

# Changes in Serum Biochemical Factors Associated with Opium Addiction after Addiction Desertion

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## Original Article

### Abstract

**Background:** The long time use of opium has some effects on serums biochemical factors, the determination of this variation is a new approach in understanding off addiction and relive of drug abuser health. Hence in this study, these indicators in person who were withdrawing of opium have been studied.

**Methods:** In this cross-sectional study bloods biochemical factors such as fasting blood sugar (FBS), sodium (Na), calcium (Ca), uric acid (UA), blood urea nitrogen (BUN), creatinine, cholesterol, total protein, and fibrinogen in three groups serum were studied: (1) Who had been permanent opium users more than 2 years (case). (2) Dependent person who has taken one month addiction withdrawal course (control). (3) A healthy group that had been demographically similar to the other groups.

**Findings:** According to these study findings, FBS serum level in the case group is lower than control group. Serum level of Na, creatinine, and blood triglyceride (TG) in case study are higher than group control. Concentration of potassium, Ca, UA, BUN, cholesterol, total serum protein, fibrinogen, and thrombin time in case study and group control showed no significant difference. Also, in withdrawing case serum level of Na, Ca, UA, BUN, creatinine, and TG significantly increase and thrombin time decrease.

**Conclusion:** According to this study not only the longtime use of opium but also opium with drawerin opium dependent people can change their serum biochemical factors. So recognition, treatment, and prevention of this change could be a new step in improving of health and condition of patients.

**Keywords:** Opium, Withdraw, Dependency, Biochemical factors

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## Introduction

Opium obtains from poppy and Serturmer exploited morphine from opium. Opium used as a port of papaverine and nasocapine. Consumption rate of opium and heroin is high in the world and nowadays drug abuse is the most important social crises, which have relation with economic and cultural aspect of society. Drug dependency is an important health threat and a great difficult. Our country has the first rank in prevalence of opium consumption in the world. Use of opium and its derivatives is an increasing potential threat in the young people.<sup>1</sup> There are studies about opioid effects on different body systems. Use of opioid can lead to physiology and structured changes in kidney that may have important domical problem. Opioid change urine output and urine sodium (Na) secretion by different neurologic and hormonal mechanism in peripheral organs, kidney and central nervous system (CNS).<sup>2</sup> These changes lead to activate opioid endogenous system. There were undiagnosed mechanisms that marriage kidney function and make changes in reassertion of tubular Na in normal and pathologic case.<sup>3</sup>

Level of some electrolytes such as Na, potassium (K), magnesium, zinc, iron, and chloride decrease in the heroin user.<sup>4,5</sup> Substance use like opium and the heroin lead to inhibition in hypothalamus-pituitary-gonad<sup>6</sup> and level of gondolas hormones such as testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and parathyroid hormone (PTH) decrease in serum.<sup>7-10</sup> Act of hypogonadism is determined as cause of osteoporosis in both sexes.<sup>7-9</sup> In this manner, long time use of hypogonadism in male is more than female.<sup>11</sup> In the other study, heroin abuse leads to hyperprolactinemia and osteopenia.<sup>10</sup> Morphine increases hormones such as adrenalin, noradrenalin, Corticosterone, and glucagon which have several effects on metabolisms.<sup>12-15</sup> In a study on heroin addicted people indicates lower total cholesterol and higher triglyceride (TG) and high-density lipoprotein (HDL).<sup>4,16</sup> In the other study indicates that morphine stimulates malondialdehyde production (a risk factor in atherosclerosis) in fat brain.<sup>17</sup> In a study on the effect of morphine on plasma is explained.<sup>18</sup> Another study on rat shows that morphine,

cocaine, and methadone metabolites can release large amounts of histamine by free oxygen radicals what raise the problem.<sup>19</sup>

Stress increases mouse serum cholesterol and this effect manages by Naltroxon,<sup>20</sup> also its indicated that in opioid addiction serum HDL, low-density lipoprotein, TG, total cholesterol, glycated hemoglobin falsely increases and there is not the signification difference between control and case group.<sup>21</sup> A study on rats indicates that morphine has a hepatotoxic effect by raising the glutathione and cause hepatocellular death.<sup>22</sup> Gomez-Lechon et al. found that human hepatocellular culture in morphine 0.8-1 and acetylmorphine (pure morphine) decreases the production of glycogen and albumin up to 50%.<sup>23</sup> Hence, it seems that hepatic morphine metabolism harms hepatic calls and causes albumin level changes and hepatic cells injury. Diagnostic level function tests in afterwards years on heroin addicted people indicated serum level of aspartate transaminase, alanine transaminase; total protein and albumin have no significant difference with control group, only biliary secretions increases.<sup>24</sup>

