British Journal of Anaesthesia **103 (2):** 268–74 (2009)
doi:10.1093/bja/aep159 Advance Access publication June 18, 2009

BJA

Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children

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Background. Caudal block is a common technique for paediatric analgesia but with the disadvantage of short duration of action after single injection. Caudal dexmedetomidine and clonidine could offer significant analgesic benefits. We compared the analgesic effects and side-effects of dexmedetomidine and clonidine added to bupivacaine in paediatric patients undergoing lower abdominal surgeries.

Methods. Sixty patients (6 months to 6 yr) were evenly and randomly assigned into three groups in a double-blinded manner. After sevoflurane in oxygen anaesthesia, each patient received a single caudal dose of bupivacaine 0.25% (1 ml kg^{-1}) combined with either dexmedetomidine 2 μg kg^{-1} in normal saline 1 ml, clonidine 2 μg kg^{-1} in normal saline 1 ml, or corresponding volume of normal saline according to group assignment. Haemodynamic variables, end-tidal sevoflurane, and emergence time were monitored. Postoperative analgesia, use of analgesics, and side-effects were assessed during the first 24 h.

Results. Addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia time [median (95% confidence interval, CI): 16 (14–18) and 12 (3–21) h, respectively] than the use of bupivacaine alone [median (95% CI): 5 (4–6) h] with $P<0.001$. However, there was no statistically significant difference between dexmedetomidine and clonidine as regards the analgesia time ($P=0.796$). No significant difference was observed in incidence of haemodynamic changes or side-effects.

Conclusions. Addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side-effects.

Br J Anaesth 2009; **103**: 268–74

Keywords: anaesthetic, analgesic regimens; anaesthetic techniques, regional, caudal; anaesthetics local, bupivacaine; analgesia, paediatric; analgesia, postoperative

Accepted for publication: May 6, 2009

Caudal epidural block is one of the most popular, reliable, and safe techniques in paediatric analgesia that can provide analgesia for a variety of infra- and supraumblical surgical procedures. The main disadvantage of caudal analgesia is the short duration of action after a single injection.[1] The use of caudal catheters to administer repeated doses or infusions of local anaesthetics is not popular, partly because of concerns about infection. Prolongation of caudal analgesia using a 'single-shot' technique has been achieved by the addition of various adjuvants, such as epinephrine, opioids, ketamine, and α_2 agonists.[2]

Clonidine action, similar to local anaesthetic action, and its interaction with local anaesthetics have been explained by three possible mechanisms. First, clonidine blocks Aδ and C fibres as a consequence of an increase in potassium conductance in isolated neurones, thus intensifying local anaesthetic conduction block.[3] Secondly, clonidine may cause local vasoconstriction, thus decreasing local anaesthetic spread and removal around neural structures. This effect is mediated by drug action on post-synaptic α_2 receptors, although there is little evidence of this mechanism with clinical doses.[4] Thirdly, clonidine combined with

spinal local anaesthetics or used in peripheral blocks intensifies and prolongs analgesia.[5] Spinal α_2 adrenergic agonists may also induce analgesia by activating spinal cholinergic neurones resulting in acetylcholine release.[6]

Dexmedetomidine has an eight-fold greater affinity for α_2 adrenergic receptors than clonidine and much less α_1 effects. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_{2A} receptors, responsible for the hypnotic and analgesic effects of such drugs.[7–9]

This study was designed to compare the analgesic effects and side-effects of dexmedetomidine and clonidine when added to bupivacaine for caudal analgesia in children undergoing lower abdominal surgeries.

Methods

After local ethical committee approval and obtaining informed parental consent, 60 ASA status I and II patients, aged 6 months to 6 yr undergoing lower abdominal surgeries, were prospectively enrolled in this study.

Study exclusion criteria included a history of developmental delay or mental retardation, which could make observational pain intensity assessment difficult; a known or suspected coagulopathy; a known allergy to any of the study drugs; and any signs of infection at the site of the proposed caudal block.

