Evaluation of a TAP Block Given During Laparoscopic Colorectal Surgery to Help Control Pain

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RESEARCH PLAN

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Title: Evaluation of a TAP block as part of an enhanced recovery pathway in laparoscopic colorectal surgery: A prospective, randomized, double-blinded multi-institution trial

Introduction/Background

A substantial component of pain experienced by patients after abdominal surgery arises from the abdominal wall incision (1, 2) even in laparoscopic surgery. Reducing post-operative pain -besides its obvious improvement in patient comfort- has been shown to decrease the physiological response to stress (3), reduce morbidity (4), and in the case of colorectal surgery, offer a potential improvement in outcome (5). Several modalities of postoperative analgesia are in place to reduce postoperative pain. The use of local anesthesia has been advocated to improve postoperative pain and reduce the need for opioid use thereby reducing potential side effects of their use; however their role in colorectal surgery is unclear (6).

A retrospective cohort analysis of local anesthetic during laparoscopic colorectal surgeries was recently completed by our institution. Findings suggested that the use of local anesthetic by traditional application techniques, either subcutaneous or subcutaneous combined with intra-peritoneal did not significantly decrease postoperative pain scores and opioid requirements or impact the duration of time spent in the PACU or total days spent in the hospital (6). The retrospective nature of this study precludes definitive conclusions and randomized studies are needed to determine whether different methodology of local anesthetic administration might show clinical improvement that would support its use in colorectal surgery.

A promising modality of pain management is to directly block the sensory nerves of the anterior abdominal wall thereby reducing pain from abdominal incisions. The transversus abdominis plane (TAP) block was first described in 2001 by Rafi et al and is a potentially valuable tool in pain management for patients undergoing abdominal surgery (7) which aims to block the sensory nerves of the anterior abdominal wall before they pierce the musculature to innervate the abdomen, thereby alleviating that pain. A TAP block places a large volume of local anesthetic into the fascial plane between the internal oblique and the transversus abdominis which contains the nerves from T7 to L1 to directly block those sensory nerves.

To date, randomized, double-blinded clinical trials with TAP blocks have focused on open abdominal surgery (1,8) and gynecological surgery (9,10,11,12) and most have been from a single group of authors. Results have been mainly positive, with all but one trial (12) showing improved postoperative pain, and reduced opioid consumption.

The only published study using TAP block for laparoscopic colorectal surgery by Conaghan et al collected data from patients undergoing laparoscopic colorectal resections. They compared analgesia usage and outcome data for patients who had a TAP block and a PCA (patient controlled analgesia) pump, with those who had a PCA alone. Their 74 patient study found a significant reduction in overall intravenous opiate use in the TAP/PCA group compared to the PCA group. They also noted a

slight trend towards a shorter hospital stay but there was no difference in postoperative complication or any other outcome measure (13).
A recent review by Peterson et al noted important shortfalls in the literature regarding TAP blocks. They stressed that the results from primary published studies, which have been mostly from a single group of authors, need to be confirmed in future studies. They also pointed out that the studies to data have been small, therefore potentially masking both positive and negative results (14).

Significance and Purpose

Tap blocks are a simple analgesic technique which might significantly benefit patients undergoing laparoscopic colorectal surgery. There is inadequate data in the literature to make this decision. Although studies to date have generally been positive, there is still a paucity of data regarding TAP blocks and only one comparative series for laparoscopic colectomy (LC).
This study will be a large, multi-center, randomized prospective trial for TAP block, evaluating postoperative pain, PONV, hospital stay and other surgical outcomes.

Study Population and Design

The study design will be a multi-center, double-blinded, prospective, randomized controlled trial comparing Marcaine (bupivacaine) with normal saline in a transversus abdominis plain block in adult patients who have undergone elective laparoscopic colorectal surgery.
The purpose of this study will be to prove the effectiveness of local anesthetic given via a TAP block in improving postoperative pain, postoperative opioid use, PONV and surgical outcomes such as hospital length of stay in laparoscopic colorectal surgery when compared to controls.
The study will randomize adult patients with benign and malignant conditions of the colon and rectum that require elective laparoscopic right, total, and left colectomy into two groups. Subjects meeting the inclusion criteria will be informed about the trial, and requested to participate after the informed consent process.

