Adjuncts to caudal blockade in children

Editor—We read with great interest the editorial by Lönqvist regarding caudal additives. The author gives an excellent description of the chronological development of caudal adjuncts. Nevertheless, we were somewhat surprised by his affirmations regarding caudal neostigmine. The author claims that two studies are proof enough to show that caudal neostigmine has no role in the caudal space and its use should be limited to the reversal of neuromuscular block—’no further studies are needed’!

Of the seven studies on caudal neostigmine in children,3–8 only two3,8 have been mentioned. Sample sizes of these two studies are quite small (n=30 and 20), therefore it seems premature to draw any sound conclusions. Four studies2,4,7,8 showed a significant prolongation of postoperative analgesia when neostigmine was added to local anaesthetic (5–8 h vs 16–22 h). A dose finding study clearly showed dose-dependent analgesia of caudal neostigmine.5 A study performed by our group showed a ketamine sparing effect of neostigmine with a postoperative analgesia of 21.8 h.3 Only one study6 so far did not observe a significant advantage in terms of analgesia when adding neostigmine to bupivacaine. Secondly, a 30% incidence of PONV as observed in two3,8 studies is defined by the author as unacceptable. Of the seven studies on caudal neostigmine in children, four studies2,4,6,7 did not show a significant increase in PONV. A dose-dependent increase of PONV has been described in the dose finding study,5 but only with doses of 30 μg kg⁻¹ or higher. The 30% incidence of PONV encountered in our study3 might be because of the higher dose of neostigmine (10 μg kg⁻¹) used, but nevertheless only mild PONV was observed as no child presented more than one single episode of vomiting. The same or even higher incidence of PONV can be observed with caudal opioids.9,10 The effectiveness of antiemetics on preventing neostigmine induced PONV still needs to be tested. With regard to safety, all studies so far show that caudal neostigmine has a reasonably benign profile with dose-dependent nausea and vomiting the only reported side-effect. In our study the preservative-free formulation has been used and this is strongly recommended. We agree with the author that prospective randomized trials of adequate size are warranted to answer important questions regarding new caudal adjuncts and prevent caudal block falling into disrepute. It might be true that caudal neostigmine will not become an alternative to clonidine or ketamine, but only a large number of studies with adequate power will enable us to decide whether caudal neostigmine should be adopted into mainstream clinical practice or not.

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Editor—We were interested in the recent editorial regarding adjuncts to caudal block in children by Lönqvist.3 Although the author has summarized the use of adjuvants well, and drawn conclusions and recommendations to safeguard the practice of caudal analgesia, the decision to condemn the caudal neostigmine seems to be a hurried one.

The author has the opinion that because of the high incidence of PONV (30%) with caudal neostigmine, no further studies are required, and its use to be restricted only to reverse neuromuscular block, on the basis of two studies.3,8 In the first study, using caudal S(+)-ketamine 1.0 mg kg⁻¹ and neostigmine 10 mg kg⁻¹, only marginal prolongation of postoperative analgesia was seen with addition of caudal neostigmine to ketamine with a high incidence (30%) of PONV.5 However, this is not surprising. In our early dose–response study of caudal neostigmine, we have already demonstrated a poor analgesic effect of caudal neostigmine given alone in doses of 10 μg kg⁻¹ with a 20% incidence of PONV which increased with higher doses of caudal neostigmine.5 Caudal ketamine, in the dose range of 0.5–1.0 mg kg⁻¹ is associated with 10–25% incidence of PONV.11 A synergistic action of caudal neostigmine with bupivacaine does mean a synergistic analgesic effect with caudal ketamine. It is possible that ketamine may potentiate the emetic action of caudal neostigmine.

In the study by Abdulatif and colleagues8 in which caudal neostigmine in dose of 2 μg kg⁻¹ with bupivacaine was found to be efficacious, albeit with a high incidence of PONV (30%). We found a dose-independent analgesic effect of caudal neostigmine, with 2 μg kg⁻¹ being the optimal dose with caudal bupivacaine.4 However, we found a 15% incidence of PONV. Similarly Turan and colleagues7 and Kumar and colleagues5 have reported 13–15% incidence of PONV with caudal neostigmine with local anaesthetics.4 All these three studies have concluded that administration of caudal neostigmine 2 μg kg⁻¹ with local anaesthetics, offers an advantage of extended duration of postoperative analgesia without increasing the incidence of adverse effects. A similar or higher incidence of PONV has been reported with the use of caudal bupivacaine alone.11

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In conclusion, notwithstanding the adverse effect of PONV, the favourable haemodynamic and respiratory profiles of epidural neostigmine, do make it an attractive alternative to currently used caudal antinociceptive drugs and its use in mainstream practice for caudal analgesia may be well advocated along with its routine i.v. use for reversing neuromuscular block.

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Editor—I would like to thank both Drs Mahajan and Almenrader for their input regarding neostigmine as an adjunct to paediatric caudal blockade. As they have an academic interest in this technique it may not be surprising that our opinions regarding the appropriateness of neostigmine as an adjunct does somewhat differ.

The core message of my editorial was, that new alternatives to opioids, ketamine, and clonidine must either be considerably more effective than these existing well-documented alternatives or should be equally effective but with fewer side-effects. Furthermore, it is now time for well-established working bodies (e.g. RCA or APA) to issue guidelines, so that the best and safest practice can be adopted at all institutions delivering regional anaesthesia to paediatric patients. Thus, the focus of the editorial was not the use of neostigmine as an adjunct per se.

Having said that, I still fail to understand that neostigmine does have a place in this context. Although it appears as if neostigmine is capable of producing enhanced postoperative pain-relief this is not at present entirely clear. Dose–response data from Dr Mahajan’s group is somewhat confusing. In one study, a dose-dependent effect within the dose range of 10–50 µg kg⁻¹ of neostigmine in saline was reported (however, with no effect of 10 µg kg⁻¹ vs a group not treated with caudal blockade) whereas a later publication described a dose-independent effect of 2–4 µg kg⁻¹ when added to bupivacaine. Furthermore, if the remaining publications on adjunct use of neostigmine were subjected to a meta-analysis, it would most likely conclude that there is still a lack of data to support its efficacy.

It may be that neostigmine’s effect on PONV is overly emphasized in my editorial, but I would suggest that the majority of current data clearly point to the fact that caudal neostigmine does increase the incidence of PONV in an unjustifiable way. In the two studies initially referenced an increase from almost 0 to 30% PONV was reported and, although not statistically significant because of sample sizes, further studies have found trends pointing to a 3-fold increase in PONV in the groups treated with neostigmine compared with plain local anaesthetics.

For fairness’ sake I would take this opportunity to emphasize that I have previously questioned whether the routine use of opioids as adjuncts to caudal blockade can still be justified because of the high incidence of unwanted side-effects.

Overall, my conclusion still is that adjunct neostigmine neither is clearly more effective than an existing alternative, nor associated with fewer side-effects. Thus, neostigmine does not fulfil the criteria for a drug that can compete with or replace the already well-established adjuncts. I will be surprised if further studies would be able to prove otherwise.

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