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Effects of intrathecal fentanyl on quality of spinal anesthesia in children undergoing inguinal hernia repair

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Summary

Background: The effect of intrathecal fentanyl on the characteristics of spinal anesthesia has not been investigated in children undergoing inguinal hernia repair. The purpose of this study was to assess whether the incidence and severity of pain during peritoneal sac traction is decreased by addition of fentanyl to bupivacaine in children undergoing inguinal hernia repair with spinal anesthesia.

Methods: Children (6–14 years) were randomized into two groups. Group F (n = 25): hyperbaric bupivacaine plus 0.2 $\mu g \cdot kg^{-1}$ of fentanyl. Group P (n = 25): hyperbaric bupivacaine plus 0.9% NaCl (placebo). The dose of bupivacaine was 0.4 $mg \cdot kg^{-1}$. The primary variable was the incidence and severity of pain during peritoneal sac traction. Spinal block characteristics, duration of spinal anesthesia assessed by recovery of hip flexion and duration of analgesia were the secondary variables measured, and the side effects were noted.

Results: There were significant differences in incidence of pain and pain scores during sac traction with lower incidence and scores in the fentanyl group (P = 0.009). Two groups were similar regarding the level of sensory block during sac traction and duration of spinal anesthesia. Duration of spinal analgesia was prolonged significantly in the fentanyl group (P = 0.025).

Conclusion: Intrathecal fentanyl at a dose of 0.2 $\mu g \cdot kg^{-1}$ added to bupivacaine significantly improves the quality of intraoperative analgesia and prolongs postoperative analgesia in children undergoing inguinal hernia repair with spinal anesthesia.

Keywords: pediatric; spinal anesthesia; fentanyl; hernia

The incidence of inguinal hernia is reported to be 0.8–4.4% in full-term babies and as high as 25% in prematures (1). As a result, repair of inguinal hernias is among the most common pediatric surgical procedures performed by pediatric surgeons. Regional analgesia for inguinal hernia repair in children has attracted increasing interest. Caudal block, lumbar epidural block, ilio-inguinal nerve block and wound infiltration have been used with

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varying success (2–6). Spinal anesthesia (SA) has become a popular technique for inguinal hernia repair infants but there are few studies for older children (7,8). Some studies report intraoperative restlessness and pain during inguinal hernia repair with SA. Previous studies report the incidence of restlessness during inguinal hernia surgery after successful subarachnoid block as 4% and 32%, respectively, for children and infants (7,9). Our clinical experience with verbal children and previous data suggest that the restlessness seen in children may be related to pain encountered during peritoneal sac traction (7,9).

The addition of intrathecal (IT) fentanyl to SA improves intraoperative and the early postoperative quality of analgesia (10,11), relieves visceral pain (12) and attenuates sympathetic activation (13) during surgery. IT fentanyl is extensively used as an adjuvant for adult spinal anesthesia but is less studied for pediatric anesthesia. Batra *et al.* (14) conducted a dose–response study of IT fentanyl on the duration of spinal block in infants mainly undergoing inguinal hernia repair but did not assess the effects of fentanyl on intraoperative anesthesia quality. The effectiveness of fentanyl in preventing sac traction pain during inguinal hernia repair in children remains to be determined. We conducted a prospective, randomized double-blind study to compare the effectiveness of intrathecal fentanyl with placebo for preventing pain during sac traction in school-age children undergoing inguinal hernia repair with spinal anesthesia. The secondary aim of the study was to investigate the duration of SA and postoperative analgesia. In addition, hemodynamic changes or other adverse events were recorded.

Methods

This study was approved by the ethics committee; it was conducted in accordance with the latest revision of the Declaration of Helsinki. Informed consent was obtained from the parents. The study included 50 children (ASA physical status I–II) aged six to fourteen, scheduled for day-case unilateral inguinal hernia repair. Children with a known history of bleeding diathesis, allergy to local anesthetics, aspirin ingestion in the preceding week or pre-existing neurological or spinal disease and who had cognitive-behavioral disturbances were excluded from the study.