Recruitment

The patients will be recruited from the Departments of Colorectal Surgery of University Hospitals of Cleveland OH as well as approximately 3 to 6 other institutions across the United States. The patient population in this study will be candidates of either sex, over 18 who have benign or malignant colonic or rectal disease in which resection is required via a laparoscopic approach. The patients will be asked to participate in the study after evaluation by either the PI or the co-investigators and candidacy for either procedure has been established. The investigator will discuss the study with the patient and the study coordinator will participate in patient recruitment. Patients will be recruited until at least 75 participants are enrolled from all institutions, with up to 75 patients enrolled from UHCMC if other institutions do not participate.
Inclusion criteria:
1. Subjects who have benign or malignant colonic or rectal disease that are being scheduled for laparoscopic colorectal resection.
2. Subjects who are 18 years of age and older
3. Subjects of either sex
4. Subjects who are willing and able to adhere to protocol requirements, agree to participate in the study program and provide written and informed consent.

Exclusion criteria:
1. Subjects who undergo conversion to the open approach will be excluded from the analysis, as the block will be given at the end of the procedure and is being evaluated for laparoscopic cases.
2. Subjects who are pregnant.

3. Subjects with a medical condition that may interfere with the use of the study medication Bupivicaine.
4. Subjects who have another condition or general disability or infirmity that in the opinion of the investigator precludes further participation in the study.

Study Procedures
Informed consent will be obtained at the time of enrollment into the study. Enrollment will take place during the preoperative visit with the surgeon in the out patient area or in the pre-surgical area on the day of surgery. The patient will undergo routine preoperative assessment, including: surgical informed consent, collection of demographic information, medical/surgical history, physical exam, and routine laboratory testing. All patients will undergo perioperative care using a standardized enhanced recovery pathway, outlined in the enhanced recovery pathway perioperative guidelines for complete care.
Randomization
Randomization will take place in the operating room. A numbered, sealed envelope, corresponding to the patients' assigned study number, will be opened, and the study nurse will provide Marcaine (bupivacaine) or placebo for the OR nurse to prepare. Patient and surgeon will not know which group the patient is randomized to.
Intraoperative
Using standard surgical procedures, the surgeon will proceed with the planned laparoscopic surgery. All procedures will be done by straight laparoscopic technique according to standard of care. At the completion of the procedure, and under laparoscopic control, patients will have a TAP block placed by the attending surgeon. The clinical research nurse involved in the research will prep the solution to be injected and the surgeon will be blinded as to whether the patient will be receiving normal saline or Marcaine in the TAP blocks. The block will be administered between the costal margin and iliac crest in the anterior axillary line. A Braun Stimuplex A insulated needle (80 mm 21 gauge) with 0.5 mL/kg solution (max of 30 ml) is passed through the skin, and then continued until two distinct "pops" are felt, which indicates the needle piercing each of the two fascial layers. The needle is then deemed to be in the inter-muscular plane between internal oblique and transversus abdominis muscles respectively, to target the spinal nerves in this plane. The laparoscope will be visualizing for the needle tip to ensure that it does not penetrate the peritoneum or inject pre-peritoneally. The local anesthetic is infiltrated in two separate injections into the same plane on each side. If a sub-peritoneal bleb is seen to be raised by the laparoscope, then the needle will be withdrawn slightly. Two thirds of the solution is injected, and the needle is withdrawn 5 mm and the remaining solution is injected. If injecting in the correct plane, then a smooth raised area of fluid, covered by transversus will be seen via the laparoscope. This procedure is repeated on the patients other side, to complete a bilateral block. Refer to the attached TAP block Procedure.doc file for a visual aid to the TAP block procedure. Depending on their randomization, patients will receive one of the following solutions:
Group A: Represents the control group and will receive 0.5 ml/kg of 0.9% normal saline for a maximum of 30 ml.
Group B: Represents the experimental group and will receive 0.5 ml/kg of 0.25% Marcaine (bupivacaine) for a maximum of 30 ml.
Enhanced Recovery Pathway
All patients will be managed via standardized accelerated postoperative recovery guidelines which are currently in use by the division of colorectal surgery at UHCMC. This includes early overnight patient-controlled analgesia pump, oral analgesia and diet on the first postoperative day, early postoperative ambulation, and defined discharge criteria. The complete guidelines can be viewed at our Guidelines.doc file included.

