Does a ketamine Infusion decrease post-operative narcotic consumption after gastric bypass surgery?

NCT03001843

Most recent approval: 2/22/2017

UNIVERSITY OF FLORIDA ACADEMIC HEALTH CENTER

Does a ketamine Infusion decrease post-operative narcotic consumption after gastric bypass surgery?

Investigators: David Smyth CRNA PI, Joshua Sappenfield MD , and Jeffrey Friedman MD

Abstract: Among the negative side effects of narcotics is respiratory depression. The risks of respiratory depression are exacerbated when coupled with pre-existing sleep apnea. The obese patient population is predisposed to sleep apnea and are a growing population, increasingly presenting for gastric bypass surgery as a means to lose the excess weight. One drug which can decrease the need for narcotics while still delivering good pain relief is ketamine. It is our hypothesis that an intra operative infusion of ketamine will decrease the amount of post-operative narcotics required for adequate pain relief and thereby the patients will be exposed to fewer narcotic side effects.

Background: According to the Centers for Disease Control (CDC), approximately one third of American adults, about 78.6 million, are obese. Obesity contributes greatly to healthcare costs in this country accounting for $147 billion in 2008, according to the most recent data available from the CDC.[1] The health risks associated with obesity cited by the CDC include, but are not limited to coronary heart disease, high blood pressure, type 2 diabetes, cancers, stroke, liver and gall bladder disease, sleep apnea, and osteoarthritis [1].

Several treatments for obesity exist with varied efficacy and long term success rates. With caloric reduction as the initial treatment it was found that after 6 months there is a reduction in initial body weight of about 8%; however beyond 4-5 years the amount of weight loss drops off to 4% .[2] In contrast Gastric Bypass Surgery has shown "that patients lose about 2/3 to 3/4 of their excess weight over the first two years. Longer term studies have shown that on average patients keep off at least 1/2 of the excess over 5 to 15 years." [3]

Obesity is an epidemic in America and surgical interventions have been shown to provide greater and longer lasting weight loss compared to conservative measures such as caloric restriction. Among surgical interventions, gastric bypass has shown better maintenance of weight loss than vertical banded gastroplasty .[4] It is therefore probable that anesthesia providers will be seeing an increasing number of obese patients presenting for gastric bypass in the coming years. The tremendous healthcare costs related to obesity as well as the high success rate of gastric bypass "a loss of 50% of excess weight as long as 14 years postoperatively"[4] make this an important issue for anesthesia providers. Managing this group of patients with their co-morbidities presents its own unique challenges and one of those challenges is effective post-operative pain control while maintaining adequate ventilation as this group is highly prone to sleep apnea even before undergoing an anesthetic and administration of narcotics.

The dangers of sleep apnea in this group should not be taken lightly. In a closed claims analysis from 1990 through 2009 it was found that there were 92 cases probably or definitely related to post-operative narcotic related respiratory depression and in 77% of those cases, the patient suffered death or severe brain damage. The review article found that the typical patient who would suffer an adverse

event due to narcotic related respiratory depression was “an obese adult patient with severe OSA receiving opioids postoperatively without continuous electronic monitoring, oxygen supplementation or CPAP” and obese adult patients are the population receiving laparoscopic gastric bypass. In the American Society of Anesthesiologists Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea, the ASA and its consultants make the statement that “the potential for respiratory compromise should be considered in selecting intraoperative medications”. The ASA also makes the desirability of opiod reduction in this population clear by stating they “strongly agree that to reduce opioid requirements, nonsteroidal anti-inflammatory agents and other modalities (e.g., ice, transcutaneous electrical nerve stimulation) should be considered if appropriate”.

One medication that shows promise in the management of this group is ketamine. Ketamine is a dissociative anesthetic with well documented analgesic properties. The primary aspect of interest is that ketamine delivers pain relief which lasts beyond its expected effective time; it was found that preemptive administration of ketamine and administration of an infusion throughout abdominal surgery resulted in a decrease narcotic requirements when compared to the group who received a bolus of ketamine at abdominal closure; even though both groups had similar pain scores the infusion group had a lower narcotic requirement for two days after surgery.[7] The next property of interest ketamine possesses is the fact that administration of ketamine has been shown to have a narcotic sparing effect.[7,9,10] Another property of interest for the obese population is that ketamine maintains functional residual capacity (FRC) and increases the rib cage’s contribution to tidal breathing[8] making respiratory depression less of a concern with ketamine than with narcotic pain medication immediately after the surgery, which can be important in a population (obese patients) already predisposed to sleep apnea.

