

# Risk Factors of Mortality Due to Acute Opium Poisoning: A Report from the Largest Intoxication Referral Center in Iran

Sahar Rismantab-Sani MD<sup>1</sup>, Babak Soltani MD<sup>2</sup>, Siamak Soltani MD<sup>3</sup>, Azadeh Memarian MD<sup>3</sup>

## Original Article

### Abstract

**Background:** Studies have shown that Iran has a high rate of opiate abuse and the most prevalently used is opium. This study was aimed to evaluate risk factors in patients with acute opium intoxication who referred to Loghman Hakim Hospital, Tehran, Iran, in 2011.

**Methods:** A total number of 383 patients with acute opium overdose, who were referred to the Emergency Department of Loghman Hakim Hospital in Tehran during 2011, were enrolled into this descriptive, cross-sectional study. Clinical data including level of consciousness, vital signs, mode of consumption, medical management, and laboratory results were recorded. Independent t-test was used to analyze the results.

**Findings:** Level of consciousness at admission was lower in patients who expired compared to survivors ( $P = 0.020$ ). Respiratory depression and tachycardia were both more common among patients who expired compared to survivors ( $P = 0.001$ ). Increase in urea, creatinine, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT) was more common among patients who died compared to survivors and the relationships between death due to opium poisoning and increase in these factors were all statistically significant ( $P \leq 0.001$ ).

**Conclusion:** The findings of this study clarify the importance of clinical and laboratory findings of patients with opium poisoning in predicting their outcome, although further studies in this context are appreciated.

**Keywords:** Opium; Poisoning; Mortality; Iran

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1- Fellowship, Department of Gastroenterology and Hepatology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2- Associate Professor, Department of Pediatrics, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran

3- Assistant Professor, Department of Forensic Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Correspondence to: Siamak Soltani MD, Email: [siamaksoltani92@yahoo.com](mailto:siamaksoltani92@yahoo.com)

## Introduction

Intoxication is defined as the extension of unwanted and adverse effects of any chemical agents, drugs, and other xenobiotic materials to the whole body.<sup>1</sup> It is the 3<sup>rd</sup> fatal accident in the United States with 11% prevalence.<sup>2</sup> There are different types of poisoning agents which have various impairing effects on brain tissue and function.<sup>3-8</sup> Opium and opioids are of the most importance. Opium is the dried extract of opium poppy (*Papaver somniferum*) and consists of 12% morphine. It also includes codeine and other non-narcotic alkaloids such as thebaine and noscapine.<sup>9</sup> Morphine itself is an alkaloid which turns into heroin after chemical processing.<sup>10</sup> Opium and its derivatives are widely used for palliating chronic pain, post-surgery pain, and cancer induced and acute pain in medical centers.<sup>9</sup> Unfortunately, opium and opiates are easily available for illegal consumption and abuse by ordinary people; thus, the risk of consequent complications and intoxication are high.<sup>11</sup> Studies have shown that Iran has a high opiate abuse rate and the most prevalently used is opium.<sup>12</sup>

Despite the increasing prevalence of opium abuse and its hazards, there is still much to be known regarding different aspects of the burden, mortality risk factor, prognosis, quality of medical care and mechanisms which cause death, and other characteristics of patients with acute opium intoxication.<sup>11</sup> Our knowledge of the epidemiologic indices of opium consumption in Iran, either due to addiction or due to medical goals, and their complications is not enough.<sup>13,14</sup> This study was aimed to evaluate the risk factors of patients with acute opium intoxication who referred to Loghman Hakim Hospital, Tehran, Iran, in 2011. The goal of this study was to evaluate the effects of vital signs, level of consciousness, and mode of consumption, history of opium addiction as well as medical management, and laboratory results on prognosis of patients with acute opium overdose.

## Methods

This study was approved by the ethical committee of Tehran University of Medical Sciences. All patients with acute opium intoxication who referred to Loghman Educational Hospital during 2011 were enrolled

into the study. Patients, who reported opium consumption, decrease in level of consciousness, respiratory rate equal to or less than 12 per minute, or meiotic pupils, were included as acute opium poisoning cases. The patients with history or laboratory results of using other drugs were excluded from the study. The patients were divided into two groups of survived and expired. Demographic and basic data including age, gender, past medical history, history of opium abuse and opium detoxification during the last year, mode of consumption, and time interval between opium consumption and admission to hospital were recorded in the provided checklists. The treatment details, duration of admission, and final outcome of all patients were also recorded. Data analysis was performed by means of independent t-test in SPSS software (version 11, SPSS Inc., Chicago, IL, USA) at the significant level of  $P < 0.05$ .

