# Higher Morbidity and Mortality in Trauma Intensive Care Unit Patients with Opium Addiction

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### **Original Article**

#### **Abstract**

**Background:** Opium addiction is associated with multiple physical, psychological, and social problems. The aim of this study was to compare the risk of morbidity and mortality in opium-addicted and non-addicted trauma patients admitted to the intensive care units (ICUs) of trauma center of Kerman Province, Iran.

**Methods:** In this cohort study, a total of 200 addict and non-addicted patients who were admitted due to trauma in ICUs of Shahid Bahonar Hospital in Kerman during 9 months of 2018 were included. Patients were compared in terms of mortality, incidence of pressure ulcers, incidence of organ failure, duration of mechanical ventilation, and duration of hospitalization. Data were analysed using Fisher's exact test and independent t-test at P < 0.05.

Findings: Out of 197 examined patients, 161 (81.7%) individuals were men and 36 (18.3%) were women. Moreover, 98 (49.7%) patients had a history of opium abuse, while 99 (50.2%) patients had no history of opium addiction. The addicted and non-addicted groups had no significant differences in terms of age (P = 0.650) and gender (P = 0.580). In addicted patients, mortality, duration of mechanical ventilation (P = 0.027), the incidence of pressure ulcer, and organ failure were significantly higher (P < 0.001), but mean ICU stay and hospitalization time was the same in both groups.

**Conclusion:** The results of this study indicated higher mortality and morbidity in opium-addicted patients admitted to ICU than non-addicted ones. This suggests that various systems of the body are affected by opium and, in certain circumstances such as severe diseases, this will cause problems for patients. Therefore, experts should pay attention to complications and side effects of addiction in the management of critical patients with a history of opium abuse.

Keywords: Mortality; Morbidity; Intensive care units; Opioid-related disorders

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#### Introduction

The opioid addiction is a growing social and public health phenomenon that involves both the individual and society. In 2011, the prevalence of drug abuse disorder was 2.44% in Iran, with opium being the most commonly-used substance. Addiction to drugs imposes a great deal of time and cost for health, social, and even political practitioners. Among common drugs, opium has the highest frequency of consumption. It is obtained from Papaver somniferum and its natural and artificial derivatives have adverse effects on the physiology and behaviour.

Opium has various pharmacological and pathologic effects due to the presence of 20 types of alkaloids and 70 other types of compounds.<sup>5,6</sup> Morphine alone has a variety of effects such as analgesia, sedation, reduced cough reflex, respiratory depression, nausea, vomiting, hot flashes, sweating, itching, addiction, coma, and death.<sup>5</sup> On the other hand, drug and alcohol abuse are known as two important causes of trauma.7 Therefore, the relative frequency of addicted patients admitted to hospitals will also increase due to the increasing prevalence of drug abuse. Results of a study in Kerman, Iran, showed that 28.8% of samples taken from the general population had drug abuse.8 In this regard, a study on patients admitted to the intensive care units (ICUs) of public hospitals in Kerman in 2012 showed that about 55.0% of patients admitted to these units had drug addiction.9 An American study showed that 12%-42% of traumatic patients were positive for opioids.<sup>10</sup>

Continuous consumption of opium and its undermines hypothalamicderivatives the pituitary-adrenal gradually (HPA) axis, weakening and suppressing the adrenal cortex and reducing cortisol levels.11,12 A study showed that pulmonary, infectious, and neurological complications were higher in an opioid-consuming group than in the control group after cardiac surgery.<sup>13</sup> In opium-addicted rabbits, changes such as urinary tract dilation (UTD), renal interstitial dilatation with severe hyperemia, hypertrophy, hyperplasia of renal glomeruli, and degeneration of urinary tubules were seen compared to the control group. There were also lobular central vein hyperemia, leukocyte infiltration, lipid droplet accumulation, hepatic necrosis, and liver sinusoidal dilatation.<sup>14</sup> A

