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# Effect of Opium Addiction on Some Serum Parameters in Rabbit

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**Abstract:** Addiction is one of the most important issues of the 21st century that received more attention all over in the world. Addiction affects blood parameters that could be led to other problems. In this study to assay biochemical effects of pure opium, 40 New Zealand white rabbits were randomly divided into two groups (control and addicted group). Addicted and control groups received opium and distilled water separately by gavage. Rabbits were weighed at the beginning and at the end of the experiment. Blood samples also were taken from ear vein at the beginning and at the end of the experiment. Samples were stored at -20 °C until used for biochemical analysis. Various parameters such as Fasting blood glucose, total cholesterol, high density lipoproteins–cholesterol, low density lipoproteins–cholesterol, triglycerides, sodium, potassium, calcium, phosphor, total protein, albumin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, amylase, Creatine phosphokinase, uric acid, creatinine and urea were measured in the serum of both groups. Addicted male and female rabbits showed higher serum FBS, AST, ALT, LDL, TG, CPK, $K^+$ and Cr values in compare to the control group. Our finding showed that addiction has profound effects on biochemical parameters that could be used for detection of side effects.

**Key words:** Addiction · Biochemical parameters · Opium · Serum · Weight

## INTRODUCTION

In traditional medicine, opium has been considered as a remedy for many disorders. This belief along with use of opium as recreation can lead to addiction. Addiction is one of the important issues of the 21st century in the world that is also imperative in Iran [1]. Two common ways of Opium consumption are inhalation or oral intake. Opium is constituted mostly from Morphine but contains more than eighty alkaloids with different effects on homeostasis [2]. Determining the serological changes caused by opium addiction can help to better understand of the biology of addiction and adoption of a proper strategy for treatment. There are lots of studies about the effects of opiate addiction on serum factors [1-7] and also on different tissues [8-10] but only limited aspects have been focused on opium. Since opium has more than 70 components, its effect on metabolism and therefore biochemical parameters varies in compare to pure morphine and other active ingredients. In mentioned studies duration, route of opium consumption, purity of consumed opium, diet status and other conditions were not similar. Because of possible effects of these parameters on serum parameters in addicted subjects this study was done to evaluate the effects of opium addiction on serum parameters under controlled conditions in healthy rabbits as animal model.

## MATERIALS AND METHODS

Forty New Zealand white rabbits (20 males and 20 females, 1.5-2 kg body weight) were purchased and housed in an animal care facility under controlled light, 12 h light/12 h dark, at 25±1°C temperature and 60±5% humidity. Rabbits were fed with standard chow diet and water was available *ad libitum*. Rabbits were randomly divided into two groups as control and addicted group. Addicted group was treated with pure opium from police office (Ilam, Iran) that was suspended in 1ml of hot water. Suspension was administered by gavage after bringing to

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room temperature. Initial dose of suspension was 250 mg per day that was gradually increased to 1000 mg per day within one week and the final dose was kept constant throughout the rest of the study. The control group received 1 ml of distilled water for 60 days [19]. In the beginning and at the end of period, Rabbits were weighed and blood samples were taken from ear vein. Blood was centrifuged and the isolated serum was kept in -20°C until analysis. After the euthanasia the weight of abdominal fat was measured. All experiments were approved by the ethics committee of the Ilam University.

A Convergys ISE Analyzer was used for determination of serum sodium ($Na^+$) and potassium ($K^+$). Calcium ($Ca^{2+}$) and phosphorus (P) of serum were determined by colorimetric methods. Fasting glucose (FBS) was determined using the glucose oxidase method. Serum value of Total cholesterol (Tch), High density lipoprotein–cholesterol (HDL-c), low-density lipoproteins (LDL) and Triglycerides (TG) were assayed by enzymatic-colorimetric method. Urea and uric acid were measured using enzymatic methods. Total protein content of serum was determined by the Biuret method. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), Creatine phosphokinase (CPK) and α-Amylase were measured by kinetic enzyme assays. Albumin and creatinine were measured by the bromocresol green method and kinetic colorimetric assay.

