

Refined Opium Extract (Shireh) Poisoning: A 10-Year Retrospective Study in a Referral Poison Control Centre in Iran

MARZIEH AZARAKHSH¹, MITRA RAHIMI^{2*}, NASIM ZAMANI^{3,4}, SEPIDEH ARBABI BIDGOLI⁵

¹Faculty of Pharmacy and Pharmaceutical Sciences, Islamic Azad University, Tehran Medical Sciences (IAUTMU)

²Toxicological Research Center, Excellence Center of Clinical Toxicology, Department of Clinical Toxicology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Social Determinants of Health Research Centre, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁴Department of Clinical Toxicology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁵Department of Toxicology and Pharmacology, Islamic Azad University, Tehran Medical Sciences (IAUTMU), Iran

Abstract

Background: There is limited data on refined opium extract (Shireh) abuse, especially the magnitude of its complications and its mortality rates. To bridge such a gap, in this study, we aimed to investigate the frequency of pure refined opium extract poisoning and its consequences in a sample of our patients.

Methods: This retrospective study was conducted on all the patients presented to our center with pure refined opium extract poisoning. Patients' demographics, clinical and laboratory data, and outcome were collected during a ten-year period between 2006 and 2016. The included patients were divided into two groups: those who remained conscious and those who developed loss of consciousness. However, they were compared subsequently.

Results: A total of 227 patients were evaluated. Most (75.8 %) of them were male. Mean age was 38.26±25.91 years. We found a significant correlation between educational (.038), marital (<.001), and occupational status (<.001) and age-gender groups of the patients. The mean amount of refined opium extract consumed was 4400 mg which had significant correlation with hospitalization period (<.001) and on-arrival rhabdomyolysis (<.001). We also found a correlation in vomiting (<.001), dizziness (.015), respiratory distress (.001), and apnea (<.001) between the two groups. The mean hospitalization period was 2.3 days and the mortality rate was 1.76%.

Conclusion: Naloxone therapy use effective in most cases of pure poisoning with refined opium extract. There were four deaths incidences three of which happened due to cardiopulmonary arrest following body packing. Further studies in this type of poisoning are recommended.

Keywords: Opium, Toxicity, Poisoning, Mortality, Iran.

How to cite this article: Azarakhshi M, Rahimi M, Zamani N, Arbabi Bidgoli S. Refined Opium Extract (Shireh) Poisoning: A 10-Year Retrospective Study in a Referral Poison Control Centre in Iran. *Asia Pac J Med Toxicol* 2021; 10(1):12-17

INTRODUCTION

Drug addiction is known as one of the health, medical, and social problems in Iran (1). Opiates, alcohol, and stimulants are used in almost all countries. However, the patterns of their use/abuse vary from country to country and across time (2,3). According to the official statistics of Iran Drug Control Headquarters, there are 2.802.800 addicts in Iran by aging between 15 and 64 years. The prevalence rate of drug addiction in Iran was reported to be 5.39 %. The most common substance abused in Iran is opium followed by heroin, crack, and methamphetamine (4). Moreover, based on the latest Iranian Legal Medicine Organization report, although there is a decline in deaths due to drug abuse in this country from 2004 to 2013 years, there are still eight people dying of addiction every day (5).

Opium is a brown gum/latex obtained from incision in unripe *Papaver somniferum* capsules and has analgesic

effects(6, 7). Thirty alkaloids exist in opium with morphine, codeine, thebaine, noscapine, narceine, and papaverine being the most common ones (8). Opioids have analgesic, central nervous system (CNS) depressant, and euphoric properties. Opioid receptors, - transmembrane neurotransmitters- are mu (μ or MOP-R) Kappa (κ or KOP-R), delta (δ or DOP-R), and NOP-R (9). They couple with G-proteins initiating signal transduction (10).

