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ORIGINAL ARTICLE

Effect of wound infiltration with bupivacaine on postoperative analgesia in neonates and infants undergoing major abdominal surgery: a pilot randomized controlled trial

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Abstract

Purpose Postoperative pain management is essential in the perioperative care of neonates and infants but it requires a high level of care. Wound infiltration with bupivacaine, a long-acting local anesthetic, is a simple method with minimal complications. However, studies on the effectiveness of wound infiltration in neonates and infants are lacking. The purpose of this study was to investigate the effectiveness of wound infiltration with bupivacaine for postoperative analgesia in neonates and infants undergoing abdominal surgery.

Methods A prospective, randomized controlled trial was conducted in 34 neonates and infants. The patients were randomized into two groups: the bupivacaine (B) group and the control (C) group. A standardized anesthetic protocol was used for each patient. Before wound closure, the surgical site of each patient in the B group was infiltrated with 2 mg/kg of bupivacaine, whereas no surgical site anesthetic infiltration was used in the C group. The neonatal infant pain scale (NIPS) score was used to evaluate postoperative pain, and fentanyl 0.5–1.5 μg/kg was administered when the NIPS score was ≥4. In regard to the fentanyl requirement, the NIPS score and the numbers of patients whose NIPS score was ≥4 were compared between the two groups.

Results The median fentanyl dose requirements in the B group and C group were 1 and 0.5 μg/kg, respectively; and the difference was not statistically significant ($p = 0.255$). The postoperative NIPS scores in the two groups were not significantly different. In addition, there were no significant differences in the numbers of patients whose NIPS score was ≥4 at 6, 12, 18, and 24 h postoperatively.

Conclusions In neonates and infants, wound infiltration with bupivacaine had no significant effect on pain relief or fentanyl requirement during the first 24 h after major abdominal surgery.

Keywords Pain · Neonates · Bupivacaine · Wound infiltration

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Introduction

In the past, there was widespread ignorance about pain management in neonates and infants. However, multiple studies have shown that neonates have a perception of pain that affects the autonomic, endocrine, metabolic, circulatory, and psychological systems [1–4]. Therefore, nowadays, effective management of pain is a major priority in improving health care in neonates and infants [5]. Postoperative pain management in neonates and infants can be accomplished by systemic and regional techniques [6]. Opioids are the most commonly used drugs for the treatment of postoperative pain. In neonates and infants, however, respiratory depression is the most deleterious side effect of opioids; therefore, vigilant monitoring is essential [7]. Regarding the regional technique, caudal and epidural analgesia are commonly used. However, these techniques require operative skills. Local infiltration of the surgical site with long-acting local anesthetics such as bupivacaine is a simple and easily performed method for postoperative analgesia in neonates and infants, with fewer complications than caudal and epidural analgesia [6]. However, conflicting results including systematic reviews [8, 9] have been reported on the effectiveness of this wound infiltration technique. Wound infiltration with bupivacaine was as effective as caudal anesthesia for inguinal herniorrhaphy in children [10] and the hormonal stress response was decreased [11]. In addition, wound infiltration was also effective in pain management after appendectomy in children [12]. However, in contrast, a number of studies have demonstrated that wound infiltration had no effect on pain after surgery either in adults [13, 14] or in children [15]. To date, there has been no study on the effectiveness of wound infiltration with local anesthetics in neonates and infants.

The aim of this study was to investigate the effectiveness of wound infiltration with bupivacaine on postoperative pain management in neonates and infants who underwent abdominal surgery. The effect was evaluated by the fentanyl requirement and the neonatal infant pain scale (NIPS) score [16] during the first 24 h after surgery (Appendix 1).

Patients, materials, and methods

After the institutional ethics committee had approved the study protocol and written informed consents had been obtained, a prospective, randomized controlled clinical study was conducted at the Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, Thailand, from January 2007 to January 2010. Neonates and infants (age 0–12 months) scheduled for abdominal surgery during the study period were recruited. The patients were randomized into two groups; namely, the B (bupivacaine) and C (control) groups, by one of the investigators, using a computer-generated algorithm. Patients who needed postoperative mechanical ventilation, those who needed reoperation within 24 h, and those with a known allergy to bupivacaine were excluded.

