

## Outcome of acute heroin overdose requiring intensive care unit admission

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### ARTICLE INFO

#### Keywords:

heroin overdose  
acute drug intoxication  
ICU management

#### Article history:

Received 17 December 2009  
Received in revised form 18 February 2010;  
1 April 2010  
Accepted 12 April 2010  
DOI:10.5055/jom.2010.0021

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### ABSTRACT

**Background:** Heroin use carries a large burden of morbidity and mortality. Heroin overdose and in particular events that need intensive care unit (ICU) admission have not been widely examined. The aim of this study was to describe the causes of ICU admission and the outcome of patients with a heroin overdose.

**Methods:** A retrospective chart review of all patients with a heroin overdose admitted to the ICU between 1987 and 2006 was conducted.

**Results:** Forty-two records were available for review. The average age of the patients was 28 years. In the field, 19 persons were found in coma Glasgow Coma Scale (GCS < 8) and respiratory depression and were treated with naloxone. The reasons for ICU admission included hypoxemia in 37 (88 percent), 28 of whom had acute lung injury (ALI) and nine aspiration pneumonia, shock in three (7.2 percent) and persistent mental compromise in two patients (4.8 percent). Intubation and mechanical ventilation (MV) were instituted in 37 patients. In 19 of the 37 patients, weaning and extubation became possible within the first 24 hours. Sixteen patients suffered complications and received MV for  $5 \pm 2$  days, with a mean length of ICU stay of  $8 \pm 1$  days, while two patients succumbed because of anoxic encephalopathy and brain death. The complications observed were acute respiratory distress syndrome in eight patients, severe sepsis in four, catheter-related bacteremia in one, iatrogenic pneumothorax in one, and rhabdomyolysis in two, while four among them died due to severe sepsis.

**Conclusions:** In our study, ALI and aspiration pneumonia were the most frequently observed respiratory complications after acute heroin overdose requiring intubation and ICU admission. Mortality rate was 14.2 percent and was attributed to septic complications and irreversible brain damage.

### INTRODUCTION

According to the United Nations World Drug Report 2009, at least 15.1 million people or 0.4 percent of the world population aged 15 to 64 years use illicit opioids; more than half use heroin and the remainder use opium or diverted pharmaceutical opioids.<sup>1</sup> The European Monitoring Centre for Drugs and Drug Addiction estimates that the prevalence of opiate use in eight European countries ranges from 0.5 to 2.1 percent, while 10-20 percent of adult mortality at ages 15-49 years is attributable to opiate use.<sup>2</sup>

Even though stimulant drugs, such as cannabis, cocaine, and amphetamines, are the illicit substances more commonly used, heroin remains by far the predominant cause of death among drug addicts.<sup>1,2</sup> In Greece, 273 drug-related deaths from acute intoxications were reported in 2006, of which 173 (63.4 percent) were confirmed by toxicological analyses. In 97.7 percent of the confirmed cases, the cause of death was heroin use.<sup>3</sup> The estimated number of heroin users in Attica for the year 2006 was 9,313 (46 percent of the estimated heroin prevalence in Greece).<sup>3</sup> Heroin overdose represents the leading

cause of death among intravenous heroin users and is usually due to severe respiratory depression.<sup>4</sup>

Apart from death at the scene, heroin overdose may have serious sequelae that need immediate intervention. The heroin overdose syndrome is usually manifested by the typical triad of reduced level of consciousness, miosis, and severely depressed respiratory drive. About 3-7 percent of patients treated for heroin overdose require hospital admission because of complications such as pneumonia, noncardiogenic pulmonary edema, coma, and infections.<sup>5</sup> Only a small number among them will finally need admission to the intensive care unit (ICU).

