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Adding of intrathecal fentanyl in hyperbaric bupivacaine improves analgesia during appendectomy

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Background : *Spinal anesthesia is commonly employed for appendectomy in Thailand. Some patients complain of pain when the appendix was been retracted or swab was put in the abdomen.*

Objective : *To determine the effectiveness of intrathecal fentanyl.*

Setting : *Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital*

Subjects : *60 patients who underwent appendectomy with spinal anesthesia*

Design : *The prospective, randomized double-blinded study.*

Methods : *Patients were randomly assigned into 3 groups: 20 in each group; subjects in the first group received 0.4 ml of fentanyl 20 μg (Group 20), the second group received 0.2 ml of fentanyl 10 μg and 0.2 ml of normal saline (Group 10) and the third group received 0.4 ml of normal saline (Group 0).*

Results : *There were no differences of the onset and the level of the highest sensory blockage between the groups. However the number of segments regressed at 60 min in Group 20 was significantly less than in Group 0 ($P<0.05$). All patients in both fentanyl groups had completed intraoperative analgesia whereas 13 patients (65%) in Group 0 had ($P<0.001$). The most severe*

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intraoperative pain by VNS scores were also siginificantly lower in both fentanyl groups compared with Group 0 (P <0.001). Time to the first request of postoperative analgesics was also extended in Group 20 compared with the other two groups (11.0 h, 5.25 h, 4.7 h respectively; P<0.05). Both fentanyl groups developed less shivering than in the control group (40 %, 45 %, 70 %; P< 0.05). No patient developed respiratory depression or PDPH.

Conclusion : *The present study revealed the improvement of analgesia without increasing side effects of the addition of fentanyl 10 and 20 μg to bupivacaine in spinal block for appendectomy. Adding 20 μg of fentanyl intrathecally could prolong analgesic effect.*

Keywords : *Intrathecal fentanyl, Spinal anesthesia, Appendectomy.*

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ปัญหา : *การทำผ่าตัดไส้ติ่งอักเสบส่วนใหญ่ถือเป็นการผ่าตัดฉุกเฉิน วิธีการให้การระงับความรู้สึกมักเลือกใช้การฉีดยาชาเข้าช่องไขสันหลัง แต่ในระหว่างการดูแลผู้ป่วยที่กำลังผ่าตัดนั้น บ่อยครั้งที่ผู้ป่วยจะบ่นปวดท้องทั้งที่ระดับชาได้ตามมาตรฐานแล้วคือระดับลิ้นปี่*

วัตถุประสงค์ : *เพื่อทดสอบสมมุติฐานที่ว่าการให้ fentanyl ร่วมไปกับการฉีดยาชาเข้าช่องไขสันหลัง ในการผ่าตัดไส้ติ่ง สามารถเพิ่มคุณภาพของการระงับความรู้สึกลดความปวดระหว่างการผ่าตัด*

สถานที่ทำการศึกษา : *ภาควิชาวิสัญญีวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย โรงพยาบาลจุฬาลงกรณ์*

การคัดเลือกผู้ป่วย : *ผู้ป่วยที่มารับการผ่าตัดไส้ติ่งจำนวน 60 ราย ผู้ป่วยทุกรายต้องไม่มีข้อห้ามในการฉีดยาชาเข้าช่องไขสันหลัง และไม่เคยมีประวัติแพ้ fentanyl หรือยาชา ผู้ป่วยได้รับการอธิบายถึงการศึกษาและได้รับการยินยอมเป็นลายลักษณ์อักษร*

รูปแบบการวิจัย : *การวิจัยเชิงทดลอง*

วิธีการทำวิจัย : *ผู้ป่วยจะถูกแบ่งเป็น 3 กลุ่ม โดยการสุ่มตัวอย่างกลุ่มละ 20 ราย กลุ่ม 20 จะได้รับการฉีด fentanyl 20 ไมโครกรัมเข้าช่องไขสันหลัง กลุ่ม 10 จะได้รับการฉีด fentanyl 10 ไมโครกรัมเข้าช่องไขสันหลัง และกลุ่ม 0 ได้รับการฉีดน้ำเกลือ 0.4 มล เข้าช่องไขสันหลังเป็นกลุ่มควบคุม, โดยวิสัญญีพยาบาลจะเป็นผู้ผสมยาให้และวิสัญญีแพทย์ผู้ซึ่งไม่ทราบว่าผู้ป่วยอยู่ในกลุ่มใดจะเป็นผู้ที่ฉีดยาเข้าช่องไขสันหลัง*