All Study Patients

The medical/surgical information below will be collected as part of this research study and is all information already available as part of the patients medical chart.

-Patient Demographics (age, gender, BMI, ASA score)
-name of surgeon
-name of procedure
-Estimated blood loss
-Opiate use in PACU (morphine equivalents)
-Time spent in PACU
-daily use of analgesics (PCA and oral) in morphine equivalents
-daily Pain scores while in hospital (maximum and average)
-daily post-operative nausea/vomiting scores
-daily use of antiemetics
-opiate use at discharge, and whether opioids are used at home
-Length of stay in hospital
-day of return of bowel function (flatus and stool)
-Post operative complications, including ileus (defined as reduction in diet and placement of a nasogastric tube)
-30 day readmission rates

Study Completion

Completion of participation in the study will be 30 days after their date of surgery. Any readmission up to 30 days post-operatively to the hospital as a direct result of their surgery will be followed. The patients will follow-up with the surgeon in the office in approximately 6 weeks which is considered standard of care for all patients undergoing colorectal surgery and is not considered part of the research study.

Patient Withdrawal

Patients can withdraw from the study at any time. Any subject who wishes to withdraw from this study on his/her own accord and for whatever reason is entitled to do so without obligation and prejudice to further treatment. In addition, the investigator may decide for reasons of medical or surgical prudence to withdraw a subject. In either event, the investigator will clearly document the date and reason for the subject's withdrawal from this investigation in the medical chart.

Risks/discomforts

The potential risks of this study are those caused by the injection itself and those caused by the medication bupivicaine. Risks of the TAP block injection itself include infection (at injection site and peritoneal), bleeding, transient nerve injury. The risks of the use of bupivicaine include intravascular injection which may cause neurological or cardiovascular complications (confusion, seizure, hypotension, and cardiovascular collapse), local anesthetic toxicity and allergic reaction. Risks of intraperitoneal injection or organ injury will be minimized by laparoscopically-assisted visualization of the needle. Risks of intravascular injection of bupivacaine will be minimized by withdrawal of the syringe to ensure it is not site intravascular prior to injecting. The full details of the risks associated with surgical procedure are explained in the surgical consent form and will be reviewed and discussed with the patient.

Benefits

Because of the nature of this research, there may or may not be any benefits. The study may benefit future patients based on our findings. It is possible that the patients randomized to Group B (Marcaine group) may benefit from decreased length of stay, decreased post-operative nausea/vomiting, less post-operative pain and earlier recovery of gastrointestinal function.

Financial Compensation and Costs

There are no extra costs for the patient associated with the research. Since the surgical procedure is standard of care, any costs related to the surgery will be the responsibility of the patient and his/her insurance company.

Alternative(s) to participation

Patients may also choose not to participate in this study without affecting their surgical treatment. They will receive post-operative analgesia for pain control according to standard of care and the colorectal surgery enhanced recovery pathway guidelines sheet, which may include a TAP block as per the individual surgeon's practice and discussion with the patient. The only other alternative to participation in the study is not to participate.

Plan for obtaining informed consent

For each subject, written informed consent will be obtained prior to any protocol-related activities. As part of this procedure, the principal investigator, a co-investigator, or study coordinator must explain orally the nature, duration, and purpose of the study in such a manner that the subject is aware of the potential risks, inconveniences, or adverse effects that may occur. All the above are members of the research team and are knowledgeable with regards to the TAP block procedure and the medication bupivicaine, and their risks/benefits. In addition, all members of the research team are Human Subjects certified. They will be informed that the subject may withdraw from the study at any time.

