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**HEROIN ADDICTION &  
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## Case series of heroin-induced non-cardiac pulmonary oedema

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### Summary

**Background.** Heroin usage is a significant health care problem in many countries. It can cause altered mental status, and even induce respiratory depression. Respiratory manifestations are generally caused by exacerbation, pulmonary oedema and respiratory distress. In this study we report eleven cases of patients that were admitted to an emergency department with dyspnoea in a ten-month period. **Methods.** The age, gender, past medical history, laboratory results and radiological images were collected retrospectively. **Results.** The median age of the patients was 27 (range: 21-70). Naloxone was administered to three of the patients because of respiratory depression. Mean WBC count was  $20136 \pm 8773$ . 10 out of 11 patients had abnormal chest x-ray findings: 8 of them had peribronchial thickening, 6 had consolidation. Chest computed tomography (CT) was obtained from 10 of the patients; in 7 of them peribronchial thickening and ground glass densities were detected. None of the patients were intubated. All of the patients but one left the emergency department in the first 24 hours. One of the patients was hospitalized; in the first 48 hours significant improvement was seen and on the 7th day after admission his chest CT was completely normal. **Conclusions.** Heroin addiction not only causes respiratory depression but also marked pulmonary oedema at an early phase. Patients with pulmonary oedema due to heroin use may respond well to supportive therapy, including oxygenation via a face mask or mechanical ventilation; in heroin users it should, however, be considered as an alarming predictor of upcoming fatalities.

**Key Words:** heroin; heroin lung; non-cardiac; pulmonary oedema.

## 1. Introduction

Heroin remains one of the large number of abused drugs that show rising trends of use and that have become a significant health care problem in many countries, with social, judicial and economic involvement. It may be injected intravenously, snorted or smoked. Heroin overdose is diagnosed on the basis of a combination of depressed consciousness. Previous studies pointed out that the respiratory manifestations of heroin use do not stop at respiratory depression, but include asthma exacerbation, pulmonary oedema and some level of respiratory distress [2, 9, 11].

In this paper we report our experiences with eleven patients who were admitted with respiratory alterations. Studies on x-ray images were performed

after heroin insufflations in the previous 24 hours.

## 2. Methods

Subjects were identified retrospectively via hospital records on all patients who had been admitted to our emergency department with acute dyspnoea and had been using heroin via the nasal route between July 2013 and April 2014. All our patients were managed individually by attending physicians, so management protocol was not required. All patients' characteristics including age, gender, past medical history, laboratory results and radiological images were collected.

**Table 1.** Patients' demographic and laboratory

|                  | N°1    | N°2    | N°3    | N°4    | N°5    | N°6    | N°7    | N°8    | N°9    | N°10   | N°11   |
|------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Age              | 24     | 28     | 60     | 27     | 36     | 21     | 32     | 23     | 24     | 23     | 27     |
| Gender           | Male   | Male   | Male   | Female | Male   |
| Glucose          | 375    | 216    | 111    | 125    | 135    | 105    | 326    | 96     | 106    | 141    | 126    |
| BUN              | 30     | 47     | 79     | 30     | 43     | 36     | 26     | 47     | 26     | 26     | 34     |
| CR               | 1.37   | 1.41   | 0.73   | 0.65   | 1.03   | 1.18   | 1.14   | 1.18   | 0.7    | 0.85   | 1.12   |
| AST              | 28     | 30     | 62     | 15     | 52     | 26     | 19     | 114    | 25     | 33     | 22     |
| ALT              | 31     | 24     | 171    | 10     | 80     | 10     | 22     | 79     | 17     | 18     | 28     |
| WBC              | 21,300 | 29,700 | 13,500 | 21,300 | 20,700 | 37,300 | 13,100 | 28,800 | 11,400 | 14,400 | 10,000 |
| NEU %            | 77.2   | 76.6   | 83.2   | 53.1   | 77.0   | 92.7   | 37.2   | 92.1   | 67.8   | 77.9   | 65.8   |
| LYM %            | 8.1    | 17.6   | 11.2   | 11.5   | 16.7   | 3.0    | 50.6   | 3.1    | 21.6   | 7.3    | 15.4   |
| MONO %           | 1.0    | 4.2    | 2.4    | 34.6   | 5.7    | 3.9    | 7.2    | 4.6    | 6.5    | 4.4    | 8.8    |
| EOS %            | 0.3    | 0.5    | 0.1    | 0.3    | 0.1    | 0.0    | 2.4    | 0.0    | 2.4    | 9.9    | 9.6    |
| BASO %           | 13.4   | 1.4    | 0.1    | 0.5    | 0.5    | 0.4    | 2.6    | 0.2    | 1.70   | 0.5    | 0.4    |
| pH               | 7.12   | 7.25   | 7.54   | 7.37   | 7.46   | 7.46   | 7.15   | 7.01   | 7.45   | 7.39   | 7.37   |
| pCO <sub>2</sub> | 49.50  | 66.20  | 30.50  | 46.30  | 36.00  | 35.90  | 76.50  | 110.90 | 33.70  | 37.00  | 46.20  |
| HCO <sub>3</sub> | 29.40  | 28.80  | 25.60  | 26.70  | 25.30  | 25.40  | 26.40  | 27.60  | 23.10  | 21.90  | 26.30  |

