Caudal neostigmine in children

Editor—I was interested in the excellent review of caudal additives in children. The review provides an elaborate description of the drugs used as additives for caudal analgesia. Although almost all of the drugs used for this purpose have been extensively reviewed by the authors, no mention of neostigmine could be found.

Neuraxial neostigmine is known to produce analgesia in animals, human volunteers and patients with pain. Neuraxial administration of this cholinesterase inhibitor inhibits breakdown of the endogenous spinal neurotransmitter acetylcholine, which has been shown to produce analgesia. The analgesic effect is thought to be mediated via spinal muscarinic (M₄) receptors. A dose–response study of caudal neostigmine has proved its efficacy and safety in paediatric patients. Dose-dependent analgesia has been observed with caudal neostigmine in the range of 20–50 μg kg⁻¹. A single caudal injection of neostigmine 2 μg kg⁻¹ when added to bupivacaine 0.25% or ropivacaine 0.2% has been found to provide an extended duration of postoperative analgesia (20–22 h), and reduced the need for supplementary analgesics in children undergoing genitourinary surgery. This duration is almost equal to the duration of analgesia provided by other caudal drugs co-administered with local anaesthetics.

Respiratory depression, sedation and pruritis ascribed to the use of caudal opioids are not encountered with caudal neostigmine. Unlike ketamine and clonidine, use of neostigmine does not require a specific preservative-free preparation. The neostigmine preparation containing methyl and propyl-parabens as preservatives has been safely used in adults and children. Furthermore, in contrast to clonidine, its use with local anaesthetics is not associated with significant haemodynamic changes. This is attributed to the ability of neostigmine to counteract the inhibitory effect of spinal bupivacaine on the sympathetic nervous system, thereby blunting the hypotension induced by neuraxial local anaesthetics and clonidine.

The main adverse effect reported with the use of neuraxial neostigmine is the frequent incidence of nausea and vomiting. Although the incidence has been reported to be significantly higher with the intrathecal route, use of extradural neostigmine in adults and children has been found to be associated with a lower incidence of nausea or vomiting (15–30%). A similar or even higher incidence of nausea and vomiting has been reported with the use of caudal bupivacaine alone. Notwithstanding this adverse effect, the favourable haemodynamic and respiratory profiles of extradural neostigmine make it an attractive alternative to currently used caudal antinociceptive drugs.

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Editor—Thank you for the opportunity to respond to Dr Mahajan’s letter. Neostigmine was deliberately omitted from our review as we felt that there was insufficient evidence at the time for its safe and efficacious use in children. However, a number of recently published studies have shown that caudal neostigmine, either alone or in combination with bupivacaine, provides effective and prolonged postoperative analgesia in children. What is not so clear is the ideal dose. The dose range used by Batra and colleagues (10–50 μg kg⁻¹) resulted from an extrapolation of the intrathecal dose used in an adult study, multiplied by a factor of 10 to account for its highly polar nature as suggested by Lauretti and colleagues. When used as the sole agent, a dose of 20–30 μg kg⁻¹ is recommended, though a much lower dose of neostigmine (2 μg kg⁻¹) has been used to good effect when combined with a local anaesthetic. With regard to safety, caudal neostigmine appears to have a reasonably benign side-effect profile, with dose-dependent nausea and vomiting being the only reported adverse effect. However, we have some reservations about the author’s comment, ‘unlike ketamine and clonidine, use of neostigmine does not require a specific preservative-free preparation’. Although methyl and propyl paraben containing neostigmine has been safely used in adults, it does not necessarily mean that it is safe to use. In particular, we do not know what long-term effects it may have on the developing spinal cord in children. In our opinion, the perceived benefits do not justify the potential risks and we cannot, on the basis of the current data, advocate the adoption of caudal neostigmine into mainstream clinical practice.

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