

*Lesson of the week***Nalbuphine and slow release morphine**

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**Nalbuphine should be avoided in patients taking long term opiate analgesia**

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Prehospital analgesia should ideally give fast and safe relief from pain without adversely affecting the clinical course of patients. Nalbuphine is the intravenous analgesic for severe pain that is most widely used by ambulance services in the United Kingdom, but morphine has now been licensed for use by paramedics and is being introduced by a number of ambulance services. We present a case highlighting an important contraindication to the use of nalbuphine.

**Case report**

A 60 year old woman fell in her garden, injuring her right leg. She had a history of renal cell carcinoma with cerebral and bony metastases, and was taking 90 mg of slow release morphine tablets twice a day to control her pain. Ambulance paramedics diagnosed a fractured femur, and her prehospital care included giving her 30 mg of nalbuphine intravenously for analgesia. She became agitated, and on arrival in the emergency department she was unable to keep still; her agitation was severe enough to cause involuntary movements of all four limbs, including the injured right leg. On questioning, she complained that the main problem at that stage was agitation, which was causing the pain in her leg to be much worse.

Examination and x ray imaging confirmed a closed fracture of the mid-shaft of the right femur, and subsequent radiological investigation showed evidence of a pathological fracture. We saw no neurovascular deficit. The woman's symptoms of agitation along with tachycardia, hypertension, and sweating were typical of opiate withdrawal.

Initially, her management was complicated by resistance to intravenous opiate analgesia (she was given incremental doses of intravenous morphine for her pain to a total of 40 mg but with little effect), and she required a femoral nerve block and application of a traction splint to control her symptoms. Also, her agitation was controlled by giving intravenous lorazepam, titrated to achieve control of her involuntary movements—a total 4 mg was given in 30 minutes. She remained agitated, although pain free, for about 4 hours after taking the nalbuphine. Subsequently she went on to have internal fixation of her femoral fracture and made an uneventful recovery from her operation.

**Discussion**

Nalbuphine is a synthetic opioid that is a mixed agonist-antagonist at opiate receptors. It binds to  $\mu$  and  $\kappa$  receptors, acting as an agonist at  $\kappa$  receptors but as a partial antagonist at the  $\mu$  receptor to primarily  $\mu$  agonist compounds such as morphine. The onset of action after intravenous administration is 2-3 minutes, and its plasma half life is about 5 hours.<sup>1</sup> It has similar analgesic properties to morphine at equivalent doses, but a lower incidence of respiratory depression with

nalbuphine has been reported. Nalbuphine is a safe and effective analgesic for use in the prehospital environment for many conditions ranging from cardiac ischaemia to trauma and burns.<sup>2-4</sup>

Authors have previously expressed concerns over the potential of nalbuphine to increase requirements of opiate analgesics after arrival at hospital due to its partial antagonist effect.<sup>5,6</sup> The potential for nalbuphine to produce withdrawal in opiate dependent people has been explored in a study using opiate dependent volunteers, where it was found that the withdrawal syndrome precipitated by nalbuphine was indistinguishable from that produced by giving naloxone.<sup>7</sup> This case highlights the potential for the induction of opiate withdrawal secondary to prehospital administration of nalbuphine for analgesia.

For those prehospital systems using nalbuphine, education should caution against using this form of analgesia in patients already taking opiate analgesic agents. History taking should specifically target whether patients have been prescribed opiates, and this should be considered a contraindication to giving nalbuphine. Handover at the interface between prehospital and hospital environments should always include a summary of drugs given, and documentation should accurately reflect the treatment given.

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- Lo MW, Lee FH, Schary WL, Whitney CC Jr. The pharmacokinetics of intravenous, intramuscular, and subcutaneous nalbuphine in healthy subjects. *Eur J Clin Pharmacol* 1987;33:297-301.
- Stene JK, Stofberg L, MacDonald G, Myers RA, Ramzy A, Burns B. Nalbuphine analgesia in the prehospital setting. *Am J Emerg Med* 1988;6:634-9.
- Chambers JA, Guly HR. Prehospital intravenous nalbuphine administered by paramedics. *Resuscitation* 1994;27:153-8.
- Johnson GS, Guly HR. The effect of pre-hospital administration of intravenous nalbuphine on on-scene times. *J Accid Emerg Med* 1995;12:20-2.
- Houlihan KP, Mitchell RG, Flapan AD, Steedman DJ. Excessive morphine requirements after pre-hospital nalbuphine analgesia. *J Accid Emerg Med* 1999;16:29-31.
- Robinson N, Burrows N. Excessive morphine requirements after pre-hospital nalbuphine analgesia. *J Accid Emerg Med* 1999;16:392.
- Preston KL, Bigelow GE, Liebson IA. Antagonist effects of nalbuphine in opioid-dependent human volunteers. *J Pharmacol Exp Ther* 1989;248:929-37.

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*Endpiece***The doctor within**

Each patient carries his own doctor inside him.  
They come to us not knowing that truth. We are at  
our best when we give the doctor who resides  
within each patient a chance to go to work.

Albert Schweitzer (1875-1965)

Fred Charatan, retired geriatric physician, Florida