Fulminant pulmonary edema after intramuscular ketamine

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Purpose: To report an unusual case of pulmonary edema following intramuscular ketamine administration.

Clinical Features: An eight-year-old, healthy girl presented for dressing of first degree burns on dorsum of hand. Ten minutes after administration of 125 mg ketamine *im*, she developed laboured breathing, cyanosis, and bilateral crepitations and arterial blood gas analysis showed PaO₂ 55 mmHg. There was no evidence of upper airway obstruction. On intubating the trachea, pink frothy fluid emerged from the tube. She was diagnosed as a case of neurogenic pulmonary edema. She was managed with positive pressure ventilation with positive end expiratory pressure, morphine and furosemide. With this treatment she showed a favourable recovery.

Conclusion: Ketamine was given *im* to aid burns dressing in this case because it has distinct advantages above the other anesthetic agents including that of being a good analgesic which is absorbed by *im* route. Its use led to the development of pulmonary edema.

Objectif : Signaler un cas inhabituel d'œdème pulmonaire survenu après l'administration intramusculaire de kétamine.

Éléments cliniques : Une fillette de 8 ans, en bonne santé, s'est présentée pour un pansement sur des brûlures de premier degré au dos de la main. Dix minutes après l'administration de 125 mg de kétamine *im*, elle a présenté une gêne respiratoire, de la cyanose et des crépitations bilatérales. La gazométrie artérielle a montré une PaO₂ de 55 mmHg. Il n'y avait pas d'évidence d'obstruction des voies aériennes supérieures. À l'intubation de la trachée, un liquide rosé spumeux sortait du tube. On a posé le diagnostic d'œdème pulmonaire neurogène. La ventilation à pression positive avec pression positive en fin d'expiration, de la morphine et du furosémide ont constitué le traitement. L'enfant a connu une bonne récupération.

Conclusion : La kétamine *im* a été utilisée pour faciliter le pansement de brûlures à cause de ses avantages particuliers par rapport aux autres anesthésiques. En effet, elle fournit une bonne analgésie absorbée par voie *im*. Son emploi a provoqué l'apparition d'un œdème pulmonaire.

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Accepted for publication June 14, 2000.

PULMONARY edema after heroin, methadone and fentanyl as well as following the abuse of crack cocaine has been reported.¹⁻⁵ Also, there is one report of pulmonary edema following ketamine administration in a patient who had a history of crack cocaine abuse.⁶ In animals, pulmonary edema has been described after administration of xylazine-ketamine.⁷ We report a case of pulmonary edema after intramuscular ketamine in a previously healthy girl who presented for burn dressing.

Case report

An eight-year-old, 20 kg girl, presented for dressing of first-degree burns approximately 5x5 cm on the dorsum of the left hand. The patient was otherwise healthy, with no underlying medical risk factors. She was not suffering from respiratory disease. On physical examination, heart rate was 98 bpm, BP 100/68 mmHg. On auscultation, the lungs were clear and the cardiovascular system was normal. Noninvasive blood pressure, pulse oximeter and ECG monitoring were applied. The child was lying supine and oxygen 30% was started via a ventimask. Ketamine, 6.25 mg·kg⁻¹, was given *im* to aid the dressing procedure and no other medication was given. Isolyte P at 3 ml·kg⁻¹·hr⁻¹ was infused. Ten minutes later, the child developed laboured breathing. Respiration was shallow and at a rate of 30·min⁻¹. There was no suprasternal or supraclavicular retraction and no "rocking horse" movement of the chest. A patent airway was ensured but she developed cyanosis and oxygen saturation decreased to 80%. Chest auscultation revealed bilateral coarse crepitations. The saturation decreased to 70% very rapidly. The trachea was immediately intubated with 5.0 cuffed endotracheal tube from which emerged a gush of pink frothy fluid. Arterial blood gas analysis showed pH 7.39, PCO₂ 28 mmHg, PO₂ 55 mmHg, HCO₃ 25 mmol·l⁻¹ and SpO₂ 86% at FiO₂ 0.5. A diagnosis of pulmonary edema was made. She was given 0.1 mg·kg⁻¹ morphine and 1 mg·kg⁻¹ furosemide and she was transferred to the intensive care unit where positive pressure ventilation with PEEP of 8 cm H₂O and FiO₂ 1 was instituted. Oxygen saturation increased to 98%. Intermittent endotracheal suction was performed. She was nursed in a propped up position and intermittent suction continued. Chest X-ray one hour after the event was normal. Two hours after positive pressure ventilation at FiO₂ of 0.4, arterial blood gas analysis showed pH 7.44, PCO₂ 38.8, PO₂ 176 mm Hg, HCO₃ 25 mmol·l⁻¹. Morphine, 0.1 mg·kg⁻¹, *iv* was repeated two hours after the event. She passed 600 ml urine in the next six hours. Isolyte P was infused as a maintenance fluid at 60 ml·hr⁻¹. She

became conscious three hours after the event and the trachea was extubated approximately five hours after arriving in the ICU. She was kept in the intensive care unit over night and was transferred to the surgical ward the next day without complication.