**Statistical Analysis:** All data are presented as mean±SD. Data were analyzed by one-way ANOVA followed by Duncan's multiple comparisons test. Multiple comparisons tests were only applied when a significant difference was determined in the ANOVA analysis, $P < 0.05$. The SPSS 13.0 (Chicago, USA) was used for analysis.

## RESULTS

Both groups gained weight during the period of the study. However, there was a significant difference in the weight of rabbits in different groups at the beginning and throughout the study. In addicted group weight gaining was lower in compare to control group. Abdominal fat was significantly decreased in addicted rabbits (Tables 1, 2). Our results showed that sex did not affect the impact of opium addiction on measured factors. In control group, all parameters did not show a significant difference at the end of the study compared to the beginning of the study in both sexes ($P \leq 0.05$). $K^+$ showed significant difference that was higher in addicted group compare to control group ($P \leq 0.05$) but other ions did not show a significant change (Table 3). Assayed enzymes, CPK, AST, ALT were increased significantly in addicted group at the end of study but ALP was significant lower in compare to control group (Table 4). Serum TG, Tch and LDL levels were increased significantly in addicted group ($P \leq 0.05$)

Table 1: Comparison of Abdominal fat and Difference of weight gaining between addicts and non addicts males Data represent mean ± SD (n=10), p<0.05 considered as significant difference

| | Addicted male | Non addicted male | P value |
|---|---|---|---|
| Difference of weight gaining(gr) | 489.93±9.50 | 889.07±12.16 | 0.001 |
| Abdominal fat(gr) | 40.25±7.37 | 60.25±15.71 | 0.003 |

Table 2: Comparison of Abdominal fat and Difference of weight gaining between addicts and non addicts females Data represent mean ± SD (n=10), p<0.05 considered as significant difference

| | Addicted female | Non addicted female | P value |
|---|---|---|---|
| Difference of weight gaining(gr) | 110.28±9.33 | 218.87±11.95 | 0.001 |
| Abdominal fat(gr) | 34.5±8.37 | 67.7±7.85 | 0.001 |

Table 3: Comparison of the biochemical factors in two groups of addicted and nonaddicted males and female. Data represent mean+SD (n=10)

| | | Addicted Male | Non Addicted Male | Addicted Female | Non Addicted Female |
|---|---|---|---|---|---|
| Ca | Baseline | 14.44±.581 | 14.46±.579 | 14.33±.570 | 14.39±.562 |
| | 60 day | 14.78±.601 | 14.54±.729 | 14.92±.767 | 14.42±.662 |
| P | Baseline | 7.35±.291 | 7.42±.289 | 7.33±.286 | 7.21±.290 |
| | 60 day | 7.79±.647 | 7.66±.411 | 7.12±.697 | 7.22±.274 |
| Na | Baseline | 147.0±4.47 | 146.0±4.36 | 144.0±5.07 | 145.12±4.31 |
| | 60 day | 154.39±12.75 | 152.2±20.72 | 155.7±14.41 | 146.4±6.07 |
| K | Baseline | 6.38±.724 | 6.29±.716 | 6.71±.702 | 6.46±.695 |
| | 60 day | 10.18±.494** | 6.95±.721 | 10.42±1.40** | 6.82±.587 |

