การศึกษาเปรียบเทียบการใส่ยาบูพิวาเคน (Bupivacaine) ในช่องหน้าต่อเยื่อบุผิวช่องท้อง (preperitoneal space) เพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนขาหนีบด้วยการส่องกล้อง

นายรณรัฐ สุวิกะปกรณ์กุล

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาการพัฒนาสุขภาพ
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2550

A RANDOMIZED CONTROLLED TRIAL OF PREPERITONEAL BUPIVACAINE INSTILLATION FOR REDUCING PAIN FOLLOWING LAPAROSCOPIC INGUINAL HERNIORRHAPHY

Mr.Ronnarat Suvikapakornkul

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Health Development

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Thesis Title	A RANDOMIZED CONTROLLED TRIAL OF PREPERITONEAL BUPIVACAINE INSTILLATION FOR REDUCING PAIN FOLLOWING LAPAROSCOPIC INGUINAL HERNIORRHAPHY
By	Mr. Ronnarat Suvikapakornkul
Field of Study	Health Development
Thesis Principal Advisor	Jule Namchaisiri, M.D., M.Sc.
Thesis Co-advisor	Associate Professor Savit Kositchaiwat, M.D., M.Sc.

Accepted by the Faculty of Medicine, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

..... Dean of the Faculty of Medicine

(Associate Professor Adisorn Patradul, M.D.)

THESIS COMMITTEE

..... Chairperson

(Associate Professor Somrat Charuluxananan, M.D., M.Sc.)

..... Thesis Advisor

(Jule Namchaisiri, M.D., M.Sc.)

..... Thesis Co-advisor

(Associate Professor Sav it Kositchaiwat, M.D., M.Sc.)

..... External Member

(Assistant Professor Yo wanush Kongdan, M.D.)

..... External Member

(Assistant Professor Chulaluk Komoltri,DrPH)

รณรัฐ สุวิกะปกรณ์กุล: การศึกษาเปรียบเทียบการใส่ยาบูพิวาเคน (Bupivacaine) ในช่องหน้าต่อเยื่อบุผิวช่องท้อง (preperitoneal space) เพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนขาหนีบด้วยการส่องกล้อง (A RANDOMIZED CONTROLLED TRIAL OF PREPERITIONEAL BUPIVACAINE INSTILLATION FOR REDUCING PAIN FOLLOWING LAPAROSCOPIC INGUINAL HERNIORRHAPHY) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: อ.นพ.จุล นำชัยศิริ, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: รศ.นพ.สาวิตร โมษิตชัยวัฒน์, 38 หน้า.

วัตถุประสงค์: เพื่อศึกษาประสิทธิผลของยาบูพิวาเคนเมื่อใส่ในช่องหน้าต่อเยื่อบุผิวช่องท้องเพื่อลดความปวดหลังการผ่าตัดไส้เลื่อนขาหนีบด้วยการส่องกล้อง

รูปแบบงานวิจัย: การวิจัยทางคลินิกแบบเปรียบเทียบบาที่ใช้ทดสอบกับยาหลอกโดยใช้การแบ่งกลุ่มด้วยการสุ่มอย่างมีระบบ

สถานที่ทำวิจัย: ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล

ผู้เข้าร่วมงานวิจัย: ผู้ป่วยไส้เลื่อนขาหนีบที่ไม่มีอาการแทรกซ้อนจำนวน 40 ราย ทั้งที่เป็น 1 ข้าง หรือ 2 ข้าง และไส้เลื่อนเกิดใหม่ หรือไส้เลื่อนเกิดซ้ำหลังการผ่าตัดครั้งแรกจะถูกแบ่งออกเป็น 2 กลุ่มโดยการสุ่มอย่างมีระบบ โดยมีกลุ่มที่ได้รับการใส่ยาบูพิวาเคนมีจำนวน 19 คนและกลุ่มที่ได้รับการใส่น้ำเกลือ (ยาหลอก) จำนวน 21 คน ทันทีที่ผ่าตัดไส้เลื่อนด้วยการส่องกล้องแบบในช่องหน้าต่อเยื่อบุช่องท้องทั้งหมดเสร็จสิ้น ยาบูพิวาเคนหรือน้ำเกลือจะถูกใส่ใสช่องหน้าต่อเยื่อบุช่องท้องอย่างทั่วถึง โดยมีศัลยแพทย์ผู้เดียวเป็นผู้ทำผ่าตัดและถูกปกปิดชนิดของยาที่ใช้ทำการทดลอง

ตัวแปรหลัก: ระดับความเจ็บปวดหลังการผ่าตัดถูกวัดโดยการใช้ไม้บรรทัดวัดระดับความปวดและตีค่าออกมาเป็นคะแนน และร่วมกับให้ผู้ป่วยตีค่าความเจ็บปวดออกเป็นระดับ "ไม่ปวด ปวดน้อย ปวดปานกลาง และปวดมาก" ความเจ็บปวดจะถูกวัดหลังการผ่าตัด 1, 2, 6, 12 และ 24 ชั่วโมงตามลำดับ โดยพยาบาลคนเดียวกัน และถูกปกปิดชนิดของยาที่ใช้ทำการทดลอง

ผลการวิจัย: คะแนนของความปวดหลังผ่าตัดในกลุ่มที่ได้รับบาบูพิวาเคนและน้ำเกลือมีดังต่อไปนี้ 3.5 และ 5.2 (p= 0.059), 2.9 และ 4.5 (p=0.117), 2.1 และ 3.2 (p= 0.101), 1.5 และ 2.7 (p= 0.145), 1.6 และ 2.0(p= 0.672) ที่ 1,2,6,12 และ 24 ชั่วโมงหลังการผ่าตัดตามลำดับ พบภาวะแทรกซ้อน 4 รายในกลุ่มที่ได้รับการใส่ยาบูพิวาเคน (น้ำเหลืองคั่ง 2 ราย ปัสสาวะไม่ออก 1 รายและหัวใจเต้นผิดจังหวะ 1 ราย) และ พบภาวะแทรกซ้อน 7 รายในกลุ่มที่ได้รับการใส่น้ำเกลือ (น้ำเหลืองคั่ง 4 ราย ปัสสาวะไม่ออก 1 รายและท้องอืดจากภาวะลำไส้ไม่ทำงาน 1ราย) ซึ่งไม่แตกต่างอย่างมีนัยสำคัญ

สรุป: ไม่มีหลักฐานหนักแน่นเพียงพอว่าการใส่ยาบูพิวาเคนในช่องหน้าต่อเยื่อบุผิวช่องท้องหลังการผ่าตัดไส้เลื่อนขาหนีบด้วยการส่องกล้องจะสามารถลดความปวดหลังผ่าตัดลงได้

สาขาวิชา การพัฒนาสุขภาพ ลายมือชื่อนิสิต .....

ปีการศึกษา 2550 ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์หลัก .....

ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์ร่วม .....

497 50061 30: MAJOR HEALTH DEVELOPMENT

KEYWORD: LAPAROSCOPIC HERNIORRHAPHY / PAIN / BUPIVACAINE / RANDOMIZED CONTROLLED TRIAL

RONNARAT SUVIKAPAKORNKUL: A RANDOMIZED CONTROLLED TRIAL OF PREPERITONEAL BUPIVACIANE INSTILLATION FOR REDUCING PAIN FOLLOWING LAPAROSCOPIC INGUINAL HERNIORRHAPHY. THESIS PRINCIPAL ADVISOR: JULE NAMCHAISIRI, M.D.,M.Sc., THESIS COADVISOR: ASSOC.PROF.SAVIT KOSITCHAIWAT, M.D.,M.Sc. 38 pp.

Objective: To determine the effectiveness of bupivacaine instillation into the preperitoneal space following laparoscopic herniorrhaphy.