### 3. Results

Eleven patients were identified as suffering from dyspnoea after having heroin insufflations in the 24 hours before their presentation. The baseline characteristics are as follows: median age was 27 years (range: 21 to 70) and ten were male. The respiratory problems of patients were evident on admission to the emergency department. Three patients had respiratory depression and showed marked alteration of their consciousness, so naloxone was administered to them. On admission, mean white blood cell count (WBC) was  $20136 \pm 8773$  (range: 10000-37300), mean neutrophil percentage was  $72 \pm 16$  (range: 37-92). None of the patients had fever.

10 of the 11 patients had a chest x-ray taken, and the findings were as follows: peribronchial thickening was present in 8 patients, consolidation in 6; 5 patients had both peribronchial thickening and consolidation, and one of them had fluid in the right fissure.

Chest CT was obtained from 10 of the 11 patients. Marked pulmonary oedema was present in 7 patients, while peribronchial thickening and ground glass densities (GGD) were observed, too (Table 1).

All of our patients were given oxygen via a face mask, and none of them were intubated. 10 of the 11 patients refused to be hospitalized and left our emergency department in the first 24 hours, after regaining consciousness. Only one patient was hospitalized in

the intensive care unit (Patient 1). He was given supportive therapy. This patient's first chest CT on admission revealed a pulmonary oedema (Figure 1a); a control chest CT was obtained at the 24th and the 48th hour after admission (Figures 1b and 1c). These control CTs revealed the resolution of the findings shown in the first chest CT. On the third day after admission he was discharged. One week later, his control chest CT was completely normal (Figure 1d).

### 4. Discussion

Accumulation of fluid in a body space occurs as the result of an imbalance between hydrostatic, osmotic and oncotic pressures between membranes that separate the body cavities. Accordingly, fluid accumulation in the lungs is the reflection of an imbalance between the forces mentioned above across the alveolar-capillary membranes. This process is generally induced by left ventricular failure. However, lung congestion is sometimes observed occurring as a result of several conditions that do not involve cardiac dysfunction. The pulmonary consequences of heroin use show a wide spectrum of life-threatening conditions, including acute respiratory depression, pulmonary oedema, asthma exacerbation and, thinking of the future, a likely long-term respiratory sequel [4].