* p<0.05 versus control and baseline * * p<0.01 versus control and baseline

Table 4: Comparison of the biochemical factors in two groups of addicted and nonaddicted males and female. Data represent mean+SD (n=10)

| | | Addicted Male | Non Addicted Male | Addicted Female | Non Addicted Female |
|---|---|---|---|---|---|
| ALT | Baseline | 62.9±14.85 | 60.9±14.60 | 60.8±16.6 | 61.9±14.5 |
| | 60 day | 116.0±12.14** | 63.3±13.97 | 115.0±30.21** | 61.1±16.78 |
| AST | Baseline | 69.1±9.66 | 68.4±9.92 | 68.11±9.83 | 68.41±9.75 |
| | 60 day | 139.1±22.97** | 72.8±14.60 | 99.0±19.84** | 69.0±10.55 |
| ALP | Baseline | 365.10±54.34 | 361.13±56.39 | 349.10±54.34 | 351.10±56.3 |
| | 60 day | 309.8±48.17** | 419.30±46.71 | 248.0±38.11** | 321.0±31.72 |
| CPK | Baseline | 299.3±45.62 | 296.3±49.73 | 295.3±48.73 | 294.3±49.23 |
| | 60 day | 413.1±65.08** | 316.9±35.17 | 430.2±65.27** | 303.6±47.48 |

* p<0.05 versus control and baseline * * p<0.01 versus control and baseline

Table 5: Comparison of the biochemical factors in two groups of addicted and nonaddicted males and female. Data represent mean+SD (n=10)

| | | Addicted Male | Non Addicted Male | Addicted Female | Non Addicted Female |
|---|---|---|---|---|---|
| Tch | Baseline | 41.3±14.76 | 40.4±14.86 | 40.1±13.96 | 40.9±14.16 |
| | 60 day | 76.7±16.77** | 42.9±11.28 | 76.1±16.9** | 41.9±8.89 |
| TG | Baseline | 51.1±9.15 | 50.1±8.95 | 50.9±9.25 | 50.5±9.15 |
| | 60 day | 79.5±14.69** | 57.6±12.69 | 79.0±14.04** | 56.6±9.15 |
| HDL-C | Baseline | 20.25±3.17 | 20.01±3.0 | 22.05±3.7 | 20.31±3.07 |
| | 60 day | 25.2±12.77 | 17.37±2.81 | 30.8±20.07 | 22.65±2.60 |
| LDL-C | Baseline | 9.9±2.20 | 10.11±2.31 | 10.02±2.29 | 10.12±2.26 |
| | 60 day | 18.11±7.85** | 10.23±3.82 | 17.87±8.68* | 10.44±4.74 |

* p<0.05 versus control and baseline * * p<0.01 versus control and baseline

Table 6: Comparison of the biochemical factors in two groups of addicted and nonaddicted males and female. Data represent mean+SD (n=10)

| | | Addicted Male | Non Addicted Male | Addicted Female | Non Addicted Female |
|---|---|---|---|---|---|
| FBS | Baseline | 126.9±17.93 | 127.2±18.95 | 127.8±17.53 | 127.1±17.91 |
| | 60 day | 238.3±33.74** | 140.4±14.33 | 223±26.31** | 137.5±20.36 |
| Pr | Baseline | 2.94±.231 | 2.84±.229 | 2.86±.222 | 2.86±.231 |
| | 60 day | 2.95±1.14 | 3.3±.713 | 2.88±1.38 | 2.89±.488 |
| Alb | Baseline | 3.29±.375 | 3.23±.368 | 3.25±.384 | 3.27±.379 |
| | 60 day | 3.45±.447 | 3.52±.854 | 3.2±.454 | 3.26±.383 |
| Amy | Baseline | 439.1±56.0 | 443.1±54.05 | 449.1±56.05 | 446.1±54.12 |
| | 60 day | 479.4±88.3 | 431.9±50.48 | 446.1±42.6 | 478.2±62.06 |

* p<0.05 versus control and baseline * * p<0.01 versus control and baseline

Table 7: Comparison of the biochemical factors in two groups of addicted and nonaddicted males and female. Data represent mean+SD (n=10)

| | | Addicted Male | Non Addicted Male | Addicted Female | Non Addicted Female |
|---|---|---|---|---|---|
| Ur | Baseline | 28.12±1.82 | 28.72±1.74 | 28.70±1.78 | 28.62±1.87 |
| | 60 day | 30.0±2.35 | 29.89±2.90 | 31.8±5.26 | 29.8±3.38 |
| Cr | Baseline | 1.02±.129 | 1.02±.131 | 1.02±.10 | 1.02±.119 |
| | 60 day | 1.17±.082** | 1.02±.103 | 1.11±.087* | 1.02±.091 |
| U.A | Baseline | 1.28±.297 | 1.27±.289 | 1.31±.287 | 1.3±.290 |
| | 60 day | 1.53±.496 | 1.4±.461 | 1.83±.879 | 1.39±.624 |