Design: Randomized controlled trial, double blinded

Setting: The elective surgery in a medical school

Participants: Forty patients, who had an inguinal hernia with no complication, unilateral or bilateral and recurrence or no recurrence after previous hernia repair were randomly assigned to receive bupivacaine (n = 19) and normal saline (n =21). The intervention or placebo was instilled into preperitoneal space after totally extraperitoneal laparoscopic herniorrhaphy by the same surgeon who was blinded to the intervention.

Main outcome measures: Pain intensity was assessed by using visual analogue scale and verbal rating scale after 1, 2, 6, 12 and 24 hours postoperatively by the same nurse who was blinded to the intervention.

Results: For bupivacaine and placebo group, mean of pain score were 3.5 vs. 5.2 respectively after 1 hour (p= 0.059), 2.9 vs. 4.5 respectively after 2 hours (p=0.117), 2.1 vs. 3.2 respectively after 6 hours (p= 0.101), 1.5 vs. 2.7 respectively after 12 hours (p= 0.145) and 1.6 vs. 2.0 respectively after 24 hour (p= 0.672). The complications developed in 4 patients (2 seroma, 1urinary retention and 1 arrhythmia) in bupivacaine group and 7 patients (5 seroma, 1 urinary retention and 1 ileus) in placebo group, which are not significant different.

Conclusions: There is no strong evidence to confirm that bupivacaine instillation into preperitoneal space after laparoscopic herniorrhaphy can reduce postoperative pain.

Field of Study: Health Development ..... Student's Signature: .....

Academic Year: 2007 ..... Principal Advisor's Signature: .....

Co-advisor's Signature: .....

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LIST OF ABBREVIATIONS

TEP Herniorrhaphy: Total ExtraPeritoneal Herniorrhaphy

TAPP Herniorrhaphy: TransAbdominal PrePeritoneal Herniorrhaphy

VAS: Visual Analogue Scale

VRS: Verbal Rating Scale

CHAPTER I

INTRODUCTION

Rationale and Backgrounds

The technique of an inguinal hernia repair still has being developed because none of available technique is the most perfect. The laparoscopic hernia repair is new modern method for an inguinal hernia repair. The short-term recurrent rate is not different from the standard tension-free repair ***(1-3)***. The laparoscopic herniorrhaphy is associated with less operative pain and more rapid return to normal activities, but it takes longer time to perform, higher cost and may slightly increase the risk of complications ***(1,4)***. It is usually preferred in recurrent hernia and bilateral hernia ***(5)***.

The refinement of the laparoscopic techniques to the now widely accepted transabdominal preperitoneal approach (TAPP) and the totally extraperitoneal (TEP) technique has established a sound basis for the laparoscopic approach to the repair of groin hernias. The TEP procedure, which is rapidly growing in popularity and in Ramathibodi hospital as well, approaches the inguinal canal through the preperitoneal space without entering the peritoneal cavity.

Nowadays, the traditional open hernia repair can be performed under local anesthesia as a day-case surgery ***(6)***. Unlike its open counterpart, laparoscopic hernia repair is not widely performed as a day-case procedure, although there were few studies, which demonstrated the possibility ***(7,8)***. It usually requires performing under general anesthesia and patients usually suffer a considerable amount of pain on the first postoperative day. Pain following laparoscopic preperitoneal repair is typically in the lower abdominal wall area and not on the small skin incisions ***(9)***. The exact etiology of pain remains unclear. It should be multifactorial and treatment of any one factor in isolation will not achieve the favorable outcome. The causes include tissue dissection, type of insufflated gas, gas temperature, humidity and unknown individual factors. The use of mesh fixation stapler to fix the mesh to the abdominal wall and Cooper's ligament may further exacerbate pain from tissue dissection ***(7)***. These could be related to the

management of postoperative pain, as a requirement for parenteral anesthesia would prevent patients from early discharge and early ambulation.

Topical instillation of local anesthetics has been shown to be useful in reducing postoperative pain in other types of laparoscopic surgery such as cholecystectomy and gynecologic surgery ***(10,11)***. The instillation of the local anesthetic agent into the preperitoneal space intraoperatively, as same as intraperitoneal blockade, in an attempt to achieve direct sensory inhibition of the most potential painful part. This technique may be useful in TEP procedure where administration of a long-acting agent such as bupivacaine may provide effective analgesia in postoperative period. Thus, attenuation of early postoperative pain may decrease the use of narcotic medications and reduce postoperative complications, thereby facilitating discharge as a day-case surgery, and reducing hospital-related expenses.

CHAPTER II

REVIEW OF RELATED LITERATURES

Review of Related Literatures

The literature search strategy used to locate the information in this review is in the MEDLINE, SCOPUS and ISI web of knowledge reference database. The following search terms were used:

1) Laparoscopic herniorrhaphy AND pain

2) Laparoscopic inguinal hernia repair AND pain

3) Laparoscopic inguinal hernia repair AND bupivacaine

4) Laparoscopic herniorrhaphy AND bupivacaine

The period covered by the search was from any date until July 2007. The 4 randomized controlled trials were retrieved. There was no meta-analysis or systematic review for this issue.

The conclusions from randomized controlled trials have been still in controversy. The following studies concluded that bupivacaine instillation in peritoneal space attenuates pain following laparoscopic inguinal hernia repair:

In 2004, Bar-Dayan, et al *(12)* conducted trial in Israel. The 44 patients were randomized in to two groups. After completion of laparoscopic herniorrhaphy, group A received 80 mg of bupivacaine in 25 cc of saline instilled into the preperitoneal space, whereas group B received normal saline instilled into the preperitoneal space. The average visual analogue scale were significantly attenuated in-group A compare to group B at 1 (4.0 vs. 5.0, respectively; p =0.0038), 2 (4.0 vs. 5.9, respectively; p=0.0015) and 4 (4.3 vs. 5.8, respectively; p=0.0015) hour after surgery. Furthermore, the analgesic intake was significantly decreased in group A compare to group B. This study has a good randomization, blinding and measurement. The weak point of the study is that the investigators did not perform a uniform anesthesia protocol defining the anesthetic and narcotic medications during surgery.

In 1998, O'Riordian DS, et al ***(7)*** studied that the 56 patients with unilateral hernia were randomized into preperitoneal instillation of bupivacaine (n=29) or normal saline (n =27). Patients were blindly assessed on discharge (4-6 hours after operation) from the hospital, at 24 hours, 1 week, and 1 month postoperatively. The patients treated with bupivacaine had lower median visual analogue pain score on discharge 1.5 vs. 3.7 (p=0.03), more frequently pain free, recover faster, stopping analgesia earlier, and returning to full activity earlier. In this study, the intention- to- treat analysis was not used. A few patients were excluded from analysis because the laparoscopic repair hernia was converted to open technique due to difficult hernia. The researcher did not mention about the amount of morphine, which prescribed to the patients as require after procedure. The morphine should effect the pain intensity. The principle of measurement is inappropriate. Bupivacaine is long-acting analgesia but its duration is not long as 24 hours. The 24 hour time point evaluation could not be correct, the patients were possible have pain relief from other analgesia that the investigators did not mention.

The following studies concluded that the bupivacaine instillation into preperitoneal space has no effect on postoperative pain relief:

In 1998, Saff GN, et al ***(13)*** recruited 42 patients which randomized in into two groups, 21 patients received 60 ml of 0.125%bupivacaine into preperitoneal space and other 21 patients received 60 ml of normal saline. All of the patients received intravenous ketorolac 45 mg and fentanyl was given as much as the patients were feeling comfortable. The study concluded that bupivacaine has no effect to attenuate postoperative pain. The major considerable factor in this study is the pain medication given as much as patient needed that will interfere the intensity of pain interpretation.

