Comparison of an Ultrasound Guided Bilateral Transversus Abdominis Plane Block with Dexamethasone and Preperitoneal Instillation of Local Anesthetic with Dexamethasone to a Standard Anesthetic Technique for Analgesic Efficacy and Patient Satisfaction Following a Total Extraperitoneal Bilateral Inguinal Hernia Repair: A Prospective Randomized Single Blinded Study

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Version: 5, Dated: 7-14-14
**Background**

Total extraperitoneal (TEP) inguinal hernia repair is a surgical procedure that is typically performed on an outpatient basis. TEP hernia repair is a relatively recent technique which has been reported to have advantages over open hernia repair including minimal complications, excellent recovery, and a high degree of patient satisfaction (1).

Multimodal or “balanced” analgesic techniques involving the use of smaller doses of opioids in combination with non-opioid analgesic drugs are becoming increasingly popular approaches to preventing pain after surgery (2). Multimodal analgesia strategies have been recognized as a potential method to improve post-operative pain management while minimizing opioid related side effects (3). These side effects include ventilatory depression, drowsiness and sedation, postoperative nausea and vomiting, pruritus, urinary retention, ileus, and constipation, which can delay hospital discharge or lead to unanticipated hospital admissions (4). Improved analgesia without increased analgesic-related side effects is an important component of the anesthetic plan for outpatient surgical procedures. In addition, it has been suggested by the Joint Commission that excessive use of post-operative opioid analgesics leads to decreased patient satisfaction (2).

Local anesthetics have been reported to improve post-operative analgesia and patient satisfaction when used in a multimodal approach (5-7). Although there have been numerous reports on the use of preperitoneal instillation of local anesthetic following TEP hernia repair, the results are contradictory (8-13). One published study has reported on the analgesic benefits of transversus abdominis plane (TAP) blocks following TEP hernia repair (14), but its analgesic benefit appears to wane after 8 hours. While both methods are currently utilized for post-operative pain control for TEP hernia repair surgery at this institution, the two techniques utilizing only local anesthetics may have a limited use in terms of prolonged analgesic efficacy and patient satisfaction.

Human studies on the addition of dexamethasone to local anesthetics have been positive in terms of improving analgesic duration of various regional techniques (15-19). While concerns of increased infection rates or poor wound healing have been suggested with a single perioperative dose of steroids, published studies have not shown this to be true (20-22). Preliminary observations of the addition of dexamethasone in TAP blocks for various lower abdominal surgeries at this institution have been encouraging. Post anesthesia care unit (PACU) observations and follow-up interviews suggest improved analgesic duration of our regional technique, reduced post-operative opioid use, and improved patient satisfaction.

**Rational and Specific Aims**

Currently, both bilateral TAP blocks and preperitoneal instillation of local anesthetics with the addition of dexamethasone are utilized for post-operative pain control for TEP inguinal hernia repair at this institution. It is unknown if these methods are efficacious for post-operative pain control and patient satisfaction following a TEP bilateral hernia repair. From our previous observations in the PACU and follow-up interviews, we are hypothesizing that the bilateral TAP block and preperitoneal instillation of local anesthetics with the addition of dexamethasone are
superior in terms of patient satisfaction and post-operative pain control when compared to a standard anesthetic technique (no regional technique).

To test our hypothesis, a randomized prospective single blinded study of the addition of dexamethasone to an ultrasound guided bilateral TAP block and preperitoneal instillation of local anesthetic under direct visualization will be compared to a standard anesthetic technique (control) following a TEP bilateral hernia repair. We will conduct this study to establish if these methods are more efficacious for post-operative pain control and patient satisfaction following a TEP bilateral hernia repair when compared to a standard anesthetic technique. Once the results from this study have been determined, recommendations will be made on which technique(s) should be utilized for this procedure at this facility.

The primary objective of this study is to assess the efficacy of the addition of dexamethasone to the bilateral TAP block and preperitoneal instillation of local anesthetic to a standard anesthetic technique on the post-operative quality of recovery using the Quality of Recovery 40 (QoR-40) questionnaire (see attachment) for patients the day following a TEP bilateral hernia repair. The global QoR-40 score consists of 40 questions that examine 5 domains of patient recovery using a 5-point Likert scale: none of the time, some of the time, usually, most of the time, and all of the time (23). The 5 domains include physical comfort, pain, physical independence, psychological support, and emotional state (23). The responsiveness of this questionnaire has been assessed in patients evaluated before and after surgery (24).

Secondary objectives will be to compare the efficacy of the addition of dexamethasone to the TAP block and preperitoneal instillation of local anesthetic on post-operative opioid usage, pain scores, side effects, and time to discharge readiness.

**Inclusion/Exclusion Criteria**

Patients will be eligible for participation if they are 18–80 years of age, have an ASA physical status I–III, and are scheduled for outpatient TEP bilateral inguinal hernia repair.

Exclusion criteria include a patient’s refusal to participate, inability to give consent, drug allergies to any medications used in this study, pregnancy, bleeding diathesis, or conversion to an open procedure. In addition, any subject whose anatomy, or surgical procedure, in the opinion of the investigator, might preclude the potential successful performance of a TAP block.