Studies examining the outcome of critically ill patients with a history of drug addiction have focused upon trauma and asthmatic attacks. Drug addicts with trauma have not been shown to be at increased risk of ICU complications.<sup>6</sup> On the other hand, patients with asthma who use heroin have greater need for mechanical ventilation (MV).<sup>7</sup> In a recent study, de Wit et al.<sup>8</sup> reviewed the records of 1.2 million medical patients and concluded that drug use is associated with increased need for MV. However, few data exist in the literature about heroin overdose requiring ICU admission, regarding complications and outcome.

The purpose of this observational retrospective study was to depict the profile of heroin addicts with severe overdose and to describe their clinical course and outcome.

## PATIENTS AND METHODS

This study was conducted in a multidisciplinary ICU of an urban academic general hospital, specialized in chest diseases. We reviewed the charts of all adult patients (aged  $\geq 16$  years) who had been admitted to the ICU during a period of 20 years with the diagnosis of heroin overdose. The average number of annual admissions in the ICU during this period was  $153 \pm 26$  patients. Of 61 cases of heroin overdose, 50 charts were available for review. In eight of these patients, there was no laboratory documentation and were excluded from the study. Neither of the remaining 42 subjects was human immunodeficiency virus-positive nor had a second hospital admission during this period. This study was approved by the institutional board review of the hospital, where the study was conducted. Informed patient consent has not been obtained as it was a retrospective chart analysis.

Hypoxemia before intubation was defined as a room air saturation  $<90$  percent with a respiratory

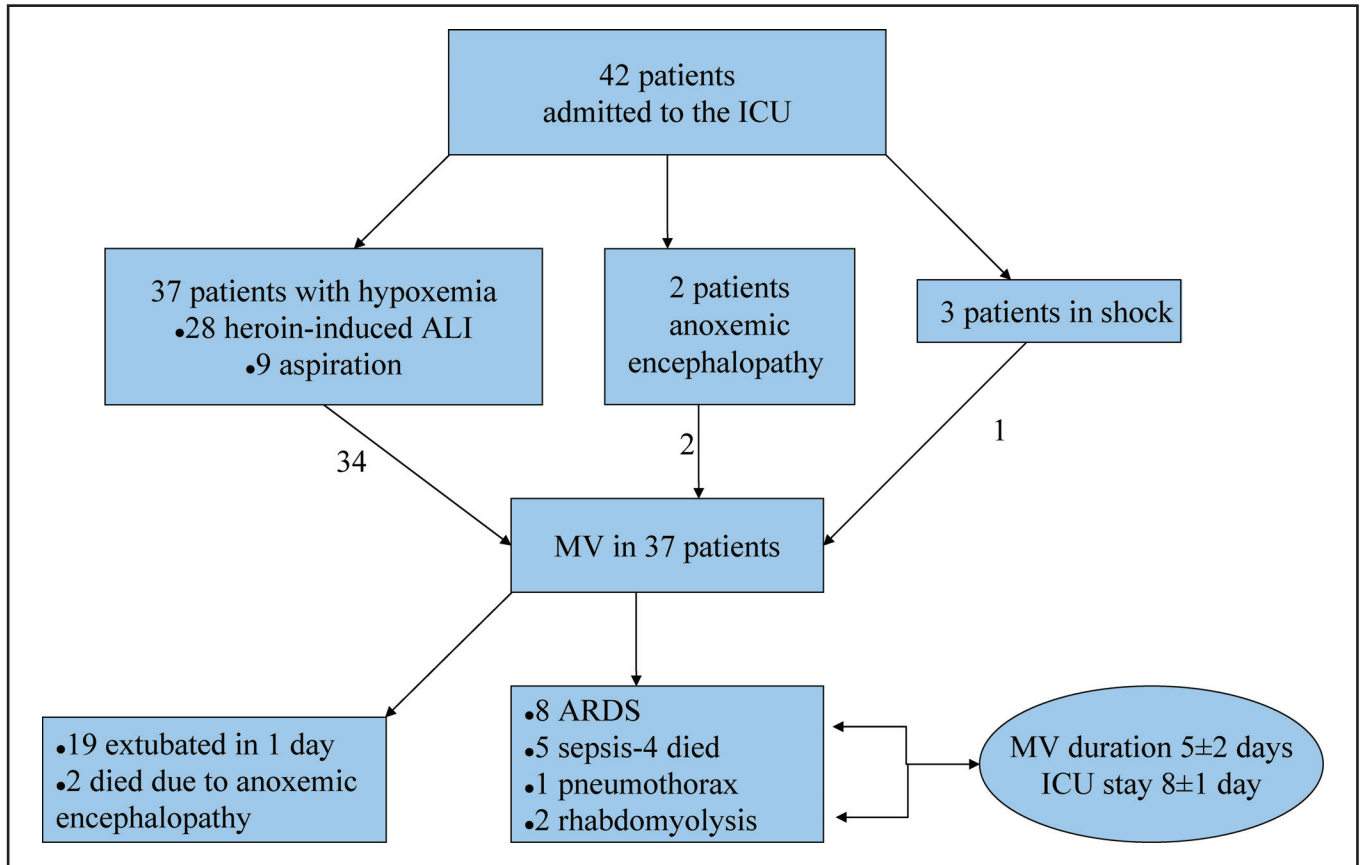
rate  $>12 \text{ min}^{-1}$ . Respiratory depression was defined as a respiratory rate  $<12 \text{ min}^{-1}$  and hypoxemia after intubation as a  $\text{PaO}_2/\text{FIO}_2$  ratio  $\leq 300$ . Heroin-induced acute lung injury (ALI) was defined as significant hypoxemia accompanied by radiographic evidence of diffuse pulmonary infiltrates, not attributable to other causes, within 24 hours after a heroin overdose that resolved clinically and radiographically within 48 hours.<sup>9</sup> Heroin use was documented by a urine screening assay that traces morphine, the metabolite of heroin. The drug screening performed by a homogenous immunoassay method with a cut-off point of 2,000 ng/mL was considered to be a positive result. A positive result indicates use of opiates within the previous 12 hours.