In 1998, Deans GT, et al ***(14)*** studied one hundred patients undergoing transabdominal preperitoneal laparoscopic hernia repair (TAPP) were allocated randomly to receive 1) bupivacaine 1.5 mg/kg (n=25) 2) bupivacaine 1.5mg/kg with 1:200,000 adrenaline (n=25) 3) bupivacaine 3 mg/kg (n=24) 4) saline (n=26). They concluded that the bupivacaine has no effect on postoperative relief at 4, 8, 12 and 24 hour after operation. This study has a good study design, but the method of the hernia repair is different that our study operation (TEP) will perform in the preperitoneal space only but TAPP technique, the intraperitoneal space was entered and the endo-tacker

was used much more than TEP technique that while the intensity of pain from TAPP is possible more than TEP.

From the literature review, we have not enough evidence to conclude that bupivacaine has or has no effect to attenuate the postoperative pain following laparoscopic inguinal hernia repair with TEP technique. We will conduct more appropriate study design to solve this question.

CHAPTER III

RESEARCH METHODOLOGY

Research Questions

1. Primary Research Question

Does bupivacaine instillation into preperitoneal space attenuate postoperative pain following laparoscopic inguinal herniorrhaphy compare to placebo?

2. Secondary Research Question

2.1 What is the duration of bupivacaine instillation into preperitoneal space for controlling postoperative pain of laparoscopic inguinal herniorrhaphy?

2.2 What is the complication of bupivacaine instillation into preperitoneal space for attenuate postoperative pain of laparoscopic inguinal herniorrhaphy?

Research Objectives

1. To evaluate the effectiveness of bupivacaine analgesia, administered into the preperitoneal space at completion of procedure, in the patients undergoing laparoscopic herniorrhaphy.

2. To evaluate the duration of bupivacaine instillation into preperitoneal space for controlling postoperative pain of laparoscopic inguinal herniorrhaphy.

3. To evaluate the complication of bupivacaine instillation into preperitoneal space for attenuate postoperative pain of laparoscopic inguinal herniorrhaphy.

Hypothesis

1. Research Hypothesis

Bupivacaine instillation into preperitoneal space can reduce postoperative pain intensity following laparoscopic inguinal herniorrhaphy compare to placebo.

2. Statistical Hypothesis

2.1 Null Hypothesis

Bupivacaine instillation into preperitoneal space cannot alter postoperative pain intensity following laparoscopic inguinal herniorrhaphy compare to placebo.

2.2 Alternative Hypothesis

Bupivacaine instillation into preperitoneal space can alter postoperative pain intensity following laparoscopic inguinal herniorrhaphy compare to placebo.

Conceptual Framework

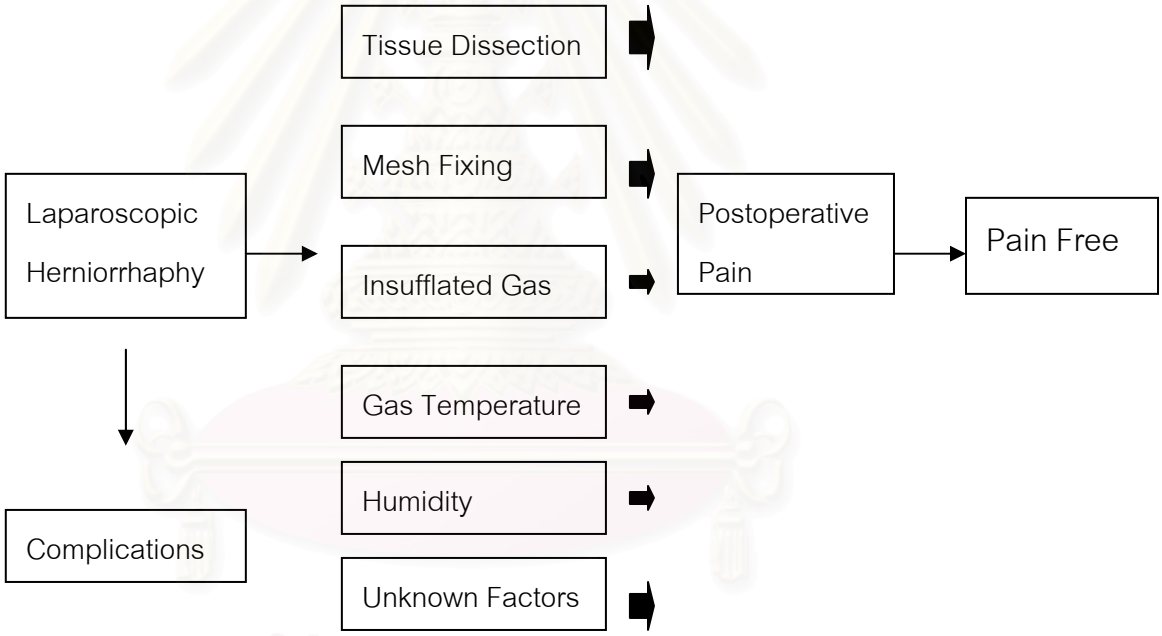

Figure 1 Conceptual framework of the study. There are 6 possible causes of postoperative pain following laparoscopic herniorrhaphy. The independent variables i.e. postoperative pain and complications will be recorded. The different levels of thickness of block arrows show relatively different level of effect to the postoperative pain.

Assumptions

1.The study indicates that a 30%-50% reduction of pain intensity on visual analogue scale corresponds to a clinically significant reduction of pain ***(15).***

2. No other analgesic medication, especially long acting medication, is administered 1 week before the operation until 24 hours after operation, and then the patient will be prescribed an oral acetaminophen and/or NSAID to relief pain.

Keywords

Laparoscopic Herniorrhaphy, Pain, Bupivacaine, Randomized Controlled Trial, Extraperitoneal Instillation

Operational Definitions

Laparoscopic herniorrhaphy or laparoscopic hernia repair is an approach to repair inguinal hernia under viewing of telescope and operated by laparoscopic instruments through the small holes on the skin.

Pain in this study means the post-operative pain, which directly caused by the operation and occurs on the operative site.

Visual Analogue Scales (VAS) is the instrument, which is used by this study to measure the pain intensity. It consists of 10-cm horizontal lines with the two end points, the left end labeled with " no pain" and the right end labeled with " worst pain ever ". The patients are required to place a mark on the line at the point that corresponds to the level of pain intensity they presently feel. The distance in centimeters from the low end of the visual analogue scale to the patient's mark is used as a numerical index of severity of pain.

Verbal Rating Scale (VRS) consists a series of verbal pain description ordered from least to most intense (no pain, mild, moderate, and severe)

Laterality means how many side that the hernia has been diagnosed, unilaterally or bilaterally.

Recurrent Hernia means the hernia, which reoccurs after the prior hernia repair in any time.

Operative Time is a duration, which starts from the time point of skin incision until finishing the skin closing.

Total Morphine Consumption is total milligram of morphine, which required by the patients postoperatively.

Time to Rescue Analgesia is the first time which the patients require morphine for pain relief.

The Duration of Pain Controlled by Bupivacaine is the duration start from immediate post operation until time to rescue analgesia.

Research Design

The study will be conducted as a superiority trial, which the intervention should decrease the postoperative pain comparing to placebo. The randomized controlled trial will be used for ensure that the influence of the unknown factors will be equally distributed in to both groups.

Population

Target Population

Thai people who has an inguinal hernia.