**Enrollment/Study Duration**

Patients will be recruited on the day of surgery by the principle investigator, co-investigator or research nurse. After obtaining written informed consent, patients will be randomized to receive an ultrasound guided bilateral TAP block with a standard anesthetic technique, preperitoneal instillation of local anesthetic with a standard anesthetic technique, or standard anesthetic technique. Group allocation will be determined by the sealed envelope method after inclusion into the study. A random number generator will be used to randomize the three groups before being placed in sealed envelopes.
The proposed duration of the study is estimated to be approximately two years. In the previous calendar year (6/25/2012-6/24/2013), we have performed forty seven initial and six recurrent inguinal hernia repairs using the TEP method. (Note: this data will not be used in this study).

Study Procedures

Anesthetic management will be performed by a 1) staff anesthesiologist, 2) anesthesiology resident under the supervision of a staff anesthesiologist or 3) nurse anesthetist under the supervision of a staff anesthesiologist. In the operating room, standard ASA monitors will be placed on all patients. All patients will receive a standardized general anesthetic consisting of premedication with midazolam, 1-2 mg intravenous (IV) and induction with 1-2 mcg/kg fentanyl IV, and propofol 1-2 mg/kg IV. Succinylcholine 1-2 mg/kg IV will be used to facilitate tracheal intubation (rocuronium will be substituted if there are any contraindications to succinylcholine). The patient’s lungs will be ventilated with a 50:50 mixture of oxygen: nitrous oxide or 100% oxygen. Sevoflurane will be added to maintain anesthia perioperatively. Neuromuscular blockade for the surgery will be provided with cisatracurium (intermittent IV boluses) or rocuronium (intermittent IV boluses) to maintain suitable operating conditions. The patients will be given 25-50 mcg fentanyl IV bolus during the case if the anesthesiologist deems necessary. Neostigmine/glycopyrrolate (0.05mg/kg/0.001 mg/kg IV) will be used at the conclusion of the surgery to reverse the neuromuscular blockade. Ondansetron 4 mg IV will be administered for antiemetic prophylaxis prior to emergence from anesthesia. (The dosing of medications listed above are typical for routine standard anesthetics given at this institution. Medication doses may be modified or omitted at the discretion of the staff anesthesiologist secondary to the patient’s weight and medical status.) At the conclusion of the surgical procedure, all patients will have their laparoscopic port site infiltrated with approximately 10 ml of 0.25% bupivacaine.

After the completion of the surgical procedure prior to emergence from anesthesia, either an ultrasound guided bilateral TAP block or preperitoneal instillation of local anesthetic under direct visualization will be performed depending on the patient’s group allocation. The ultrasound guided TAP block will be performed by three different staff anesthesiologists (principle investigator and two co-investigators). The surgical procedure and preperitoneal instillation of local anesthetic under direct visualization will be performed by one staff surgeon (co-investigator). Using aseptic techniques, a bilateral TAP block will be performed under ultrasound guidance (25). Fifteen ml of 0.5% bupivacaine (diluted to a total volume of 30 ml with normal saline) and 4 mg of preservative-free dexamethasone will be injected for each side of the abdomen. A preperitoneal instillation of 30 ml of 0.5% bupivacaine and 8 mg of preservative free dexamethasone will be placed by the surgeon under direct visualization.

**Dosing rational of preservative free dexamethasone and bupivacaine:**
All patients receiving a bilateral TAP block or preperitoneal instillation of local anesthetics will receive 8 mg of preservative free dexamethasone and 175 mg bupivacaine (30 ml of 0.5% bupivacaine and 10 ml of 0.25% bupivacaine). Doses given are at or below the FDA recommended dosing guidelines (26, 27).
While not specifically approved by the FDA as an adjuvant for regional anesthesia, multiple clinical studies have supported the use of dexamethasone (8mg) as an adjuvant for regional anesthesia. Human studies on the addition of dexamethasone to local anesthetics have been positive in terms of improving analgesic duration of various regional techniques (15-19). While concerns of increased infection rates or poor wound healing have been suggested with a single perioperative dose of steroids, published studies have not shown this to be true (20-22).

The FDA suggests a single dose of 175 mg of bupivacaine which can be adjusted up or down depending on the patient’s medical history and location of the injection (27). In addition, the FDA recommends a limit of 400 mg bupivacaine a day (27). The current amount of bupivacaine usage proposed in this study is below this limit.

