Laparoscopic TAP Block for Sleeve Gastrectomy: Does Timing Matter

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Document: Protocol + statistical analysis

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HENRY FORD HEALTH SYSTEM IRB PROTOCOL FORMAT

Appendix 1

(Incomplete applications will be returned, & inadequate responses may lead to a delay in review.) You may mark your responses in the shaded areas following each question. Supporting documents (articles, drug toxicity information, etc.) must be submitted when applicable. A "See Attached" response will not be accepted for review. Be concise & clear.

Directions:

Sponsored protocol: If you have a sponsored protocol (e.g., pharmaceutical), a grant application (e.g., National Institutes of Health), or another peer-reviewed protocol, you may submit that protocol/application along with the application elements. It is the responsibility of the Principal Investigator to assure, however, that the protocol/application contains the information requested in this "IRB Protocol Format". Additional sheets should be attached to the protocol/application as necessary to provide the information (e.g., a description of the process of consent) required for IRB review. When available, the Investigator's Brochure must be submitted along with the research protocol, or a summary of the preclinical/animal data and any relevant clinical data.

Physician Initiated protocol: If you have not been provided a protocol from an outside source, you must develop one. The following is the "Henry Ford Health System "IRB Protocol Format".

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1. **PURPOSE:** State in one or two sentences the purpose or objective of this project. **The purpose of this study is to investigate whether an early intraoperative transverse abdominus plane block (TAP block) will provide superior analgesia to a late intraoperative TAP block in laparoscopic sleeve gastrectomy patients.**

2. **SPECIFIC AIMS:** Number your aims so that the aims can be referred to in the Project Design and Data Analysis sections of this outline. **Our aims are to establish a statistifically significant correlation between timing of administration of TAP block and**
3. **Narcotic use post-operatively**
4. **Early post-operative numerical pain score (NAS) @ immediately post-op, 4, 8, 12, 16, 20, and 24 hours to be performed by nursing aids taking vital signs**
5. **Length of stay (in hours)**

3. **RATIONALE FOR THE PROJECT:**
   a. State the rationale for the project and support it with background information about the project. Critically evaluate existing knowledge, and specifically identify the gaps in knowledge the project will fill. **Transverse abdominus plane (TAP) block has been proven to be an effective tool in reducing pain after laparoscopic sleeve gastrectomy. A meta-analysis was performed utilizing 10 studies primarily looking at the efficacy of TAP block in laparoscopic surgery. There was a clear benefit of TAP block for post-operative pain control. One of the findings of their study in comparing trials where TAP was administered pre-operatively vs post-operatively suggested that pre-operative administration provided superior analgesia; however to our knowledge, no prospective study has ever been done investigating the timing of administration. With this in mind, we would like to investigate whether an early intraoperative TAP block will provide superior analgesia to a late intraoperative TAP block.**
   b. State the applicant's prior research and experience in this research area. **The PI of this study has no prior research regarding TAP blocks; however he has routinely been performing TAP blocks intra-operatively on his sleeve gastrectomy patients for several years.**

4. **SIGNIFICANCE:** State concisely the importance of this project by relating the purpose to broader, long-range objectives. **We would like to determine if early vs late intraoperative TAP block is provides superior analgesia as to make it the standard block for bariatric patients undergoing sleeve gastrectomy.**

5. **SUBJECTS IN THE PROJECT:**
   a. State the inclusion and exclusion criteria for enrollment of subjects.**Inclusion criteria: Patients between the ages of 18 and 65 undergoing laparoscopic sleeve gastrectomy at Henry Ford Macomb Hospital. Exclusion: Conversion to open procedure, prior history of narcotic use (which will be defined as any narcotics used on a recreational basis or any narcotic used for pain relief without having had recent operation or injury), current narcotic use at time of surgery, and prolonged case time defined as >1 SD over average time. Currently, the primary investigator has a %<1 conversion rate of**

laparoscopic to open sleeve gastrectomies in the last 10 years. The anticipated conversion rate is <1% given this data.