Refined opium extract which is called Shireh in Iran, is a very strong opium extract. The pure opium or burned remains of used opium is first dissolved in hot water and then heated. Following filtration, it is re-heated to the boiling point until all the water evaporates resulting in a firm substance. Refined opium extract is only made from opium-soluble compounds. Therefore, morphine and codeine alkaloids have a higher concentration in the refined opium extract in comparison to the pure opium (11). There are no insoluble compounds in refined opium extract including papaverine and noscapine. The effects

*Correspondence to: Mitra Rahimi, MD, Department of Clinical Toxicology, Loghman Hakim Hospital, South Karegar Street, Tehran, Iran. Tel/ Fax: 00982155424041, Email: mrahimi744@gmail.com

of refined opium extract consumption include analgesia and sleepiness, dizziness, blurred vision, nausea, respiratory depression, hypothermia, hypotension, constipation, urinary retention, decreased LH and TRH and ACTH hormones, and increased prolactin levels. Effects which are particularly noticeable in addicts include weight loss, chronic constipation, chronic fatigue and sleepiness, pulmonary obstructive diseases, reduced fertility, and altered memory (11).

In cases of toxicity, the primary step is checking three major physical findings: mental alteration, pinpoint pupils, and respiratory depression. Following the diagnosis, the treatment begins with ventilation support, gastric lavage or administration of activated charcoal, and an opioid antagonist (12).

In spite of the significance of this social and health issue, to the best of our knowledge, only six studies have been conducted on refined opium extract poisoning. Addiction to refined opium extract was mentioned in Yazd (31 cases, 33.7%) (13), Sanandaj (62 cases, 41.3%), Tehran (14 cases, 8.75%), Quechan (490 cases, 65%), Mashhad (2 cases, 3.77%), and Gorgan (490 cases, 16.31%) [14-18]. Nonetheless, there is no exact data on the use of refined opium extract in other provinces and countries, and in particular the magnitude of the complications and deaths caused by it. Hence, we aimed to investigate the prevalence of refined opium extract consumption and its consequences in patients who referred to the emergency room of a referral toxicology center in Tehran, Iran.

METHODS

This cross-sectional retrospective study was carried out on all refined opium extract-poisoned patients who referred to Loghman Hakim Hospital in Tehran-Iran from March 2006 to March 2016. Patients with pure refined opium extract poisoning and a positive opium test were selected for this research. To gather the required data, a questionnaire was designed and developed by the researcher which contained the patients' demographic information, on-presentation vital signs and laboratory tests, the duration of hospitalization, the treatments given, and the outcome. The questionnaire was completed by all the selected patients. The ingested dose was calculated based on the amount of the refined opium extract ingested by the patients given by the history and considering the mean morphine amount of the opium to be 5%. The participants of the study were divided into two groups: those who remained conscious and those who developed loss of consciousness (LOC) which were both compared subsequently.

The collected data was analyzed through the social package for statistical analysis (SPSS) software version 20. The data was presented by mean \pm SD for continuous variables and frequency for categorical variables. Distribution of the data was tested by the Kolmogorov-Smirnov test. The Chi-square and Fisher's exact tests were used to analyze the qualitative variables. Statistical comparison was made using Mann-Whitney U-test for nonparametric variables and independent t-test for parametric ones. A P-value of 0.05 or less was considered to be statistically significant. Written informed consent was waived

by our local ethics committee because of the retrospective nature of the study. The ethics committee in Islamic Azad University Pharmaceutical Science Branch and Shahid Beheshti University of Medical Sciences approved the study.

RESULTS

A total of 302 patients had been admitted to our center with refined opium extract poisoning during the study period, 75 of whom were excluded because of mixed drug poisoning. The number of refined opium extract-poisoned patients referring to our center had increased since 2006 with most of the cases being reported between 2013 and 2015 years (135 cases, 59.5%), and the least from 2016 (12 cases, 5.3%). The mortality rate was 1.76% (four patients). All patients had ingested refined opium extract. Fifty-six cases (24.66%) had been accidentally poisoned by its consumption especially age under 10 years. while the rest (75.33%) were refined opium extract abusers who had overdosed on it. The average duration of addiction in the latter group was 10.75 years.

