 2.67 ± 0.10         | 2.67 ± 0.18        | 2.67 ± 0.10       |
|          | Female  | 2.86 ± 0.20              | 2.83 ± 0.27         | 2.76 ± 0.17        | 2.80 ± 0.18       |
| U.A      | Male    | 0.60 ± 0.16              | 0.69 ± 0.11         | 0.61 ± 0.09        | 0.67 ± 0.14       |
|          | Female  | 0.76 ± 0.10              | 0.71 ± 0.15         | 0.71 ± 0.09        | 0.61 ± 0.29       |

SD: Standard deviation; Cr: Creatinine; TG: Triglycerides; Alb: Albumin; U.A: Uric acid

Results

Mean serum levels of biochemical factors measured among opium-treated rats in diabetic conditions are presented in table 1. Furthermore, the results of three-way ANOVA for measured biofactors are provided in table 2.
Cholesterol and total protein levels were significantly affected by opium (P = 0.035 and P = 0.023, respectively) and sex (P < 0.001 for both comparisons), such that overall, there was a cholesterol and total protein decrease among opium-addicted rats compared to non-opium-addicted ones. Moreover, female rats experienced higher cholesterol levels as compared to male ones. Likewise, females showed higher levels of TG compared to male rats (P = 0.035). However, opium addiction and diabetes conditions did not affect the TG levels (P > 0.050). Albumin and TG were affected by sex, but not opium addiction and diabetes, such that both albumin and TG factors were significantly higher in female rats compared to male ones (P = 0.001 and P = 0.035, respectively). It is noteworthy that uric acid and creatinine factors were not significantly affected by sex, diabetes, and opium addictions (P > 0.050). Firstly, in the present study, the interactions of the diabetes, gender, and addiction, as well as their triple interactions were included with the main effects in the models, however, none was statistically significant. Therefore, the mutual effects were omitted from the models and only the main effects were included.

### Discussion

In the present study, opium consumption demonstrated significant effects on cholesterol and total protein levels. The findings showed that opium consumption significantly reduced cholesterol and total protein levels compared to non-opium-addicted. On the other hand,

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| Parameter       | B    | SE  | t     | P    | 95% CI       |
|-----------------|------|-----|-------|------|--------------|
|                 |      |     |       |      | LB           |
|                 |      |     |       |      | UP           |
| Cholesterol     |      |     |       |      |              |
| Intercept       | 57.071 | 1.729 | 33.010 | < 0.001 | 53.602       |
| Group (Non Diabetes) | -1.718 | 1.729 | -0.994 | 0.325 | -5.187       |
| Opium (Addicted) | -3.754 | 1.729 | -2.171 | 0.035* | -7.223       |
| Gender (Male)   | -6.604 | 1.729 | -3.819 | < 0.001*** | -10.073 |
| Total protein   |      |     |       |      |              |
| Intercept       | 6.889  | 0.159 | 43.291 | < 0.001 | 6.570        |
| Group (Non Diabetes) | 0.043  | 0.159 | 0.269  | 0.789  | -0.276       |
| Opium (Addicted) | -0.371 | 0.159 | -2.334 | 0.023* | -0.691       |
| Gender (Male)   | -1.193 | 0.159 | -7.496 | < 0.001*** | -1.512       |
| U.A             |      |     |       |      |              |
| Intercept       | 0.682  | 0.041 | 16.727 | < 0.001 | 0.600        |
| Group (Non Diabetes) | 0.036  | 0.041 | 0.876  | 0.385  | -0.046       |
| Opium (Addicted) | -0.070 | 0.041 | 0     | < 0.999 | -0.082       |
| Gender (Male)   | -0.057 | 0.041 | 1.401  | 0.167  | -0.139       |
| TG              |      |     |       |      |              |
| Intercept       | 91.250 | 6.592 | 13.843 | < 0.001 | 78.022       |
| Group (Non Diabetes) | -7.714 | 6.592 | -1.170 | 0.247  | -20.942      |
| Opium (Addicted) | -0.643 | 6.592 | -0.098 | 0.923  | -13.870      |
| Gender (Male)   | -14.286 | 6.592 | -2.167 | 0.035* | -27.513      |
| Cr              |      |     |       |      |              |
| Intercept       | 0.732  | 0.035 | 20.765 | < 0.001 | 0.661        |
| Group (Non Diabetes) | -0.014 | 0.035 | -0.405 | 0.687  | -0.085       |
| Opium (Addicted) | -0.014 | 0.035 | -0.405 | 0.687  | -0.085       |
| Gender (Male)   | 0.029  | 0.035 | 0.810  | 0.421  | -0.042       |
| Alb             |      |     |       |      |              |
| Intercept       | 2.814  | 0.046 | 60.657 | < 0.001 | 2.721        |
| Group (Non Diabetes) | 0.014  | 0.046 | 0.308  | 0.759  | -0.079       |
| Opium (Addicted) | -0.021 | 0.046 | -0.462 | 0.646  | -0.115       |
| Gender (Male)   | -0.157 | 0.046 | -3.387 | 0.001** | -0.250       |