Data collected included patient age, sex, vital signs, and level of consciousness as measured by the Glasgow Coma Scale (GCS) in the field before and after naloxone administration, cause of ICU admission, need and length of MV, length of ICU stay, blood gases and chest X-ray findings upon ICU admission, laboratory and radiographic findings, complications during ICU stay, and final outcome. Concurrent drug use and length of heroin use were also recorded.

## RESULTS

Between January 1987 and December 2006, 42 patients were admitted to the ICU with documented heroin overdose. Of them, 29 were males (69 percent) and 13 were females (31 percent), and the average age was 28 years (range, 16-55 years). Most of the admitted patients (73 percent) were alcohol abusers, and a smaller percentage (23 percent) of them reported occasional use of other drugs, mostly cannabis and benzodiazepines. No definite conclusion could be made about co-intoxication with other substances for the under examination event. The average time of heroin use was  $5.6 \pm 4.7$  years. None of the patients was following a detoxification program and none was receiving methadone.

They were all transferred to the ICU from the Emergency Department. In the field, 19 persons (45.2 percent) were found in coma (GCS  $< 8$ ) and respiratory depression, and both responded to naloxone, except for two patients. The rest of the patients had a GCS of 9-12. Hypoxemia, not sufficiently corrected by supplemental oxygen, was evident in 32 patients. Of the 42 patients, three were in shock, partially corrected after the administration of 2 liters of crystalloid fluids.



**Figure 1. Diagrammatic presentation of the reasons of ICU admission and outcome. ALI, acute lung injury; ARDS, acute respiratory distress syndrome; MV, mechanical ventilation; ICU, intensive care unit.**

The reasons for ICU admission (Figure 1) were as follows: hypoxemia in 37 (88 percent), shock in three (7.2 percent), and persistent unconsciousness in two patients (4.8 percent). Intubation and MV were instituted in 37 patients; in 34 patients due to refractory hypoxemia, in two cases due to persistent coma, and in one patient due to profound shock. Hypoxemia was attributed to ALI in 28 patients with diffuse fluffy infiltrates on chest X-ray and to aspiration pneumonia in nine patients.