The majority of the patients were male 75.8 % (172 cases). Mean age was 38.26 ± 25.91 years (range; 3 days to 86 years). The average age was 41.77 ± 25.13 and 27.29 ± 25.45 in males and females, respectively. The majority of the cases were younger than 10 years (22.5%), followed by 51-60 years (15.4%) and 21-30 years (14.5%). Of the patients younger than 15 years, 93% had been poisoned by refined opium extract accidentally. On the other hand, all of the patients older than 15 years had consumed refined opium extract intentionally. Table 1 shows demographic information including the educational, marital, and occupational status of the studied population revealing this toxicity to have a significant correlation with age and gender.

The mean amount of the ingested refined opium extract was 4443 mg of opium (range; 0.5 to 40.000 mg). The abused amount was 4570 mg in men and 4202 mg in women. Individuals younger than 15 years had consumed a mean of

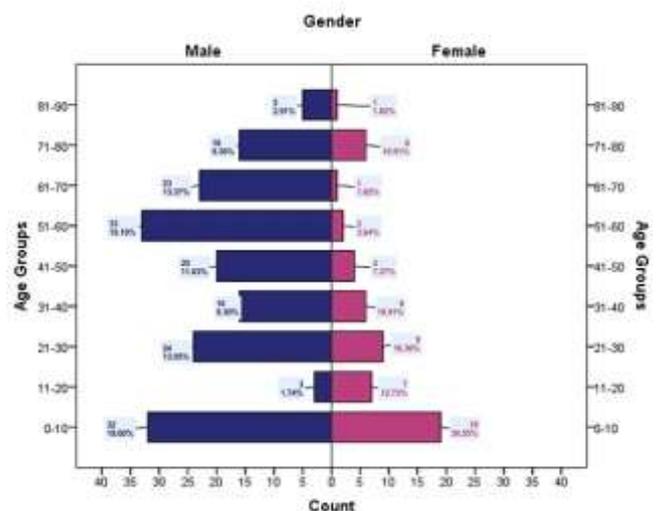


Figure 1. Patients' age groups among males and females

103.49 mg and those who were older than 15 had taken a mean of 5385 mg. Correlations were found between the abused amount of refined opium extract and hospitalization period ($<.001$), and on-arrival rhabdomyolysis ($p= <.001$). Rhabdomyolysis was present in three men aged 28, 77, and 81 years.

Most of the cases had presented with vomiting ($n=41$, 18.06%) followed by respiratory acidosis ($n=29$, 12.77%) and apnea ($n=24$, 10.57%). Arterial fibrillation and abdominal pain were observed in only one case (0.44%). As mentioned earlier, we classified our patients into two groups

of conscious and unconscious. Table 2 demonstrates the physical findings of the patients. A correlation was found in the frequency of vomiting, dizziness, respiratory distress, cyanosis, and apnea between the two groups.

Table 3 presents the on-arrival presentation of our patients along with vital signs and arterial blood gases. In a multiple regression analysis using Table 3 variables, no independent factor could prognosticate loss of consciousness in our series.

Apart from the administration of activated charcoal, gastric lavage, and ventilation support, most of the patients received naloxone (206 cases, 90.74%). The mean

Table 1. Demographic characteristics comprising A) Age groups. B) The educational, marital and occupational status of the studied population.