## Results

In this study, a total number of 383 patients, including 323 men, with mean age of  $43.28 \pm 16.5$  years were included during a one year period. Regarding significant difference in the number of cases between the two genders, the evaluation of gender effect on mortality is impossible.

The distribution of mortality among the age groups of 15-29 years, 30-45 years, 46-59 years, and older than 60 years was 15.6%, 28.1%, 21.9%, and 34.4%, respectively. There was no significant difference regarding age distribution between the two groups. Tables 1 and 2 show clinical and laboratory data of the studied patients, respectively. Regarding electrocardiography (ECG) findings, there was no significant difference between the two groups; 89.3% of survived and 83.9% of expired patients had normal ECGs. The most common cardiac arrhythmia in survived patients was QT interval prolongation (4.6%), whereas ST segment elevation was the most common recorded arrhythmia in non-survived patients (9.7%).

The overall prevalence of underlying diseases was 18.3%, with 16.8% in survived and 34.4% in expired patients. Cardiac disease was reported in 15.6% and 8.3% of expired and survived patients, respectively. Infectious disease affected 12.5% and 0.6% of expired and survived subjects, respectively.

**Table 1.** Comparison of clinical data of survived and expired patients

Clinical data		Survived (%)	Expired (%)	P
Level of consciousness (GCS) at arrival	15	23.1	3.1	0.021
	13-15	30.5	25.0	
	10-13	23.1	37.5	
	< 13	23.3	34.4	
Time interval between consumption and admission (hour)	< 1	3.4	9.4	0.029
	1-6	26.6	15.6	
	> 6	30.4	15.6	
Mode of consumption	unknown	39.5	59.4	< 0.001
	Inhalation	24.9	0	
Respiratory rate (minute)	oral	75.1	100	< 0.001
	12-30	70.2	34.4	
	> 30	1.8	18.8	
	< 12	21.9	25.0	
Pulse rate (minute)	apnea	6.1	21.9	< 0.001
	60-100	60.3	40.6	
	> 100	25.8	59.4	
MAP (mmHg)	< 100	13.9	0	0.030
	> 90	98.8	93.3	
Pupils' size	< 90	1.2	6.7	NS
	Meiosis	78.7	70.0	
Intubation	Non-meiosis	21.3	30.0	< 0.001
	Yes	11.5	87.5	
Dose of naloxone	No	12.5	88.5	0.011
	Not infused	38.2	25.8	
	Diluted	2.9	9.7	
	Full dose	20.4	41.9	
	Diluted +booster	8.9	3.2	
Duration of admission (day)	Full dose +booster	29.6	19.4	< 0.001
	< 1	47.4	18.8	
	1-3	35.4	37.5	
	3-7	8.6	9.4	
Past medical history	> 7	8.6	34.4	0.001
	+	17.1	34.4	
	-	79.8	53.1	
History of opium abuse	unknown	3.2	12.5	0.001
	Yes	100	78.0	
History of opium detoxification during the last year	No	0	22.0	NS
	Yes	6.7	0	
	No	31.4	22.6	
The ward the patient was admitted to	Unknown	61.9	77.4	< 0.001
	Emergency room (< 6 hours)	0.3	0	
	ICU	5.2	53.1	
	Intoxication ward	86.0	21.9	
Motivate	ICU and intoxication ward	8.6	25.0	0.038
	Addiction	62.0	87.5	
	Suicide	35.1	12.5	
	Pain relief	0.6	0	
	Murder	2.3	0	