Discussion

Ketamine is a hypnotic agent, possessing well-defined analgesic properties and is often used for induction of anesthesia because it has a rapid onset of action, short duration and is less likely to be followed by psychotic symptoms in children. These properties, combined with superb analgesia, give it an advantage in children undergoing repeated neurological investigation, radiotherapy or other minor surgical procedures where it can be given by intramuscular, intravenous, oral or nasal routes.⁸

Pulmonary edema may be caused by either increased pulmonary vascular pressure (cardiogenic), or increased permeability (noncardiogenic).^{7,9} Increased pressure pulmonary edema is characterised by lack of cellular damage, and a benign course of development. In contrast, increased permeability pulmonary edema is characterised by presence of cellular damage, protein rich edema fluid and rapid onset. Pulmonary edema following the use of heroin has been attributed to hypoxia, acute allergic reactions, neurogenic effect or a direct toxic effect of heroin on the alveolar capillary membrane.^{1,2} Hypoxia produces mild vasoconstriction of pulmonary arteries and arterioles, and increased permeability of alveolar walls.^{1,10} This would lead to over-perfusion and raised capillary pressures in uninvolved areas of the lung, which in turn might cause edema of the hydrostatic type. Our patient did have a period of respiratory depression, as was manifested by cyanosis; decreased respiratory depth followed a period of marked hypoventilation and decreased SpO₂. However, since experimental evidence shows that hypoxia causes no such effect, either alone or in conjunction with other forces,¹⁰ the concept of hypoxia induced pulmonary edema is not relevant in this case.

The pulmonary edema associated with airway obstruction, negative pressure pulmonary edema¹¹ is another possible mechanism but is less likely to be the cause because the patient did not develop clinically detectable airway obstruction at any time.

Acute injury to the central nervous system of both man and experimental animals may be followed by the development of acute pulmonary edema.¹²⁻¹⁵ This type of edema develops in the absence of pulmonary or cardiac disease and has been reported with many clinical disorders of the central nervous system (CNS). Immediately after injury, there is a massive increase in

systemic arterial and venous pressures, and pulmonary arterial, capillary and venous pressures. These changes reflect an extensive transfer of blood from the systemic to the pulmonary circulation, and are similar to the findings after a massive infusion of adrenaline.¹⁰ The injury to the CNS provokes a massive sympathetic discharge, which causes marked increase in pulmonary intravascular pressures, which leads to hydrostatic type edema.¹²⁻¹⁵ The increase in the intravascular pressure is short lived, but is of such a degree that it injures the endothelium of small pulmonary blood vessels. This results in increased vascular permeability and small hemorrhages. The increased permeability persists after intravascular pressures have returned to normal, and leads to the escape of edema fluid with a high protein content. This variety of pulmonary edema has been called neurogenic pulmonary edema to distinguish it from other varieties of pulmonary edema and to emphasize the primary role played by the CNS in the pathogenesis.^{9,10,13-15} Studies suggest that neurogenic pulmonary edema (NPE) is mediated largely through the sympathetic nervous system, specifically the alpha adrenergic system. The ability to prevent NPE by pre-treatment with adrenergic blocker agents indicates that massive neural discharge is primarily sympathetic in nature. Alpha adrenergic blocking drugs suppress the peripheral effects of sympathetic discharge and thus prevent pulmonary edema. The ability to prevent NPE with a variety of CNS depressants that operate by different pharmacological mechanism suggests that sympathetic discharge is centrally mediated and can be blocked by non-specific central depression.^{9,10,12,13} The use of morphine produces dramatic improvement in many cases of acute pulmonary edema.¹⁰ The most probable explanation is that neurogenic induced vasoconstriction, contributes to the rise in intravascular pressure, that precipitates an attack of acute edema, and that morphine abolishes this neurogenic vasoconstriction.

Ketamine is a potent sympathomimetic.⁸ There is at least one report of pulmonary hypertension and pulmonary edema caused by intravenous ketamine in a patient with coronary artery disease.⁶ Even in normal patients, ketamine produces increased pulmonary artery pressure, increased pulmonary vascular resistance and, secondarily, an increase in right ventricular stroke work.⁸ The cardiovascular effects produced by ketamine resemble sympathetic nervous system stimulation. The mechanism for the ketamine induced cardiovascular effects is complex.⁸ Direct stimulation of the central nervous system leading to increased sympathetic nervous system outflow seems to be the most important mechanism.⁸ Another proposed mechanism of the cardiac stimulating effect of ketamine, which has not been confirmed, is inhibition of norepineph-

rine uptake into postganglionic sympathetic nerve endings resulting in elevated plasma catecholamine concentration.⁸ This seems to be an appropriate explanation for the development of pulmonary edema in the case discussed here.

In view of the widespread casual use of ketamine by surgeons and other clinicians unaware of the possible complications, our case is a precautionary note to avoid misuse of the drug.

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