A study performed by Fu compared pre-incisional ketamine along with an infusion to a single dose given post incision closure. After the surgery, pain scales and amount of narcotic used by each group were compared and an infusion of ketamine was found to decrease narcotic requirements more than a single bolus of ketamine.[7] The proposed study compares a pre-incision bolus and intra-op infusion of ketamine to the standard practice of narcotic bolusing in gastric bypass surgery. Additionally this study will compare the total amount of narcotic used as well as average pain relief scores between the two groups. Therefore, the purpose of this research project is to determine if an intraoperative infusion of ketamine during bariatric surgery decreases narcotic requirements in the first 48 hours post operation.

Specific Aims: This study will attempt to determine if it is possible to reduce the post-operative opioid requirements for patients undergoing laparoscopic gastric bypass surgery while still providing acceptable levels of pain relief by utilizing an intra-operative infusion of ketamine. This study will compare two groups of patients presenting for gastric bypass surgery. The two groups will be randomized to a control group who will receive a standard, narcotic based pain relief anesthetic and the study group which will receive an intra operative ketamine infusion. After the surgery the patients’ narcotic use and pain scores will be followed for 48 hours to determine if the intra operative ketamine infusion is effective at decreasing post-operative narcotic requirements.

Research Plan: The study will be a head to head experiment with one group receiving narcotic medication during the surgery and the other group receiving a ketamine infusion. Both groups will receive 2 mg of versed on the way from pre op holding to the operating room, which is standard practice.

We plan to enroll at least 48 patients in this study, with 10 additional patients in case patients are removed from the study for any reason. This number was arrived at by a power analysis performed by Terry Vasilopoulos last year and it was estimated that to see a 30% reduction in narcotic use we would need two groups of 24, emphasizing that this would be a pilot study. The study by Fu utilized two groups of twenty participants each and fount that "cumulative morphine consumption on D1 and D2 was reduced by approximately 40%".[7] The surgeon, Dr Friedman, performs between three and five laparoscopic gastric bypasses per week so this number of patients should be able to be enrolled in a reasonable amount of time.

The ketamine group will receive 100 mcg of fentanyl at induction of anesthesia and then no further narcotics during the surgery. During induction the patient will receive a 20 mg bolus of ketamine, a dose of propofol deemed appropriate by the anesthesia team to render the patient unconscious and a dose of neuromuscular blocking medication followed by an intraoperative infusion of ketamine at 5 mcg/kg/min beginning after induction, and ending at the beginning of wound closure.

The narcotic group will receive no ketamine but rather a more standard anesthetic consisting of 100 mcg of fentanyl, a dose of propofol deemed appropriate by the anesthesia team to render the patient unconscious and a dose of neuromuscular blocking medication for induction. Intraoperatively only the narcotic group will be given intraoperative boluses of fentanyl and 0.3 mg of hydromorphone approximately 45 minutes prior to the end of surgery.

Both groups will receive 1 gram of Ofirmev (acetaminophen) infused over 15 minutes starting when wound closure begins. They will also both receive neuromuscular blockade reversal medication and a dose of Zofran at the end of the surgery. These medications are routine for this surgery. Anesthesia providers will be allowed to provide other non-analgesic medications to the patient which is consistent with their usual practice.

The amount of narcotics a patient receives is part of the medical record. Beginning in the PACU amount of narcotics needed to control the patient's pain (converted to morphine equivalent units) and pain scores (a hospital standard measure) will be collected for 48 hours for the study , or until discharge, whichever occurs sooner. The conversion to a morphine equivalent unit is to allow us to compare different narcotics the patient may receive in a more standardized way. The results will be analyzed and compared between the two groups.

Patients will be eligible for inclusion in this study if they are between 18 and 65 years old presenting for laparoscopic gastric bypass surgery at Shands Hospital.

Patients would be excluded if they are below 18 or older than 65 or have hypersensitivity, allergy, or contraindications to fentanyl, propofol, hydromorphone or ketamine; the medications which could be administered in this study. Patients with cardiovascular disease who cannot tolerate the sympathomimetic effects of ketmine and ASA 4 patients will be excluded from this study.

