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Original Article

Effect of Bupivacaine on Preperitoneal in Laparoscopic Total Extraperitoneal Hernioplasty: Prospective Randomized Double Blind Controlled Trial

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Abstract

Objectives: **The aim of the study was to evaluate the analgesic effect after instillation of bupivacaine in preperitoneal space in patients undergoing unilateral laparoscopic totally extraperitoneal (TEP) hernioplasty.**

Methods: **A total of 44 patients with unilateral reducible inguinal hernia were randomly assigned into two groups. The bupivacaine group received 40 mL of 0.25% bupivacaine, and the control group received 40 mL of normal saline, instilled into the preperitoneal space during the TEP procedure. Surgeons, anesthesiologists, and patients were blinded to the assigned treatments. A nurse assessor also blindly assessed the pain score, using the visual analogue scale (VAS) and the numeric rating scale (NRS). Postoperative pain scores were recorded at 2, 4, 8, 12, 24 hours after operation. Complications, time of first analgesia and fentanyl consumption were recorded. All operations were performed by one surgeon.**

Results: **The age, sex, BMI, operative time did not significantly differ between the two groups. Similarly, there were no significant differences between groups with regard to postoperative pain, time to first analgesia, fentanyl consumption and complications.**

Conclusions: **The instillation of bupivacaine in the preperitoneal space during laparoscopic totally extraperitoneal hernioplasty did not reduce postoperative pain compared with placebo.**

The study was registered on www.clinicaltrial.in.th with number TCTR2016712004

Keywords: **bupivacaine, preperitoneal, laparoscopic total extraperitonealhernioplasty inguinal hernia**

INTRODUCTION

An inguinal hernia occurs in the groin area when fatty or intestinal tissues push through the inguinal canal. Modality of treatment of inguinal hernia includes open and laparoscopic techniques. Laparoscopic technique is associated with less pain, rapid recovery, quick return to work and shorter hospital stay than the open procedure[1]. There are two laparoscopic techniques; laparoscopic transabdominal preperitoneal (TAPP) hernioplasty and laparoscopic totally extraperitoneal (TEP) hernioplasty. The choice of surgical technique depends on the surgeon's skills,

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patient and surgeon preferences, available instruments, and patient's condition. The site of pain in TEP hernioplasty included the port site wound and the dissected preperitoneal space. Postoperative pain may prolong hospital stay and recovery. Preperitoneal infusion of bupivacaine may significantly reduce postoperative pain[2-4,7]. Several randomized controlled trials have addressed pain reduction after instillation of bupivacaine in the preperitoneal space in patients undergoing TEP, but results have been inconclusive[5,6,8]. This study aims to compare the pain reduction by preperitoneal infusion of 0.25% bupivacaine versus normal saline solution during TEP hernioplasty. Secondary outcomes included postoperative complications, fentanyl consumption and time to first use of analgesic drugs.

Materials and Methods

This prospective randomized double blind controlled trial was conducted at Hatyai Hospital, Songkhla, Thailand, from March 2016 to February 2017. The protocol was approved by the Hatyai Research Ethics Committee. Patientswith reducible unilateral inguinal hernia and scheduled for elective TEP hernioplasty, who had American Society Anesthesiologist (ASA) status I-II, and aged between 14 to 70 years, were enrolled into the study after informed consent was obtained. Exclusion criteria included high risk for general anesthesia, allergy to bupivacaine, pregnancy, denying consent, history of previous lower abdominal surgery, recurrent inguinal hernia, bilateral inguinal hernia, and history of drug abuse.

All patients were admitted one day prior to surgery and familiarized with the visual analogue scale (VAS) and numeric rating scale (NRS). For VAS, a continuous 10 cm line was used, with the 0 point defined as no pain to the 10 cm point defined as the most severe pain. For NRS, 0 was defined as no pain, to the score of 10 defined as the most severe pain.

The patients were premeditated by receiving 10 mg diazepam before bedtime and diazepam 5 mg on the morning of operation. All patients were instructed to void prior to operation, and urinary bladder catheterization was not performed. Patients received 1gm cefazolin intravenous within 30 minutes before skin incision. The operation was carried out under general anesthesia using the same protocol. General anesthesia was induced with propofol 2.5 mg/kg and fentanyl 1.5 mg/kg. Oropharyngeal intubation was facilitated by the administration of cisatracurium 0.1 to 0.2 mg/kg and maintained with incremental IV dose of 1 to 2 mg. After intubation, anesthesia was maintained with oxygen, 70% N2O, 1 to 2% sevoflurane, and fentanyl 0.5 to 1 mg/kg to maintain blood pressure and pulse within 20% of patient's baseline values. Patients were ventilated with positive pressure ventilation to keep at ETCO2 30 to 35 mmHg. The anesthesiologist team was blinded to patient's assignment.

