Journal of Clinical Anesthesia (2009) **21**, 113–119

ELSEVIER

Journal of Clinical Anesthesia

Original contribution

Addition of midazolam to continuous postoperative epidural bupivacaine infusion reduces requirement for rescue analgesia in children undergoing upper abdominal and flank surgery

Babita Ghai MD, DNB (Associate Professor)[a,*], Jeetinder Kaur Makkar MD, DNB (Assistant Professor)[a], Pramila Chari MD, FAMS (Ex-Professor and Head)[a], Katragadda Lakshmi Narasimha Rao MS, Mch, FACS, FAMS (Professor and Head)[b]

[a]*Department of Anesthesia and Intensive Care, Post Graduate Institute of Medical Education and Research, Chandigarh-160012, India*
[b]*Department of Pediatric Surgery, Post Graduate Institute of Medical Education and Research, Chandigarh-160012, India*

Received 26 September 2007; revised 26 June 2008; accepted 26 June 2008

Keywords:
Patients;
Children;
Postoperative analgesia;
Epidural infusion;
Bupivacaine;
Midazolam;
Procedure;
Abdominal surgery

Abstract

Study Objective: To investigate the effect of adding midazolam to continuous epidural infusion of bupivacaine for postoperative analgesia in children.

Design: Prospective, randomized, double-blind, controlled study.

Setting: Tertiary-care center.

Patients: 44 ASA physical status I and II children in age groups of two to 10 years, undergoing elective upper abdominal and flank surgery.

Interventions: At the end of surgery, patients were randomly allocated to receive epidural infusion of 0.125% bupivacaine alone (Group B) or with 20 μg/kg/hr midazolam (Group BM) for 12 hours at the rate of 0.2 mL/kg/hr.

Measurements: Pain, motor block, and sedation were assessed at predetermined times over 24 hours. Intravenous fentanyl was used as rescue analgesic for the first 12 hours, and tramadol for next 12 hours. Patients were followed at one week, one month, and one year for any neurological deficits.

Main Results: The number of patients requiring rescue analgesia during infusion was significantly lower in Group BM (7 vs. 17 in Group B; $P < 0.001$). Time to first rescue analgesia was significantly prolonged in Group BM compared with Group B ($P < 0.001$). Frequency of fentanyl ($P < 0.001$) and tramadol ($P = 0.001$) administration as rescue analgesia was significantly less in Group BM. Significantly lower median pain scores were obtained in Group BM than Group B at all time intervals ($P < 0.05$). Greater sedation scores were noted in Group BM at all time intervals postoperatively except

* Corresponding author. Tel.: +91 172 274 6622; fax: +91 172 274 4401.
E-mail address: ghaibabita@hotmail.com (B. Ghai).

0952-8180/$ – see front matter
doi:10.1016/j.jclinane.2008.06.029

at 4 hours ($P < 0.05$). No motor block was observed in any child during the study. No neurological deficit was reported in any child in the one year of follow-up.
Conclusion: Addition of 20 μg/kg/hr of midazolam to postoperative continuous epidural infusion of 0.125% bupivacaine reduces the requirement for rescue analgesia in children following upper abdominal and flank surgery.

1. Introduction

Epidural analgesia is reported to be effective in managing the postoperative pain in children undergoing abdominal surgery with less sedation and improved respiratory function compared with intravenous (IV) opioids [1]. When used alone, higher doses of local anesthetics required for effective epidural analgesia may be associated with autonomic and motor block. To decrease these "dose-dependent" side effects and prolong the duration of analgesia of local anesthetics, opioids are commonly added. However, epidural opioids may be associated with distressing side effects like nausea, vomiting, pruritus, urinary retention, and respiratory depression [2]. Therefore, the nonopioid drugs like clonidine, ketamine, and others, have been investigated as adjuvants to epidural local anesthetics. Epidural clonidine has been associated with limited hypotension [3]. However, limited availability of injectable clonidine in many countries restricts its use. Epidural ketamine is associated with psychomimetic effects [4].

Gamma amino butyric acid (GABA) receptors also modify nociception [5]. An epidural infusion of midazolam has been used in adults and causes amnesia and sedation [6-8]. "Single shot" caudal epidural injection of midazolam prolongs the analgesic effect of bupivacaine in children [9-11], but we have found no published data on the effect of epidural infusion of midazolam. This study investigated the analgesic effect and side effects of adding midazolam to continuous epidural infusion of bupivacaine for postoperative analgesia in children undergoing upper abdominal and flank surgery.

2. Materials and methods

Forty-seven ASA physical status I and II children of either gender, in age groups of two to 10 years, and undergoing elective upper abdominal and flank surgery, were recruited to this prospective, randomized, double-blind study. Patients with a history of bleeding disorders, hepatorenal disorder, local spine deformity, neurological or spinal pathology, or allergy to midazolam or bupivacaine were excluded from the study.

PGIMER Institutional ethics committee approval and written, informed consent from the parent/guardian were obtained. Anesthesia was induced with halothane in O_2 administered via face mask. Fentanyl one μg/kg was administered. Intraoperative monitoring included electrocardiogram, oxygen saturation, noninvasive blood pressure (BP), end-tidal CO_2, end-tidal halothane concentration, and temperature. Tracheal intubation was facilitated using atracurium 0.5 mg/kg. Anesthesia was maintained with halothane and nitrous oxide (67%) in O_2 , maintaining the end-tidal cumulative minimum alveolar concentration (MAC) of 1.3-1.5. An epidural catheter (19-gauge needle/22-gauge catheter, Mini Kit; Vygon, Ecouen, France) was inserted in the lateral position at the L_2 - L_3 level using the loss-of-resistance technique. Catheter length inside the epidural space was calculated by measuring the distance from the site of insertion to the T_{12} level; this calculation was used as a guide for correct catheter placement. Placement of the catheter tip at the T_{12} level was confirmed by fluoroscopy. After the test dose (0.1 mL/kg of 1% lidocaine with 5 μg/mL of epinephrine), patients received 0.125% bupivacaine 0.2 mL/kg bolus through the epidural catheter before the start of surgery. At the start of skin closure, patients were allocated to one of two groups for epidural infusion, using computer-generated random numbers. In Group B, patients received an epidural infusion of 0.2 mL/kg/hr 0.125% bupivacaine, and Group BM patients received a similar volume of 0.125% bupivacaine with 20 μg/kg/hr midazolam (Claris Lifesciences, Ltd., Ahmedabad, India) for 12 hours. The midazolam concentration used in Group BM was 0.001%; the pH of the solution was 6.0 in Group B and 5.9 in Group BM. The randomization codes were kept in sealed envelopes. An anesthesiologist not involved in the study selected one envelope for each patient and prepared the infusion in normal saline. Both patient and investigators involved in the study were blinded as to the drug used.

After completion of surgery, halothane was discontinued. Neuromuscular block was reversed with neostigmine and atropine, and the trachea was extubated. Patients were observed in the Postanesthesia Care Unit (PACU) for 12 hours and transferred to surgical wards after the infusion was discontinued. Vital signs, pain, sedation, and degree of motor block were recorded at the immediate postoperative period (0 hr), then hourly for 4 hours, then at 8, 12, and 24 hours postoperatively. All observations were made by a single trained observer. Pain was assessed based on a scoring system as described by Hannallah et al. [12], which obtains a summed value of between 0 and 10 from observations of arterial BP, crying, movement, agitation, and localization of pain [Appendix A]. During the infusion period, IV fentanyl