positive correlation was also found between opium consumption and liver damage, particularly liver fibrosis, especially in patients with hepatitis C.15 Finally, it was shown that drugs had destructive effects on the liver and kidney tissues, while the dangerous addictive substance morphine;<sup>16</sup> however, there are conflicting studies. In another study, it was found that drug abuse did not increase cardiovascular, pulmonary, and neurological complications, as well as mortality rates in comparison with a non-addicted group.<sup>17</sup> There are some beliefs about the positive effects of opium consumption on the regulation of serum lipids, blood glucose, and blood pressure.18 A study was also conducted to investigate the positive impacts of opium consumption on metabolic and cardiovascular status. 19 Considering the controversial results of the mentioned studies concerning the effects of drugs on complications and mortality, the present study was conducted to compare the frequency of mortality and morbidity in trauma patients admitted to ICU in nonaddicted and addicted groups.

#### **Methods**

Study design and setting: This cohort study was conducted since January 2018 on 200 adult trauma patients who were consecutively admitted to the ICU of Shahid Bahonar Hospital in Kerman (southeast trauma center of Iran). Three of the patients were excluded from the study due to incomplete information. Therefore, 98 patients admitted to ICU with a history of drug addiction [based on the Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-V) criteria] were placed in the first group and 99 patients without any history of addiction in the second group.

Sample size: In each group, 90 subjects were calculated to be required to detect a difference of 30% in mortality rates between the opium-addict and non-addicted groups, with a power of 0.80 and a significance level of 0.05. Inclusion criteria was patients aged > 18 years who were admitted to trauma ICU. Exclusion criteria were: patients with Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score > 25, incomplete medical records, age < 18 years, and previous chronic disease.

*Measurements:* The ethical code was obtained from the Ethics Committee of Kerman University of Medical Sciences. Written consent forms were

then received from the legal guardians of patients. Required data, namely demographic characteristics, opium addiction history based on the DSM-V, incidence of pressure ulcer and organ failure, duration of mechanical ventilation, length of ICU and hospital stay, and mortality were recorded in a checklist.

Data were analysed by SPSS software (version 20, IBM Corporation, Armonk, NY, USA). Frequency, percentage, mean, and standard deviation (SD) were used to describe the sociodemographic characteristics of the participants. Mean ± SD was used to describe the informational needs of the participants. Given the normal distribution of the continuous variables, the Pearson correlation coefficient, independent samples t-test, and analysis of variance (ANOVA) tests were used to examine the associations between drug addiction history and age of patients, length of hospital stay, etc. The level of significance in all statistical analyses was set at less than 0.05.

Ethical considerations: The **Ethics** Committee of Kerman University of Medical Sciences approved the study protocol (IR.KMU.AH.REC.1398.011). An explanation was about voluntary presence provided withdrawal of samples as well as the safety of the study. The patients' companions were also assured that the information collected was confidential and would only be used for research purposes. Informed written consent was also taken from patients' companions.

#### **Results**

Out of 197 patients, 98 (49.75%) and 99 (50.25%) subjects were, respectively, with and without a history of opium addiction. As depicted in table 1, mean values of age, length of hospitalization, and ICU stay were not significantly different between the two groups. Mean age of the patients in the addicted and non-addicted groups was  $41.7 \pm 11.7$  and  $42.6 \pm 15.0$  years, respectively (P = 0.650).

Length of hospital stay in the addicted group was  $20.3 \pm 8.4$  days versus  $19.0 \pm 7.8$  days in non-addicted patients (P = 0.070) and duration of ICU stay was  $13.0 \pm 7.1$  days in the addicted group versus  $11.9 \pm 6.6$  days in non-addicted patients (P = 0.060). However, the duration of mechanical ventilation was significantly higher in the addicted group (10.1  $\pm$  6.8 days versus 7.5  $\pm$  5.9, P = 0.020) (Table 1).