Using a computer-generated list, the subjects were randomly and evenly assigned into three groups: A, B, and C. All health-care personnel providing direct patient care, the subjects, and their parents or guardians were blinded to the caudal medications administered. All medications were prepared by pharmacy staff not participating in the study except for preparing the drugs. They received and kept the computer-generated table of random numbers according to which random group assignment was performed. After obtaining subjects weight, and according to the randomizing table, the volume to be injected in the caudal block was prepared in syringes with labels indicating only the serial number of the patient.

All subjects received a conventional preoperative dose of oral midazolam (0.5 mg kg^{-1}) 20–30 min before anaesthetic induction, and then underwent a standard inhalation induction with sevoflurane in oxygen followed by insertion of an i.v. canula and administration of a neuromuscular blocking agent to facilitate endotracheal intubation. Induction was strictly inhalation and atropine was not administered routinely. After endotracheal intubation, patients were placed in the lateral decubitus position, and a single-dose caudal block was performed according to the group under sterile conditions using a 23 G needle and standard loss of resistance technique.

Group 'A' received: bupivacaine 0.25% (1 ml kg^{-1}) with dexmedetomidine 2 μg kg^{-1} in normal saline 1 ml; Group 'B' received: bupivacaine 0.25% (1 ml kg^{-1}) with clonidine 2 μg kg^{-1} in normal saline 1 ml; and Group 'C' received: bupivacaine 0.25% (1 ml kg^{-1}) with normal saline 1 ml, with a maximum volume of 30 ml for all three groups.

General anaesthesia was maintained with sevoflurane delivered in oxygen. The inhaled concentration of sevoflurane was adjusted to achieve haemodynamic changes <30% of the baseline values. No other narcotics, analgesics, sedatives, or antiemetics were administered intraoperatively. At the conclusion of surgery, the patient was awakened and transported to the post-anaesthetic care unit (PACU).

Standard monitoring was used during anaesthesia and surgery. Heart rate and arterial pressure were recorded before operation and every 5 min until the end of surgery. The occurrence of intraoperative hypotension requiring a fluid bolus, bradycardia requiring atropine, and the maximum maintenance end-tidal concentration of sevoflurane (%) were recorded. Perioperative blood loss was replaced meticulously using crystalloids and blood, as appropriate. The anaesthesia time (the time from induction of anaesthesia to the end of surgery when the inhalation agent was discontinued), emergence time (the time from the end of surgery to opening the eyes on calling the patient's name), a delayed anaesthetic emergence (defined as >20 min elapsing from the end of surgery to exiting the operating theatre), or all were also noted.

Using the paediatric observational FLACC pain scale with its 0–10 score range (Table 1),[10] each study participant's pain intensity was assessed upon arrival in and at the time of discharge from the PACU, and then every 4 h for the first 24 h after operation. If the FLACC pain scale score was noted at any time to be 4 or more, morphine 0.2 mg kg^{-1} i.m. was administered to achieve an FLACC scale score of 3 or less. The duration of adequate caudal analgesia (from the time of caudal injection to the first time the FLACC pain scale score was noted to be 4 or more) was also recorded.

Once transferred to the in-patient care unit, the oxygen saturation, heart rate, and arterial pressure were continuously monitored in the presence of a staff nurse. The occurrence of postoperative respiratory depression (defined as oxygen saturation of <95%), hypotension (defined as systolic arterial pressure <70 plus twice the age in years and associated with altered peripheral perfusion), bradycardia (defined as heart rate below 80 beats min^{-1} for ages <1 yr and <60 beats min^{-1} for ages above 1 yr) requiring medical intervention, or all was also noted. Postoperative nausea and vomiting (PONV) was treated as needed with i.v. ondansetron 0.06 mg kg^{-1} every 4 h, postoperative pruritis was treated as needed with i.v. diphenhydramine 0.2 mg kg^{-1} every 6 h.

Postoperative recordings also included: the duration of PACU stay, time of first administration of morphine for each patient, occurrence and treatment of PONV and pruritis, time to first micturition after caudal injection, and the incidence of bladder catheterization. The initiation of clear liquid and solid oral intake and time of discharge home were also recorded.