In the course of this study we have detected some degree of tachypnoea in patients who did not show

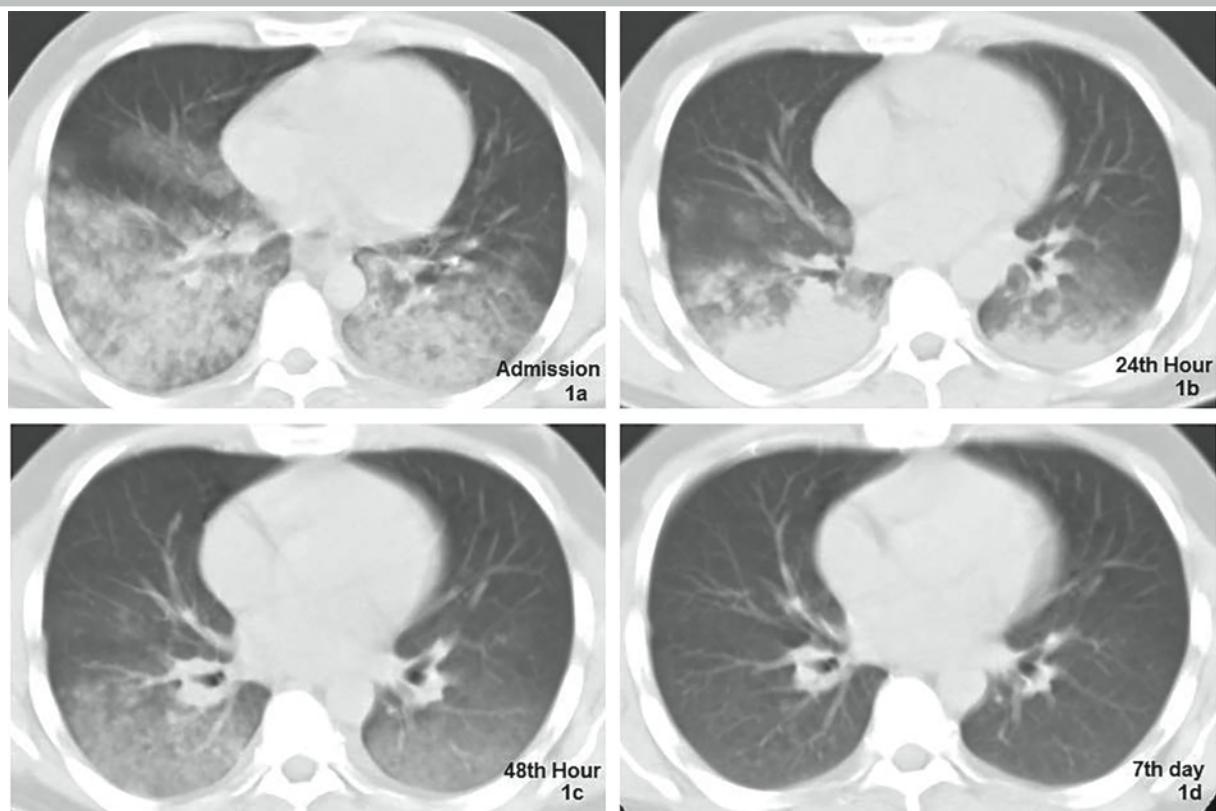
mental alterations, but the most probable outcome of heroin use turned out to be respiratory depression. The absence of fever and the rapid resolution of symptoms in all patients as a result of supportive therapy alone, and rapid improvement in one patient's x-ray image findings, led us to formulate a diagnosis of pneumonia as being likely, and a condition of heroin-induced non-cardiogenic pulmonary oedema (HI-NCPE) as being the best grounded.

In a previous study, pulmonary oedema was detected in 95% of subjects who were recorded as having had heroin- or methadone-related deaths; in all these cases a post-mortem whole-body computed tomography were obtained [10]. In another study mainly centred on heroin user autopsies, pulmonary oedema was the most common finding, followed by alveolar hemorrhages and emphysematous changes. Bronchiolitis obliterans and interstitial fibrosis were also observed in the same study [8]. Based on these studies, non-cardiogenic pulmonary oedema (HI-NCPE) is likely to be present in heroin addicts more often than is currently supposed. Although it was first described more than 13 decades ago, the pathophysiology of HI-NCPE is still not well understood, and seems to be more complex than is usually suggested.