* p<0.05 versus control and baseline * * p<0.01 versus control and baseline

but HDL values did not show a significant change (Table 5). FBS, creatinin were higher in addicted rabbits in compare to control group (Tables 6, 7) but other parameters did not show significant difference in both groups ($P \leq 0.05$).

## DISCUSSION

Opium addiction had a considerable effect on weight gain and abdominal fat weight in rabbits as seen in this study. Opium addict rabbits had lower body weight and abdominal fat than non-addicts. Weight loss might be caused by hypophagia as Boghossian *et al*. [11] showed that morphine induced this phenomena. But our finding is inconsistent with the findings of Mohamadi *et al*. [7] who reported that opium addiction had no effect on body weight in rabbits. In this study effects of opium addiction on measured factors were not sex dependent ($P \leq 0.05$).

FBS was significantly higher in addicted rabbits but considerable controversies about the role of opioids in regulation of glucose homeostasis should be considered. In some reports blood glucose had been increased

[1, 2, 9, 12, 13] but in others, it had been decreased [3, 14-16]. Increased glucose could be attributed to the effect of morphine [9]. Dosage of opium has a crucial role in serum level of FBS [5]. Morphine at high doses increased glucose production by liver and decreases clearance of glucose by peripheral tissue and leads to hyperglycemia in dog but at low dose did not affect FBS in dog [13].

Serum $Na^+$ concentration was not affected by addiction while serum $K^+$ values in addicts had increased considerably ($P \leq 0.05$), that is in agreement with a study that showed morphine injection increases plasma $K^+$ in chronically morphine administrated pigs [18]. Heprkalemia could be due to kidney dysfunction in addicted group that could interfere with regulation of water volume and blood pressure [10].

Total cholesterol, triglyceride and LDL were significantly higher in addicted group which was in contrast to the other reports in rabbit [7] and also in human [2, 3, 19] but was consistent with results obtained in rat by Bryant *et al.* [17]. Increase in serum values of these parameters can be caused by lypolytic effect of opioids [20]. Direct effect of morphine on isolated epididymal fat pads of rats also had been demonstrated [21].

In this study blood urea and uric acid was not affected by opium addiction, but Sumathi *et al.* [26] and Divsalar *et al.* [22] reported decrease of UA and increase of UA, blood urea and Cr, respectively. This controversy may be caused by different type of used opium. Opium makes histopathological changes in kidney that result in changes in biochemical parameters that are related to severity of histopathological changes [22].

Increased ALT, AST and creatinine could be attributed to nephrotoxicity and hepatotoxicity of morphine as showed in rat [4, 10, 22-24]. CPK was significantly higher in addicted group. This phenomenon may be due to effect of opioids on muscle as Sylvester *et al.* [25] proposed the toxic effect of chronic opioid therapy on muscle. ALP was significantly lower in addicted group. Total protein and albumin showed no significant difference between opium addicts and non opium addicts that are in agree with findings of Divsalar *et al.* [26] in opium and heroin addicts human.

Our findings show that opium addiction in rabbit has many biological consequences. Opium consumption decrease FBS, AST, ALT, LDL, TG, CPK, $K^+$ and Cr and increase ALP in both male and female rabbits. These alterations in serological parameters can deteriorate the some situations such as diabetes mellitus, hyperlipidemia and kidney and liver disorders that should be considered in medical evaluation of addicted patients. More studies need to be conducted for a better understanding of the effects of the individual components of opium on the biochemical factors and mechanism of these changes.

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