b. Describe the control population (if utilized) and justify its selection.**No control**

c. Support the likelihood of recruiting the number of subjects required to complete the project. Relate this to other projects recruiting similar subjects. **Approximately 200 patients will be asked to participate in this study. This is based on the PI's case load for the alotted clinical trial time period. We anticipate that the majority of patients will agree to participate given the relatively low risk of participation compared to current practice.**

6. **PROJECT DESIGN AND PROTOCOL:**

a. Describe the experimental design/methodology.**This is a single blinded, prospective study designed to determine optimal timing of TAP block in laparoscopic gastric sleeve patients. Research has shown that administration of TAP block during these cases does show improved post-operative pain control. There are no trials specifically evaluating the timing of administration in regards to superiority of pain control. To our knowledge, no prospective study has ever been done investigating whether TAP block performed at the beginning of the case versus at the end of the case makes a difference in the amount of relief experienced by the patient. We hypothesize that early intra-operative block will be superior to late intra-operative block in both post-operative pain as well as decreased LOS in hospital secondary to reduction in peripheral and central nervous system hyper excitability. Before beginning the research study, ~200 plain envelopes will be made each containing one option written on paper indicating early intra-operative or late intra-operative TAP block. There will be equal numbers of both options. Office staff in the bariatric clinic independent of the research project will select at random an envelope marked either early-intraoperative or late-intraoperative TAP block. It will be the responsibility of either the PI or sub-investigators to collect selected envelope from the office and bring it to the operating room at the time of surgery. All patients involved in the study will have given informed consent in the office prior to surgery. On the day of surgery after the patient is induced and intubated, the PI or sub-investigator will open the envelope revealing the timing of the TAP block. Depending on what is revealed from the envelope, the patient will either receive the early intra-operative TAP block or the late intra-operative TAP block. The TAP block will be performed using 60 ml for right sided TAP block (side of specimen extraction) and 30 ml for left sided TAP block (non extraction side). 30 ml of bupivicaine solution will also be used for intraperitoneal irrigation as is already routinely done during these cases by the primary surgeon for additional analgesia. This will be performed at the conclusion of all cases regardless of which arm the patient is in. For the early intra-operative TAP block, optiview trocar entrance will be performed in the upper abdomen followed by CO2 insufflation. After introduction of the camera into this trocar, the right lateral abdominal wall will be visualized with the laparoscope. An 18-gauge needle will be introduced externally at the center of the mid axillary line between the lower costal margin and the iliac crest until the surgeon feels a "pop," after which the surgeon will inject the first 2 mL of 0.25% bupivicaine to verify the correct position. Doyle's internal bulge sign (the bulge seen when the transversus abdominis muscle and peritoneum is pushed internally) will be visualized and the remainder of the 60 mL of 0.25% bupivacaine will be injected. The contralateral block will be performed according to the same technique but with only 30 ml of bupivicaine. The late post-operative block will be performed in the same fashion but after completion of the surgery just prior to removing the trocars and desufflation. The intraperitoneal irrigation with 0.25% bupiviaine solution will be performed at the end of the case using 30 ml total sprayed above the stomach, under the diaphragm, and over the bed of the spleen. All other medications intra-op and post-op including anesthesia will remain standardized according to the current HF Macomb bariatrics protocols. Our primary endpoint will be narcotic use. Per the standard bariatric protocol at Henry Ford Macomb Hospital, narcotic pain medications are only given if the pain score is 7 or higher and the pt's pain is unable to be controlled with non-narcotic pain medication. On POD #0, pt's receive IV acetaminophen 1000 mg IV q6h x24 hours as well as pregabalin 75 mg PO one time. If their pain is unable to be controlled and their pain score is 7 or higher, they will be given oxycodone immediate release 5 mg PO q4h. On POD #0, there will be an additional PRN order for hydromorphone 0.5 mg IV q4h PRN only if pain is persistently 7 or greater after receiving all other pain medications including oxycodone. On POD #1, the hydromorphone PRN order is discontinued. The patient receives celecoxib 200 mg PO daily, acetaminophen liquid 960 mg PO q8h ATC, and pregabalin 75 mg PO BID for non-narcotic pain control. There will continue to be a PRN order for oxycodone immediate release 5 mg PO q4h for pain 7 or greater unable to be controlled with non-narctoic medication. Typically, these patients are discharged home on POD #1. They are sent with 5-10 tablets of oxycodone 5 mg for breakthrough**

pain ONLY if it was used during the hospital stay. We will be analyzing the total amount of hydromorphone and oxycodone in mg used during the hospital stay as it compares to whether they received their TAP block early intra-op vs late intra-op. We will also be analyzing post-operative pain scores as secondary endpoints. This data collection will take place immediately post-op, 4, 8, 12, 16, 20, and 24 hours post-op using the numerical assessment score (NAS) for pain which will be performed at the time vitals are taken by the nursing aids. As the pt's We will also be analyzing length of stay in hours as an additional secondary endpoint.