**Table 1.** Comparison of mean of age and duration of mechanical ventilation in addicted and non-addicted patients

Variable	Addicted	Non- addicted	$\mathbf{P}^*$
	Mean ± SD	Mean ± SD	
Age (year)	$41.7 \pm 11.7$	$42.6 \pm 15.0$	0.600
Duration of	$10.1 \pm 6.8$	$7.5 \pm 5.9$	0.020
mechanical			
ventilation (day)			
Length of ICU	$13.0 \pm 7.1$	$11.9 \pm 6.6$	0.060
stay (day)			
Length of hospital	$20.3 \pm 8.4$	$19.0 \pm 7.8$	0.070
stay (day)			

\*T-test

SD: Standard deviation; ICU: Intensive care unit

Of 98 addicted patients, 82 (83.7%) and 16 (16.3%) individuals were men and women, respectively. In the non-addicted group, 79 (79.8%) and 20 (20.2%) patients were men and women, respectively. In terms of gender, there was no significant difference between the two groups (P = 0.580) (Table 2). Results of Fisher's exact test showed that the incidence of mortality was significantly higher in addicted patients (26.5%) than that of non-addicted (7.1%) patients (P < 0.001). Moreover, Fisher's exact test revealed that the incidence of pressure ulcer and organ failure (P = 0.012) was significantly higher in addicted patients (Table 2).

**Table 2.** Comparison of the frequency distribution of addicted and non-addicted patients based on gender, life status, infection, delirium, bedsore, and organ failure

Variable	Addicted	Non- addicted	<b>P</b> *
	n (%)	n (%)	
Men	82 (83.7)	79 (79.8)	0.580
Women	16 (16.3)	20 (20.2)	
Alive	72 (73.5)	92 (92.9)	< 0.001
Deceased	26 (26.5)	7 (7.1)	
Pressure ulcer	11 (11.2)	7 (7.1)	0.012
No pressure ulcer	87 (88.7)	92 (92.9)	
Organ failure	34 (34.7)	9 (9.1)	< 0.001
No organ failure	64 (65.3)	90 (90.9)	

\*Fisher's exact test

#### **Discussion**

Drug addiction as one of the most common problems impresses the different parts of society, such as the health care system. Drug abuse has a direct effect on the incidence of disease and traffic accidents, which in turn has increased the rate of hospitalization of

addicted patients. On the other hand, it seems that addicts who are hospitalized have weaker outcomes than non-addicts due to the involvement of various organs, which can cause heavy costs and a lot of time for the health care system.

The results of our study showed that opium-addicted patients hospitalized in the ICU due to multiple trauma had poor outcomes compared to non-addicted patients. The duration of mechanical ventilation, the incidence of pressure ulcers, organ failure, and mortality were significantly higher in the addicted group, but the length of hospitalization and ICU stay did not differ significantly.

In the present study, the mean age of patients admitted to ICU was the same as those of similar studies such as Soleimani et al. (47.7 years),<sup>20</sup> Khatami and Sedaghat Siyahkal (52.7 years),<sup>21</sup> Rafiei and Ayat Elahi (40 years),<sup>22</sup> and Yasemi et al. (47.6 years).<sup>23</sup> Of 197 patients examined in ICU, 81.7% were men, which is consistent with other studies, including Bahrami et al.,<sup>24</sup> Modabernia et al.,<sup>25</sup> and Jabalameli et al.<sup>26</sup> This is because the incidence of crashes and trauma is higher in men than in women.<sup>27</sup>

In this study, 26.5% and 7.1% of ICU-admitted addicted and non-addicted patients, respectively, away due to multiple Motamedolshariati et al. found that the mortality rate was significantly higher in addicted burn patients,28 because critically-ill patients, such as those suffering from multiple trauma and burns, are more susceptible to complication with opium addiction adverse effects. Alonso et al. showed that outcomes of stroke patients with opium addiction were poorer than non-addicts.<sup>29</sup> Similarly, our results showed that outcomes of opium-addicted patients who suffered from multiple trauma were significantly poorer than non-addicted patients because the mortality rate of the former was 26.5% versus 7.1% in the latter. The frequency of mortality was significantly higher in addicted patients (P < 0.050).

Khorvash et al. showed that some opioids, such as Norgesic, also had a higher mortality rate due to more severe complications such as heart attacks.<sup>30</sup> Therefore, it is important to pay attention to the type of substances that are abused, because the adverse effects of one substance may be different from another, but our study only focused on opioid consumption.