Heroin increases male and female mouse serum glucose, Na, and K. But how much opium withdrawal changes the biochemical indexes of the body? Assessment of biochemical parameters in drug abusers serum in withdrawal could help futures studies. The purpose of the present study is answers to these questions and furthermore in foreigner and Iranian references and articles had not found any study about perfect assessment of opium withdrawal patients biochemical parameters, last studies only cover a few biochemical parameters in animal and human being. This study could be used as the most perfect study about the effect of opium on important serum biochemical parameters in opium withdrawal patients. So could be a base for next studies about basic addiction arguments and especially studies about addiction prevention, etiology and treatment.

## Methods

This cross-sectional study consists of 120 men between 24 and 45 years old with opium addiction that had gone to a clinic to wean from addiction were studied. Person who had been opium users more than 2 years were as opium

dependent group and the people who were users more than 1 month was withdrawal group and some volunteer from non-addicted men who were similar to this population from age and education as control group were selected.

Only opium dependent person according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition brought to the study and the person who were multiple drug users, recreational user or substance abuser were omitted too. In addition, among opium addicted people who had diabetes and kidney failure were excluded. The patient who were infected by syphilis, hepatitis, AIDS and any infectious disease or obvious clinical sign of them like skin rash were omitted too. To being sure that using the opium in permanent urine morphine test was used. In the first step in opium dependent group a screening test on urine sample was done. Rapid immunochromatography test and then on the positive cases of screening test for the confirmation of opium use a liquid-solid chromatography test and then also a thin layer chromatography was done. To be sure about not opium using by control and withdraw group the diagnostic examinations with rapid immunochromatography technique were done. Opioid rapid situation assessment too was done on the urine sample of these people (only screening test or rapid chromatography).

At first the goal of this study explains to the patients' steps then a letter of satisfaction was taken before urine and blood sampling. Demographic information about age, drug type, last using time and addiction period is collected and connect by a code to each patient and sample for biochemical blood parameters were taken by researchers.<sup>4,25</sup> To determine the biochemical serum parameter of the both dependent and witness, case group, control and experimental group the following procedurals are performed.

All groups of study were fasted for at least 12 h. To get the blood serum, we need about 5 mg of the newly gathered blood vein. Separating the serum 30 min after sampling and taking blood by centrifugation was in this case that the sample centrifuged for about 5 min/800 g. This blood serum will be frizzed in 20° C and protected till the day of the experiment. The rate of the Na and K measured, through using electrolyte analyzer. Calcium (Ca) density measured through

cresolphthalein complex method (Darman Kav Co. kit). Uric acid (UA) measured through the phosphotungstic acid method (Zist-Shimi Co. kit). And also, creatinine with the help of "Jaffe" method (Pars Azmun Co. kit), fasting blood sugar (FBS) density, through photometric and enzymatic (GPO-PAP) (Iran Shimi Co. kit) were evaluated. Cholesterol, TG, and blood urea nitrogen (BUN) were measured through photometric method (GPO-PAP) (Iran Shimi Co. kit). Colorimetric "End point" method (Zist-Shimi Co. kit) utilized for evaluation of the fibrin-tion as well as time needed for thrombin were measure (coagulometric methods) (kit of the Estago Co. of France).<sup>4,25</sup>

The data were analyzed by SPSS for Windows 11.5 (version 11.5, SPSS Inc., Chicago, IL, USA) software. The group's comparison performed through one-way ANOVA test. Toki-Kramer post-test was utilized for founding a meaningful place in between the above groups. The meaningful level of 0.05 was considered in this test. Moreover, data were delivered in the form of average of the  $\pm$  standard deviation.

## Results

FBS parameter indicated a meaningful decrease ( $P < 0.001$ ) in people who were dependent to opium and also people who were trying to give up comparing to under controlled group, but no meaningful difference were observed between FBS serum of the people who tried to give up as well as the dependent ones to opium.