Sample Population

The patient with an inguinal hernia who visits the surgical clinic of Ramathibodi hospital has agreement for participation and gives the informed consent. The participants should meet the following criteria:

Inclusion Criteria

1. The patient has any type of an inguinal hernia (direct, indirect, femoral, recurrent and combined-hernia)
2. Unilateral or bilateral hernia
3. Reducible hernia
4. ASA status I or II

Exclusion Criteria

1. Inguinal hernia with complications i.e. incarceration, strangulation, obstruction, gangrene and perforation of hernia content

2. The patient has a history of operation in Retzious' space.

3. The patient has severe cardiovascular and/or pulmonary disease that could not tolerate the gas insufflation i.e. chronic obstructive pulmonary disease, congestive heart failure.

4. ASA status III or IV

5. Bleeding disorder

6. Alcohol or drug abuse

7. Intolerance or adverse reaction to medications (especially bupivacaine, morphine) uses in this study

8. Patient who cannot comprehend the instruction and have perceptual-motor system problem

Sample Size Calculation

Sample sized was estimated based on a comparison of mean VAS pain score between bupivacaine and placebo. To have a 90% chance of detecting 30% reduction in VAS pain score using a two-tail test at the 5% level of significance, 20 subjects per group was required as shown in the detailed calculation below. It was assume that pain score is continuous and normally distributed in each group. Furthermore, standard deviation of VAS pain score in each group was assumed to be equal.

Ho: $\mu_1 - \mu_2 = 0$

Ha: $\mu_1 - \mu_2 \neq 0$

Where μ_1, μ_2 = mean VAS pain score at 1 hour in group 1 and 2 respectively.

σ = common standard deviation of VAS pain score at 1 hour

$$n|group = \frac{2\sigma^2 [Z_\alpha + Z_\beta]^2}{[\mu_1 - \mu_2]^2}$$

$Z\alpha$ = 1.96 for two-tailed type I error of 0.05

$Z\beta$ = 1.28 for power 90%

SD $\approx$ range/6 = (8-1)/6 =1.16 [from Dean GT, et al ***(14)***]

Mean of pain score (14) = 4 , 30% reduction of pain score = 2.8

$$n|group = \frac{2\,(1.16)^2\,[\,1.96+1.28]^2}{[4-2.8]^2}$$

$$= 19.5$$

Randomization and Concealment

Randomization lists were produced in advance by computer-generated sequence using simple randomization and kept secret in the sealed opaque envelope at the randomization center. When the operation starts, the randomization center will be called for the randomization code.

Blinding

The patients, surgeons, assistances, anesthesiologists, outcome assessors and nursing staff were all blinded to the intervention.

Anesthetic Technique

No pre-emptive analgesia was allowed before operation. Intravenous antibiotic were administered preoperatively. Anesthesia was induced with Pentothal 5 mg/kg, fentanyl 1.5 mcg/kg was used as analgesia, and the muscle relaxant was with atracurium 0.6 mg/kg. Patient was intubated and ventilated with intermittent positive pressure ventilation. Anesthesia was maintained with N_2O, O_2 and isoflurane, and supplemental analgesia was provided with fentanyl 0.5 to 1 mcg/kg. On the completion of surgery, neuromuscular blockade was reversed with atropine 1.2 mg and neostigmine 2.5 mg. Postoperative analgesia included fentanyl intravenously as required in the operating room.

Surgical Technique

The TEP procedure was underwent by the same surgeon. The operative technique was performed as describe by McKernan and Laws ***(16)***. After urinary catheterization, the first incision was start on the infraumbilical area, the anterior rectus sheath was cut slightly lateral away from midline, and the rectus muscle retracted laterally to create a plane between posterior aspect of rectus muscle and the peritoneum. Via a 12 –mm port, using blunt dissection with telescope, blunted-tip laparoscopic instruments and helping from CO_2 insufflation developed the preperitoneal space. The space was developed beyond the symphysis pubis and laterally to the anterior superior iliac spine. The space was maintained with CO_2 at a pressure of 10 mmHg. In addition two 5-mm working ports were placed in the midline below the umbilicus.

The direct hernia was reduced and indirect sac was dissected from the spermatic cord and either fully reduced or ligated and transected. A 15 x 12 to 15 x 15 cm knitted polypropylene mesh without a slit was placed in the preperitoneal space behind the posterior wall of the inguinal canal and secured to the Cooper's ligament medially with double tacks and superiorly two tacks using an endo- tacker (Endo Anchor®) instrument. Prior completion of the procedure, a small catheter was inserted through a 5-mm trocar and guided to the space beneath mesh using the grasping instrument. The study solution was then instilled into the preperitoneal space. The abdomen was deflated and all ports were removed. The surgical wounds were not infiltrated with local anesthetic.

Intervention

After completion of mesh placing and fixing, the 40 ml of normal saline (placebo) or 0.25% bupivacaine in unlabelled syringes (intervention) was put into the preperitoneal space via small catheter under viewing by telescope to ensure that the whole preperitoneal space was covered with solution. The nurse who opened the randomization envelope prepared the solution. The surgeon who operated was blinded to the solution, which was no labeled, clear, no color and no smell.

Outcome Measurement and Follow-up

The nurse who was blinded to the intervention assessed the pain and none of case was assessed by the operating surgeon. The pain was measured at fixed time interval 1, 2, 6, 12, and 24 hour after operation. If the post- operative pain intensity is up to the level of the patient requires the analgesic, morphine will be administered intravenously until the patient feels pain relief in the first 24 hours. After 24hours after operation, the patient will be prescribed an oral acetaminophen as require to relief pain. The patient will be discharged on the second day of post-operation.

Side Effect

The serious side effects of bupivacaine rarely occurs but the potential side effect, such as excessive shivering, confusion, seizure or cardiac arrhythmia, should be closely monitored ***(17)***. The minor side effects occur more often in bupivacaine group, such as urinary hesitancy, transient numbness of thigh, mostly recovered in 24 hours ***(7)***. We have protocol for monitoring and treatment for all of these complications

Data Collection

The eligible participants who visit the surgical clinic in 1 May 2007until 29 Feb 2008 will be recruited to the study. All the participants who meet the inclusion and exclusion criteria, read and agree with protocol (appendix II) and give informed consent (appendix III) will be randomly allocated into group A or B. The construct informed consent (appendix I) will be recorded. The research assistant will fill the baseline characteristic of patients.

On the day of operation, the assistant nurse will open the randomization number, which kept in the opaque envelope. The bupivacaine or normal saline will be prepared by nurse according to the randomization code and keep blind to the surgeon. The operative time will be recorded by the assistant nurse. After operation, the nurse who blind to the intervention will measure the pain intensity and immediate complication. And then the patients will be discharged from the hospital after 24 hours postoperation. The postoperative follow-up by the surgeon will be on 7 days after operation. The complication will be detected.

Data Analysis

Statistical data analysis was based on intention-to-treat principle. To compare VAS pain score between two groups, Mann-Whitney U test was applied. Regarding comparison of VRS pain score, a linear-by-linear test of association was used. For total morphine consumption (mg) and time to rescue analgesia (min), Mann-Whitney U test was performed to test the difference between two groups. Fisher's exact test was used to compare complications between two groups.

Ethical Consideration

The proposal will be submitted for approving by the ethic committee of Faculty of Medicine Ramathibodi Hospital, Mahidol University and Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University. The informed consent will be obtained from every the patients. The patients can refuse to participate in the study at any time during the study period without interference with the standard treatment. All of the data will be kept confidential and only use in the study. In case of any complication or adverse event, the investigator will take full responsibility until full recovery.

Limitation

The main limitation of visual analogue scales is the assumption that the pain is a uni-dimensional experience that can be measured with a single-item scale. The pain is measured in term of severity. The sensory qualities of the experience in pressure, discomfort, thermal and other properties that are not been measured. The pain experience is not be evaluated in all dimensions. In the different time of assessments, the patients may be responded to the severity of pain in different dimensions.