ผลการศึกษา : *ระดับการชาที่ 5, 10, 15, 30, 45 นาทีหลังการฉีดยาชาเข้าช่องไขสันหลังและระดับชาสูงสุดไม่แตกต่างกัน แต่ที่ 60 นาทีพบว่าระดับชาในกลุ่ม 20 ลดลงน้อยกว่ากลุ่ม 10 และกลุ่ม 0 ($P < 0.05$) ในระหว่างการผ่าตัดพบว่าผู้ป่วยทุกรายในทั้งสองกลุ่มที่ได้รับ fentanyl ไม่มีอาการปวดในขณะที่พบ 13 รายในกลุ่ม 0 ($p < 0.001$) โดยมีระดับความปวดสูงสุดเฉลี่ย (VNS scores) ในทั้งสองกลุ่มที่ได้รับ fentanyl ต่ำกว่ากลุ่ม 0 ($P < 0.001$) หลังผ่าตัดพบว่าผู้ป่วยกลุ่ม 20 เริ่มขอยาแก้ปวดครั้งแรก*

ช้ากว่ากลุ่ม10 และกลุ่ม 0 ($P < 0.05$) อาการข้างเคียงได้แก่ อาการสั่นระหว่างการผ่าตัดพบว่าในทั้งสองกลุ่มที่ได้รับ fentanyl พบน้อยกว่ากลุ่ม 0 ($P< 0.05$) ภาวะความดันโลหิตลดลง อาการคัน คลื่นไส้ อาเจียน และปัสสาวะไม่ออกพบไม่แตกต่างกัน ไม่พบอาการปวดศีรษะหรือการกดการหายใจ ผู้ป่วยทุกรายในทั้งสองกลุ่มที่ได้รับ fentanyl และ 18 รายในกลุ่ม 0 พึงพอใจในการให้ยาชาระงับความรู้สึก

สรุป : การผสม fentanyl ทั้งขนาด 10 และ 20 ไมโครกรัมเข้าไปกับยาชาในการฉีดยาชาเข้าช่องไขสันหลัง สำหรับผู้ป่วยผ่าตัดไส้ติ่งช่วยเพิ่มคุณภาพการชาและลดอาการสั่นในระหว่างการผ่าตัดไส้ติ่ง และในขนาด 20 ไมโครกรัมยังช่วยเพิ่มระยะเวลาการชาและลดความปวดหลังการผ่าตัด

คำสำคัญ : Intrathecal fentanyl, การฉีดยาชาเข้าช่องไขสันหลัง, การผ่าตัดไส้ติ่ง

Spinal anesthesia is commonly employed for appendectomy in Thailand. The advantage of spinal anesthesia includes the simplicity of the technique, its rapid onset and the exclusion of aspiration. Some patients complain of pain when the appendix is retracted or swab is put in the abdomen.

Experimental studies have shown that opioids administered intrathecally was able to relieve visceral pain. [1-6] The clinical efficacy of intrathecal opioids to relieve visceral pain has also been demonstrated. [7-8]

Fentanyl is well known for its rapid onset and shorter duration of action following intrathecal administration. [9-10]

This study was designed to assess efficacy and safety of intrathecal fentanyl 10 and 20 μg on the improvement of analgesia of hyperbaric bupivacaine in patients who were undergoing appendectomy.

Materials and Methods

After obtaining the approval of the Ethics Committee of the Faculty of Medicine and written informed consent from each patient, this prospective, randomized, double-blind, placebo-controlled study was conducted at King Chulalongkorn Memorial Hospital. Patients of ASA physical status I E who were scheduled for appendectomy under spinal anesthesia were recruited into the study. The exclusion criteria employed in the study were known history of bupivacaine or fentanyl allergy, past history of severe headache or backache, narcotic dependence, inability to quantify pain by verbal numeric scale (VNS).