**SE**: Standard error; **CI**: Confidence interval; **LB**: Lower bound; **UP**: Upper bound; **Cr**: Creatinine; **TG**: Triglycerides; **Alb**: Albumin; **U.A**: Uric acid

*Significant at 0.050, **Significant at 0.010, and ***Significant at 0.001
Opium Effects on Biochemical Factors in Diabetes

Asadikaram et al.

cholesterol, total protein, TG, and albumin levels were significantly different in both female and male rats.

The findings of the current study were in agreement with the results of the study by Mohammadi et al. on opium addicted mice. Contrary to these results, Sadeghian et al. and Shahryari et al. reported that opium and its derivatives caused no changes in cholesterol levels. However, Bryant et al. showed that morphine, as a main opium alkaloid, increased cholesterol levels in animals. Change in cholesterol levels following opium consumption is one of the notable findings of the present study. It seems that differences in doses and types of opium may be possible reasons for the differing results obtained in previous studies.

Opium can cause changes to liver and kidney metabolism that affect the amount of cholesterol in diabetic animals. Based on the current findings and given the remarkable effects of opium on cholesterol reduction, regardless of diabetes condition, it seems that feeling a reduction in symptoms and complications of chronic diseases (such as DM) through the consumption of opium or its derivatives has psychological aspects rather than physiologic features. Occasionally, opium consumption has been reported to increase the severity of a disease; thus, consumers of narcotics should be made aware of this erroneous belief. Findings of the current study showed that opium consumption did not significantly change the measured biofactors in diabetic animals; however, some biofactors underwent significant changes in both male and female rats. In agreement with the present study, the results of a study by Karam et al. revealed that total protein levels were lower in addicted individuals compared to the non-addicted patients with DM of both men and women. In contrast, Asgary et al. showed that the chronic consumption of opium led to increase in some circulating proteins, especially those known to be risk factors for CVDs. Interestingly, the inhalation of opium (Sikh-Sang) caused more increase in blood proteins. The lack of significant changes in the some measured biofactors in the present study may be due to the dose or low duration of opium consumption. Taken together, results of the current study indicated the key role of opium in total protein and cholesterol levels regardless of diabetes conditions in both sexes.

There is an old belief that consuming opium can alleviate chronic diseases like DM. DM, as a metabolic disease, can cause changes in the functions of body organs. Liver and kidney are two organs directly affected by DM. Serum levels of creatinine and uric acid are known as key indicators of renal and liver function. The present findings showed no significant changes among individuals exposed to opium and/or diabetic circumstances with regard to the creatinine and uric acid. However, the previous studies reported the significant changes in serum levels of creatinine among individuals with DM. These discrepancies may be due to the diversity of samples (animal vs. human), severity of DM, and other possible metabolic disorders existing in experimented cases.