Demographics	<15 years Female (n=20)	<15 years Male (n=32)	>15 years Female (n=35)	>15 years Male (n=140)	P-value
Education					
<high school diploma (%)	20 (9.5)	32 (15.2)	34 (16.2)	124 (59.0)	.038
≥high school diploma	0	0	1(5.88)	16 (94.1)	
Marital Status					
Single	20 (20.4)	32 (32.6)	19 (19.3)	27 (27.5)	<.001
Married/Divorced	0	0	16 (12.4)	113 (87.6)	
Employment					
Unemployed	20 (21.5)	32 (34.4)	18 (19.3)	23 (24.7)	<.001
Housewife	0	0	16 (100%)	0	
Employed	0	0	1 (1.1)	89 (98.8)	
Retired	0	0	0	28 (100)	

Table 2. the physical findings of the included patients

Clinical Manifestations	Non-conscious subjects (n=167)	Conscious subjects (n=60)	P-values*	Odds Ratio	95% Confidence Interval
Vomiting	16(9.58%)	25(41.66%)	<.001	.148	.072-.307
Diarrhea	5(2.99%)	1(1.66%)	NS	1.821	.208-15.911
Abdominal pain	0	1(1.66%)	NS	3.831	3.076-4.770
Headache	2(1.19%)	1(1.66%)	NS	.715	.064-8.033
Dizziness	8(4.79%)	11(18.33%)	.001	.224	.085-.589
Seizure	3(1.79%)	2(3.33%)	NS	.530	.086-3.255
Respiratory Distress	2(1.19%)	5(8.33%)	.015	.133	.025-.707
Apnea	8(4.79%)	16(26.66%)	<.001	.138	.058-.344
Cyanosis	5(2.99%)	7(11.66%)	.017	.234	.071-.767
Agitation	16(9.58%)	3(5%)	NS	2.013	.565-7.170
Tremor	4(2.39%)	2(3.33%)	NS	.712	.127-3.989
Weakness	3(1.79%)	3(5%)	NS	.348	.068-1.771
Rhabdomyolysis	3(1.79%)	0	NS	1.366	1.262-1.478
Arterial Fibrillation	1(0.59%)	0	NS	1.361	1.259-1.472
Respiratory Acidosis	24(14.37%)	5(8.33%)	NS	.542	.197-1.491

*Significance at the 95% level
NS: Not significant

Table 3. On arrival presentations, vital signs and arterial blood gases of 227 patients.

Predictor Factors	Mean		Std. Deviation		Significant P-values*	Multivariate analysis R Square and P value
	LOC (n=167)	No LOC (n=60)	LOC (n=167)	No LOC (n=60)		
Age(year)	38.29	38.18	26.87	23.25	NS	R2= .087 P= .414
Time between consumption and admission (hour)	9.30	14.30	9.53	19.45	.019	
Refined opium extract dose (mg)	3905.56	5992.88	10218.06	12480.06	NS	
Hospital Stay (day)	2.40	2.11	3.65	2.10	NS	
Naloxone dose (mg)	1.50	1.36	2.10	1.46	.005	
Vital Signs						
Pulse rate (/min)	92.07	92.22	20.00	18.49	NS	R2= .041 P= .251
Respiratory rate (/min)	18.85	17.82	7.22	5.41	NS	
Systolic Blood Pressure	109.46	117.05	22.63	23.29	.027	
Diastolic Blood Pressure	70.74	74.55	13.38	13.14	NS	
Temperature	36.75	36.76	.74	.48	NS	
Acid-Base Status						
PH	7.31	7.35	.10	.14	NS	R2= .038 P= .157
PCO2	48.39	49.12	14.87	14.37	NS	
HCO3	24.59	26.58	6.21	7.19	.029	

LOC= Loss of Consciousness at arrival

*Significance at the 95% level

NS: Not significant

intubation and intensive care unit surveillance. Despite the continuous care of the staff, four patients died, three of whom were body packers and one had committed suicide.

DISCUSSION

The main purpose of the current study was to investigate the prevalence and characteristics of refined opium extract poisoning in patients who referred to emergency department of Loghman Hakim Hospital in a 10-year-period. Despite the high prevalence of this poisoning in Iran, few studies are available on it in the literature. As demographics revealed, there was a strong relationship between poor education, unemployment, and marital status of the patients and refined opium extract consumption/abuse.