These conclusions also indicated that, density of the Na<sup>+</sup> ion did not observed in the blood serum of the dependent people comparing to under controlled ones, but on the contrary, density of Na<sup>+</sup> ion showed a meaningful increase ( $P < 0.001$ ) in people who were trying to give up opium comparing to under controlled groups as well as dependent ones. The density of K<sup>+</sup> ion indicated a meaningful decrease ( $P < 0.050$ ) in dependent group comparing to under controlled group. The serum level of K did not change in giving up group comparing to under controlling ones. The density of Ca<sup>2+</sup> ion showed a meaningful decrease ( $P < 0.001$ ) in dependent groups to opium comparing to under controlled ones. No meaningful difference observed in between the serum level of Ca of dependent people who were trying to give up opium as well

as under controlled people. The density of this ion indicated meaningful increase ( $P < 0.001$ ) in the serum of people who were trying to give up comparing to dependent group to opium. UA and BUN had a meaningful decrease ( $P < 0.001$ ) in dependent groups to opium comparing to under controlled group. UA and BUN did not show any meaningful difference in giving up group comparing to under controlled ones, but, these parameters showed a meaningful increase ( $P < 0.001$ ) in giving up people comparing to dependent ones.

Creatinine serum indicated a meaningful decrease ( $P < 0.001$ ) in dependent people to opium comparing to under controlled ones and indicated a meaningful increase ( $P < 0.010$ ) in giving up People comparing to under controlled ones. Present result indicated that there is a significant increase in creatinine concentrations in patients leaving the opium poppy compared to patients who are dependent to puppy. However, cholesterol serum decreased in the dependent people comparing to under control ones, but this decrease did not show any meaningful difference. Also this parameter did not show any meaningful

difference in giving up people comparing to under controlled ones. TG serum did not show any meaningful difference in dependent people comparing to under controlled ones.

This parameter indicated a meaningful increase ( $P < 0.010$ ) in giving up people comparing to under controlled ones. The data showed that TG serum is going to have a meaningful increase ( $P < 0.010$ ) in giving up people comparing to dependent ones to opioid (Table 1). Total protein and fibrinogen serum did not show any meaningful difference ( $P < 0.001$ ) in between three groups; dependent people to opium and giving up ones groups as well as under controlled ones (Table 2).

## Discussion

In this research, after finishing the period of "the giving up" the bio-chemical indications, such as FBS,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ , BUN, UA, TG, creatinine, blood cholesterol, total protein, fibrinogen, and time needed for prothrombin were considered, in dependent people to opium. Regarding what is obtained from above studies, long time consuming opium increased the FBS serum level in dependent

**Table 1.** The values of Biochemical Parameters in three groups of Control, Opium and Withdrawal

Biochemical parameters	Groups					
	Control		Opium		Withdrawal	
	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n
FBS (mg/dl)	86.96 $\pm$ 1.19	90	**80.94 $\pm$ 1.02	89	**80.80 $\pm$ 0.93	89
$\text{Na}^+$ (mmol/l)	139.30 $\pm$ 0.39	100	139.20 $\pm$ 0.49	89	€€144.30 $\pm$ 0.83	89
$\text{K}^+$ (mmol/l)	4.47 $\pm$ 0.07	100	*4.17 $\pm$ 0.60	89	4.33 $\pm$ 0.07	89
$\text{Ca}^{2+}$ (mg/dl)	9.37 $\pm$ 0.08	100	**8.81 $\pm$ 0.09	89	€9.46 $\pm$ 0.12	109
Uric acid (mg/dl)	5.34 $\pm$ 0.13	100	**3.67 $\pm$ 0.08	89	€5.16 $\pm$ 0.11	89
BUN	15.70 $\pm$ 0.36	100	**15.55 $\pm$ 0.49	89	€15.74 $\pm$ 0.36	96
Creatinine	0.92 $\pm$ 0.02	101	**0.83 $\pm$ 0.01	89	€€1.01 $\pm$ 0.01	85
Cholesterol (mg/dl)	180.06 $\pm$ 6.25	110	173.30 $\pm$ 3.92	89	181.80 $\pm$ 3.77	121
Triglyceride	105.70 $\pm$ 4.63	110	105.40 $\pm$ 4.30	89	¥,€128.80 $\pm$ 4.72	121

FBS: Fasting blood sugar; BUN: Blood urea nitrogen; SD: Standard deviation; Data are expressed as mean  $\pm$  SD and  $P < 0.050$  was considered statistically significant

\* $P < 0.050$  and \*\* $P < 0.001$  Opium group Vs. Control group; ¥ $P < 0.010$  and ¥¥ $P < 0.001$  Withdrawal group Vs. Control group; € $P < 0.010$  and €€ $P < 0.001$  Withdrawal group Vs. Opium group

**Table 2.** The values of Blood Clotting Factors in three groups of Control, Opium and Withdrawal

Blood clotting factors	Groups					
	Control		Opium		Withdrawal	
	Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n
Total protein	7.08 $\pm$ 0.08	59	6.95 $\pm$ 0.07	89	7.09 $\pm$ 0.06	89
Fibrinogen (mg/dl)	3.11 $\pm$ 0.05	100	3.23 $\pm$ 0.07	89	3.21 $\pm$ 0.05	89
Protrombine time	12.25 $\pm$ 0.09	100	*15.10 $\pm$ 0.23	89	11.98 $\pm$ 0.08	89

