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Morphine-induced pruritus after epidural administration followed by treatment with naloxone in a cat

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Abstract

Case summary A young male domestic shorthair cat weighing 1.6 kg was admitted to a veterinary teaching hospital for elective orchiectomy. A lumbosacral epidural injection of preservative-free morphine (0.1 mg/kg) and lidocaine (0.25 ml/kg) was performed under general anesthesia. One hour after extubation, the cat became agitated. Severe licking and biting of the hindlimbs, tail and lumbar area were observed. Pruritus was suspected and likely to be caused by epidural morphine. Acepromazine (0.02 mg/kg IM) was administered but clinical signs did not cease. Naloxone (2 µg/kg IV) was administered and clinical signs resolved within 20 mins.

Relevance and novel information Different therapeutic approaches are available for the treatment of morphine-induced pruritus. This case describes an additional treatment option using opioid antagonism with naloxone.

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Case description

A young male domestic shorthair cat weighing 1.6 kg was admitted to the veterinary teaching hospital of the Sao Paulo State University (UNESP-Botucatu) for an elective orchiectomy as part of a teaching laboratory for third-year veterinary students. The cat was judged to be healthy on the basis of physical examination and medical history (American Society of Anesthesiologists grade I). After premedication with an intramuscular injection of acepromazine (Acepran 0.2%, 0.05 mg/kg; Vetnil), ketamine (Dopalen, 5 mg/kg; Ceva), morphine (Dimorf 1%, 0.2 mg/kg; Cristália) and xylazine (Xilazin, 0.5 mg/kg; Syntec), a 24 G intravenous catheter was aseptically placed in the cephalic vein. Anesthesia was induced with IV propofol (Propovan, 2 mg/kg; Cristália). Endotracheal intubation was performed with a 3.5 mm cuffed endotracheal tube connected to a non-rebreathing system and anesthesia was maintained with isoflurane (Isoforine; Cristália) in 100% oxygen. An isotonic crystalloid solution (Lactated Ringer's solution; Fresenius-Kabi) was administered at a rate of 10 ml/kg/h IV throughout surgery.

Monitoring included thoracic auscultation for heart and respiratory rate, mucous membranes evaluation, rectal temperature and systolic arterial blood pressure using a Doppler ultrasonic device (811-B; Parks Medical Electronics). Under aseptic conditions and for teaching purposes, a veterinarian with experience in anesthesia (LKK) performed a lumbosacral epidural injection of preservative-free morphine (Dimorf 1%, 0.1 mg/kg; Cristália) and lidocaine (Xylestesin 2%, 0.25 ml/kg; Cristália) over 1 min, and using the stylet of a 24 G catheter. Orchiectomy was performed uneventfully by an experienced surgeon, and meloxicam (Melocox, 0.1 mg/kg; Eurofarma) was given intramuscularly at extubation.

During anesthetic recovery, approximately 1 h after extubation, the cat became agitated and restless. Severe licking and biting of the hindlimbs, tail and lumbar area were observed (see video 1 in Supplementary material). Pain was excluded after physical examination but without using a pain scoring system. The cat was able to stand

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freely and walk around the cage. Pruritus induced by epidural administration of morphine was suspected. Acepromazine (0.02 mg/kg) was given intramuscularly (approximately 30 mins) without any significant changes in behavior. Naloxone (Narcan 2 µg/kg; Cristália) was administered slowly intravenously. Approximately 20 mins later, the cat was calm and not showing signs of discomfort or pruritus (see video 2 in Supplementary material). The cat was discharged 3 h later when transportation was available.

Discussion

Morphine, administered epidurally, is a popular opioid used for the treatment of pain in dogs and cats. In cats, epidural administration of morphine has long-lasting antinociceptive effects.[1] However, the technique has been associated with adverse effects.[2–4] Morphine-induced pruritus is a possible adverse effect. The mechanism is still unclear, but some hypotheses include the involvement of serotoninergic receptors, the activation of areas in the dorsal horn of the spinal cord and the presence of an 'itch center'.[5]

There are some potential explanations for the pruritus observed in this case report. A lack of resistance during the epidural technique was noted, which normally suggests appropriate needle placement. In addition, cerebrospinal fluid was not observed in the needle hub, but it can be difficult to see because of the small size of the epidural space in this species. Both epidural and intrathecal administration of morphine have been associated with pruritus in cats.[3,4] Another explanation could be the volume administered. High volumes may induce cephalad migration of opioids. Experimental studies have shown that injection of high doses of morphine (0.2–1.0 mg/kg) into the cisterna cerebellomedullaris induces itch behavior in cats.[6]

In people, the onset of pruritus occurs between 0.5 and 3 h after epidural morphine.[7] In this case, clinical signs occurred 1 h after extubation (approximately 1.5 h after epidural injection). At that time, lidocaine-induced motor blockade had probably ended as the cat could ambulate normally.

There is no consensus about the treatment of opioid-induced pruritus. The reversal of analgesia is a common fear among researchers, but human studies show that opioid antagonism is effective in the treatment of pruritus caused by epidural and intrathecal morphine.[8] Opioid antagonists are administered by constant rate infusion or boluses using patient-controlled devices in humans to treat opioid-induced adverse effects.[9] Pruritus appears to be closely associated with stimulation of mu receptors as partial and full opioid antagonists are effective in the prophylaxis and treatment of opioid-associated pruritus. Low-dose naloxone was associated with a decrease in pruritus and nausea without changes in pain scores in humans.[10] Similar information is not available in cats.

In cats, pruritus might be under-reported and interpreted as agitation in the anesthetic recovery, pain or dysphoria. The intense grooming behavior in cases reported earlier were successfully treated with low doses of propofol and ondansetron,[3,4] a serotoninergic receptor antagonist. This is the first case report using naloxone, an opioid antagonist for the treatment of morphine-induced pruritus. It showed that naloxone crosses the blood–brain barrier to exert its effects in the central nervous system and reversing opioids that are administered by the epidural route. A low dose of acepromazine was administered in an attempt to produce sedation and anxiolysis without reversing the analgesic effects of morphine. Acepromazine has sedative and anti-histaminic properties that could have contributed to the treatment of pruritus;[11] however, this effect was not observed in this case. Finally, a low dose of naloxone (2 µg/kg) was administered intravenously over 1 min and it seemed to reverse the clinical effects. This response provides a suggested dose for opioid antagonism in cats. The duration of action of naloxone is unknown in cats; however, reoccurrence of pruritus was not observed until at least 3 h later when the patient was discharged. The cat did not return to the hospital for further treatment.

The anesthetic and analgesic protocols used in this case are not commonly employed at our veterinary teaching hospital. For example, epidural morphine is not routinely administered for routine orchiectomy. The injection was performed in one cat for didactic purposes.

Conclusions

This case describes an additional treatment option for opioid-induced pruritus in cats. Veterinarians should be aware of this possible complication after intrathecal or epidural administration of opioids, and naloxone can be considered as a treatment option. The literature suggests that clinicians treat postoperative pruritus in various ways.

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Supplementary material The following files are available:
Video 1: Severe licking and biting of the hindlimb, tail and lumbar area
Video 2: The cat was calm and not showing signs of discomfort or pruritus 20 mins after receiving naloxone

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