All subjects received a standardized anesthetic protocol. Anesthesia was induced with sevoflurane in oxygen. The neuromuscular blocker atracurium (0.5 mg/kg) was used to facilitate tracheal intubation. Maintenance of anesthesia was achieved with isoflurane in an oxygen and air mixture. Intraoperative analgesia was provided by using a fentanyl 1-μg/kg bolus and with fentanyl infused at the rate of 0.2 μg/kg/h. An incremental dose of fentanyl, of 0.5 μg/kg, was given when there was a sign of light anesthesia. Before wound closure, 2 mg/kg of 0.125% bupivacaine was infiltrated in the subcutaneous layer of the incision site in each patient in the B group, whereas the patients in the C group received no wound infiltration. At the end of anesthesia, the neuromuscular blocker was antagonized with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. When the patient was awake and had signs of adequate respiration, the endotracheal tube was removed.

During the postoperative period, the NIPS score was recorded immediately in the postanesthesia care unit and every 2 h for 24 h by the nursing staff, who were blinded to the study. When the NIPS score was ≥4, an incremental dose of intravenous fentanyl, of 0.5 μg/kg, was administered, with the maximm dose being 1.5 μg/kg (3 doses).

The Mann–Whitney rank sum test was used to compare the fentanyl requirements during the first operative day, and the Kaplan–Meier test was used to compare the times to the first dose of fentanyl. Otherwise, the *t*-test was used for comparisons between the two groups.

Table 1 General demographic data

Data	Group B	Group C	*p* value
Male/female	10/7	10/7	
Age (months ± SD)	3.55 ± 2.47	3.79 ± 2.61	0.785
Weight (kg ± SD)	5.4 ± 1.7	4.0 ± 2.0	0.469
Operative time (min)	180 ± 98	179 ± 63	0.971
Anesthetic time (min)	223 ± 96	222 ± 65	0.99

Table 2 The operation data

	Group B	Group C
Pancreatic, hepato-biliary surgery	11	12
Intestinal surgery	6	5

Results

Thirty-four neonates and infants were enrolled in the study. No patients were excluded from the study. The two groups were comparable in regard to sex, age, weight, operation time, and anesthetic time (Table 1). The operation data are shown in Table 2.

There were no significant differences in the intraoperative fentanyl dosages between the two groups. After the surgery, the time to the first dose of fentanyl administration (NIPS score ≥4) was not different between the two groups. Regarding postoperative analgesia treatment during the 24 h after surgery, the median dosages of fentanyl requirement were not significantly different between the B and C groups (Table 3). In addition, the numbers of patients with NIPS scores of ≥4 were not different at 6, 12, 18, and 24 h postoperatively (Table 4).

Table 3 Comparison of fentanyl dosages and times to first dose of fentanyl between the two groups

	Group B	Group C	p value	Statistics
Intraoperative fentanyl dosage (mean ± SD)	2.4 ± 2.5 μg/kg	2.2 ± 1.1 μg/kg	0.76	t-test
Time to first dose (median ± SE)	6 ± 4.1 h	10 ± 1.6 h	0.46	Kaplan–Meier test
Fentanyl requirement during the first 24 h after surgery (median)	1 μg/kg	0.5 μg/kg	0.255	Mann–Whitney rank sum test

Table 4 Numbers of patients whose NIPS score was ≥4

	Group B	Group C	p value	Statistics
Hour 6	5 (29.4%)	2 (11.8%)	0.398	t-test
Hour 12	5 (29.4%)	3 (17.6%)	0.688	t-test
Hour 18	3 (17.6%)	2 (11.8%)	1	t-test
Hour 24	0	0	Not applicable	t-test