Based on previous studies conducted by the authors of the present study, the effect of opium on apoptosis, electrolytes, DNA methylation, complete blood count (CBC) indices, and hormones were different among male and female genders. In the current study, opium merely altered the serum levels of cholesterol and total protein in a significant way, but not uric acid, TG, albumin, and creatinine, differently in male and female rats regardless of diabetes conditions. Meanwhile, uric acid, TG, albumin, and creatinine experienced significant changes among male and female rats regardless of opium and/or diabetes conditions. Since no significant changes in creatinine levels were observed between addicted and non-addicted animals, it is postulated that opium does not attenuate renal function in male and female animals. However, more evidence is required to clarify the exact contributing mechanisms.

The current study was accompanied by some limitations including the severity of diabetes in the addicted and non-addicted groups was not addressed. In addition, different effects of conventional opium consumption methods such as eating, sniffing, injecting, or inhalation on biofactors were not examined. It is recommended that future studies focus on the signaling mechanisms involved in the biochemical biofactors. Since the effects of addiction on living organisms appear over a long period of time, the effects of both acute and chronic narcotic consumption on blood biochemical factors should
also be investigated.

**Conclusion**

In addition to addiction and its negative social effects, opium causes changes to some biochemical factors. In this study, opium significantly decreased cholesterol and total protein regardless of diabetes conditions compared to the non-opium-addicted rats. However, opium did not significantly change creatinine, uric acid, TG, and albumin levels. Therefore, it could be concluded that although opium affect the cholesterol and total protein levels, it may not have significant effects on diabetic conditions.

**Conflict of Interests**

The authors have no conflict of interest.

**Acknowledgements**

This study was supported by a grant from Rafsanjan University of Medical Sciences. The authors appreciate the university officials allocating the support of the dissertation grant. In addition, the authors would like to appreciate professor Hamid Najafipoor for his helpful scientific advice.

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اثرات تریاک بر برخی فاکتورهای بیوشیمیایی در رت‌های مبتلا به دیابت

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مقاله بیوشیمیایی

چکیده

مقدمه: هدف از انجام پژوهش حاضر، بررسی اثرات تریاک بر روی برخی از فاکتورهای اورومیکویت در رت‌های نر مبتلا و غیر مبتلا به دیابت بود.

روش‌ها: این مطالعه تک‌زمینی بر روی ۸۸ نفر نر و ۶۸ غیر نر مبتلا به دیابت و غیر مبتلا به دیابت انجام شد. تریاک به شکل درون‌صفاقی به گروه‌های تریاک داده شد. نتایج مجموعه مقایسه‌های فاکتورهای بیوشیمیایی بین گروه‌های مبتلا و غیر مبتلا نشان داد که در برخی از موارد اثرات تریاک تأثیر کمی و ناگهانی ندارد.

نتایج‌گیری: تریاک به طور معنی‌داری قلدرن و پروپتین نمودار را در رت‌های نر مبتلا به دیابت و غیر مبتلا به دیابت کاهش داد. علاوه بر این، مصرف تریاک در شرایط اپتئا به دیابت، تأثیر قابل توجهی بر فاکتورهای بیوشیمیایی دارد.

واژگان کلیدی: نشانگرهای بیوشیمیایی، تریاک، اثرات تریاک، انتقال به تریاک، پروپتین نمودار

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نتیجه‌گیری: نتیجه‌گیری به این معناست که اثرات تریاک بر رت‌های مبتلا به دیابت می‌تواند در تأثیرات فاکتورهای بیوشیمیایی ممکن باشد.

تاریخ دریافت: 96/11/25

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DOI: http://dx.doi.org/10.22122/ahj.v10i2.40

130

Addict Health, Spring 2018; Vol 10, No 2

http://ahj.kmu.ac.ir, 04 April