

## Analysis of Hematological and Biochemical Parameters in Methamphetamine Addicts Compared with Healthy Individuals

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**Received:** 19 Oct 2014

**Revised:** 08 Dec 2014

**Accepted:** 16 Dec 2014

**ABSTRACT**

**Background and Objective:** Methamphetamine has strong stimulating effects on various systems of the human body. The aim of this study was to evaluate the hematological and biochemical parameters in methamphetamine addicts and to compare them with healthy individuals.

**Methods:** This is a retrospective case-control study that was conducted in 1390-91 in Ibn Sina Hospital in Shiraz, Iran. Measurement of lipids (cholesterol, triglycerides), liver enzymes (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase), albumin, blood urea nitrogen, creatinine and blood parameters such as platelets and white blood cells (WBCs) count, hemoglobin concentration and hematocrit of 60 individuals addicted to methamphetamine and 60 healthy subjects as a control group was carried out.

**Results:** Alanine aminotransferase, aspartate amino transferase, alkaline phosphatase, WBCs and platelet count and serum creatinine levels in methamphetamine addicts were significantly higher than the control group (p-value <0.001), while hemoglobin, hematocrit and albumin levels were lower in these patients (p-value <0.001).

**Conclusion:** The use of methamphetamine increases lipid peroxidation, changes levels of inflammatory markers and increases liver enzymes, which may increase the risk of liver diseases. It also increases WBCs and platelets count as an early sign of inflammatory disease progression, associated with methamphetamine abuse. Decreased hemoglobin and hematocrit can also increase the risk of anemia in these patients. These observations may give us a better understanding about the biological mechanisms associated with the pathology of methamphetamine consumption in Iran and help us prevent and solve the problems arising from this drug.

**Keywords:** Methamphetamine, Hematological Tests, Biological Markers, Oxidative Stress.

## INTRODUCTION

The number of methamphetamine (MA) addicts in Iran is rising, a condition which can lead to serious health and social problems. It can also increase the risk of various diseases including acute kidney problems, cardiovascular and neurological diseases in older individuals (1-3). Methamphetamine has strong stimulating effects on the central nervous system (CNS), increases euphoria and consciousness and decreases appetite (4). Methamphetamine's mechanism of effect is mainly through dopamine and serotonin release in the CNS (5). Animal studies have shown that methamphetamine increases inflammation and oxidative stress (5), which in turn may cause respiratory, cardiovascular and neurological disorders (6). Oxidative stress is defined as the imbalance between oxidants and antioxidants in biological systems. Macromolecules are damaged by free radicals when this imbalance occurs (7, 8). A study on the oxidative effects of methamphetamine on dopamine in rats has shown that the production of reactive oxygen intermediates in synaptosomes increases, while Methamphetamine is unable to induce the production of reactive oxygen intermediates in animals lacking dopamine synaptosomes(9). Since our knowledge about the biochemical mechanisms and pathological conditions related to methamphetamine addiction is insufficient, this study was aimed to examine the hematological and biochemical parameters in methamphetamine addicts compared to healthy subjects.

## MATERIAL AND METHODS

**Subjects:** Study population consisted 120 adult males, 60 of whom had a history of methamphetamine use and 60 healthy subjects with no history of drug abuse. All the subjects underwent physical examination and medical history was obtained to identify healthy individuals from addicts. Individuals who were classified in the group of methamphetamine consumers had the following criteria: Age between 20-50. Use of methamphetamine on a regular basis for at least 3 months and at least 5 days a week Exclusion criteria included: HIV infection, History of drug dependence (other than methamphetamine, nicotine, caffeine)

History of any chronic disease, nervous and mental illness (e.g. Convulsion, depression, high blood pressure, heart disease, diabetes or liver disease). Sera was used to determine the biochemical variables such as albumin, blood urea nitrogen (BUN), creatinine, total cholesterol, triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and uric acid. Blood containing anticoagulant EDTA was used to determine hemoglobin, hematocrit, platelets and white blood cells (WBC) count. This experimental study was approved by the research ethics committee. **Laboratory Techniques:** Blood samples were collected after 12 hours fasting. Total cholesterol, triglycerides, BUN, creatinine, uric acid, AST, ALT and ALP were measured by enzymatic methods using commercial kits (MAN Co.). WBC hemoglobin, hematocrit, platelets were measured by Sysmex Kx21 cell counter. **Statistical analysis:** Statistical analysis was performed using SPSS version 16 statistical software. Mean and confidence intervals (CI) of 95% were measured in groups. The difference between the means was analyzed using the Student's t-Tests and P-value of <0.05 was considered as statistical significance.

## RESULTS

The mean duration of methamphetamine abuse among the test groups was about 3 years. The mean and confidence intervals (CI = 95%) for biochemical and blood parameters in addicts and controls are shown in Table 1. There was no significant difference in the amount of BUN, fat and uric acid between the two test groups. The number of platelets and WBC among methamphetamine consumers was notably higher than the controls (P-value <0.001). However, albumin, hemoglobin and hematocrit in the methamphetamine group were significantly lower than the control group (P-value <0.001). Increased levels of creatinine and liver enzymes such as AST, ALT and ALP was observed among drug abusers compared to the healthy subjects (P value <0.001).