Children were premedicated with 0.5 $mg \cdot kg^{-1}$ midazolam (maximum dose of 10 mg) orally about 30 min before the operation. Prilocaine–lidocaine cream (EMLA® %5; Astra Zeneca, Istanbul, Turkey) was applied to the potential lumbar puncture and venous access sites of the patients about 60 min before entering the operating room. Monitoring comprised ECG, pulse oximetry and automated, non-invasive blood pressure. After establishing peripheral intravenous access, intravenous fluids (0.45% saline in 5% dextrose) were administered at a rate of 5 $ml \cdot kg^{-1} \cdot h^{-1}$.

The children were randomly allocated to one of two spinal anesthesia groups according to sealed envelopes. Group F (n = 25): hyperbaric bupivacaine (Marcaine® Spinal Heavy; Astra Zeneca) plus 0.2 $\mu g \cdot kg^{-1}$ of fentanyl (Fentanyl-Janssen®; Janssen-Cilag, Beerse, Belgium). Group P (n = 25): hyperbaric bupivacaine plus 0.9% NaCl (placebo). Placebo volume was equal to calculated fentanyl dose for each child. The dose of bupivacaine was 0.4 $mg \cdot kg^{-1}$. An application of amounts up to the maximum dose 10 mg. Fentanyl was prepared with in a separate 1-ml syringe by mixing fentanyl and 0.9% NaCl (20 $\mu g \cdot ml^{-1}$). Bupivacaine and fentanyl or placebo solutions were combined into a single syringe before administration.

Following sterile preparation, a lumbar puncture was performed at the L4–L5 level using a 27G pencil point needle (Pencan®, B. Braun Melsungen AG, Melsungen, Germany) in the sitting position. For children who were restless despite premedication, to provide an adequate level of sedation for a comfortable lumber puncture, sevoflurane was administered in a 50% N_2O–50% O_2 mixture during spontaneous breathing via a facemask by placing the child in the lateral decubitus position. Correct placement of the spinal needle was verified by the free flow of cerebrospinal fluid. The study solutions were injected at a rate of 1 ml over 10 s with cephalad orientation of the spinal needle's distal orifice. Upon completion of the injection, 0.2–0.4 ml of cerebrospinal fluid was again aspirated and re-injected to clear the dead space of the needle. Children breathed room air spontaneously during surgery.

The study solutions were prepared aseptically by an anesthesiologist not involved further in the study.

All of the staff who gave treatment to the patients, including the anesthesiologist performing the block and the nurses collecting the postoperative data, were blinded to group asignments. Parents were also unaware as to which study group their child had been allocated.

Sensory block level was measured every minute by pinprick in the midline starting at 3 min after the block until block level reached T11 dermatome. Block level was re-evaluated during sac traction. The surgeon commenced surgery when sensory block reached the T11 dermatome. In case of inadequate spread or inadequate duration of spinal anesthesia, surgery was completed with general anesthesia.

Intraoperative abdominal pain was scored according to a four-point scale: 0, no pain; 1, slight pain (minor verbal/no facial response to traction); 2, moderate pain (clear verbal/facial response to traction); and 3, severe pain (the patient complained of pain moved arms and/or cried) during sac traction. Time of sac traction from spinal block was also noted. To prevent the child misleading the anesthesiologist by confusing any other previous pain with pain of peritoneal handling, the following question was asked to the child; '*Do you feel any pain in your hand, arm, head, nose, chin, chest, abdomen, or feet?*' just before traction of the peritoneal sac. Any child who was not cooperative or responded '*yes*' to the question was excluded from further study. During sac traction, the children were again asked '*Do you feel any pain now?*' and abdominal pain score was recorded.

Children who were anxious before initiation of surgery were sedated with 0.5–1 $mg{\cdot}kg^{-1}$ of propofol i.v. (Propofol-Lipuro 1%; B. Braun Melsungen AG). Children who were not fully awake during the sac traction as a result of propofol sedation were excluded from the study.

The incidence of episodes of changes (>20% from control) in systolic arterial pressure and heart rate was evaluated. After termination of surgery, all children were transferred to the postanesthesia care unit (PACU) for continuous monitoring of their vital signs and assessment of motor recovery, and pain scores was evaluated every 10 min. The motor recovery was assessed until hip flexion recovered, which was considered the end of SA duration measured from the completion of the subarachnoid injection. Children were discharged from the PACU when they were able to flex their hips, fully awake and stable hemodynamic and respiratory conditions were ascertained. Time to be ready for PACU discharge was recorded. Children were then transferred to the pediatric surgical ward until discharged from the hospital. Postoperatively, pain was assessed for 6 h by a trained recovery nurse, at 1-h intervals until discharge. Rescue analgesics (paracetamol 20 $mg{\cdot}kg^{-1}$, i.v.) were given at the request of the child or if the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) >5 as assessed hourly at the regular floor (15). Number of patients receiving i.v. analgesics and time to the first rescue analgesic was recorded, which was considered the end of spinal analgesia duration measured from the completion of the subarachnoid injection.