After a potential study patient is identified, a member of the research team will be responsible for instituting the informed consent process in a face-to-face manner. Before starting any study procedures, the investigator will discuss the proposed research study in detail with the potential subject during the office visit or pre-surgery visit on the day of surgery to discuss treatment options. The subject will be allowed ample time to read, review and ask questions. The informed consent document will be reviewed with the subject in depth by the participating investigator to ensure the potential participant has a good understanding of the study, what is required from them, risks, benefits and their rights as a participant. The investigators are available by phone or in the office to answer any questions the participant may have. If the consenting process takes place in the office the subject may return for another visit with the investigator to discuss the study, ask questions and sign the document to participate in this study.

After the subject has read and reviewed the informed consent document and has agreed to participate, he/she will be asked to sign and date the document. The person obtaining consent will also sign and date the form, and documentation of the informed consent process will be included in the research file (i.e., the person who obtained consent, where and when consent was obtained, and who was present during the process). A copy of the consent form will be given to the subject.

In those instances where potential participants cannot read the consent form because they do not speak English, every effort will be made to give an informed consent document written in a language understandable to them which will be submitted, reviewed and approved by the IRB before implementation. The IRB will be provided with all appropriate information such as qualifications of the individual translating the document. A qualified translator will present the consent to the participant. The consent form will be signed and dated by the translator and the participant.

In addition, in the unusual situation where a subject cannot read a consent form (illiterate, blind) we will follow the appropriate steps indicated by the IRB such as submitting a document summarizing the consent or reading the consent form to the subject. There will be a witness to the oral presentation who will also sign and date the consent form as well as the summary if indicated.

Provisions for subjects from vulnerable populations

There are no vulnerable populations to be studied.

Data Safety Monitoring Plan

This study will be monitored to ensure the identification, documentation and analysis of all adverse events, compliance with the protocol, and compliance with the terms of the participating Institutional Review Boards (IRB) to protect the safety and rights of all patients, and federal and local regulations. As a transversus abdominis plane block is standard therapy after other procedures, and is extremely safe, no adverse events are expected due to the block. Nevertheless, all complications and adverse events during the pre-operative, intra-operative, and post operative periods will be monitored and recorded for analysis by principal investigator and the research team. Data safety will be evaluated after each 25% patient accrual.

Subject privacy and data confidentiality

Subject charts and clinical records will be requested and reviewed so that protocol adherence and source documentation can be verified. Information collected from the medical file will be entered into a study spreadsheet to collect data on each subject. The data collection spreadsheet will be kept password protected on Shared Drive in the Department of Surgery in which the principal investigator and the study coordinator have access. Initials will only be used along with surgery date. A separate spreadsheet will be kept of the subject's date of surgery and patient number will be kept on the study coordinator's hard drive in which only she has the password. All data collection forms will be kept under lock and key in the Department of Surgery. Only members of the research team will have access to the documents. The information will only be disclosed with the subject's permission or as required by law. Upon publication, no subjects will be identified and all information will be reported conclusively. There is a possibility that the University Hospitals of Cleveland Institutional Review Board, Food and Drug Administration and possibly foreign regulatory agencies may review the study records.

Data analysis/statistics

Routine statistical analyses will be utilized for parametric and non-parametric datasets, as appropriate. Demographic data will be analyzed using students t-test or Fishers exact test as appropriate. Repeated measurements (pain, nausea scores) will be analyzed by repeated measures ANOVA or ANOVA on ranks. Further paired comparisons at each time interval will be analyzed using the t-test of Mann-Whitney U-test as appropriate. Categorical data will be analyzed using X_2 analysis or Fishers exact test where applicable. Normally distributed data will be presented as means +/-SD of the mean, non-normally distributed data will be presented as medians +/- quartiles and categorical data will be presented as raw data and frequencies. A P value of > 0.05 will be considered statistically significant.

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