The patient was placed in the Trendelenburg position with the ipsilateral side rotated up. All patients were operated by one surgeon. A 2-cm transverse infraumbilical incision was performed and the anterior rectus sheath was incised horizontally. The ipsilateral rectus muscle was retracted laterally. Preperitoneum space was created by sharp dissection (not using balloon dissection) initially, a 12 mm port was inserted, and CO2 was insufflated. The pressure was maintained at less than 12 mmHg. A zero-degree 10 mm laparoscope was inserted, and a second port was made in the midline between the first and third port, the third port created 3 cm above pubic symphysis. The preperitoneal space was developed by sharp dissection under vision from midline to pubic symphysis, and Cooper's ligament and hernia sac were identified. The sac was separated from spermatic cord while preserving all blood vessels and vas deferens. The hernia sac was ligated with silk 2-0. The proximal sac was pulled back and distal sac was left alone.

All of patients were randomized in blocks of 4, with concealment using numbered closed envelopes, into 2 groups by scrub nurse: one instilled with 40 mL of 0.25% bupivacaine, and the other 40 mL of normal saline into the preperitoneal space. The scrub nurse opened the envelope to reveal the allocated treatment when the hernia sac was closed. The surgeon, the anesthesiology team, and nurse assessors were blinded to the allocation. A small catheter was inserted through a 5 mm trocar and guided to instill the allocated treatment into the preperitoneal space under direct vision.

After instillation, the operating table was rotated to the reverse Trendelenburg position and down towards the ipsilateral side for 3 to 5 minutes. After

rotating the table back to the operative position, a 15 × 10 cm polypropylene mesh was inserted through subumbilicus port. The mesh was placed and transfixed with trackers 2 pieces at the Cooper's ligament, and at transversalis fascia above the iliopubic tract with tackers (Protack, Autosuture, Norwalk, CT, USA). After the preperitoneum space was deflated, laparoscopic ports were removed. Bupivacaine, 5 to 10 mL, was infiltrated at the port incisions. The subumbilical fascia was closed with 1-0 interrupted absorbable suture. The skin was closed with 4-0 absorbable, subcuticular suture. At the end of the operation, residual neuromuscular blockade was antagonized with 2.5 mg of neostigmine and 1.2 mg of atropine. After endotracheal tube extubation, patients were transferred to the recovery room and were attended by anesthetic nurses who were also blinded to the patient's treatment assignment.

Intravenous fentanyl of 50 μg was given if the patient had VAS or NRS pain score more than 5, or at the patient's request. Postoperative pain scores were assessed at 2, 4, 8, 12, and 24 hours after surgery, using both VAS and NRS, by nurses. All patients were clinically assessed at the Outpatients Clinic at 1 week and 30 days after operation by the same surgeon.

Operative time was defined as the duration in minutes between skin incision to skin closure. Postoperative complications such as nausea or vomiting, pruritus, constipation, urinary retention, hematoma, and infection were recorded. Superficial surgical site infection (SSSI) was defined as tender and redness at the surgical wound. Seroma was defined as a fluid mass in the scrotal sac or at the groin. Hematoma was defined blood in scrotal sac or under the area of dissection. Groin pain was defined pain around the surgical wound. Readmission and reasons for readmission to the hospital were recorded, as well as time to first analgesia (fentanyl) use, and the amount of analgesics used.

The parameters obtained were summarized in computerized spreadsheets and statistical analysis was performed by using STATA MP-13. The two groups were compared using Student's t test for continuous variables. Categorical variables were analyzes by Chi square test or Fisher's exact test. Numerical data were presented as mean ±SD and categorical data was expressed as counts and percentages. Statistical significance was defined as a *P* value of 0.05 or less.