The number of patients with nausea, retching or vomiting was recorded. Patients received 0.5 $mg{\cdot}kg^{-1}$ of diphenhydramine on two or more episodes of retching or vomiting. Pruritus was assessed on a four-point categorical scale: 0, none; 1, mild; 2, moderate; 3, severe pruritus (requiring naloxone). Respiratory depression (defined as pulse oximetry saturation, <95% on room air and/or respiratory breathing rate <10 min^{-1}) was treated with oxygen via face mask, and incremental doses of naloxone were used at the discretion of the anesthetist. All parents received a follow-up telephone call the day after surgery by the same recovery nurse and were asked if they observed any side effect. On discharge, oral paracetamol (20 $mg{\cdot}kg^{-1}$) were prescribed for all children as needed (maximum four times in 24 h).

Statistical analysis was performed using the incidence of intraoperative visceral pain during the sac traction as the main criterion. Power was not calculated before the study because of the lack of data regarding the incidence of pain during sac traction under spinal anesthesia in children. Sample size was based upon previous studies (16,17). Data were presented as mean (SD) or median (range). Student's *t*-test or Mann–Whitney *U*-test were used as appropriate. Categorical variables were analyzed using chi-square test to determine the differences among the groups. The Fischer's exact test was used as appropriate. The level of significance was set at $P < 0.05$.

Results

Forty three patients completed the trial: 20 in group F and 23 in group P. Seven patients did not complete the trial for the reasons outlined in Figure 1. Power calculation for the study with incidence of pain reduced from 52% (placebo group) to 10% (fentanyl group) with 20 patients has a power between 81% and 87%.

The groups were similar with respect to age, weight, height and sex distribution (Table 1). There were no failed blocks in either group. The interval between spinal puncture and surgical incision, spinal puncture and sac traction, as well as the duration of surgery and duration of SA was similar between the groups (Table 1).

There were significant differences in incidence of pain and pain scores during the sac traction with lower incidence and scores in the fentanyl group ($P = 0.009$) (Table 2). Two groups were similar in the level of sensory block during sac traction (Table 2). In the placebo group, sac traction pain scores were higher in children with sensory block <T4 dermatome compared to children with sensory block ≥T4 dermatome ($P = 0.009$) (Table 2). Duration of spinal analgesia was prolonged significantly in the fentanyl group ($P = 0.025$) (Table 3). The perioperative and

Table 1
Demographic data and block characteristics

	Group F (n = 20)	*Group* P (n = 23)
Age (year)	8.7 ± 1	8.6 ± 2
≥8 year/<8 year	18/2	21/2
Height (cm)	130 ± 7	128 ± 13
Weight (kg)	27 ± 5	27 ± 7
Gender (male/female)	14/6	16/7
Patients who received propofol	5	9
Time from spinal block to surgical incision (min)	4 ± 1	4 ± 1
Time from spinal block to sac traction (min)	8 ± 3	8 ± 3
Duration of surgery (min)	13 ± 3	12 ± 4
Duration of SA (min)	76 ± 25	79 ± 23
Time to ready for discharge from PACU (min)	80 ± 26	80 ± 22

Data are number of cases and mean ± SD. There were no significant differences between the groups.

