Acute respiratory distress syndrome induced by oral methadone managed with non-invasive ventilation

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Non-cardiogenic pulmonary oedema is an uncommon complication of both methadone and heroin overdose, often requiring a period of invasive ventilation due to its severity. We report the successful, early use of non-invasive ventilation in the management of non-cardiogenic pulmonary oedema secondary to a non-fatal overdose of oral methadone.

A 54-year-old, previously healthy man presented to the emergency department with shortness of breath, following an overdose of an unknown amount of methadone. He denied previous or current abuse of any form of illegal substances or opioids. The ambulance crew found the patient to be ''gurgling'' and ''gasping'' for breath, with oxygen saturations of 84% on room air. They administered high flow oxygen and 5 mg salbutamol via a nebuliser en route to hospital.

On arrival in the ED, the patient's Glasgow Coma Score (GCS) was 9/15, with pinpoint pupils, and he had severe respiratory distress. He was maintaining his own airway, but had a respiratory rate of 50 breaths/min and was using his accessory muscles for respiration. He had generalised poor air entry with widespread coarse, ''wet'' sounding crepitations. His oxygen saturations soon fell to 72% despite a fractional inspired oxygen (F_{IO_2}) of 0.8. He was tachycardic (140 beats/min) with a blood pressure of 179/84 mm Hg. There was no clinical evidence of raised left atrial pressure.

His initial arterial blood gas, with F_{IO_2} of 0.8, showed a pH of 7.18, arterial carbon dioxide pressure (Pa_{CO_2}) of 10.11 kPa (75.8 mm Hg), and arterial oxygen pressure (Pa_{O_2}) of 6.13 kPa (45.98 mm Hg) (Pa_{O_2}: F_{IO_2} ratio of 57.46 mm Hg). A portable chest *x* ray showed bilateral florid pulmonary oedema. An electrocardiogram demonstrated sinus tachycardia.

After an initial intravenous dose of 400 μg naloxone, his conscious level improved to a GCS of 15/15. He was also given 50 mg furosemide intravenously and a 1% glyceryl trinitrate infusion, titrated to the patient's blood pressure.

There was no improvement in his respiratory failure with this initial treatment, and he remained hypoxic and tachypnoeic. The patient was commenced on bi-level positive airway pressure (BiPAP) non-invasive ventilation from a BiPAP Vision Ventilatory Support System (Respironics Inc) via a facemask. The initial inspiratory positive airways pressure (IPAP) was 10 cm H_2O, and expiratory positive airways pressure (EPAP) 5 cm H_2O. Over the next hour his respiratory rate fell to 24, Pa_{CO_2} to 5.57 kPa, and pH to 7.34. However, his GCS fell to 14/15 with pinpoint pupils, and he remained significantly hypoxic with a Pa_{O_2} of 6.60 kPa on an F_{IO_2} of 0.8. Three further doses of 400 μg naloxone intravenously were needed to maintain a normal conscious level and therefore a naloxone infusion was commenced.

Following increasing IPAP and EPAP to 12 and 7 cm H_2O, respectively, his Pa_{O_2} gradually rose to 23.96 kPa. His respiratory rate continued to return to normal. The patient was admitted to the coronary care unit for further care. He required a further 12 h of BiPAP before being weaned onto high flow oxygen as his pulmonary oedema gradually improved. Invasive ventilation was not required during his hospital stay. Further investigations failed to reveal any evidence of cardiac failure as the cause for his pulmonary oedema.

DISCUSSION

We found it surprising, given the availability of methadone in the community, that such cases are not seen more frequently, although it is possible that in regular users, the degree of opiate tolerance may offer protection against developing pulmonary oedema.[1–3]

Opiate antagonists will reverse central nervous system and respiratory depression but will not correct opiate-induced pulmonary oedema.[4] In our case, methadone caused severe respiratory failure.

Clinicians should consider commencing non-invasive ventilation in patients presenting with respiratory compromise early as such measures might improve outcome in non-cardiogenic pulmonary oedema.

The exact pathogenesis of opiate-induced pulmonary oedema is unclear.[1 2] One theory is that hypoxaemia and respiratory acidosis secondary to central respiratory depression in opiate overdose lead to increased capillary permeability.

Another theory is that the pulmonary capillary leak may be secondary to histamine release. Opiates are potent stimulators of both local and systemic histamine release, and histamine has been shown to increase both pulmonary lymph flow and capillary permeability. Surrogate markers of histamine release (plasma tryptase concentrations) have also been found to be elevated in fatal heroin overdose when compared to control subjects.

In non-cardiogenic pulmonary oedema secondary to methadone overdose, non-invasive respiratory support should be considered early and may reduce the need for invasive ventilation.

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