b. Outline the protocol, corresponding it to the specific aims; identify the data or endpoints to be analyzed to reach the specific aims.**We will randomly give early or late intra-operative TAP blocks to our laparoscopic sleeve gastrectomy patients. All other aspects of the anesthesia and post operative analgesia protocols will remain the same. Our primary endpoint will be post-operative narcotic use. Our secondary outcomes include length of stay in hours and post-operative self reported pain scores. We will quantify results in terms of subjective pain scoring using NAS performed by nursing.**

c. Discuss potential limitations and difficulties in the protocol.**Potential limitations of this protocol include using a subjective matter (numerical assessment score) to measure our patient's pain level. Another limitation/difficulty involves relying on nursing staff to collect our data vs. collecting the data ourselves.**

d. Provide a tentative schedule for conducting and completing this project and, if applicable, the multicenter study.**We would like to have all of the data collected and analyzed in a 12 month time period. Acceptance of manuscript can take up to 24 months if multiple submissions or revisions are requested by prospective journals/bodies.**

e. Data collection: Submit a copy of the data collection tool or list the data fields to be collected (review IRB policy, *Access to Medical Records for Research* on intranet at http://henry.hfhs.org).**Data will be collected by the surgical team and clinical trial personnel. All collected data will be recorded on paper sheets and kept in the patients' individual charts, and on electronic files. Paper copies of patient data will be kept in a locked file and only accessible by the trial investigators and staff. All electronic files will be kept in password protected folders on USB drives and personal computers. At the end of the study, all paper files will be shredded. All electronic files will be permanently removed from all computers and USB devices. Refer to 6b of the protocol for variables. Excel spreadsheets and visual analogue scale for pain (VAS score) will be used for data analysis/collection.**

7. **DATA ANALYSIS:** Describe the analysis of the data and relate this to the specific aims. Describe the statistical analysis in detail (referral to analysis by a multicenter sponsor is not acceptable). The Committee recommends free consultation with the Division of Biostatistics and Research Epidemiology. **The primary anaslysis will be to compare the total amount of hydromorphone and oxycodone between the two groups. We will use a Student's t-test for this comparison. If the data is not normally distributed we will use a two-sample Wilcoxon test.**

The secondary endpoint, pain score, will be analyzed using an analysis of variance for repeated measures (ANOVA). The design will have a between factor, group (early or late), and a single within factor, time (0,4,8,12,16,20 and 24 hours). The analysis will test for each factor and their two-way interaction. We believe all patients should start on post-op care approximately at the same time so that the time of day should not be a factor. In this analysis, we anticipate that the interaction term will not be signicant. If this is not that case a Student's t-test will be used to compare the groups at each time point that the test of group effect looks to see if the groups are the same difference apart at each time point so that no one time point is the primary endpoint.

8. **JUSTIFICATION FOR NUMBER OF SUBJECTS OR DATA:**

a. State the number of subjects or data points to be analyzed in the project at this institution and the total number for multicenter studies. The Committee recommends consultation with the Division of Biostatistics and Research Epidemiology. **Approximately 200**

b. *Describe the statistical justification for this number of subjects or data points.*

We propose to enroll a total of 200 individuals randomly put into two groups of 100 each. The test for differences in drug use will have 80% power to detect an effect size, with a two-sided 0.05 alpha level, or 0.40. This is considered a small to medium effect size and should be sufficient for the study

For the ANOVA analysis with a non-significant interaction term the test will have 80% power, with a two-sided 0.05 alpha level and an anticipated standard deviation of pain scores of 1.8, to detect a difference