Mathers et al. reported that the overall

mortality rate in drug abusers was higher than the general population, although mortality rate varied in different regions based on geographical, cultural, economic, and social conditions.<sup>31</sup> It was attributed to destructive effects of opium on organs, which is consistent with our results in terms of a higher mortality rate in addicted group.

Based on the findings of this study, it seems that the incidence of organ failure, including hepatic, renal, and respiratory failure, was significantly higher in addicted patients. In a study by Javad Mousavi et al., a higher incidence of chronic obstructive pulmonary disease (COPD) was reported in opium-smoking addicts,<sup>32</sup> which had a negative impact on the outcome of critically-ill conditions as observed in our patients.

Active chemical components in opium, particularly morphine, seem to be metabolites resulting from opioid metabolism in the liver that causes structural changes in the liver tissue. Shavakhy et al. found that the consumption of opium resulted in liver fibrosis, especially in patients with hepatitis C.<sup>16</sup> Atici et al. presented evidence of morphine destructive effects on the liver and kidney tissues of mice.<sup>17</sup>

In the present study, the overall organ failure rate was 34.7% in the addicted group, which was significantly higher than that of the non-addicted group (9.1%) (P < 0.001).

Dewan et al. found that the cardiac surgery complications such as blood transfusion, pulmonary embolism (PE), mechanical ventilation, prolonged postoperative pain, and longer hospital stay were significantly higher in opium-addicted patients, but the mortality rate did not differ between the two groups.<sup>33</sup> In our study, the mean ICU stay periods were  $13.0 \pm 7.1$  and  $11.9 \pm 6.6$ days in addicted and non-addicted groups, respectively (P = 0.060). Also, there was no significant difference between the length of hospital stay in addicted (20.3 ± 8.4 days) and non-addicted (19.0  $\pm$  7.8 days) groups (P = 0.070). The length of hospital stay after non-complicated cardiac surgery is very shorter than multiple trauma patients, which may be a reason for the difference in our results.

Cardiovascular disease (CVD) is one of the most important causes of mortality in the general population, which is more common among addicts than non-addicts.

Mean duration of mechanical ventilation was

 $10.1 \pm 6.8$  days in the addicted group, which was significantly more than non-addicted group  $(7.5 \pm 5.9 \text{ days})$  (P = 0.02).

As with our results, Vahedian-Azimi et al. observed that the duration of mechanical ventilation was longer in addicted than non-addict patients.<sup>34</sup> Many addicts have chronic respiratory disease, and by weakening the respiratory efforts and cough reflex with narcotics, these patients are prone to atelectasis, increased pulmonary secretions, and pneumonia.<sup>35,36</sup> These problems can increase the length of the mechanical ventilation period.

Studies have shown that the duration of mechanical ventilation is directly related to the mortality rate.<sup>37</sup> It seems that regular and correct implementation of rehabilitation programs and lung care protocols in opium addicts can be effective in reducing the length of mechanical ventilation.

Our findings showed that the incidence of bedsore was significantly higher in addicts (11.2%) than in non-addicts (7.1%) (P = 0.012). Common risk factors of pressure ulcers include advanced age, immobility, friction, shear, poor nutrition, excessive moisture and incontinence, altered level of consciousness, poor perfusion, certain skin infections, and comorbid conditions.<sup>38</sup>

Most opium addicts suffer from malnutrition due to poor eating behaviors, anorexia, lack of proper skills and knowledge in preparing healthy foods, and poor economic conditions,<sup>39</sup> as well as hormonal and immunological disorders<sup>40</sup> which prolong recovery from such diseases as human immunodeficiency virus (HIV) infection<sup>41</sup> and predispose patients to pressure ulcer.

In addition, another predisposing factor for bedsore is diarrhea experienced by many addicts during the hospitalization period due to the withdrawal syndrome.