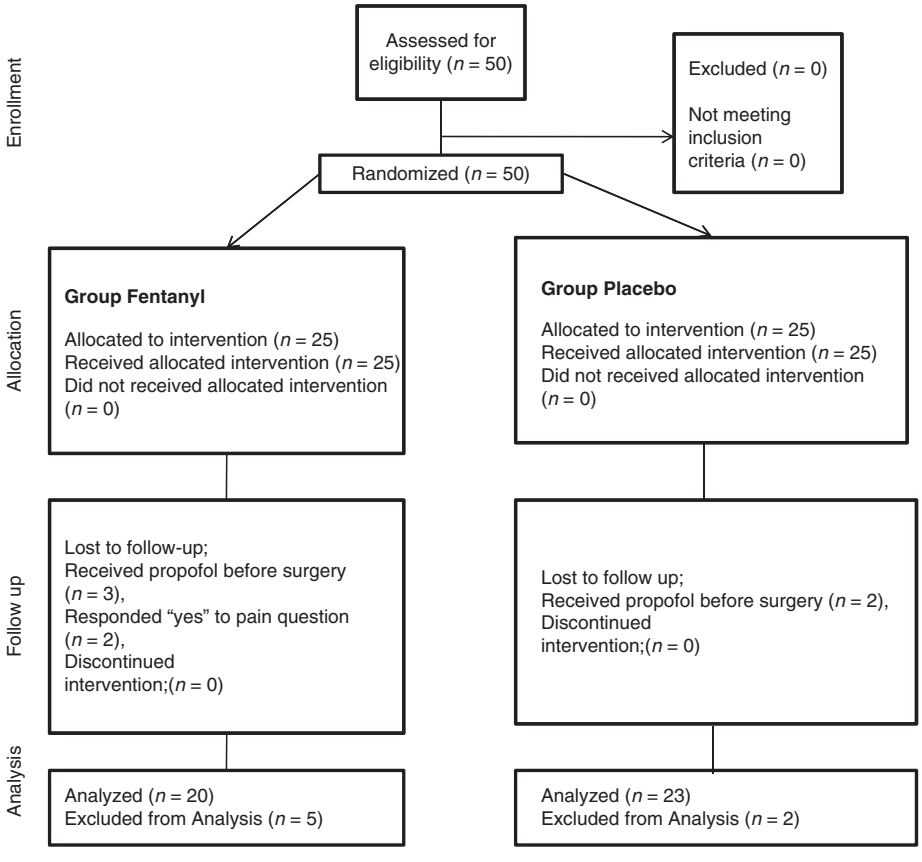

Figure 1
Flow diagram of patient distribution.

Table 2
Sensory block levels and characteristics of pain during sac traction

	Group F (n = 20)	*Group* P (n = 23)
Median sensory block level (min–max)	T4 (1–7)	T4 (1–8)
Pain during sac traction *n* (%)	2 (10%)*	12 (52%)
T12–T5 dermatome (*n*)	0*	8
T4–T1 dermatome (*n*)	2	4
Abdominal pain scores (*n*) 0/1/2/3	18/2/0/0*	11/4/4/4

*P = 0.009 compared to placebo.

postoperative adverse events are presented in Table 4. In the operating room, hypotension was seen in one patient and was treated with a bolus 5 ml·kg^{-1} bolus of intravenous fluid. Transient bradycardia requiring no medical treatment developed in three children in the placebo group and one child in the fentanyl group during sac traction. No hemodynamic adverse effect was seen during the PACU stay.

Discussion

This study demonstrates that compared with placebo, adding fentanyl to bupivacaine decreases the incidence and severity of sac traction pain and increases the time for first postoperative rescue analgesic use in children undergoing inguinal hernia repair with spinal anesthesia.

Of the several opioids available for neuraxial administration, morphine and fentanyl remain the most commonly used agents. Because of the more lipophilic nature of fentanyl, it has a more rapid onset of action than morphine (18). IT fentanyl produces profound analgesia by making direct contact with the substantia gelatinosa of the cord, and it also provided cephalad extend of sensorial block (19). Clinical effect requires the absorption of the opioid across lipid membranes into the cord

Table 3
Need for postoperative rescue analgesia

	Group F (n = 20)	*Group* P (n = 23)
Number of patients receiving i.v. paracetamol *n* (%)	7 (35%)	13 (56%)
Time to the first rescue analgesic (min) mean ± SD	219 ± 60*	168 ± 70

*P = 0.02 compared to placebo.

Table 4
Perioperative and postoperative adverse events

	Group F (n = 20)	*Group* P (n = 23)
Hypotension	1	0
Bradycardia	1	3
Tachycardia	0	1
Nausea–vomiting	2	4
Pruritus: mild/moderate/severe	2/0/0	1/0/0
Urinary retention	0	0
Respiratory depression	0	0

Data are presented as number of patients.