Upon arrival in the PACU, subjects will be asked to rate their pain at rest using a 0 to 10 numeric rating scale (NRS), where 0 means no pain and 10 is the worst pain imaginable. After the initial rating, pain ratings will be repeated at regular intervals during the remainder of the PACU stay. PACU nurses will be blinded to the patient’s group allocation. Postoperative pain will be treated with hydromorphone 0.2-0.4 mg IV every 5 minutes. Patients will be medicated to achieve a pain score less than or equal to 3/10, or until they report being “comfortable.” After 2mg of hydromorphone is given, patients will be assessed by a staff anesthesiologist to determine if hydromorphone is required. Since each patient will have different opioid requirement and respond differently to opioids secondary to their medical and previous opioid history, no maximum dose of hydromorphone is given. Our PACU nursing and anesthesia staff are expertly trained in delivering opioids and monitoring/treating complications from opioids if they arise (please see attached RL Roudebush VAMC Pain Management Policy). Additional anti-emetics will be given for post-operative nausea/vomiting (ondansetron 4mg IV, droperidol 0.625mg IV and/or haloperidol 1mg IV) anti-emetics will be available for post-operative nausea/vomiting. (Note: All patients will have their 5-lead EKG, blood pressure, oxygen saturation, respiratory rate, and temperature monitored for the entire duration of their PACU stay.) Discharge criteria will include adequate control of pain, nausea, and bleeding, as well as a patient’s ability to ambulate and void. Patients who cannot void will have their bladder emptied by catheterization. Pain after discharge will be managed with hydrocodone 5 mg plus acetaminophen 325 mg (1-2 tablets by mouth every 4-6 hrs. as needed).

Subjects will be contacted by telephone the following day after the procedure by an investigator or research nurse unaware of group allocation. At that time, questions regarding analgesic consumption and pain score will be asked. The QoR-40 questionnaire will also be administered at this time. Additional data collected will include subject’s age, sex, weight, height, ASA physical status, total amount of hydromorphone used in the PACU, pain scores in the PACU, nausea and vomiting in the PACU, and time spent in the PACU (time to discharge readiness).

Note: This is a quality control study. The anesthetic and surgical techniques described above are standard of care at this facility for this surgery. The randomization of the specific post-operative analgesic technique, performance of the specific post-operative analgesic technique, administration of the QoR-40 questionnaire, and phone call following the day after the procedure are unique for this study and will only be performed by research personnel.
Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

A review of patient charts will be performed every six months by Dr. Bryan Sakamoto. Any adverse events should be reported to the principle investigator, Dr. Bryan Sakamoto at (317) 988-2475. Any adverse event secondary to the experimental protocol will be reported to the VAMC and IRB.

Study Withdrawal/Discontinuation

Participants may withdraw from the study at any time.

Statistical Consideration

Based on the assumption of an overall standard deviation of 12 (5), a sample size of 23 subjects per group was estimated to achieve 80% power in detecting a 10-point difference in the aggregated QoR-40 score between the 2 study groups and control. A 10-point difference represents a clinically relevant improvement in quality of recovery based on previously reported values on the mean and range of the QoR-40 score in patients after anesthesia and surgery (23). To account for dropouts, 75 subjects will be randomized.

The global QoR-40 scores will be reported as medians. The 25th and 75th percentiles will be included to show the spread of the global QoR-40 score distributions. Dimensions of the QoR-40 questionnaire will be reported as median, 95% confidence interval, and analyzed using Mann-Whitney U-test. Continuous variables will be reported as mean ± SD and analyzed using Student’s t-test. Categorical data will be compared using $\chi^2$ test, $\chi^2$ test with Fisher’s exact correction, or Wilcoxon’s test. Pain scores will be reported as medians. The 25th and 75th percentiles will be included to show the spread of the pain score distributions. Differences in pain scores will be tested using the nonparametric Mann-Whitney U-test (independent samples). Differences between pain scores at discharge and the day after discharge will be tested by using the Wilcoxon matched-pairs signed-ranks tests (dependent samples). ANOVA will be performed to compare the 3 groups. Statistical inference will be evaluated at the 5% level of significance with Bonferroni’s correction for multiple comparisons.

Privacy/Confidentiality

All patient data which contains any identifiers will be secured on the VA research server. Any data which contains any patient identifiers will never leave the VAMC. Only data that is de-identified will be entered on a password secured VAMC computer. The biostatistician will only have access to de-identified data. Any other patient information will be properly destroyed. Only the principle investigator, co-investigators, and research nurse will have access to any identifiable data during the study.

Follow-up and Record Retention
The study begins once the participant agrees to be enrolled and ends the following day after a phone call to the patient to collect the study data. Participants will be followed up roughly four weeks after their procedure to ensure there were no surgical complications (not part of the study).

Patient data related to the study will be passed on to the principle or co-investigators. Upon completion of the study, any data will be retained by the investigator for as long as the applicable regulations at the VAMC requires and after the study is closed by the IRB. Once regulatory requirements are fulfilled, all copies of the data collected will be properly destroyed.

REFERENCES:

13. Abbas MH, Hamade A, Choudhry MN, Hamza N, Nadeem R, Ammori BJ. Infiltration of wounds and extraperitoneal space with local anesthetic in patients undergoing...


26. Dexamethasone Sodium Phosphate Injection, USP. Drug Packaging Information. APP Pharmaceuticals, LLC., Schaumburg, IL, USA.

27. Bupivacaine Hydrochloride Injection, USP. Drug Packaging Information. Hospira Inc., Lake Forest, IL, USA.