The patients were randomly allocated into 3 groups; each subject in Group 20 (n=20) received 0.4 ml of 20 μg fentanyl in 4 ml of 0.5 % hyperbaric bupivacaine intrathecally, Group 10 (n=20) received 0.2 ml of 10 μg fentanyl with 0.2 ml of normal saline in 4 ml of 0.5 % hyperbaric bupivacaine intrathecally and in Group 0 (n=20) received 0.4 ml of normal saline in 4 ml of 0.5 % hyperbaric bupivacaine intrathecally. The randomization sequence was selected based on a table of random number. Randomly allocated coded syringes of drugs were prepared by an anesthesiologist who was not involved in the spinal block or recording of the outcome. No patient was premedicated.

After the standard monitors were placed and intravenous access was established, patients were preloaded with 20 ml/kg of normal saline solution. Spinal block was performed with 27-gauge spinal needle at the L3-4 interspace in lateral decubitus position and 4 ml of 0.5 % hyperbaric bupivacaine with 0.4 ml of the studied solution was injected. The total volume of the subarachnoid injection was 4.4 ml. Patients were immediately returned to supine position after completing the blocking procedure.

Noninvasive blood pressure was monitored every 5 min. Oxygen saturation, EKG and respiratory rate were continuously monitored. The analgesic level was determined by the loss of pinprick sensation at the midline of the body every 5 min for the first 15 min and then every 15 min for 1 h.

The patient was asked to quantify their most severe intraoperative pain by using 10 scores VNS with 0 corresponding to no pain and 10 to the worst imaginable pain. The most severe pain pain was also grouped to 4-point rating score (0 = absence of pain; 1-3 = mild pain; 4-6 = moderate pain;>6 = severe pain and therapy incremented dose of 25 μg fentanyl IV was then given). The patients were scored for sedation using 4-point rating score (0 = fully awake;

1 = somnolent, responds to call; 2 = somnolent, responds to tactile stimuli; 3 = deep sedation, responds to painful stimuli), itching by a 4-point rating score (0 = no itching; 1=mild itching; 2 = moderate itching, treatment not requested; 3 = severe itching, treatment requested), nausea and vomiting by a 4-point rating score (0 = no nausea and vomiting; 1 = nausea; 2 = retching; 3 = vomiting), shivering by a 4-point rating score (0 = no shivering; 1=mild shivering; 2 = moderate shivering, treatment not requested; 3 = severe shivering, treatment requested). Intravenous metoclopramide 10 mg, pethidine 20 mg and nalbuphine 3 mg were used to treat vomiting, shivering and itching respectively.

Episodes of perioperative side effects such as hypotension (SBP < 30 % from baseline), bradycardia (HR < 50 bpm), oxygen desaturation (SpO_2)< 92 % and respiratory depression (RR < 12 bpm) were recorded. Hypotension was treated with bolus of fluid and incremental dose of ephedrine 6 my IV. Bradycardia was treated with atropine 0.6 my IV.

At 24 h postoperative, the patients were evaluated for the duration of effective analgesia (time from subarachnoid injection to the first request of analgesics) and the pain score at that time by VNS. The episodes of PDPH, urinary retention and patient's satisfaction of spinal anesthesia were also recorded.

The number of patients required in each group was determined by power analysis based on the following assumptions: the rate of pain-free episodes (the primary end point) in patients receiving placebo was 50 %; an improvement from 50 % to 100 % was clinical important; and $\alpha = 0.05$ with a power $(1-\beta)$ of 80 %. Based on these assumptions, it was determined that 20 patients were required per group. All statistical analysis was performed with SPSS version 7.0. Data were present as mean ± SD, median (range) value, and number (percent). Continuous scales were compared by one-way ANOVA followed by Scheff's test for intergroup comparisons. Ordinal scales were compared by Kruskal-Wallis test followed by a Mann-Whitney U-test with Bonferroni correction for intergroup comparisons. And nominal scales were compared by Chi-Square test. The P value < 0.05 was considered statistically significant.

Results

A total of 60 patients (32 men, 28 women) were included in the study. The three groups were not statistically different in age, weight, height, NPO time and duration of surgery (Table 1).

Table 1. Patient parameters.