Discussion

The use of wound infiltration with local anesthetics is an attractive method for postoperative pain relief because of its simplicity, safety, and low cost. This technique has gained wide popularity during the past few decades, particularly in children. However, its effectiveness is still controversial. In the present study, wound infiltration with bupivacaine had no demonstrable effect on pain relief, as evaluated by the total fentanyl dosage and NIPS score. This finding is in agreement with many previous studies on post-appendectomy pain both in adults and children [13–15]. This finding of wound infiltration with bupivacaine having no demonstrable effect on pain relief can be explained in relation to the pain following major abdominal surgery, which is derived from both visceral and post-incision or somatic components. Bupivacaine infiltration can only relieve somatic pain, but not visceral pain. In our protocol, we have shown the lack of analgesic effect of bupivacaine infiltration, so pain from visceral receptors must have played a major role in this study. This made bupivacaine infiltration not an appropriate choice to control postoperative pain following major abdominal surgery [13–15].

The NIPS score was chosen for pain evaluation in our study [16]. The reliability and validity of this pain scale were the essential factors that we considered. There is a study that compares three pain scales–CRIES, CHIPPS, and NIPS–for pain evaluation in neonates after major surgery, in terms of validity, reliability, and practicality. The NIPS score was recommended as a valid, reliable, and practical tool for pain evaluation in this context [17]. However, when each item on the above pain scales was considered, it could be seen that these items were clinical observations of indirect evidence, such as facial expression, crying, movement, vital signs, and oxygenation, and the pain scores could be confounded by various factors. The presence of an intravenous line, gastric tube, or urinary catheter, and the presence of thirst and hunger (which is commonly found after major abdominal surgery) could increase the score in the evaluation of pain. This may be another explanation of the lack of a pain relief effect of wound infiltration.

Limitations of the study

The main limitation of this study was the relatively small number of patients, which could call our conclusion into question. A small number of patients is a common flaw in studies performed in neonates and infants. However, we had already included all patients who met the criteria and underwent surgery during the study period. When the sample size calculation was applied ($\alpha = 0.05$, $\beta = 0.10$, two-tailed), there should have been 133 patients in each group [18] (Appendix 2). A larger study or a multicenter study should be conducted in order to confirm our finding. In addition, more effective regimens such as central neural blockade and other regional techniques such as transverse abdominis plane (TAP) block [19] or opioid infusion could be other options to provide postoperative analgesia in neonates and infants undergoing major abdominal surgery.

Conclusion

This preliminary study showed that wound infiltration with bupivacaine had no significant effect on the pain score or the fentanyl requirement in neonates and infants during the first 24 h after major abdominal surgery.

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Appendix

See Table 5.

Table 5 Neonatal infant pain scale (NIPS) score [16]

Parameter	Finding	Points
Facial expression	Relaxed	0
	Grimace	1
Cry	No crying	0
	Whimpering	1
	Vigorous crying	2
Breathing patterns	Relaxed	0
	Change in breathing	1
Arms	Relaxed/restrained	0
	Flexed/extended	1
Legs	Relaxed/restrained	0
	Flexed/extended	1
State of arousal	Sleeping	0
	Awake	0
	Fussy	1

Appendix 2: Sample size calculation [18]

From this study, $X_1 = 1.55$, $X_2 = 0.96$, $S_1 = 1.62$, $S_2 = 1.35$.

The results were not presented in the study, because a nonparametric test was used for comparison.

$$\sigma^2 = \text{pooled variance} = \frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2} = \frac{(17-1)(1.62)^2 + (17-1)(1.35)^2}{34 - 2} = 2.22$$

$$\text{Sample size for each group} = 2(Z_{\alpha/2} + Z_\beta)^2 \sigma^2 / (X_1 - X_2)^2 = 2(1.96 + 1.28)^2 (2.22) / (1.55 - 0.96)^2 = 133$$

When $\alpha = 0.05$, $\beta = 0.10$, $Z_{\alpha/2} = Z_{0.05/2} = 1.96$ (two tailed), $Z_\beta = Z_{0.10} = 1.28$.

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