MAP: Mean arterial pressure; ICU: Intensive care unit; NS: Not significant

**Table 2.** Comparison of laboratory data between survived and expired patients

Laboratory data		Survived (%)	Expired (%)	P
ABG	Normal	17.3	19.4	NS
	Metabolic acidosis	15.5	29.0	
	Metabolic alkalosis	0.9	0	
	Respiratory acidosis	43.4	35.5	
	Respiratory alkalosis	3.2	0	
	Mix	19.6	16.1	
Urea	Normal	79.7	37.5	< 0.001
	> normal	15.7	59.4	
	< normal	4.6	3.1	
Creatinine (mg/dl)	Normal	86.6	56.2	< 0.001
	> 1.6	12.8	43.8	
	< 1.6	0.6	0	
Blood sugar (mg/dl)	55-200	83.5	80.6	NS
	> 200	14.2	19.4	
	< 55	2.4	0	
CPK (U/L)	24-170	68.9	21.9	< 0.001
	> 170	30.8	78.1	
	< 170	0.3	0	
LDH (U/L)	< 480	72.7	9.4	< 0.001
	> 480	27.3	90.6	
Na (mEq/l)	135-145	79.4	77.4	NS
	> 145	18.9	16.1	
	< 135	1.7	6.5	
K (mEq/l)	3.5-5	86.0	74.2	0.001
	> 5	7.3	25.8	
	< 3.5	6.7	0	
SGOT (U/L)	Normal	69.1	25.0	< 0.001
	> 37	30.9	75.0	
SGPT (U/L)	Normal	79.0	53.1	< 0.001
	> 41	21.0	46.9	
ALP (U/L)	80-360	88.0	78.1	NS
	> 360	12.0	21.9	

ABG: Arterial blood gas; CPK: Creatine phosphokinase; LDH: Lactate dehydrogenase; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; ALP: Alkaline phosphatase; NS: Not significant

None of the expired patients had a history of pulmonary, hepatic, brain, or glandular diseases. However, pulmonary diseases were more prevalent in survived patients than non-survived subjects (18.6% vs. 0). The prevalence of other diseases, though higher than expired patients, was unremarkable in survived patients. Type of underlying diseases showed a statistically significant difference between the two groups ( $P = 0.001$ ).

### Discussion

In this study, the mortality risk factors of acute opium poisoning were investigated. The study sample consisted of patients who were purely intoxicated with opium, according to the American Association of Poison Control Centers

(AAPCC) criteria,<sup>9</sup> and referred to the largest intoxication center of Iran (Loghman Hakim Hospital, Tehran). The results showed that the prevalence of acute opium intoxication was higher in men than women. In addition, the highest frequency of intoxication was observed in the 30-45 years age group. These results are both in accordance with that of the study by Shadnia et al.<sup>15</sup>, who reported that 24179 cases of intoxication referred to the same center during 2003. They found that although narcotic poisoning is the most prevalent cause of intoxication, opium poisoning is the most fatal cause with a mortality rate of up to 41.5%. Karbakhsh and Zandi<sup>16</sup> reported the mean age of patients with acute opium intoxication as  $36.9 \pm 15.0$  years in Iran which is 7 years higher

than the present study. This difference might be due to sampling; they included all patients with opium poisoning who used other drugs and agents at the same time. They reported an 8.8% overall rate of mortality due to opium intoxication which is in good consistency with the present study result (8.4%). In the present study, it was concluded that oral consumption was the most prevalent mode which is compatible with previous reports.<sup>17</sup>

The high rate of mortality seen in patients older than 60 years suggests the need for prompt and intensive care for the management of this age group. Moreover, having an underlying disease was a significant risk factor of mortality which caused a 3-fold increase in mortality rate with 95% CI: 1.3-6.7. Taking into account the higher probability of having an underlying disease in the elder patients, age is an important factor in confronting patients with opium intoxication.

Intubation, oral consumption of opium, hospitalization in the intensive care unit (ICU), admission course of more than 7 days, tachycardia, mean arterial pressure (MAP) of less than 90 mmHg, time interval of more than 6 hours between opium consumption and admission, and having an underlying disease are all risk factors which were directly related with acute opium intoxication mortality.

On the other hand, suicidal attempt, hypokalemia, normal blood levels of Cr, LDH, urea and liver enzymes, in addition to negative history of opium consumption and booster dose of naloxone are preventive factors for mortality due to acute opium poisoning. However, logistic regression, which omits the confounding effect of variables on each other, showed that MAP of less than 90 mmHg and suffering from an underlying

disease were independently related to mortality. Hence, MAP of less than 90 mmHg increased the mortality rate up to 38 fold [95% Confidence interval (CI): 3.24-444.7] which is a striking finding.