	Group 20 (n = 20)	Group 10 (n = 20)	Group 0 (n = 20)
Age (yr)	30.6 ± 6.6	29.4 ± 9.5	331.8 ± 8.6
Weight (kg)	61.4 ± 9.9	56.0 ± 11.9	55.6 ± 9.0
Height (cm)	163.9 ± 1.7	161.7± 7.7	161.3 ± 9.0
NPO time (h)	9.1 ± 1.7	9.6 ± 3.3	9.2 ± 2.6
Duration of surgery (min)	54.2 ± 15.	61.7 ± 15.3	62.0 ± 17.7

Values are mean ± SD

No statistical difference among the groups

There were no significant difference in median analgesic level at 5, 10, 15, 30 and 45 min after spinal block among the three groups. The median times in all groups to achieved T6 sensory level and the highest sensory level had no significant difference between the groups. We found differences of the number of segments regressed at 60 min among the three groups. After multiple intergroup comparisons, only Group 20 showed statistically decrease of segments regressed at 60 min in compared with Group 0 ($P < 0.05$) (Table 2).

All patients in both fentanyl groups had completed intraoperative analgesia (pain-free) whereas 13 patients (65%) in Group 0 did so ($P < 0.001$) (Table 3). The most severe intraoperative pain scaled by VNS was also siginificantly lower in both fentanyl groups compared to Group 0 ($P <0.001$). There were no difference between the two groups of fentanyl. There were 2 patients in Group 0 who needed 25-50 μg fentanyl IV because their pain scores were higher than 6 when the appendix was retracted or the abdominal swab was applied in the abdominal cavity. General anesthesia was never used. Time to first required postoperative analgesics in Group 20 was longer than in the other two groups (11.0 h, 5.25 h, 4.7 h; $P < 0.05$). There was no difference in the median VNS pain scores at the time of first request of postoperative analgesics.

During operation, there was no difference in the incidences and severity of nausea and vomiting. Metoclopramide was administered to treat vomiting of 2 patients in both fentanyl groups, and 6 patients in Group 0 (Table 4). The severity of shivering in both fentanyl groups was significantly higher than in Group 0 ($P < 0.05$). There was no intergroup difference for severity of shivering. Four patients (20 %) in Group 20, 3 patients (15 %) in Group 10 and 12 patients (60 %) in Group 0 experienced severe shivering requiring treatment with intravenous pethidine 20 mg. There was no difference in the incidence of hypotension between the two groups of fentanyl. Eight patients (40 %) in Group 20, 6 patients (30 %) in Group 10 and 7 patients (35 %) in Group 0 had hypotension that required treatment with 6-18 mg of ephedrine. One patient (5 %) in Group 0 developed bradycardia which was treated by 0.6 mg of intravenous atropine. None developed respiratory depression (RR<12 bpm), SpO2 < 92 %, itching nor sedation.

Table 2. Onset and regression of sensory blockage.

	Group 20 (n = 20)	**Group 10 (n = 20)**	**Group 0 (n = 20)**
Onset time T6 (min)	5 (5-10)	5 (5-10)	5 (5-10)
The highest sensory level	T_4 (T_1-T_4)	T_3 (T_2-T_4)	T_3 (T_1-T_4)
Number of segment regression at 60 min	0 (0-2)*	0 (0-3)	2 (0-6)

Values are median (range)

* $P < 0.05$ (by Mann-Whitney U-test with Bonferroni correction) from Group 0

Table 3. Intraoperative and postoperative analgesia.

	Group 20 (n = 20)	Group 10 (n = 20)	Group0 (n = 20)
No. of patient who had intraoperative pain			
no pain (VNS =0)	[a]20 (100%) [+]	20 (100%) [+]	13 (65%)
mild pain (VNS =1-3)	0	0	4 (20%)
moderate pain(VNS =4-6)	0	0	1 (5%)
severe pain (VNS =>6)	0	0	2 (10%)
The most severe intraoperative pain (VNS)	[b]0 (0-0) [+]	0 (0-0) [+]	3 (0-9)
Time to first request of postoperative analgesics (h)	[b]11.0 (4-24) *	5.2 (2-17)	4.7 (2.5-20)
The pain at the time of first request of postoperative analgesics (VNS)	[b]5 (0-8)	5 (3-7)	5 (0-10)

[a] Value are numbers of patient (percent)

[b] Values are median (range)

[+] $P < 0.001$ (by Chi-Square test) from Group 0

* $P < 0.05$ (by Mann-Whitney U-test with Bonferroni correction) from Group 0 and Group 10

Table 4. Intraoperative side effects.