Expected Benefit and Application

1. The early postoperative pain is attenuated that will facilitate discharge as a day-case surgery.

2. To decrease the use of narcotic medications therefore the complications from will lower as well.

3. If the postoperative pain is less, the early postoperative ambulation will be obtained and the patients will have fewer complications.

Obstacles

1.The appropriated technique of instillation is not well setting. The preperitoneal instillation with a small catheter may not disperse the solution covering entire the space that may result ineffective reduction of pain. The more effective method could be an aerosolized technique that was describe by Alkhamesi NA ***(10)***. The instrument for aerosolizing is not available in our hospital.

2. The effective dose of bupivacaine is not well defined. If the dose is not enough, the difference between intervention and placebo will have not been found. If the dose is over, the patients will have toxicity. Until now, there was no study about the peritoneal absorption of bupivacaine to the blood steam and maximum tolerated dose that will affect the patients. The dose of bupivacaine using in this study is similar to the previous study ***(7)*** which possible obtained the effective pain reduction and no toxicity.

Administration and Time Schedule

The thesis planning was demonstrated in table 1.

Table 1 Time schedule is planned for conducting clinical trial.

	2007						2008		
	Jan-Feb	Mar-Apr	May-Jun	Jul-Aug	Sep-Oct	Nov-Dec	Jan-Feb	Mar-Apr	May-Jun
Project development	×								
Protocol approval		×							
Data collection			×	×	×	×	×		
Data analysis								×	
Thesis writing								×	
Thesis defense									×

Budget

1. Management fee, such as principle investigator, Co –investigator, nurse, is not included.

2. Patient related fee, such as, routine blood test, EKG, X-ray, operative charge is not included because it is the normal process of surgery except the charge for bupivacaine and normal saline.

Bupivacaine;

0.25% bupivacaine 20 ml = 150 baht, we need 2 vial/ patient, 20 patients

Total charge for bupivacaine = 150 x 2 x 20 = 6,000 baht

Normal saline (placebo);

Normal saline 50 ml = 14 baht, we need 1 bottle/ patient, 20 patients

Total charge for normal saline = 14x 1 x 20 = 280 baht

Total charge for bupivacaine + normal saline = 6,000 + 280 = 6,280 baht

3. Other fee:

Material preparation fee	5,000 baht,
Copy fee	3,000 baht,
Telephone /mail fee	2000 baht

4. Total 6,280+10,000 = 16,280 baht

CHAPTER IV

RESULTS

Participant Flow and Recruitment

A total of 40 eligible patients who visited the surgical clinic of Ramathibodi hospital in 1 May 2007 until 29 February 2008 ASA status 3-4 and 40 participant gave informed consent and agreed with protocol. They were randomly allocated into bupivacaine or normal saline instillation (figure 2). There was no loss follow-up.

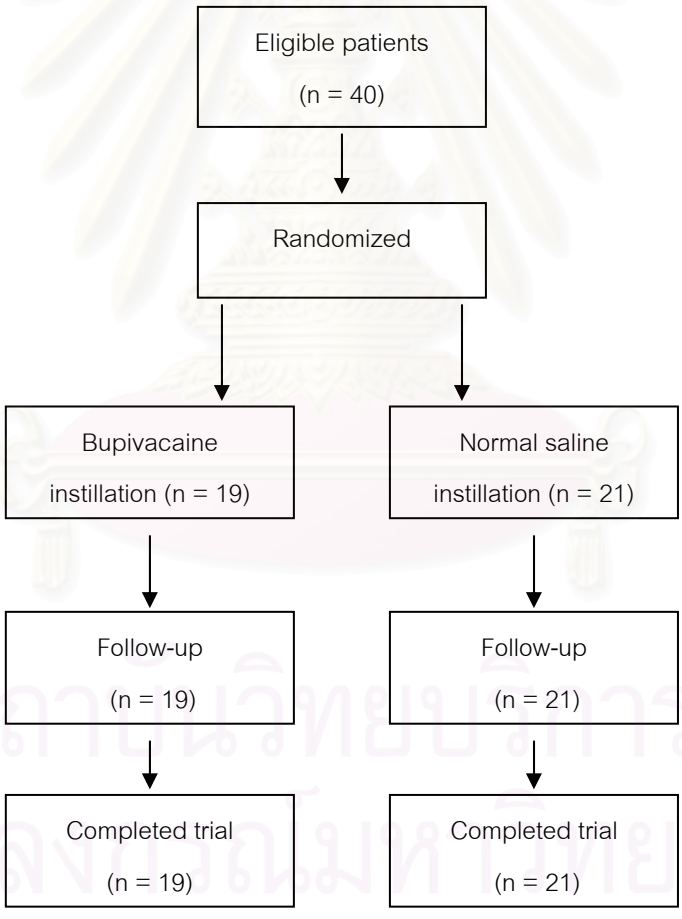

Figure 2 Flow chart of the randomized controlled trial of bupivacaine compare to placebo instillation into preperitoneal space after laparoscopic herniorrhaphy

Baseline Characteristic of Patients

The baseline characteristic of the patients group is shown in table 2. The distribution of the variables i.e. age, sex, ASA physical status and laterality in between groups were similar except the mean operative time and percentage of recurrent hernia after prior operation in normal saline group are higher than those in bupivacaine group.

Table 2 Baseline characteristics of the patients randomized to bupivacaine or normal saline instillation.

	Mean ± SD (Min,Max)	
	Bupivacaine (n=19)	Normal saline (n=21)
Age (years)	66.9 ± 9.3 (46,84)	59.8 ±14.3 (30,88)
Sex (M: F)	18:1	17:4
ASA physical status		
I	6 (31.6)	10 (47.6)
II	13 (68.4)	11 (52.4)
Laterality		
Unilateral repair	17 (89.5)	18 (85.7)
Bilateral repair	2 (10.5)	3(14.3)
Recurrent hernia after prior repair	1(5.3)	4(19)
Operative time (min)	45.5 ±16.0 (20,80)	61.2 ±21.3 (30,95)

Outcomes

Postoperative pain was measured by using both visual analogue scale and verbal rating scale after 1,2,6,12 and 24 hour postoperatively table 3 and 4. Postoperative pain in 1 hour of bupivacaine group seemed to be lower than that of placebo with borderline P-value (0.059 and 0.062,for VAS and VRS pain score respectively). Postoperative pain in the remaining time period of bupivacaine group was not significantly different from those of normal saline group (P>0.05). The total morphine consumption and the time to rescue analgesia were not significantly different between two groups (P>0.05).

The complications developed in 4 patients (2 seroma, 1 urinary retention and 1 arrhythmia) in bupivacaine group and 7 patients (5 seroma, 1 urinary retention and 1 ileus) in placebo group. One of patient with seroma of bupivacaine group completely resolves after one aspiration as well as two seroma in the placebo group. The remainders of patients with seroma spontaneous recover in 4-6 weeks. The single urinary catheterization was performed in both of patients with urinary retention. The arrhythmic episode developed in the patient with well-controlled valvular heart disease and was controlled with medication few days after operation. Small bowel ileus developed in one of the patient of placebo group and fully recovered in next few days with a conservative therapy. There was no recurrence of hernia in both groups.

Table 3 Postoperative outcomes of patients randomized to bupivacaine or normal saline solution groups.