## Conclusion

Some key points should always be kept in mind when treating patients with acute opium intoxication. First, the precise recording of medical history, especially regarding chronic and underlying diseases, could help physicians manage patients much better, particularly for those patients whose past medical history are remarkable. Second, considering the 33 times higher probability of death in patients with MAP of less than 90 mmHg, hemodynamic stabilization must be the first and most important step in treating patients with acute opium poisoning.

As Loghman Hakim Hospital is the largest referral intoxication center in Iran and is located in the center of Tehran, the capital, we can assume that it has almost all the criteria of a suitable population. Thus, we can generalize these results to the Iranian population with approximate estimation. Further studies regarding data registering in this group of patients are suggested.

## Conflict of Interests

The Authors have no conflict of interest.

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## عوامل خطر مؤثر بر مرگ و میر ناشی از مسمومیت حاد اوپیوم: گزارشی از بزرگ‌ترین مرکز مسمومیت در ایران

دکتر سحر ریسمان تاب ثانی<sup>۱</sup>، دکتر بابک سلطانی<sup>۲</sup>، دکتر سیامک سلطانی<sup>۳</sup>، دکتر آزاده معماریان<sup>۳</sup>

### مقاله پژوهشی

### چکیده

**مقدمه:** نتایج مطالعات انجام شده، میزان بالایی از سوء مصرف مواد را در ایران نشان می‌دهد. هدف از انجام پژوهش حاضر، ارزیابی تأثیر علایم حیاتی، سطح هوشیاری، نحوه مصرف، شرح حال اعتیاد به اوپیوم، اقدامات درمانی و نتایج آزمایشگاهی بر روی پیش‌آگهی بیماران با مصرف حاد اوپیوم بود.

**روش‌ها:** ۳۸۳ بیمار که در سال ۱۳۹۰ با مصرف حاد اوپیوم به بخش اورژانس بیمارستان لقمان حکیم مراجعه کرده بودند، به مطالعه وارد شدند. اطلاعات بالینی شامل سطح هوشیاری، علایم حیاتی، نحوه مصرف، اقدامات درمانی و نتایج آزمایشگاهی در چکلیست ثبت گردید و مورد تجزیه و تحلیل قرار گرفت.

**یافته‌ها:** سطح هوشیاری در زمان بستری، در بیماران فوت شده در مقایسه با بیماران نجات یافته پایین‌تر ( $P = ۰/۰۲۰$ ) و دپرسیون تنفسی و تاکی‌کاردی در بیماران فوت شده در مقایسه با بیماران نجات یافته شایع‌تر بود ( $P = ۰/۰۰۱$ ). سطح اوره، کراتینین، (CPK) Creatine phosphokinase، (LDH) Lactate dehydrogenase، (SGOT) Serum glutamic oxaloacetic transaminase و (SGPT) Serum glutamic-pyruvic transaminase در بیماران فوت شده در مقایسه با بیماران نجات یافته افزایش یافته بود. همچنین، ارتباط معنی‌داری بین مرگ ناشی از مسمومیت با اویپوئیدها و افزایش عوامل مذکور مشاهده شد ( $P \leq ۰/۰۰۱$ ).

**نتیجه‌گیری:** نتایج مطالعه حاضر، اهمیت یافته‌های بالینی و آزمایشگاهی را در بیماران مبتلا به مسمومیت با اوپیوم جهت پیش‌بینی پیامد آن روشن می‌سازد؛ اگرچه مطالعات بیشتری در این زمینه باید انجام گیرد.

**واژگان کلیدی:** اوپیوم، مسمومیت، مرگ و میر، ایران

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۱- فلوشیپ، گروه گوارش و کبد، دانشکده پزشکی، دانشگاه علوم پزشکی شهید بهشتی، تهران، ایران

۲- دانشیار، گروه اطفال، دانشکده پزشکی، دانشگاه علوم پزشکی کاشان، کاشان، ایران

۳- استادیار، گروه پزشکی قانونی، دانشکده پزشکی، دانشگاه علوم پزشکی ایران، تهران، ایران