Results

The study included 44 patients with unilateral reducible inguinal hernia, and were randomly allocated into two groups. There was one patient with unilateral pantaloon hernia in the bupivacaine group. The mean ages were 48.86 ± 13.58 years in bupivacaine group and 47.00 ± 11.32 years in control group. There were no differences between the two groups in terms of age, sex and body mass index (Table 1). The mean operative time in the bupivacaine and control groups (67.00 ± 16.36 and 80.23 ± 26.39) were statistically comparable (*P*=0.52). No patient was converted to the open technique. The mean time to first analgesia (fentanyl) and the mean fentanyl consumption were not statistically different between the two groups.The mean postoperative pain (VAS and NRS) at 2, 4, 8, 12, and 24 hours after surgery were not statistically different between two groups (Table 2). There were no wound infection, groin pain, hematoma, nausea vomiting, pruritus, constipation, urinary retention in this study. All patients were discharged within 48 hours after surgery. The overall incidence of complications (seroma) within 30 days was not significantly different between the 2 groups.

Table 1 Demographic data of randomized patients who underwent TEP

Demographic data	Bupivacaine (n=22)	Normal Saline (n=22)	*p*-value
Age (years)	48.86 ± 13.58	47.00 ± 11.32	0.624
Men (%)	22 (100)	21 (95)	0999
Body mass index (kg/m^2)	21.90 ± 1.92	22.09 ± 2.07	0.762

Table 2 Outcomes of the study

Outcomes	Bupivacaine (n=22)	Normal Saline (n=22)	*p*-value
Operative time (min)	67.00 ±16.36	80.23 ± 26.39	0.52
VAS 2 hour	4.50 ± 3.11	5.45 ± 2.70	0.284
VAS 4 hour	4.32 ± 2.46	3.59 ± 1.59	0.251
VAS 8 hour	3.59 ± 2.46	2.32 ± 1.94	0.064
VAS 12 hour	2.41 ± 2.52	1.82 ± 1.89	0.384
VAS 24 hour	2.55 ± 1.92	1.95 ± 2.44	0.380
NRS 2 hour	3.94 ± 2.97	5.00 ± 2.89	0.240
NRS 4 hour	3.75 ± 2.43	2.72 ± 2.00	0.136
NRS 8 hour	3.05 ± 2.68	1.95 ± 1.89	0.123
NRS 12 hour	2.13 ± 2.31	1.77 ± 1.98	0.409
NRS 24 hour	2.11 ± 1.87	1.77 ± 1.98	0.561
Fentanyl consumption	0.95 ± 0.95	0.59 ± 0.85	0.189
First fentanyl (hour)	1.75 ± 2.17	1.06 ± 2.05	0.281
Seroma	3 (14%)	3 (14%)	0.999

VAS: visual analog scale, NRS: Numeric rating scale, *: time to first analgesia

Discussion

Postoperative pain is often a concern after hernia repair. The reduction of postoperative pain can decrease hospital stay and facilitates recovery, with faster return to work or normal activity. The laparoscopic technique is associated with less pain than the open technique. Factors associated with postoperative pain in laparoscopic TEP hernioplasty include preperitoneal blunt dissection, stretching of surrounding muscles during gas insufflations, the presence of skin incisions, and the use of mesh fixation[9,10]. The mechanism of chronic pain following TEP hernioplasty is unknown but probable causes include nerve damage or irritation, chronic inflammation, reaction to the mesh, and irritation from staples[11]. Preemptive anesthesia may prevent nervous system hyperexcitability and postoperative hyperalgesia, but the efficacy of various preemptive anesthesia techniques is unclear[12,13]. Hon et al.[7] have shown that preemptive preperitoneal infiltration with 0.5% bupivacaine significantly reduced postoperative pain in laparoscopic TEP hernioplasty.

The present study was conducted to evaluate the analgesic effect of bupivacaine instillation during TEP hernia repair. We compared 40 mL of 0.25% bupivacaine instilled via a small catheter under direct vision into the preperitoneal space through the trocar site, withthe same amount of normal saline. The operating table was tilted for good distribution of both solutions, and 3 to 5 minutes was given for sufficient absorption. There were no significant differences in postoperative pain between patients receiving either bupivacaine or normal saline instillation.

There may be several reasons that might explain the results of the present study. Firstly, balloon trocar was not used for preperitoneal dissection. Secondly, tackers were used to fix the mesh. There have been 3 RCTs in which tackers were used. Instillation of bupivacaine into thepreperitoneal space had no significant impact on postoperative pain in these studies[5,6,8]. In 3 RCTs where tackers were not used, however, bupivacaine instillation was associated with significant relief of postoperative pain[2,4,7]. Thirdly, this study did not use preemptive analgesia. Fourthly, tissue injury after dissection might decrease the absorption of bupivacaine. Fifthly, in cases where tearing of the peritoneum occurred during the procedure, residual CO2 in the peritoneal cavity might increase postoperative pain. Finally, pain has at least two dimensions, sensory and affective. VAS and NRS are unidimensional pain scales. These scales might not fully capture the experience of pain, and thus may be less sensitive measures of pain.

