Opiate toxicity in patients with renal failure

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Lesson of the week
Opiate toxicity in patients with renal failure

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Opiates and their metabolites are known to accumulate in renal failure, with increased potential for toxicity, the most serious aspect of which is respiratory failure.1 Despite this knowledge, we continue to see life-threatening cases of opiate toxicity in patients with renal failure, two recent examples of which we present below.

Case reports

Case 1

A 68 year old woman with type 2 diabetes, angina, and obesity had an uncomplicated below knee amputation. Baseline creatinine was 133 μmol/l (estimated glomerular filtration rate 36 ml/min).2 In the first 36 hours after surgery she received 50 mg of morphine for analgesia. It was ascertained that she had been taking four tablets of Distalgesic (32.5 mg dextropropoxyphene hydrochloride and 325 mg paracetamol) a day for back pain for several days. We haemodialysed her three times, after which she was transferred to the intensive care unit. Investigations found 17.4 mmol/l (estimated 2 7.9 kPa, and P _a_O_2 9.5 kPa. We gave 400 μg of naloxone via a new cannula, and her Glasgow coma scale score improved to 14/15, and her respiratory rate rose to 14 breaths/min. We started a naloxone infusion, which was titrated to maintain her respiratory rate above 12 breaths/min. Her hyperkalaemia was managed conservatively. Within hours her urinary output increased, and in the following days her serum creatinine returned to baseline.

Case 2

A 63 year old woman with end stage renal failure, type 2 diabetes, and ischaemic heart disease was found semiconscious in bed. On the way to hospital she stopped breathing, and on arrival at the emergency department she was in cardiorespiratory arrest. We started cardiopulmonary resuscitation, and we intubated and ventilated her. After 90 seconds of pulseless electrical activity, we obtained cardiac output, and she became haemodynamically stable. Although she was obeying commands and resisting the endotracheal tube, she made no respiratory effort, therefore we sedated and paralysed her, and transferred her to the intensive care unit. Investigations found 17.4 mmol/l blood sugar, pH 7.02, P _O_2 23.9 kPa, and P_CO_2 9.5 kPa. An electrocardiogram showed a junctional rhythm, rate 50 beats/min, with no ischaemic changes. A chest radiograph was normal.

In the intensive care unit her pupils were noted to be small despite previous atropine and adrenaline administration. It was ascertained that she had been taking four tablets of Distalgesic (32.5 mg dextropropoxyphene hydrochloride and 325 mg paracetamol) a day for back pain for several days. We haemodialysed her for three hours, after which we exubrated her. She

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Students forever

An elderly woman was admitted under my care after an extensive postoperative pain in patients with renal disease, including patients who appear to have relatively mild renal dysfunction when assessed by measurement of serum creatinine. We suspected opiate toxicity at an early stage but discounted it because of an inadequate response to naloxone, which had unwittingly been administered subcutaneously. Subsequently, we gave naloxone via an intravenous infusion. We continued this for 48 hours, as the half life of naloxone is much shorter than that of morphine-6-glucuronide in patients with renal failure. Respiratory depression has been reported up to 12 hours after stopping the naloxone infusion. Indeed, we have previously observed life threatening opiate toxicity occurring more than 12 hours after withdrawal of patient controlled analgesia, when the protocol driven monitoring of respiratory function had already been discontinued. Finally, reversal of opiate toxicity coincided with the resolution of acute renal failure, a phenomenon previously described and probably reflecting morphine's haemodynamic effects.

The second case emphasises that life threatening side effects may also result from conventional doses of less potent opioid drugs in patients with chronic kidney disease. Similar effects have been encountered with other weak opiates, including over the counter preparations. Although we do not have definitive evidence of opiate toxicity, because naloxone was not given in this case, strong circumstantial evidence exists. Firstly, the patient's pupils were small despite giving her atropine and adrenaline. Secondly, the patient had recovered sufficiently from her cardiorespiratory arrest to obey commands and yet made no respiratory effort. Finally, there was a rapid improvement in respiratory function after removal of opiate metabolites during haemodialysis.

In conclusion, in patients with renal dysfunction, opiates and their active metabolites may accumulate, resulting in potentially life threatening toxicity. Use of non-opioid drugs should be considered and when opiates are necessary, those that tend not to accumulate in renal disease, such as buprenorphine or alfentanil, may be preferred for mild and more severe pain, respectively. Both medical staff and patients must be aware that patients with renal dysfunction have an increased risk of toxicity due to opiates, including over the counter preparations.

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References


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