(thus the more rapid onset of lipophilic fentanyl compared with morphine). Also, there appears to be little cephalad spread with fentanyl, especially when compared with morphine, because of this lipophilicity. It is known from previous clinical adult and experimental studies that intrathecal opioids effectively relieve visceral pain and increase the intraoperative as well as early postoperative quality of subarachnoid block (12). Although this is a common practice in adults, there is limited reported experience concerning this technique in children.

Optimal IT fentanyl dose yet remains to be determined for different age groups and different types of surgery (14,20). Studies on children used IT fentanyl in a range of 2 μg·kg^{-1} for children undergoing cardiac surgery with general anesthesia to 1 μg·kg^{-1} for lower abdominal and urologic surgery of the neonates with spinal anesthesia (14,20). The anatomy and physiology of the spinal structures are different in neonates and older children (14). The cerebrospinal fluid volume/body weight ratio decreases as the child grows older. It is reduced from 4 ml·kg^{-1} in neonates to 2 ml·kg^{-1} in adulthood causing less dilution of IT drugs (21). In our preliminary study in school-age children undergoing inguinal hernia repair, IT 0.5 μg·kg^{-1} of fentanyl resulted in high incidence of side effects such as nausea, retching, profound sedation and delayed PACU discharge (22). Based on adult studies that employ 10–25 μg of fentanyl to patients who weigh an average of 65–75 kg (0.15–0.33 μg·kg^{-1} of fentanyl), we calculated the equivalent intrathecal fentanyl dose as 0.2 μg·kg^{-1} for children.

The inguinal region receives sensory innervation from the ilioinguinal, iliohypogastric and genitofemoral nerves. The peripheral nerves supplying the

inguinal region are derived from the spinal nerve roots of T12–L2 (2). Because of the visceral afferent nerves that supply the hernia sac, a sensory blockade to T4 is considered necessary in conscious neonates to prevent response to peritoneal traction (9). Because of visceral afferent innervations, it was not surprising that children in the bupivacaine group experienced different incidence of pain when the sensorial block was higher or lower than the T4 dermatome. Webster *et al.*'s (9) experience of spinal anesthesia also suggested that high afferent blockade, to T4–T2, was necessary to achieve tranquil operating conditions in neonates.

Short duration of SA is one of the limitations for its use in pediatric patients. Studies have been performed in children with the use of different IT additives like epinephrine, clonidine, morphine and sufentanil (14). However, no study has been performed to determine the dose–response characteristics of IT fentanyl in pediatric patients, except Batra *et al.*'s (14) study in infants. Batra *et al.* (14) studied infants undergoing lower abdominal and urologic procedures with the use of different IT fentanyl doses. The addition of 1 $\mu g \cdot kg^{-1}$ but not 0.25 $\mu g \cdot kg^{-1}$ fentanyl significantly increased the duration of SA. Likewise, in our study 0.2 $\mu g \cdot kg^{-1}$ of fentanyl did not prolong the duration of SA as assessed by motor block. As mentioned earlier, the sensory block duration provided with bupivacaine was sufficient for unilateral hernioraphy procedures. PACU discharge times were not prolonged with the use of 0.2 $\mu g \cdot kg^{-1}$ of fentanyl, and this dose of fentanyl was not associated with clinically significant hemodynamic or respiratory alterations. In clinical practice, unwanted side effects such as pruritus, nausea and vomiting affect the use intrathecal opioids. The data with children are limited. Unfortunately, the power of this study is too small to allow any comparison of the incidence of side effects between the two groups. Further studies with larger groups of patients are needed to assess the incidence of important side effects seen after intrathecal opioids such as respiratory depression, nausea and vomiting and pruritus.

The main limitation for our study is that we did not assess block properties such as the highest level of sensory block, time to two dermatome regression of analgesia. Pinprick method for analgesia assessment is troublesome in children. It causes pain, discomfort and restlessness. Therefore not to disturb the children further, we only assessed the level of sensory block only once (just before sac traction) after it reached the dermatome required for incision. Another limitation needs mentioning is the surgical procedure for unilateral inguinal hernia repair in our hospital is considerably short. The mean time from spinal block to sac traction was about 8 min in our patients. Our results reflect the block level at this time point, which may change with a slower surgical technique or procedure.

Intrathecal fentanyl at a dose of 0.2 $\mu g \cdot kg^{-1}$ added to bupivacaine significantly improves the quality of intraoperative analgesia and prolongs postoperative analgesia in children undergoing inguinal hernia repair with spinal anesthesia.

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