

## Risk factors for endotracheal intubation and mechanical ventilation in patients with opioids intoxication

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### ABSTRACT

**Objectives:** Patients poisoned with opioids sometimes need endotracheal intubation with or without the use of mechanical ventilation. This study was done to determine the prognostic risk factors for of the need for endotracheal intubation and mechanical ventilation.

**Methodology:** In this cross-sectional study which was performed in Isfahan (Iran), one hundred (n=100) opioid poisoned patients whom their overdoses were diagnosed by their full and reliable history, physical examination and positive response to naloxone; vital signs at the hospital admission, blood biochemistry, ABG details and also the type and estimated dosage of opioid, route of consumption, and their need to mechanical ventilation were evaluated.

**Results:** Patients were mostly aged between 20-40 years old. Seventy nine patients were male and 26 cases (21 men) required endotracheal intubation and 15 cases (14 men) needed both intubation and mechanical ventilation. The most consumed opiates among the poisoned patients were opium (35%), heroin (16%), Tramadol (15%), Methadone (9%), crack (6%), Diphenoxylate (4%) and others (15%). There was a significant difference between the mean heart rates and respiratory rate of the patients who were connected to the ventilator and others (99.8±21.8 and 87.3±16.3; p=0.01). The lower level of consciousness [OR: 2.2 95% Confidence Interval (CI): 1.2-4.2], and lower admission level of hemoglobin (OR: 3.6; CI:1.2-10.8) were among the factors for predicting the need for intubation and ventilation.

**Conclusion:** Determining the risk factors with prognostic value for the need to intubation or ventilation seems to be necessary for improving the standard of therapy in opioids poisoned patients.

**KEY WORDS:** Intoxication, Opioids, Addiction, Risk factor, Intubation, Mechanical ventilation.

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### INTRODUCTION

Opioid poisoning is one of the most important causes of mortality due to poisoning in some countries and has currently an increasing trend.<sup>1-3</sup>

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Opioid poisoning is the third common poisoning and the most common cause of mortality in our referral poisoning emergency department.<sup>4,7</sup>

Respiratory failure due to reduction in sensitivity to carbon dioxide or respiratory muscle fatigue is one of the consequents of opioid overdose.<sup>8,9</sup> In addition it is now documented that noncardiogenic pulmonary edema is also one of the most important complication of opiate overdose which typically occurs within 24 to 36 hours.<sup>10</sup> The time of presence of toxic symptoms and course of treatment are different according to the type of the opioid and its pharmacokinetic properties and also the usage methods.

Naloxan is a safe, non-abusable and FDA approved substance which reverses the effects of opioids on the brain and respiratory system and restores breathing.<sup>3,11,12</sup> Endotracheal intubation procedure by nasal or orotracheal proper ventilation support must be conducted as soon as possible in case of the presence of acute respiratory distress syndrome (ARDS). The diagnosis of ARDS is based on clinical, hemodynamic and oxygenation.<sup>13</sup>

Unfortunately in some cases, opioid poisoned patients do not show a complete response such as awakening or the establishment of normal respiration to the prescription of naloxone and will thus require endotracheal intubation with or without the use of mechanical ventilation.<sup>14-17</sup> Risk factors affecting the need of intubation and mechanical ventilation in patients poisoned with opioids have not been determined yet. Only in a study in Spain, benzodiazepine use was associated with absence of respiratory arrest in opiate overdose cases.<sup>18</sup>

Therefore, considering that opioids poisoning is the most common cause of mortality in poison management departments in Iran and due to the limitation of available medical facilities and equipments, awareness of the risk factors could be of help to the emergency physicians in making decisions about the patient need to intubation and connection to the ventilator. Hence, in this study, we have tried to determine and compare various factors as probable risk factors among patients with endotracheal intubation with or without the use of ventilator, and those patients who do not need such actions. This study was done to determine the prognostic risk factors for the need of endotracheal intubation and mechanical ventilation in order to deal more preparedly with patients poisoned with opioids.