SD: Standard deviation; Data are expressed as mean  $\pm$  SD and  $P < 0.050$  was considered statistically significant

$P < 0.050$  was considered statistically significant; \* $P < 0.001$  Opium group Vs. Control group

people as well as giving up groups, but, no meaningful difference, related to FBS level observed between these people (both dependent and giving up groups). There are some controversial attitudes regarding the role of opioids in adjusting the glucose homeostasis. Although, a few studies have reported that opioids are the cause of hyperglycemia.<sup>13,26,27</sup> Simultaneously, some other studies indicated that opioids can be the cause of hypoglycemia.<sup>28,29</sup> Some studies indicated that the increase of the adrenocorticotrophic, cholesterol<sup>15</sup> and glucagon<sup>12</sup> are the cause of such effects.

In chronic consuming morphine, because of its effect on adjusting decrease of morphine receptors, the cell's activity rejects to normal level, but, following cutting off morphine consummation, their activities increases and this activity itself is one of the reasons for the appearance of the giving up syndrome indications.<sup>30</sup> That's why, after cutting off morphine and cocaine, plasma corticosterone level increases and causes suppression of the immunity system. Even though, after cutting it off, corticosterone level reaches to its basic level, but, immunity system would not stop.<sup>31</sup> In present study, giving up group who have past 1 month of their last opium consummation, but, they are affected by hypoglycemia, which could be the result of up-regulation mechanisms.

Moreover, studies are needed to recognizing that, if these are central or peripheral hypoglycemia effects.<sup>27</sup> Their duration of dependency, nutrition and social life or the presence of a few harmonic disorders which are the result of consuming drags and their effects on kidney as well as liver might be the cause of FBS decrease after giving it up in dependent people. Opioids are the cause of changes in urinary exocrine as well as Na urinary exocrine through multi-nerves and harmonic mechanism, in peripheral organs, CNS and kidney.<sup>32</sup> Density of some electrolytes, such as K, Ca, magnesium, zinc, iron, manganese, and chloride decrease in people who are addicted to heroin.<sup>4,5</sup> Hypokalemia increased the risk of heart diseases in patients dependent on opioids.<sup>33</sup> The recent studies conclusion indicates that, the Na serums did not changed in dependent people, but the Na serum level is obviously higher in giving up people comparing to under controlled ones. K ion density has decreased in dependent groups; these

conclusions are similar to the other studies which have shown that K decreased independent people to uploads.<sup>5</sup> Decreasing Na and K ion after a long time opium consummation might be the result of structural changed in adrenal cortex, especially in zona glomerulosa and zona fasciculate cells.<sup>34</sup> But in studies regarding animals, one doze of opium has caused increase of Na and K.<sup>26</sup>

Consuming drags is the cause of controlling hypothalamus-pituitary-gonad and moreover it will cause decreases of surface of gonads hormones, such as PTH, FSH, and LH testosterone serum<sup>7-10</sup> increase of osteoporosis observed in both gender.<sup>7-9</sup> In our studies, we have observed meaningful decrease in Ca serum level, in dependent people. But Ca level was increasing and approaching to level of under controlled group, and also bone density decreased in patient under methadone therapy.<sup>35</sup> In a study, it has observed that consuming opium is the cause of no meaningful decrease in Ca serum level. On the bases of previous studies, consuming opium can directly decrease bone density through its effects on osteogenesis. Controlling the growth of osteoblasts in plant environmental and decrease of osteocalcin in serum is among a few effects on osteoporosis that caused by osteogenesis.<sup>7</sup>

In this study, the rate of UA decreased in serum of dependent people in opium. In a research about laboratory animals, while, in giving up people it reaches to the level of under controlled people. In a research about laboratory animals, it determined that, long term consuming morphine probably along with increasing of purine nucleotide dissimilation increased the UA as well as creatinine level.<sup>36</sup> But in giving up group just like the result of these studies, one more time, the UA rejected to the normal level.<sup>37</sup>

The level of total protein and fibrinogen did not show any meaningful difference in under controlled group. Result of the present study revealed that there is significant increase in thrombin time in people who are dependent to dopey compared to control group. While result of the present study indicated that there is not significant different in patients leaving **dopey** compared to control group. The decrease of the protein level in dependent people might be the result of not suitable nourishment in dependent people to upload.<sup>38</sup> Electrophoresis profile of protein serum in dependent people changes in

dependent people to opioid.<sup>25</sup> Moreover, liver disorder might be an important matter in decreasing of protein serum. It is determined that producing morphine and increasing of glutathione is the result of using hepatotoxic, morphine, and finally it will be the cause of death of liver cells.<sup>22</sup>