	Group 20 (n = 20)	Group 10 (n = 20)	Group 0 (n = 20)
Nausea / vomiting	5 (25 %)	5 (25 %)	10 (50 %)
nausea	3	0	3
retching	0	3	1
vomiting	2	2	6
Shivering	8 (40 %)*	9 (45 %)*	14 (70 %)
mild	1	1	2
moderate	3	5	0
severe	4	3	12
Hypotension	8 (40 %)	6 (30 %)	7 (35 %)
Bradycardia	1 (5 %)	0 (0 %)	0 (0 %)
Urinary retention	2 (10 %)	4 (20 %)	1 (5 %)

Value are members of patient (percent)

* $P < 0.05$ (by Mann-Whitney U-test with Bonferroni correction) from Group 0

Table 5. Patient's satisfaction in spinal anesthesia.

	Group 20 N = 20	Group 10 N = 20	Group 0 N = 20
Yes	20 (100%)	20 (100%)	16 (80%)
No	0	0	4 (20%)

The patients could void in mean time of 6.3 h, 7.9 h and 6.9 h in Group 20, Group 10 and Group 0 respectively. There were 2 patients (10 %) in Group 20, 4 patients (20 %) in Group 10 and 1 patient (5 %) in Group 0 who needed intermittent urinary catheterization. There was no postdural puncture headache. One patient in Group 0 complained of backache. The backache was treated by NSIADS and disappeared in the fourth day postoperatively. There was no statistically significant difference in patient's satisfaction between the groups. All patients in the both fentanyl groups were satisfied with their spinal analgesia. Four patients in Group 0 were dissatisfied from inadequate analgesia (2 patients), severe shivering (1 patient) and backache (1 patient) (Table 5).

Discussion

The result indicated that the addition of fentanyl to hyperbaric bupivacaine for spinal anesthesia in patients who underwent appendectomy significantly improves the quality of intraoperative analgesia without increasing the side effects such as respiratory depression, itching, nausea, vomiting, hypotension, bradycardia, or urinary retention.

In this study all patient who received intrathecal fentanyl in dose of 20 μg and 10 μg did not experience any pain during the operation. This compared to 13 of 20 patients in Group 0 (65 %) who had no pain.

Fentanyl is a lipophilic opioid similar to meperidine, which is more readily eliminated from CSF than hydrophilic opioids such as morphine. [11-12] However, opioid that are lipophilic have a potential of a short duration of action. Duration of action of fentanyl may be dose-dependent.[9-10] Hunt et al. reported that the addition of fentanyl > 6.25 μg (6.25, 12.5, 25, 37 and 50 μg) to hyperbaric bupivacaine was shown to reduce the intraoperative opioid supplement IV from 67 % to 0 % and provided postoperative analgesia of 3-4 h in patient who underwent caesarean delivery under spinal anesthesia.[7] Dahlgren et al.also reported that fentanyl 10 μg added in hyperbaric bupivacaine spinal block produced complete analgesia and increased the duration of analgesia in early postoperative period compared to placebo.[13] In our study, we found that the addition of fentanyl 10 and 20 μg to bupivacaine in spinal anesthesia for appendectomy provided excellent surgical anesthesia. Improved perioperative analgesia following co-administration of fentanyl and bupivacaine can be explained by a synergistic inhibitory action of these two agents on A-gamma and C-fiber conduction.[6]

We found that there was no statistically significant difference in the onset and the highest level between the groups. Despite a previously demonstration of faster onset of the block by intrathecal fentanyl, [14] the effect was not observed in this study. The number of segments regressed at 60 min was decreased in Group 20 compared with Group 0, but there was no statistic difference in Group 10 compared with Group 0. Time to first analgesics request was also extended in the group that received higher dose of 20 μg fentanyl compared with the other two groups. This indicated that the duration of surgical anesthesia and early postoperative analgesia for appendectomy was prolonged with the higher dose administered intrathecal fentanyl (20 μg), but not with the smaller dose (10 μg). Belzarena et al. reported that the dose of 0.25 μg/kg intrathecal fentanyl provided excellent surgical anesthesia with short-lasting postoperative analgesia, and the dose of 0.5 - 0.75 μg/kg intrathecal fentanyl, could prolonged the postoperative pain relief.[14] Most of anesthesiologists agree that a dense block to at least T6 is needed for lower abdominal surgery in order to avoid visceral pain. In our study all of the patients had the highest sensory level of T4 or higher. One might have suspected an associated between injected volume and level of sensory blockade.[16] In order to complete of surgical analgesia in the study, we did not reduced the dosage of hyperbaric bupivacaine. Adding of study solution of 0.4 ml in the standard dosage of 0.5 % bupivacaine 4 ml was resulted in the total volume of 4.4 ml of spinal anesthesia. This may result in too high sensory blockade. For prevention of too high sensory blokade, the volume of study drug or bupivacaine should be reduced, or the operating table should be adjusted head higher before the spinal block.