In 19 of the 37 patients, weaning and extubation became possible within the first 24 hours, while the patients with hemodynamic instability were also stabilized on the first day. Sixteen patients suffered complications and received MV for  $5 \pm 2$  days and stayed in the ICU for  $8 \pm 1$  days. The complications observed were acute respiratory distress syndrome in eight patients, severe sepsis in four, catheter-related bacteremia in one, iatrogenic pneumothorax in one, and rhabdomyolysis in two patients. Rhabdomyolysis was of moderate severity in one of them, resolving after aggressive fluid administration and forced diuresis. The second one presented acute renal failure

requiring several sessions of continuous renal replacement therapy (CRRT). In total, six patients died (14.2 percent); two patients succumbed because of anoxic encephalopathy and brain death, while four died from severe sepsis.

## DISCUSSION

We reviewed the medical records of the heroin overdose patients admitted to our ICU in a period of 20 years in an effort to recognize causes for ICU admission and to describe ICU complications and outcome. Heroin overdose was diagnosed both on clinical and laboratory grounds. The typical presentation of heroin overdose consists of depressed mental status, miotic pupils, and decreased respiration. According to the study of Hoffman et al.,<sup>10</sup> clinical criteria alone have a sensitivity of 92 percent and a specificity of 76 percent for diagnosing opiate overdose.

Our patients had a mean age of 28 years and most of them were men. They had been using heroin for 5.6 years on the average and the majority consumed alcohol as well. According to the literature, most

cases of fatal heroin overdose occur among intravenous heroin users in their late 20s to early 30s, who have used heroin for 5 to 10 years.<sup>11</sup> A male preponderance among heroin addicts is also observed. The clinical epidemiology of nonfatal overdose is quite similar, as heroin users admitted for a nonfatal overdose are more likely to have a longer history of drug use, a previous episode and concurrent use of other drugs and alcohol.<sup>12</sup>

All patients in our study were found in a depressed mental status with concomitant respiratory compromise. All but two responded to naloxone, and the two nonresponders are the ones who eventually died in the ICU with the diagnosis of anoxic encephalopathy. Delayed medical intervention and cardiopulmonary resuscitation were possibly responsible for this outcome. Death is estimated to supervene 1 to 4 hours after injection, a time interval that would allow intervention.<sup>13</sup> Several strategies are being implemented in Greece, concerning prevention of overdose cases, such as informing and training of dependent drug users on safe drug use and first aid in overdose cases.<sup>3</sup> Four patients died from severe sepsis, secondary, either to aspiration- or ventilator-associated pneumonia.

Naloxone is the first aid in the field of a possible heroin overdose, along with cardiopulmonary resuscitation. Naloxone is a specific opiate antagonist with no agonist properties. It readily reverses the respiratory depression and sedation caused by heroin and has been shown to be very effective in treating acute overdose, given by the intravenous, intramuscular, or subcutaneous route.<sup>14</sup> An initial intramuscular or subcutaneous dose of 0.4 mg of naloxone is recommended, followed by incremental doses of 1-2 mg, if no response occurs within 3 to 5 minutes. Naloxone is a relatively safe drug with rarely reported adverse reactions. However, in a prospective study, Osterwalder<sup>15</sup> noted significant adverse reactions when naloxone was given in the emergency department. He reported that 1.6 percent of patients developed severe complications, including asystole, seizures, pulmonary edema, and violent behavior. Most important of all, one must be aware of the short half-life of naloxone, shorter than that of heroin, so that repeated doses may be needed, for sedation and hypoventilation not to recur.