The instillation of analgesic drugs and the amount of analgesic drug in the preperitoneal space during TEP procedure may increase the risk of seroma formation. Our incidence of seroma formation is 14 %. Seroma was found in six patients (three patients in

each group). There incidence of seroma was not significantly different between both groups.

Previous studies on postoperative pain after instillation of bupivacaine into the preperitoneal space during TEP hernioplasty differ in how they were conducted. Some used balloon trocars for tissue dissection[2,4,5,8]; the methods of mesh fixation were different[3,5,6,8]; some controlled for pain at the port site[2,3,6,7]; some included bilateral or recurrent hernia as well[2,6,8]. The timing, technique of instillation, volume and concentration of bupivacaine instillation were also different across the studies. The optimal volume and concentration of bupivacaine for instillation into the preperitoneal space during TEP inguinal hernioplasty have not been standardized. These differences may explain the differing results between studies. Tong et al.[15], in a meta-analysis of these studies, showed that extraperitoneal instillation of bupivacaine during TEP inguinal hernioplasty was not associated with greater reduction in postoperative pain compared with placebo.

Conclusion

The preperitoneal instillation of 40 mL of 0.25% bupivacaine had similar analgesic effects as the placebo in the patients undergoing unilateral laparoscopic totally extraperitonealhernioplasty.

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บทคัดย่อ **การศึกษาแบบสุ่มไปข้างหน้า ปกปิดการจับกลุ่ม ผลของการใช้ยาชา Bupivacaine ในเนื้อเยื่อนอกช่องท้องหลังการผ่าตัดไส้เลื่อนแบบส่องกล้องนอกช่องท้อง**

ชูแสง ธีระวิวัฒน์ชัย
กลุ่มงานศัลยกรรม โรงพยาบาลหาดใหญ่ จังหวัดสงขลา

จุดประสงค์: เพื่อประเมินผลของการลดปวดจากการใส่ยาชา Bupivacaine ในเนื้อเยื่อนอกช่องท้องหลังผ่าตัดไส้เลื่อนแบบส่องกล้องในผู้ป่วยที่เป็นไส้เลื่อนข้างเดียวแบบดันกลับได้

วัสดุและวิธีการ: ผู้ป่วยที่เป็นไส้เลื่อนข้างเดียวแบบดันกลับได้จำนวน 44 ราย แบ่งเป็น 2 กลุ่ม กลุ่มที่ 1 ให้ยา 0.25% bupivacaine 40 มิลลิลิตร กลุ่มที่ 2 ให้น้ำเกลือ 40 มิลลิลิตร ในเนื้อเยื่อนอกช่องท้อง โดยศัลยแพทย์ที่ผ่าตัด, ทีมวิสัญญีแพทย์, ทีมพยาบาลผู้ประเมินความปวดแบบ NRS และ VAS ไม่ทราบว่าผู้ป่วยอยู่กลุ่มใด คะแนนความปวดจะถูกเก็บหลังผ่าตัดเป็นระยะเวลาที่ 2, 4, 8, 12 และ 24 ชั่วโมง ภาวะแทรกซ้อน, เวลาที่เริ่มใช้ยาแก้ปวด, ปริมาณยา fentanyl ที่ใช้ จะถูกเก็บข้อมูล การผ่าตัดทั้งหมดได้รับการผ่าตัดโดยศัลยแพทย์คนเดียว

ผลการศึกษา: ข้อมูลทั่วไป เช่น อายุ เพศ ดัชนีมวลกาย ระยะเวลาที่ใช้ในการผ่าตัด ทั้ง 2 กลุ่มไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ระดับความปวด เวลาที่เริ่มใช้ยาแก้ปวด, ปริมาณยา fentanyl ที่ใช้ และภาวะแทรกซ้อนไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ

สรุปการศึกษา: การใส่ยา Bupivacaine ในช่องในเนื้อเยื่อนอกช่องท้องในผู้ป่วยเป็นไส้เลื่อนข้างเดียวแบบดันกลับได้เอง ไม่มีผลต่อการลดระดับความปวดหลังผ่าตัดไส้เลื่อนแบบส่องกล้อง