The findings associated with marital status are all parallel with other inquiries conducted in Tehran, Yazd, Quechan, Sanandaj, Mashhad, and Gorgan provinces (13-19); however, they are in contrast with a study piloted in Tehran (15). The most justifiable reasons for the increased presence of married refined opium extract addicts are mandatory drug test before marriage, unsuitable acquaintances and companionship after marriage, unsuccessful matrimonies, and raising economic poverty. However, these parameters could not be tracked in our 10-year study due to its retrospective nature. The slight difference in one study might be because of low sample size limited to certain addiction treatment centers of Tehran. Furthermore, based on the demographic data, most of the cases of refined opium extract intoxications were unemployed

individuals. Although this finding is similar to most of the available studies in this domain (14-17), it contradicts with a study conducted by Lotfi and colleagues in Yazd which may show the cultural differences between the users all around the country [13]. Additionally, all the abovementioned studies showed similar results regarding the higher rate of abusing refined opium extract among poorly-educated individuals (13-20). Thus, early training in educational centers is an important step to prevent drug abuse that has been neglected thus far.

Drug toxicity can be affected by the patient's age and gender. Most of the cases were males under 10 years old, followed by 51- to 60-year-old men. Despite the fact that in all of the studies conducted in Iran the

However, the existence of the inactive substances in opium along with the benzyloisoquinoline postpones absorption and reduces the set of symptoms. Moreover, papaverine and noscapine alkaloids have a relaxation effect on intestinal muscle. This makes the absorption of orally consumed opium prolonged and decreases nausea and vomiting symptoms. Hence, the signs and symptoms of ingested opium begin after 8 hours in the untreated cases. As stated earlier, due to the process of making refined opium extract, the toxic effects of morphine magnify in it causing loss of consciousness, respiratory distress, apnea, coma, and death (21).

Among the manifestations, we found a significant correlation between loss of consciousness and respiratory distress and apnea. Besides, we found vomiting to have a substantial correlation with loss of consciousness. These are comparable to other studies to some extent (23). In addition, we found significant correlations between the abused amount of refined opium extract and rhabdomyolysis ($p < .001$). Rhabdomyolysis has not only been reported in patients presenting with acute opiate intoxication, but also can be due to its routine daily consumption (24) as seen in three of our cases. In our cases, rhabdomyolysis may have occurred due to changes in refined opium extract doses. Furthermore, in the present study, the central nervous system signs existed in 10.6% of the patients, which is lower than other studies (25.4%, 64%, 30.3 %)(25–27). Yet, CNS signs are stated to be common primary signs of opium-poisoned patients (28).

In the present study, the mean time elapsed between the consumption of refined opium extract and admission to the emergency department was 11 hours. Remarkably, this average interval time was lower in patients presented with loss of consciousness. Despite emergency treatment, four of our patients died. Considering mortality rates in other studies on crude opium or opioid-substance toxicity, we had less fatalities (19,23). Studies have shown that mortality due to opioid toxicity increase with aging. This finding proposes the necessity of prompting intensive care for managing older cases. In addition, it poses the prominence of evaluating underlying disease as a significant risk factor for fatality.

The retrospective nature of the current study is probably the most important limitation of our work. Although some studies have been conducted in Iran on refined opium extract consumption, the present study is the largest one reporting all refined opium extract-poisoned patients referring to a referral center in 10 years. Researchers who are keen on running similar studies should consider that refined opium extract consumption and addiction is a native problem in Iran and the literature is not sufficiently rich especially regarding the prevalence and outcome of consuming refined opium extract.

CONCLUSION

Naloxone therapy is effective in most refined opium extract-poisoned patients probably due to its slow absorption. Refined opium extract is a native problem in Iran and literature is not available on its prevalence, complications and outcome. Further studies on this social and health issue are recommended to avid scholars.

ACKNOWLEDGEMENT

The authors express their sincere thanks to the staff of archive section of Loghman Hakim Hospital for their assistance.

Conflict of Interest: None to be declared.

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