Summarizing the results of the present study and the aforementioned studies, it seems that opium addiction can increase the risk of mortality, pressure ulcers, organ failure, and the duration of mechanical ventilation in traumatic patients hospitalized in ICU. However, our findings showed that the length of hospital and ICU stays did not differ between the two groups.

## Conclusion

ICU-admitted opium-addicted patients due to traumatic injuries require special attention and multidisciplinary care to reduce complications and increase the chance of survival.

It is recommended to perform similar studies on general ICU patients in a multicenter study with more patients to use the results of such studies to develop specific protocols for the treatment of opium-addicted patients.

*Limitations:* The most important limitations of present study were lack of co-operation of some patients for giving history of opium addiction and having missing data.

#### **Conflict of Interests**

The Authors have no conflict of interest.

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#### **Authors' Contribution**

Have made a substantial contribution to the concept or design of the article or the acquisition, analysis, or interpretation of data for the article: MA; drafted the article or revised it critically for important intellectual content: HKA; approved the version to be published: MD and PM; agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated: ST.

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# میزان مرگ و میر و عوارض بالاتر در بیماران ترومایی معتاد به تریاک در بخش مراقبتهای ویژه

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# مقاله يژوهشي

# چکیده

مقدمه: اعتیاد به تریاک با مشکلات جسمی، روانی و اجتماعی متعددی همراه است. هدف از انجام پژوهش حاضر، مقایسه میزان عوارض و مرگ و میر در بیماران مبتلا به ترومای معتاد به تریاک و غیر معتاد بستری در بخشهای مراقبت ویژه (ICU یا Intensive care unit) مرکز تروما در استان کرمان بود.

روشها: در این مطالعه هم گروهی، ۲۰۰ بیمار معتاد و غیر معتاد که به دلیل تروما طی ۹ ماه در سال ۱۳۹۶ در ICU بیمارستان شهید باهنر کرمان بستری شده بودند، مورد مقایسه قرار گرفتند. بیماران از نظر میزان مرگ و میر، میزان بروز زخم فشاری، میزان بروز نارسایی ارگانها، مدت زمان تهویه مکانیکی و طول مدت بستری بررسی شدند. داده ها با استفاده از آزمونهای Fisher's exact و Topology در سطح  $P < \cdot \cdot \cdot \circ$  مورد تجزیه و تحلیل قرار گرفت.

یافتهها: از ۱۹۷ بیمار مورد بررسی، ۱۶۱ نفر (۸۱/۷ درصد) مرد و ۳۶ نفر (۱۸/۳ درصد) زن بودند. علاوه بر این، ۹۸ بیمار (۴۹/۷۵ درصد) سابقه سوء مصرف تریاک داشتند؛ در حالی که ۹۹ نفر (۵۰/۲۵ درصد) سابقه اعتیاد به تریاک نداشتند. تفاوت معنی داری بین گروههای معتاد و غیر معتاد از نظر سن (۴۹/۵۰ درصد) و میزان مرگ و میر و مدت زمان تهویه مکانیکی (۲۰۲۷ - (P = 0.0000))، میزان بروز زخم فشاری و نارسایی ارگانها در بیماران معتاد به طور قابل توجهی بالاتر بود (۲۰/۰۰۱)، اما میانگین اقامت در (P = 0.0000) و مدت بستری در هر دو گروه یکسان بود.

نتیجه گیری: نتایج به دست آمده، میزان مرگ و میر و عوارض بالاتر را در بیماران ترومایی معتاد به تریاک بستری در ICU نسبت به بیماران غیر معتاد نشان می دهد که خود تأییدکننده تأثیر تریاک بر سیستمهای مختلف بدن می باشد و در برخی شرایط خاص مانند بیماری های شدید، می تواند مشکلاتی را برای بیماران ایجاد کند. بنابراین، متخصصان باید در مدیریت بیماران بحرانی با سابقه سوء مصرف تریاک، به عوارض جانبی اعتیاد توجه نمایند.

واژگان کلیدی: مرگ و میر؛ عوارض؛ بخش مراقبتهای ویژه؛ اختلالات مرتبط با مواد افیونی

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