Participants for this study will be recruited by Dr Friedman in his surgical clinic. If they are going to require gastric bypass surgery they will be informed of the study and asked to participate. The patients will be randomized into the two treatment groups utilizing a computer generated block randomization to get groups of equal size in each treatment. There will be 9 blocks of 6 and 1 block of 4 in order to evenly divide the 58 patients.

Patients PHI will be accessed by the study staff in collecting the data and clinicians in providing care to the patients. The only data which will be recorded will be pain scores and narcotic usage during the 48 hours after surgery. Consent for participation in the study will be scanned into the patient's record. Hard copies of the data will be saved in a locked drawer in Dr. Sappenfield's lock office until converted into a digital format, consistent with the department's protocol. The data will be analyzed with the help of the anesthesia departments statistical consultant.

Possible Discomforts and Risks: The patients will be undergoing gastric bypass surgery which, by its nature, is painful. They will be given FDA approved medications, consistent with their labeling, during the operation to minimize that pain. Post operatively the patients will be given whatever medications they need to control their pain. The largest potential side effects of ketamine is vivid dreams which may be unpleasant, this side effect should be blunted or avoided by the pre-operative administration of versed. As ketamine is a standard anesthetic drug, in the event of a temporary state of confusion or agitation related to ketamine the PACU would do as they do with any patient who has this reaction to ketamine and dim the lights and draw the curtains, allowing the patient to remain calmer as they wake from anesthesia. If the emergence is too distressing an additional dose of versed may be administered to blunt the reaction.

Possible Benefits: The patients could experience satisfactory pain relief while using less narcotics a goal recommended by the ASA. In receiving less narcotics the patients should have a lower incidence of negative side effects of narcotics including respiratory depression. The benefit to future patients will be if we are able to show that we can both decrease use of post-operative narcotics while maintaining satisfactory pain relief we can utilize this as a standard anesthetic regimen and avoid some of the negative and dangerous side effects of narcotics.

Conflict of Interest: Neither I nor the study team have any conflicts of interest involved in this study.

Bibliography:

1. Cdc.gov. Adult Obesity Facts | Data | Adult | Obesity | DNPAO | CDC. 2015. Available at: http://www.cdc.gov/obesity/data/adult.html. Accessed June 25, 2015.

2. Kopelman P. Obesity Reviews - Volume 8, Issue Supplement s1 - March 2007 - Wiley Online Library. Onlinelibrarywileycom. 2007. Available at: http://onlinelibrary.wiley.com/doi/10.1111/obr.2007.8.issue-s1/issuetoc. Accessed June 14, 2015.

3. Callery C. Gastric Bypass Expectations | Gastric Bypass | Weight Loss Surgery. Thinnertimescom. 2015. Available at: http://www.thinnertimes.com/weight-loss-surgery/gastric-bypass/gastric-bypass-expectations.html. Accessed June 25, 2015.

4. Fabricatore A, Wadden T. Treatment of Obesity: An Overview. Clinical Diabetes. 2003;21(2):67-72. doi:10.2337/diaclin.21.2.67.

5. March 3, 2015 Factors Related to Postoperative Respiratory Depression. (n.d.). Retrieved June 2, 2016, from http://www.patientsafetysolutions.com/docs/March_3_2015_Factors_Related_to_Postoperative_Respiratory_Depression.htm

6. (2014). Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep

7. Fu E, Miguel R, Scharf J. Preemptive Ketamine Decreases Postoperative Narcotic Requirements in Patients Undergoing Abdominal Surgery. Anesthesia & Analgesia. 1997;84(5):1086-1090. doi:10.1213/00000539-199705000-00024.

8. Mankikian B, Cantineau J, Sartene R, Clergue F, Viars P. Ventilatory Pattern and Chest Wall Mechanics during Ketamine Anesthesia in Humans. Anesthesiology. 1986;65(5):492-499. doi:10.1097/00000542-198611000-00007.

9. Lofsky A. Sleep Apnea and Narcotic Postoperative Pain. Apsforg. 2002. Available at: http://www.apsf.org/newsletters/html/2002/summer/04sleepapnea.htm. Accessed June 1, 2015.

10. Schmid R, Sandler A, Katz J. Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. Pain. 1999;82(2):111-125. doi:10.1016/s0304-3959(99)00044-5.