* Mann-Whitney U test

θ Fisher' s exact test

Outcomes	Mean ±SD (min, max)		P-value
	Bupivacaine (n=19)	Normal saline solution (n=21)	
VAS Pain score			
1 hour	3.5 ± 2.5 (0,8)	5.2 ± 2.5 (0,10)	0.059*
2 hour	2.9 ± 2.4 (0,8)	4.5 ± 3.0 (0,10)	0.117*
6 hour	2.1 ± 2.7 (0,10)	3.2 ± 2.5 (0,8)	0.101*
12 hour	1.5 ± 1.9 (0,5)	2.7 ± 2.7 (0,10)	0.145*
24 hour	1.6 ±1.9 (0,5)	2.0 ± 2.6 (0,9)	0.672*
Total morphine consumption (mg)	0.63 ± 1.26 (0,3)	1.38 ± 2.13 (0,6)	0.294*
Time to rescue analgesia (min)	28.4 ± 73.1 (0,300)	52.4 ± 87.7 (0,240)	0.357*
Number of complication (%)	4 (21.1)	7 (33.3)	0.488θ

Table 4 Postoperative verbal rating score of patients randomized to bupivacaine or normal saline solution groups.

Linear-by-linear association test

	Number (%)		P-value#
	Bupivacaine (n=19)	Normal saline solution (n=21)	
VRS: 1 hour			
No	5 (26.3)	1 (4.8)	0.062
Mild	7 (36.8)	7 (33.3)	
Moderate	5 (26.3)	9 (42.9)	
Severe	2 (10.5)	4 (19.0)	
VRS: 2 hour			
No	4 (21.1)	3 (14.3)	0.145
Mild	8 (42.1)	7 (33.3)	
Moderate	7 (36.8)	7 (33.3)	
Severe	0	4 (19.0)	
VRS: 6 hour			
No	8 (42.1)	4 (19.0)	0.100
Mild	8 (42.1)	9 (42.9)	
Moderate	2 (10.5)	7 (33.3)	
Severe	1 (5.3)	1 (4.8)	
VRS: 12 hour			
No	10 (52.6)	8 (38.1)	0.203
Mild	7 (36.8)	8 (38.1)	
Moderate	2 (10.5)	4 (19.0)	
Severe	0	1 (4.8)	
VRS: 24 hour			
No	10 (52.6)	10 (47.6)	0.468
Mild	7 (36.8)	7 (33.3)	
Moderate	2 (10.5)	3 (14.3)	
Severe	0	1 (4.8)	

CHAPTER V

DISCUSSION, CONCLUSION AND RECOMENDATION

Discussion

The purpose of this study was to determine the effectiveness of bupivacaine instillation into preperitoneal space for reducing postoperative pain after totally extraperitoneal laparoscopic herniorrhaphy and we found that the postoperative pain intensity, which was measured with visual analogue scale and verbal rating scale were not significant difference when it was compared with placebo. The mean VAS in 1 hour, the bupivacaine trended to have lower score than placebo (3.5 and 5.2,respectively) but the P-value was in borderline range (P=0.059). Similarly, VRS of the bupivacaine group in 1 hour is lower than the placebo with borderline P-value (P=0.062). We aim to measure the total morphine consumption as indirect measurement of pain intensity. We found that there was no difference of total milligram of morphine between the bupivacaine and the placebo group (0.63 and 1.38, P=0.294). There were some limitations for interpreting the total morphine consumption. Some participants had high pain score but they did not require morphine and vice versa some had low pain score but they called for pain relief.

The characteristic of participants of both group were comparable except the mean operative time. We found that the mean operative time of placebo group was longer than intervention group (61.2 min. and 45.5 min.) that should be cause by the placebo group had more patients with recurrent hernia. Did the mean operative time correlate with the postoperative pain score? From the univariate analysis, the mean operative time did not correlate to postoperative pain score (table 5). That was the higher postoperative pain intensity was not cause by a longer of mean the operative time.

Table 5 Spearman rank correlation between operative time and visual analogue pain score.

	Bupivacaine	Normal saline
VAS: 1 hour	0.114 (P=0.641)	0.153 (P=0.508)
2 hour	-0.015 (P=0.950)	-0.133 (P=0.565)
6 hour	0.046 (P=0.852)	-0.029 (P=0.900)
12 hour	-0.272 (P=0.259)	-0.039 (P=0.867)
24 hour	-0.182 (P=0.457)	0.124 (P=0.592)

Our results were similar to the study by Saff GN, et al ***(13)*** that recruited 42 patients randomized in into two groups, 21 patients received 60 ml of 0.125%bupivacaine into preperitoneal space and other 21 patients received 60 ml of normal saline. All of the patients routinely received intravenous ketorolac 45 mg and fentanyl was given as much as the patients were feeling comfortable (VAS<4) before the pain score would be recorded. The study concluded that bupivacaine has no effect to attenuate postoperative pain. The major considerable factor in this study is the pain medication given as much as patient needed that will interfere the intensity of pain interpretation. As same as, Deans GT, et al ***(14)*** studied one hundred patients undergoing transabdominal preperitoneal laparoscopic hernia repair (TAPP) were allocated randomly to receive 1) bupivacaine 1.5 mg/kg (n=25) 2) bupivacaine 1.5mg/kg with 1:200,000 adrenaline (n=25) 3) bupivacaine 3 mg/kg(n=24) 4) saline (n=26). They concluded that the bupivacaine has no effect on postoperative relief at 4, 8, 12 and 24 hour after operation. The procedure of the hernia repair is different from our study that cannot be applicable to our study.

The results were different from Bar-Dayan, et al ***(12)***. The 44 patients were randomized in to two groups. The average visual analogue scale were significantly attenuated in group of bupivacaine compare to group of normal saline at 1, 2 and 4 hour after surgery. Furthermore, the analgesic intake was significantly decreased. The limitation of the study is that the investigators did not control a uniform anesthesia protocol defining the anesthetic and narcotic medications during surgery. O'Riordian DS, et al ***(7)***, 56 patients with unilateral hernia were randomized into bupivacaine or

normal saline instillation and blindly assessed on discharge (4-6 hours after operation) from the hospital, at 24 hours, 1 week, and 1 month postoperatively. The patients treated with bupivacaine had lower median visual analogue pain score on discharge 1.5 vs. 3.7 (p=0.03), more frequently pain free, recover faster, stopping analgesia earlier and returning to full activity earlier, and. The researcher did not mention about the amount of morphine, which prescribed to the patients as require after procedure. The morphine should effect the pain intensity.

The complications in bupivacaine and placebo group were not different (4 and 7 patients, p=0.488). The seroma is the common complication after laparoscopic herniorrhaphy with incidence of 14-30%***(18,19).*** We found 2 (10.5%) seroma in bupivacaine group and 5 (23.8%) seroma in placebo group. Mostly of the seroma spontaneously absorbed. The cardiac arrhythmia was developed in one participant in bupivacaine group. The arrhythmia is the one of the systemic side effect of bupivacaine. In this study, it did not related to bupivacaine because the patient had underlining valvular heart disease and arrhythmia developed before bupivacaine instillation.

In our study, the factors possible weaken the research protocol were controlled such as pre- and intraoperative analgesia protocol, postoperative morphine, ensuring that entire preperitoneal space was profuse with drugs via catheter and extent of tissue dissection is not much difference in both groups because the procedures were performed by the same surgeon. The postoperative pain after laparoscopic herniorrhaphy mainly originated from blunt and sharp tissue dissection in preperitoneal space, ligation of hernia sac and mesh fixing. Thus, the small incisions related to port assess do not seem to be the major source of pain ***(8)***. The bupivacaine local instillation allows the direct contact with the dissected tissues when the space is collapsed on completion of the procedure might theoretically result in local pain relief activity and less systemic toxicity. However, our study did not demonstrate the benefit of bupivacaine.