## METHODOLOGY

In this descriptive cross-sectional study which was conducted in Noor and Ali Asghar [PBUH] general teaching hospital one hundred (n=100) poisoned patients with different opiate overdoses were recruited. This University hospital is located in Isfahan and is the referral poisoning management center for the central part of Iran. The protocol of our study was approved by the Bioethics committee of Isfahan University of Medical Science (IUMS). Opioid poisoning was diagnosed by a full and reliable history, physical examination (miotic or pinpoint pupils, decreased consciousness level, respiratory depression), complete or partial response to naloxone, or noncardiogenic pulmonary edema. Patients with

past history of cardiac problem were excluded. Patients were chosen with census-type sampling. To determine the predicting variables associated with intubation and mechanical ventilation in study patients, a check list was prepared according to the opinion of our clinical toxicology experts and was including: vital signs on admission to the hospital such as respiratory rate, pulse rate, temperature, arterial blood pressure; laboratory tests including sodium, potassium, fasting blood sugar, urea, creatinine, white blood cells, hemoglobin, Arterial Blood Gas (ABG), opiates type, amount and the route of abusing it, and the time elapsed from the usage of naloxone. Patients who needed intubation or mechanical ventilation were compared to those with no medically indicated need for intubation or mechanical ventilation.

The data was analyzed using SPSS version 17.0 statistical software. Descriptive analysis was used for reporting relevant qualitative variables and quantitative variables were compared and analyzed using independent samples T test. Logistic regression was used to predict the effect of variables related to intubation and mechanical ventilation. P value less than 0.05 was considered significant.

## RESULTS

Seventy nine (out of 100) of study patients were male. 26 cases (21 men and 5 women) had a certain medical indication for endotracheal intubation and fifteen cases (14 men and a woman) needed mechanical ventilation as well.

Although the need for intubation was more common in 20-40 years old poisoned patients, but there was not a significant difference between the patients aged under 20 years old and the patients over 40 (p= 0.07). Mechanical ventilation was more prevalently needed in patients with 40 years old or more (P= 0.003).

The most consumed opiates among the poisoned patients were opium (35%), heroin (16%), Tramadol (15%), Methadone (9%), crack (6%), Diphenoxylate (4%) and others (15%). Although the need of mechanical ventilation was more common in Diphenoxylate poisoned patients (75%); there was no significant difference between the type of opioids used and the need for endotracheal intubation and ventilation in poisoned patient.

Among different routes of opiates abuse, the need for intubation and mechanical ventilation were more needed in opiate inhalation (33.3%) and oral opiate users and abusers (20.3%). However there was no statistically significant difference between

Table-I: Admission vital signs in opioid poisoned patients with respect to the need for intubation and mechanical ventilation.

Vital signs	Intubation		P value	Mechanical ventilation		P value
	Yes	No		Yes	No	
Heart rate (/min)	96.3±18.3	86.7±16.3	0.01	99.8±21.8	87.3±16.3	0.01
Respiratory rate (/min)	12.4±11.7	13.2±7.48	0.69	17.7±11.1	12.21±8.05	0.02
Arterial Blood pressure (mmHg)	88.5±16.9	84.6±9.60	0.17	94.1±19.3	84.07±9.60	0.07
Temperature (C)	36.9±0.37	37.06±0.59	0.30	36.9±0.39	37.05±0.56	0.49

The results are expressed in (mean±SD)

the way of drug consumption and the intubation ( $p=0.24$ ) and also mechanical ventilation ( $p=0.19$ ). The survey revealed that there was no statistically significant correlation between the need for intubation and the consumption of other medications along with opioids ( $P = 0.47$ ). In addition, there was no statistically significant correlation between concomitant consumption of medications and the need for mechanical ventilation ( $P = 0.41$ )

The need for intubation and mechanical ventilation according to vital signs is presented in Table-I. The mean amount of naloxone dosage was significantly different in patients who need for intubation ( $1.6 \text{ mg} \pm 0.8$ ,  $P = 0.02$ ) and those who needed intubation and were connected to mechanical ventilation ( $1.73 \pm 0.83$ ;  $P$  value 0.01).