In our study, heroin-induced ALI was the leading cause of ICU admission. It was first diagnosed by William Osler in 1880, and it is reported at a rate of 0.8-2.4 percent. The exact cause of the increased

pulmonary capillary permeability that leads to ALI remains unclear, but the finding of an increased protein concentration in bronchoalveolar lavage fluid implies increased pulmonary capillary permeability, perhaps secondary to hypoxia.<sup>9</sup> Neurogenic pulmonary edema accompanying central nervous system depression may also contribute to opiate-induced ALI. Naloxone is also implicated in some cases, where the reversal of opioid toxicity may cause a surge in catecholamine levels, thereby increasing cardiac afterload, which causes interstitial edema and alveolar flooding. ALI due to heroin overdose occurs shortly after injection, usually within 4-6 hours and rarely within 24 hours. It typically resolves within 36 to 48 hours.<sup>16</sup>

The second commonest complication observed in our patients was aspiration pneumonia. The central nervous system depression that accompanies heroin overdose impairs airway protection, thus increasing susceptibility to aspiration pneumonia. Bronchiectasis has been reported among heroin users as a result of recurrent lung infections.<sup>17</sup>

Three patients were admitted to the ICU due to cardiovascular compromise. Hemodynamic instability was mild and easily restored with intravenous fluids, while inotropic support was required for only a few hours. Heroin use is commonly associated with hypotension and mild bradycardia. Heroin acts directly on the vasomotor center leading to an increased parasympathetic activity and reduced sympathetic activity. These effects combined with histamine release from the mast cells may result in excessive bradycardia and hypotension. However, profound shock after heroin overdose is rarely encountered and is mainly attributed to depression of left ventricular contractility.<sup>18,19</sup>

Two patients developed rhabdomyolysis, a complication that lengthened their ICU stay. One of them required CRRT because of nonresolving acute renal failure. The pathophysiologic mechanisms of rhabdomyolysis after heroin overdose are not completely elucidated. Direct cell toxicity and quinine, a common adulterant, have been implicated. Another plausible explanation is that prolonged immobilization after drug injection, without fluid intake, increases the risk of developing rhabdomyolysis.<sup>20,21</sup>

Our study is limited by its retrospective nature. We were confined to the data that were recorded in the medical charts, so we could not reach safe conclusions about epidemiological issues. Another drawback is the fact that we used a qualitative method for heroin identification, and therefore, no conclusions

can be made regarding the relationship between drug levels and risk of complications and/or death. The scenarios for a heroin overdose include the use of a higher or of greater purity dose, the use of heroin after a prolonged period of abstinence, and the rare incidence of an intentional overdose. Nevertheless, morphine levels do not sufficiently correlate to the fatality risk. Actually, concurrent alcohol and/or drug use seem to be the most significant precipitants of a fatal outcome. In various studies, a great percentage of 29-75 percent of heroin-related deaths was associated with significant alcohol levels. In the study of Ruttender et al.,<sup>12</sup> with high alcohol levels much lower morphine levels were required to cause death. High benzodiazepine levels were identified in 5-12 percent of fatalities. It is plausible that the combination of heroin with a respiratory depressant reduces the threshold for central nervous compromise.<sup>22</sup>

## CONCLUSIONS

We have reported a high prevalence of respiratory complications among patients with acute heroin overdose admitted to the ICU. Heroin-induced ALI was the commonest complication requiring intensive care management, followed by aspiration pneumonia, hemodynamic instability, and rhabdomyolysis. Death supervened in 14.2 percent of patients as a result of anoxic encephalopathy and severe sepsis. In the rest of the patients, complications were mild and the ICU stay was quite short.

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## ACKNOWLEDGMENTS

*Data were collected and reviewed by Prof. L. Grigorakos, Dr. G. Nikolopoulos, Dr. D. Veldekis, and Dr. K. Sakagianni. Dr. G. Apostolakos conducted review of the literature. Prof. L. Grigorakos, Dr. E. Tsigou, and Dr. K. Sakagianni prepared this article. The authors have no conflicts of interest to disclose.*

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