The lack of benefit from bupivacaine instillation into preperitoneal space in our study are possible related to high vascularity and high blood flow of the preperitoneal space which enhance the local clearance the bupivacaine ***(20).*** The retention of carbon dioxide in the preperitoneal space is another factor, which reduces local pH, that possible stimulates vasodilatation mechanism resulting in increase the drug clearance

(21) and low pH environment is also attenuate pharmacologic effect of bupivacaine*(20).* The bupivacaine has vasodilatation effect *(21)*, which may increase drug absorption. The alkalinization or epinephrine may enhance effect and prolong duration of pain reduction. The limitation of the study was the post-hoc power for detecting the difference was only 57.4%.

Conclusion

There is no strong evidence to confirm that bupivacaine instillation into preperitoneal space after laparoscopic herniorrhaphy can reduce postoperative pain.

Recommendation

Bupivacaine instillation into preperitoneal space is not recommended for reducing postoperative pain after total extraperitoneal laparoscopic herniorrhaphy. The future investigation for the effect of alkalinization and/or epinephrine adds to bupivacaine may enhance effect and prolong duration of pain reduction.

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APPENDICES

APPENDIX A

Patient ID number □ – □ □

Constructed Case Record Form

“การศึกษาเปรียบเทียบการใส่ยาบูพิวาเคน (Bupivacaine)
ในช่องหน้าต่อเยื่อบุผิวช่องท้อง
(preperitoneal space) เพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนด้วยการส่องกล้อง”

“A Randomized Controlled Trial of Preperitoneal Bupivacaine Instillation for Reducing Pain following Laparoscopic Inguinal Herniorrhaphy”

ผู้วิจัยหลัก: ผศ.นพ. รณรัฐ สุวิกะปกรณ์กุล ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี

งานวิจัยนี้เป็นส่วนหนึ่งของวิทยานิพนธ์ หลักสูตรวิทยาศาสตร์มหาบัณฑิต สาขาวิชาการพัฒนาสุขภาพ
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย พ.ศ. 2549-2550

Patient ID number □ — □ □

Entry Procedure and Criteria For Enrollment

Inclusion criteria	**yes**	**no**
1) The patient has any type of an inguinal hernia (direct, indirect, femoral, recurrent and combined-hernia)		
2) Unilateral or bilateral hernia		
3) Reducible hernia		
4) ASA I and II		

Exclusion criteria	**yes**	**no**
1) Inguinal hernia with complications i.e. incarceration, strangulation, obstruction, gangrene and perforation of hernia content		
2) The patient has a history of operation in Retzious' space.		
3) The patient has severe cardiovascular and/or pulmonary disease who could not tolerate the gas insufflation i.e. chronic obstructive pulmonary disease, congestive heart failure.		
4) ASA status III or IV		
5) Bleeding disorder		
6) Alcohol or drug abuse		
7) Intolerance or adverse reaction to medications (especially bupivacaine, morphine) uses in this study		
8) Patient who cannot comprehend the instruction and have perceptual -motor system problem.		

Patient ID number ☐ ☐ ☐

Date of enrollment at OPD

Baseline characteristics

Age [age]

Sex [sex] 1) M 2) F

Province [pro]

1. ☐ Bangkok include Nontaburi, Samutprakarn, Patumtani
2. ☐ Central 3. ☐ East 4. ☐ West 5. ☐ North 6. ☐ Northeast 7. ☐ South

Laterality [Lat]

1. ☐ **Unilateral**
2. ☐ bilateral

Recurrence [recur]

1. ☐ no recurrence
2. ☐ recurrence

ASA status [ASA]

1. ☐ I
2. ☐ II

Patient ID number □ – □ □

Date of Operation

Operative time [optime]

Start □□ : □□

End □□ : □□

Summary □□ : □□

Intervention [inter] 1. □ **A** 2. □ **B**

Pain score at: **VAS (mm)** **VRS** (no pain, mild, mod, severe)

1hour[VAS1], [VRS1]

2 hour [VAS2], [VRS2]

4 hour [VAS4], [VRS4]

6 hour [VAS6], [VRS6]

12 hour [VAS12], [VRS12]

24 hour [VAS24], [VRS24]

Total morphine consumption [mor]

Time to rescue analgesia [Time_R] □□ : □□

Complication [Com]

0. □ No

1. □ Yes……..

APPENDIX B

เอกสารชี้แจงข้อมูล / คำแนะนำแก่ผู้เข้าร่วมการวิจัย

(Patient/Participant Information Sheet)

การศึกษาเปรียบเทียบการใส่ยาบูพิวาเคน (Bupivacaine) ในช่องหน้าต่อเยื่อบุผิวช่องท้อง (preperitoneal space) เพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนด้วยการส่องกล้อง

ท่านเป็นผู้ได้รับเชิญจากแพทย์ให้เข้าร่วมการศึกษาวิจัยเพื่อประเมินผลการใช้ยาชาบูพิวาเคนเพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนด้วยการส่องกล้องก่อนที่ท่านจะตกลงเข้าร่วมการศึกษาครั้งนี้ ขอเรียนชี้แจงเหตุผลและรายละเอียดในการศึกษาวิจัยครั้งนี้

วิธีการรักษาไส้เลื่อนที่ดีที่สุดในปัจจุบันคือ **การผ่าตัด** การผ่าตัดไส้เลื่อนมีหลายวิธีขึ้นอยู่กับความเหมาะสม ของคนไข้แต่ละท่านการผ่าตัดไส้เลื่อนด้วยการส่องกล้องเป็นวิธีการหนึ่งที่ได้ผลการรักษาที่ดีเทียบเท่ากับการผ่าตัดแบบเปิด **แต่การผ่าตัดไส้เลื่อนด้วยการส่องกล้องมีแผลขนาดเล็กความเจ็บปวดหลังผ่าตัดน้อยกว่า ฟื้นตัวเร็วกว่า และ กลับไปทำงานได้เร็วกว่า**

อย่างไรก็ตามความเจ็บปวดหลังผ่าตัดใหม่ๆยังเกิดในการการผ่าตัดไส้เลื่อนด้วยการส่องกล้องทำให้ผู้ป่วยรู้สึกไม่สบายหลังการผ่าตัดได้ ทางผู้วิจัยกำลังทำการศึกษาวิธีการลดความเจ็บปวดหลังผ่าตัดด้วยวิธีการต่างๆ **การใช้ยาชาบูพิวาเคน** ใส่ลงในบริเวณที่ผ่าตัดเป็นวิธีหนึ่งที่คาดว่าจะได้ผลดี ซึ่งปัจจุบันเรายังไม่ทราบว่าการใช้ยาชาบูพิวาเคนจะได้ผลดีหรือไม่ การที่จะได้คำตอบจะต้องทำการศึกษาวิจัยในครั้งนี้ ผู้ร่วมวิจัยจะเป็นส่วนหนึ่งของการสร้างองค์ความรู้ใหม่แก่วงการแพทย์และอาจจะได้รับประโยชน์ในแง่ของการลดปวดจากการวิจัยนี้

อนึ่งยาบูพิวาเคนเป็นยาชาเฉพาะที่ที่นิยมใช้กันมาหลายสิบปีไม่ใช่ยาใหม่ เพียงแต่ดัดแปลงวิธีให้ยาเท่านั้น โดยที่ยามีผลข้างเคียงน้อยมากซึ่งผลข้างเคียงที่อาจจะเกิดขึ้นได้แก่ สั่น ปัสสาวะลำบาก และต้นขาชา ผลข้างเคียงเหล่านี้สามารถหายได้เองภายใน 24 ชั่วโมง ซึ่งจะได้รับการเฝ้าระวังอย่างใกล้ชิดและแก้ไขอย่างทันท่วงทีถ้ามีผลแทรกซ้อนเกิดขึ้น

การศึกษาครั้งนี้ผู้ป่วยที่เข้าหลักเกณฑ์และยินยอมเข้ารับการรักษาวิจัยจะถูกแบ่งเป็น 2 กลุ่มด้วยวิธีสุ่มอย่างเป็นระบบ ได้แก่