The level of urea, creatinine, sodium, potassium, fasting blood sugar (FBS), and the count for platelets, white blood cells, and also indexes for arterial blood gas analysis ( $\text{PaCO}_2$ , PH,  $\text{PaO}_2$ ,  $\text{HCO}_3$ ) were not significantly different between the intubated and non-intubated patients.

Only 13.3% and 2.7% of the patients with intubation and ventilation survived without complications respectively and most of the patients with intubation (52.6%) and ventilation (36.8%) survived with complications.

In our analysis the level of consciousness [OR: 2.2 95% Confidence Interval (CI): 1.2-4.2], and hemoglobin level (OR: 3.6; CI: 1.2-10.8) were the determining factors in predicting need for intubation and ventilation.

The level of consciousness on admission, the time interval between the ingestion of opiate and

Naloxone therapy and the patients' hemoglobin were among the determining factors in predicting the need for mechanical ventilation (Table-II).

## DISCUSSION

To our best of knowledge there are limited and few studies which presented related factors to intubation and mechanical ventilation in opiate poisoned patients. One study in Spain has described the factors associated with respiratory arrest in opiate overdoses among injecting drug abusers. It showed that the concomitant use of alcohol, cocaine or methadone is not associated with suffering respiratory arrest in opiate overdose and lack of previous consumption of benzodiazepines was proved to have a statistically significant association with suffering of a respiratory arrest (OR:0.462;  $p=0.017$ ).<sup>18</sup> In our study we did not find any relationship between concomitant drug use and intubation or ventilation which may be due to the differences between the type of abused opiate. In another study it was shown that co administration of other intoxicants was not associated with increased risk of death or adverse events in the first 24 hours of follow up.<sup>19</sup>

Our study showed that anemia at the time of admission was associated for the medical indication of intubation. Interestingly heart rate was not a predicting factor of intubation and mechanical ventilation, but it was significantly higher in patients who needed intubation and ventilation. Higher heart rates were seen in poisonings with Diphenoxylate and acute pulmonary edema due to heroin and methadone overdose.

Table-II: Factors for prediction of need for mechanical ventilation in patients with opioids poisoning.

Intubation and Mechanical ventilation Risk factors	Odds ratio (OR)	P value	95% Confidence interval (CI)	
			Lower	Upper
Delayed Naloxone therapy	0.23	0.02*	1.03	1.53
Lower level of consciousness	0.99	0.000*	1.57	4.6
Low admission blood hemoglobin	2.4	0.012*	1.7	84.9

Our results also showed that the frequency of tachypnea is higher in patients who needed ventilation. Some opiates such as heroin induced noncardiogenic pulmonary edema that may have resulted in increasing respiratory rate as one of the indications of mechanical ventilation.

However, there exists statistically significant correlation between the type of the abused drug and the need for mechanical ventilation. Patients who had consumed more Diphenoxylate, have been connected to the ventilator more frequently which may be due to the prolonged effect of this abused drug or the possibility of further dosage consumption of this medication by the patients. The level of consciousness and hemoglobin level were important determining factors in predicting the need for intubation and ventilation.

In conclusion determining risk factors with prognostic value for the need to intubation or ventilation seems to be necessary for improving the standard of therapy in opioids poisoned patients. Our limitations for this study were determining the amount of drug which was abused by the poisoned patients and recall bias.

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#### Author's Contribution:

NEM, AMS and AY contributed for the idea and design of the study. FH, GD and SMMM gathered the data. NEM and AMS and PM made data interpretation. PM drafted the manuscript and all authors critically revised it for important intellectual content and approved the final version. Authors had no conflict of interest.

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