**Table 1- Mean and 95% confidence intervals for hematological and biochemical parameters in methamphetamine consumers and healthy subjects**

Parameters	Mean	95% CI	Total Mean	Healthy control group (n = 60) 95% CI	P value
<b>MA abuse group (n=60)</b>					
Age (years)	33.68	30 – 37	35.47	31 – 41	0.10
BUN(mg/dL)	14.03	13.02 – 14.80	13.13	12.00 – 14.35	0.000
Creatinine(mg/dL)	1.10	1.00 – 1.20	1.02	0.90 – 1.10	0.001
<b>Total Cholesterol(mg/dL)</b>					
	221.0	210-231	219.0	209-241	0.391
Triglycerides(mg/dL)	139.82	124 – 154	141.12	120 – 152	0.474
AST(u/L)	31.23	28-3	28.45	27-31	0.000
ALT(u/L)	29.97	25-33	26.10	23-29	0.000
ALP(u/L)	65.17	58-77	56.98	51-63	0.000
Uric acid(mg/dL)	5.86	5.02-6.38	5.31	5.17-5.40	0.000
Albumin(g/dL)	4.29	4.20-4.48	4.61	4.39-4.71	0.000
Hemoglobin(g/dL)	12.43	12.32-13.47	13.48	13.60-14.22	0.000
Hematocrit (%)	39.24	37.94-40.09	42.62	42.30-4 4.65	0.000
<b>White Blood Cell</b>					
Count(109 /L)	7.87	7.32-8.67	6.44	5.97-7.09	0.000
Platelet count (109/L)	292.57	274-315	261.95	246-275	0.000

## DISCUSSION

Methamphetamine release in Presynaptic nerve terminals of neurotransmitters such as norepinephrine, dopamine and catecholamine leads to poisoning, stimulates post-synaptic receptors and inhibits reuptake of the neurotransmitters (10, 11). High levels of these neurotransmitters by auto-oxidation mechanism or destruction of monoamine oxygenase are responsible for the production of reactive oxygen species (ROS) and oxidative stress (5, 12, 13). Animal studies have well-established the effects of methamphetamine in the production of ROS (11, 14). ROS can response to macromolecules such as proteins, lipids and DNA which result in cellular dysfunction (9, 15), reaction of ROS with lipids and consequently lipid peroxidation. Many studies have shown that methamphetamine can activate transcription factors that play an important role in the signaling pathway, inflammatory gene regulation such as tumor necrosis factor (TNF- $\alpha$ ) (16). Oxidative stress can cause damage to many biological molecules in the body and is a factor involved in the pathogenesis of inflammatory diseases (17, 18). It has been demonstrated that increased inflammatory reactions after methamphetamine consumption increases microglial activity and results in secretion of pro-inflammatory cytokine, prostaglandin, nitric oxide and superoxide, all of which damage the nervous tissue. Moreover, microglia can cause inflammation by increasing the secretion of

inflammatory cytokines such as IL-1 $\beta$ , IL-6 and TNF $\alpha$  (5, 19). The results of a recent study has shown that methamphetamine can significantly change inflammatory markers such as the number of WBCs, platelets and albumin levels compared to healthy controls and increases the risk of inflammatory diseases. Another study on animals showed that methamphetamine can change biochemical variables including creatinine and albumin levels and blood cell count (20). The number of WBCs may indicate the exposure to oxidative and inflammatory response and host susceptibility to inflammatory stimuli (21). It was also demonstrated that methamphetamine increases oxidative damage and impairs the function of T-cells (22). Platelets represent an important link between inflammation and thrombosis due to their ability to interact with WBC and endothelial cells. They can also release factors that are involved in inflammation and coagulation (23). Albumin is one of the acute phase proteins with antioxidant properties that can be used as an indicator of inflammation (24, 25). As mentioned previously, the use of methamphetamine causes inflammation and oxidative stress, thus it may affect inflammatory markers such as the number of WBCs, platelets and albumin levels.

However, the mechanisms by which methamphetamine can induce inflammation is not clearly understood. Yamaguchi and his colleagues have shown that methamphetamine increases the level of pro inflammatory cytokines such as IL-1 (26, 27). Flora et al. have represented that methamphetamine can activate activator protein-1 (AP-1) which plays a role in the signaling pathways, resulting in inflammatory gene regulation within the body (6). Thus, this study shows the association of Methamphetamine use with increased oxidative stress, inflammatory markers and increased adverse effects on health. Methamphetamine is metabolized in the liver microsomes by cytochrome P450s with half-life of about 10-12 hours (28,29). Liver injury can be another effect of methamphetamine use and a range of clinical protests from acute and chronic hepatitis have been demonstrated in previous studies (30, 31). Possible mechanisms of liver damage by methamphetamine includes; lipid peroxidation and toxic effects on liver cells (32). A recent study showed that methamphetamine use increases the level of liver enzymes and increases the risk of liver diseases. Methamphetamine is a stimulant with large side effects on appetite which can lead to weight loss and malnutrition (33). It was also demonstrated

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that methamphetamine consumers have reduced hemoglobin and hematocrit concentrations compared to healthy individuals, which increases the risk of anemia in this population (34). Thus, it can be concluded that methamphetamine consumption can affect public health both directly and indirectly.

## CONCLUSION

Methamphetamine addicts have increased levels of inflammatory markers, elevated liver enzymes and increased number of WBCs and platelets, which may increase the risk of acute and chronic liver diseases. Reduction in hemoglobin and hematocrit concentrations will also increase the risk of anemia. These observations may give us a better approach to pathobiological mechanisms associated with methamphetamine use and help us solve the problems arising from the use of this drug.

## ACKNOWLEDGMENT

I would like to thank all the colleagues who worked with us in this study, especially the management and staff of Ibn Sina Hospital.

## CONFLICT OF INTEREST

The authors declare no conflict of interest between them.

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