1. กลุ่มที่ได้รับยาชาบูพิวาเคนใส่ลงในบริเวณที่ผ่าตัด ในระหว่างการผ่าตัด
2. กลุ่มที่ได้รับยาหลอก (น้ำเกลือ)ใส่ลงในบริเวณที่ผ่าตัด ในระหว่างการผ่าตัด

หลังผ่าตัดผู้ป่วยจะถูกประเมินเรื่องระดับของความเจ็บปวดเป็นระยะ และผู้ป่วยสามารถขอยาแก้ปวดได้ตามปกติ ผลการศึกษาในครั้งนี้ใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น ข้อมูลที่เกี่ยวกับตัวท่านจะถูกเก็บเป็นความลับ การเผยแพร่ผลงานทางวิชาการจะ ไม่มีการระบุชื่อของผู้เข้าร่วมการศึกษาวิจัยและไม่สามารถเชื่อมโยงถึงผู้ป่วยได้

การศึกษาวิจัยในครั้งนี้ได้รับความเห็นชอบและการควบคุมดูแลจากกรรมการทางจริยธรรมทางการแพทย์ของคณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล และคณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย การวิจัยร่วมการศึกษาครั้งนี้เป็นไปด้วยความสมัครใจ ท่านสามารถปฏิเสธเข้าร่วมโครงการ หรือขอถอนตัวจากโครงการได้ตลอดเวลาเวลาโดยไม่กระทบต่อการดูแลรักษาบริการทางการแพทย์ หากมีผลแทรกซ้อนใดๆ ที่เกิดจากการศึกษานี้ ผู้วิจัยจะยุติการศึกษาและให้การดูแลแก้ไขปัญหาอย่างทันท่วงที

หากท่านมีปัญหาหรือข้อสงสัยใดๆ กรุณาติดต่อ ผศ.นพ. รณรัฐ สุวิกะปกรณ์กุล ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล โทร. 02-201-1527, 086-6101053 ตลอด 24 ชั่วโมง

ถ้าท่านมีปัญหาข้องใจหรือรู้สึกกังวลใจกับการเข้าร่วมในโครงการวิจัยนี้ ท่านสามารถติดต่อกับประธานกรรมการจริยธรรมการวิจัยในคน
สำนักงานวิจัยคณะฯ อาคารวิจัยและสวัสดิการ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี โทรศัพท์ 02-201-1544
หรือสำนักงานคณะกรรมการจริยธรรมการวิจัย คณะแพทยศาสตร์จุฬาลงกรณ์มหาวิทยาลัย โทรศัพท์ 02-256-4455 ต่อ 14,15

เอกสารประกอบ 5ก

APPENDIX III

หนังสือยินยอมโดยได้รับการบอกกล่าวและเต็มใจ

(Informed Consent Form)

ชื่อโครงการ **การศึกษาเปรียบเทียบการใส่ยาบูพิวาเคน (Bupivacaine) ในช่องหน้าต่อเยื่อบุผิวช่องท้อง (preperitoneal space) เพื่อลดความเจ็บปวดหลังการผ่าตัดไส้เลื่อนด้วยการส่องกล้อง**

ชื่อผู้วิจัย ผศ.นพ. รณรัฐ สุวิกะปกรณ์กุล

*ชื่อผู้เข้าร่วมการวิจัย .....

อายุ ..... ปี

คำยินยอมของผู้เข้าร่วมการวิจัย

ข้าพเจ้า นาย/นาง/นางสาว .....

ได้ทราบรายละเอียดของโครงการวิจัย ตลอดจนประโยชน์ และข้อเสี่ยงที่จะเกิดขึ้นต่อข้าพเจ้าจากผู้วิจัยแล้วอย่างชัดเจน ไม่มีสิ่งใดปิดบังซ่อนเร้นและยินยอมให้ทำการวิจัยในโครงการที่มีชื่อข้างต้น

และข้าพเจ้ารู้ว่าถ้ามีปัญหาหรือข้อสงสัยเกิดขึ้นข้าพเจ้าสามารถสอบถามผู้วิจัยได้

และข้าพเจ้าสามารถไม่เข้าร่วมโครงการวิจัยนี้เมื่อใดก็ได้ โดยไม่มีผลกระทบต่อการรักษาที่ข้าพเจ้าพึงได้รับ

นอกจากนี้ผู้วิจัยจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับและจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆที่เกี่ยวข้อง กระทำได้เฉพาะกรณีจำเป็นด้วยเหตุผลทางวิชาการเท่านั้น

ลงชื่อ ..... (ผู้เข้าร่วมการวิจัย)

..... (พยาน)

..... (พยาน)

วันที่ .....

คำอธิบายของแพทย์หรือผู้วิจัย

ข้าพเจ้าได้อธิบายรายละเอียดของโครงการ ตลอดจนประโยชน์ของการวิจัย รวมทั้งข้อเสี่ยงที่อาจจะเกิดขึ้นแก่ผู้เข้าร่วมการวิจัยทราบแล้วอย่างชัดเจนโดยไม่มีสิ่งใดปิดบังซ่อนเร้น

ลงชื่อ ..... (แพทย์หรือผู้วิจัย)

วันที่ .....

หมายเหตุ : กรณีผู้เข้าร่วมการวิจัยไม่สามารถอ่านหนังสือได้ ให้ผู้วิจัยอ่านข้อความในหนังสือยินยอมฯ นี้ให้แก่ผู้เข้าร่วมการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้เข้าร่วมการวิจัยลงนามหรือพิมพ์ลายนิ้วหัวแม่มือรับทราบในการให้ความยินยอมดังกล่าวข้างต้นไว้ด้วย

* ผู้เข้าร่วมการวิจัย หมายถึง ผู้ยินยอมตนให้ทำวิจัย

VITAE

Mr. Ronnarat Suvikapakornkul was born in 2 April 1973, Bangkok, Thailand. He graduated the Doctor of Medicine degree with second-class honor from Ramathibodi Hospital, Mahidol University in 1996, Diploma of clinical science (Surgery) in 2000 and Thai board of general surgery from Ramathibodi Hospital in 2002. He works as a lecturer in general surgery in Department of Surgery, Ramathibodi Hospital, Mahidol University from 2002 until present. He interests in breast surgery, endocrine surgery and minimally invasive surgery. The academic position is Assistant Professor of Surgery from 9 May 2006. The already published papers were;

Suvikapakornkul R, Kositchaiwat S, Lertsithichai P. Retrospective comparison of one-stage versus sequential ERCP and laparoscopic cholecystectomy in patients with symptomatic gallstones and suspected common bile duct stones. Thai J Surg 2005;26:17-21

Sitathanee C, Puataweepong P, Swangsilpa T, Narkwong L, Kongdan Y, **Suvikapakornkul R**. Acute effects of postmastectomy radiotherapy after immediate TRAM flap reconstruction in breast cancer patients. J Med Assoc Thai 2005; 88(12):1861-6.

Kositchiwat S, Suwanthamma W, **Suvikapakornkul R**, et al. Comparative study of two bowel preparation regimens for colonoscopy: Senna tablets vs. sodium phosphate solution. World J Gastroenterol 2006; 12(34): 5536-5539

In June 2006, he admitted into the Master's degree program in Health Development in Thai-CERT consortium, Faculty of Medicine, Chulalongkorn University, as funded by Faculty of Medicine Ramathibodi Hospital, Mahidol University. During the course, he had conducted the clinical trial "A Randomized Controlled Trial of Preperitoneal Bupivacaine Analgesia for Reducing Pain following Laparoscopic Inguinal Herniorrhaphy "