There are several other potential adverse effects from intrathecal opioid administration, such as nausea, vomiting, sedation, itching, respiratory depression and urinary retention. Belzarena et al. demonstrated that fentanyl 0.25 μg/kg with bupivacaine 0.5 % provided excellent surgical anesthesia with a few side effects. [14] Gielen et al. and Sudarshan et al. also reported that intrathecal fentanyl is one of the safest opioid that was not associated with any troublesome side effects. [17-18]

Hunt et al. reported that it was significant increase of the incidence of nausea in only the group that received 6.25 μg fentanyl but Dahlgren et al. reported that the addition of intrathecal fentanyl 60 μg for caesarean section reduced the need for intraoperative antiemetic medication. In this study the incidence of nausea and vomiting did not increase.

Itching is another frequent complication of subarachnoid and epidural opioid administration. Hunt et al. observed a significant increase in the overall incidence of itching in the 25 μg and 50 μg fentanyl groups. In another study there was no evidence of itching after an intrathecal injection of 10 μg fentanyl intraoperatively and postoperatively. [13] Rueben et al. reported 50 % of patients received high dose (50 μg) intrathecal fentanyl added in lidocaine complained of itching, but only 20 % of the patients in each 10 and 40 μg fentanyl, and none in 5 μg and 20 μg developed itching. [10] In this study, however, none of the patient experienced itching.

Hypotension commonly accompanies spinal block as a result of sympathetic nervous system block causing venous and arterial vasodilatation.[20]

In spite of the intravenous administration of 10 ml/kg of normal saline solution, the comparable decrease in blood pressure was in three groups. This supports the finding that prehydration does not regularly preclude hypotension induced by sympathetic block from spinal anesthesia with or without fentanyl. This effect is also found in geriatric patients: 25 μg of spinal fentanyl does not alter the cardiovascular response to the spinal block.[21]

The patients who had extensive sympathetic block (at least T4), the cardiac accelerated nerves (T1-T4) might affected and leaded to bradycardia. We found only one patient in group 20 who had bradycardia.

High anesthetic level of block also results in respiratory compromise. Rueben et al. reported that none of the patient who received intrathecal fentanyl up to 50 μg experienced respiratory depression, even in elderly patients who had cardiac and pulmonary diseases.[10] The same as in our study, none of the patient experienced RR <12 BPM and SpO_2 < 92 % during the operation.

We found that the severity of intraoperative shivering was decreased when fentanyl was added to intrathecal bupivacaine. However, the incidence and the severity of shivering has never been reported in previous intrathecal fentanyl study before. Alfousi et al. reported that intravenous fentanyl 1.7 μg/kg is about 77 % effective in the treatment of postoperative shivering in patients who underwent abdominal or orthopedic surgery. [22] Wheelahan reported that adding epidural fentanyl to epidural lidocaine decreases the shivering threshold compared with epidural lidocaine alone. [23] The spinal cord makes a major contribution to afferent thermal input and also it involves with the integration of thermal input. [24] The reduction of shivering in this study may be attributable to the effect of fentanyl that was added into the subarachnoid space on thermoregulator. The disadvantage of adding fentanyl to epidural lidocaine is that it increased the risk of hypothermia. In this study we did not monitor the body temperature of the patient. Most patients who underwent appendectomy had fever, so the effect of fentanyl on thermoregulator by decreasing the body temperature may not be harmful.

In conclusion, the present study reveals a beneficial effect of adding fentanyl into bupivacaine in spinal anesthesia for appendectomy. There is significant improvement in intraoperative anesthesia without any effect on the height of the sensory level and it also reduces the severity of shivering.

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