Damage to the alveolo-capillary membrane and increased permeability of the vascular endothelium had been supposed to be the final pathway of this oedema. Damage to alveolar integrity should occur as a result of hypoxia, the direct effects of snorted particles and additives in less pure forms. Besides, Dettmeyer et al. [1] detected similar defects on alveolar-capillary membranes in victims of sudden cardiovascular deaths and heroin-related deaths. All our patients used heroin via the nasal route, which may result in the effects mentioned above. It should be noted that oedema has been observed in intravenous heroin users, too. In these circumstances hypoxia is suggested as a factor that contributes strongly to this oedema. Sterrett and colleagues speculated that increased pulmonary capillary permeability was secondary to hypoxia [7].

Histamine has been proposed as an important mediator of this oedema. It was thought that histamine release resulted in large gaps in the endothelium of bronchial venules leading to the oedema. Maruer et al. [3] reported that baseline histamine concentrations were high in chronic intravenous heroin users. When histamine and some other vasoactive peptides are released, the result is increased capillary perme-

**Figure 1.** CT of the first patient: on admission (a); at 24th hour (b); at 48th hour (c) and control at 7th day (d)



ability in the pulmonary system – the very feature that appears to be responsible for this kind of oedema.

Mell and colleagues suggested that pulmonary oedema was due to naloxone-precipitated withdrawal and associated catecholamine surge [5]. In opposition to this suggestion, Sporer et al. [6] concluded that the lower rates of HI-NCPE observed in the most recent studies, rather than in the earlier ones, is the result of administrating naloxone at an earlier stage and more liberally. In the present study 3 patients received naloxone, whereas 8 of them did not receive any. It should be stressed that all of our patients had marked pulmonary oedema. Accordingly, we may speculate that naloxone does not have any role in developing pulmonary oedema in patients whose hypoxic insult is completed, but may have some positive effects in preventing pulmonary oedema before hypoxic insult has been completed.

The purity of the heroin taken should be kept in mind as another factor contributing to the development of pulmonary oedema. The purity of street heroin varies widely, and variations can be recognized at the moment of assessing its effects. Besides this, the additives to be found in less pure heroin may play a role in developing or preventing pulmonary oedema. Wong et al. [11] reported a patient who had marked pulmonary oedema at an acute phase, micronodular lung findings on a chest x-ray and lung CT at a subacute phase. The patient also underwent a lung biopsy that showed large amounts of foreign-body granulomas distributed over the same region as that shown in the image studies obtained at a subacute phase. Most of our patients too were suffering from marked pulmonary oedema, mild peribronchial thickening, and GGD that may reflect interstitial pneumonitis similar to that reported by Wong et al. It is true, however, that we obtained the x-ray images only at the moment of admission of patients and obtained no further images at a later stage, with just one exception. In the lung CT obtained on the 3rd day, counting from the admission of one of our patients, the CT indicated the pulmonary oedema had improved and that the patient had only moderate peribronchial thickening and GGD. In addition, the lung CT that had been obtained on the 9th day counting from his admission showed a normal condition. Furthermore, our chest x-ray and chest CT findings were not unique to our patients, either. These differences between the cases reported by Wong and colleagues and ours probably depend on the duration of heroin use and hypoxic insult, and on the purity of the heroin used.

All of our patients responded well to oxygen

therapy via a face mask, and the respiratory symptoms resolved rapidly within 24 hours. The rapid resolution of respiratory symptoms leads us to suggest that hypoxia was the most important contributing factor to the development of heroin-induced non-cardiogenic pulmonary oedema.

## 5. Conclusions

Heroin addiction not only causes respiratory depression, but also marked pulmonary oedema at an early phase. Patients with pulmonary oedema arising from heroin use may respond well to supportive therapy, including oxygenation via a face mask or through mechanical ventilation. This kind of oedema should, in any case, be considered as an alarming predictor of upcoming fatalities in heroin users.

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#### *Contributors*

All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

#### *Conflict of interest*

Authors declared no conflict of interest.

#### *Ethics*

Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The study does not have IRB review/approval; this study does not require ethics committee approval because 'Case reports' does not require ethics committee aproval but informed consent signed by patients.

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