Gomez-Lechon et al. through utilizing cell cultivation technique observed that liver cells plant in front of 0.8-1 ml morphine and 3 and 6 dye acetyl morphine (pure opium) decreased the production of glycogen and albumin to 50%.<sup>23</sup> In this case, metabolism of morphine liver through ruing the lever cell not only liver cell resulted to a change in albumin doze and also created liver disorder. Of course, diagnostic liver function tests, which has been taken few years later on serum of addicted people in heroin indicated that the rate of the serum aminotransferase, total proteins as well as albumin had no meaningful difference comparing to under controlling group and just biliary excretion was increased.<sup>24</sup>

### Conclusion

In the present study, dependent people in opium as well as giving u one did not show any meaningful difference regarding cholesterol serum level. Regarding TG level, these studies

indicated that, there is no meaningful difference between serum levels of this parameter in under controlled as well as independent groups. Any distinguished increase did not observed in TG serum level of giving up people. The studies which is done about people who are addicted to heroin shows fewer doze of total TG and higher doze of TG and HDL in these people comparing to witness group.<sup>4,16</sup> Karam et al. indicated that total cholesterol in diabetic people which are depended to opium abnormally decreased.<sup>39</sup> Overall we conclude that: long-term consuming opium changes the protein and lipid serum level, so in this case, not only "addiction" is the result of higher risks of diseases but also is the cause of increasing the cause of diseases' risk, such as cardiovascular disorders, osteoporosis, liver, and kidney disorders as well as HIV.

### Conflict of Interests

The Authors have no conflict of interest.

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## تغییرات عوامل بیوشیمیایی در سرم بیماران وابسته به تریاک پس از ترک اعتیاد

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### مقاله پژوهشی

### چکیده

**مقدمه:** مصرف طولانی مدت اوپیوئیدها اثراتی را بر عوامل بیوشیمیایی سرم دارد. تعیین این تغییرات رویکرد جدیدی در شناخت اعتیاد و بهبود وضعیت مصرف کنندگان این مواد می باشد. مطالعه حاضر به بررسی شاخص های مذکور در افراد در حال ترک پرداخت.

**روش ها:** در این مطالعه مقطعی، عوامل بیوشیمیایی خون از جمله قند خون ناشتا (Fasting blood sugar یا FBS)، سدیم، پتاسیم، کلسیم، اسید اوریک (Uric acid یا UA)، اوره، BUN (Blood urea nitrogen)، کراتینین، کلسترول تام، تری گلیسرید، پروتئین تام، فیبرینوژن و زمان ترومبین در سرم سه گروه ۱- کسانی که بیش از دو سال مصرف کننده مداوم تریاک بودند (گروه مورد)، ۲- افراد وابسته ای که دوره یک ماهه ترک اعتیاد را سپری کردند (گروه شاهد) و ۳- گروه سالم بررسی شد که هر سه گروه از نظر دموگرافیک تطبیق داشتند.

**یافته ها:** سطح سرمی قند ناشتا در افراد در حال ترک نسبت به گروه شاهد کاهش یافت و سطح سرمی سدیم، کراتینین و تری گلیسرید خون به طور معنی داری در افراد در حال ترک بالاتر از گروه شاهد بود. غلظت یون پتاسیم، کلسیم، اسید اوریک، BUN، کلسترول، پروتئین تام سرم، فیبرینوژن و زمان ترومبین در افراد در حال ترک با گروه شاهد اختلاف معنی داری را نشان نداد. سطح سرمی سدیم، کلسیم، اسید اوریک، BUN، کراتینین و تری گلیسرید در افراد در حال ترک در مقایسه با گروه وابسته به تریاک افزایش معنی دار و زمان ترومبین کاهش معنی داری داشت.

**نتیجه گیری:** بر اساس نتایج حاصل شده، نه تنها مصرف طولانی مدت تریاک بلکه ترک اعتیاد در افراد وابسته به تریاک می تواند عوامل بیوشیمیایی مربوط به سرم بیماران را تغییر دهد. بنابراین شناخت، درمان و پیشگیری از این تغییرات می تواند گام جدیدی در بهبود سلامت و وضعیت این بیماران باشد.

**واژگان کلیدی:** تریاک، ترک اعتیاد، وابستگی، عوامل بیوشیمیایی

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