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Original article

Combined preemptive and preventive analgesia in morbidly obese patients undergoing open gastric bypass: a pilot study

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Abstract

Purpose: It is difficult to balance adequate pain control against the risk of sedation and depressed breathing in severely obese patients. This study assesses the effects of combined preemptive and preventive analgesia on narcotic use after open gastric bypass.

Methods: Twenty patients were randomized in this prospective double-blind trial comparing preoperative 30 mg intravenous ketorolac (Toradol), 0.25% subcutaneous bupivacaine (Marcaine) with epinephrine along the planned incision, and 0.25% bupivacaine in the rectus fascia before closing with identical injections with 0.9% saline. The patients' self-assessed pain on a visual analogue scale (VAS) and total narcotic use by patient-controlled analgesia (PCA) and rescue medication were recorded.

Results: Age, body mass index (BMI), incision length, and operative times were similar between the two groups, as was the average length of hospital stay (2.9 days). Self-reported pain was less in the treatment group 1 hour postoperatively ($P = .01$). Narcotic use was less in the treatment group during the first 2 hospital days (51% less on day 1 vs 44.5% less on day 2). Total narcotic use during the hospital stay was reduced by 40% ($P = .02$).

Conclusions: Patients receiving combined preemptive and preventive analgesia used significantly less narcotic pain medication than the patients receiving placebo. The effect lasted beyond the duration of action of the local anesthetic.

Keywords: Preemptive analgesia; Preventive analgesia; Gastric bypass; Pain management; Narcotic usage

Severe obesity is a risk factor for numerous cardiopulmonary complications associated with general endotracheal anesthesia [1,2]. Postoperative sedation with immobilization and hypoventilation from narcotic analgesics contributes significantly to these complications. Preemptive and preventive analgesia regimens have been demonstrated to reduce postoperative narcotic use in several studies [3,4]. Remarkably, however, such regimens have not been reported in obese patients, who would be expected to benefit the most from reduced postoperative narcotic use. Consequently, we designed a prospective randomized double-blind study of combined preemptive and preventive analgesia in severely obese patients undergoing open gastric bypass surgery.

Definitions of preemptive and preventive analgesia vary greatly in the medical literature [5–9]. Since the perioperative period can be divided into three distinct phases: preoperative, intraoperative, and postoperative, some authors narrowly define "preemptive" analgesia as pertaining to the preoperative phase and "preventive" analgesia to the intraoperative phase. We use a slightly broader definition, maintaining two key elements universally qualifying as preemptive analgesia: administration of a pharmacologic agent before the perception of pain,

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and an effect lasting beyond the time when the agent is clinically active [10,11].

Materials and methods

Patients

Twenty morbidly obese patients (16 women and 4 men), with a mean age of 42 years (range, 24–61 years), and mean body mass index (BMI) of 51 kg/m^2 (range, 40.3–74.5 kg/m^2) were scheduled for open gastric bypass by a single surgeon (J.K.) at a university hospital during January and February 2003.

Patients with known aspirin or nonsteroidal anti-inflammatory drug (NSAID) allergies were excluded, as were patients with active reactive airway disease, significant alcohol consumption, or a smoking history within the preceding 3 months. Other comorbid conditions were not considered criteria for exclusion for this study and thus were not recorded. No patient had a history of previous bariatric surgery. As part of the preoperative protocol, all patients underwent training with a physical therapist on the proper use of incentive spirometry.

All patients gave written consent. The protocol was approved by the Institutional Review Board of the University Hospital, University of Medicine and Dentistry of New Jersey, Newark, New Jersey.

Anesthesia

Preoperative assessment included verification of normal baseline "room air" resting arterial blood gas (ABG) analysis and carboxy hemoglobin level. Each patient received unit doses of 2 mg of midazolam (Versed) intravenously (IV) and 150–250 μ of fentanyl IV during preoxygenation, followed by 300–400 mg of propofol (Diprivan) and 50 mg of lidocaine IV. A "test breath" was performed and a "mask airway" was established in all patients, before 1 mg/kg IV of succinylcholine was administered. General anesthesia was maintained with desflurane 7–9 volume % and oxygen. Further muscle relaxation was facilitated with cis-atracurium. Reversal was achieved with 5 mg neostigmine and 1 mg glycopyrollate IV. Patients received a total maximum amount of 250 μg of fentanyl, including the amount given during induction. No morphine was used intraoperatively.

All patients received 8 mg of ondansetron (Zofran) IV, to prevent postoperative nausea and vomiting, and were transported with oxygen to the postanesthesia care unit (PACU). While in the PACU, all patients were started on identical postoperative pain regimens, including unit doses of 30 mg of ketorolac (Toradol) every 6 hours, morphine administered by a patient-controlled analgesia (PCA) pump, and intramuscular injection of hydromorphone (Dilaudid) for breakthrough pain.

The preemptive analgesia protocol being tested comprised three elements. The first element was a single IV injection of 30 mg ketoralac before the induction of anesthesia. The second element was infiltration of the skin along the planned incision line 1–2 minutes before incision with approximately 75 ml of 0.25% bupivacaine (Marcaine) with epinephrine. The third element consisted of a rectus fascia block using approximately 75 ml of 0.25% (plain) bupivacaine before wound closure. The placebo control group received injections with equal volumes of 0.9% saline. Coding of all study medications was performed by the hospital pharmacy. The code was not broken until all patients had been discharged from the hospital.

Table 1
Conversion of doses of narcotics to intravenous (iv) morphine equivalents

Drug (1 cc volume)	Narcotic content	IV Morphine Equivalence
Tylenol #3 Elixir	2.4 mg Codeine	0.24 mg
Roxanol	2.0 mg Morphine (oral)	0.33 mg
Dilaudid	1.0 mg Hydromorphone	6.67 mg

Procedure

A vertical banded gastroplasty–Roux-en-Y gastric bypass (VBG-RGB)[12] was performed in a retrocolic/retrogastric fashion with a two-layer hand-sewn gastrojejunostomy, a 15-cm biliopancreatic limb, a 100-cm alimentary limb, and a stapled jejunojejunostomy. A poly-track Gomez self-retaining retraction system was used in all cases.

Pain management

Postoperatively, a standard 10-cm linear visual analog scale (VAS) was used to assess each patient's pain perception. The patient rated the amount of pain on the scale and marked it with a pen. Data were collected at 1 hour and 4 hours after completion of the surgery, as well as once in the morning (between 6 and 8 AM) and once in the evening (between 6 and 8 PM) each day until discharge. Narcotic use was recorded from the nursing records and the PCA pumps at the time of the morning pain assessments, except in patients discharged after the evening pain assessment on postoperative day (POD) 2. All narcotics were recorded in absolute volumes (ml) or mg. After all data were collected, narcotic doses were converted to their IV morphine equivalence (Table 1) [13].

Statistics

An a priori analysis of power was computed to determine an adequate study group size, anticipating a 10% reduction in narcotic use among treatment group patients (σ within each group = 5, α = 0.05, 1-β = 0.95, effect size = 2). Results are reported as mean ± standard error of the mean (SEM) throughout. Data were analyzed using power analysis paired *t*-tests after first applying *F*-testing for variances.

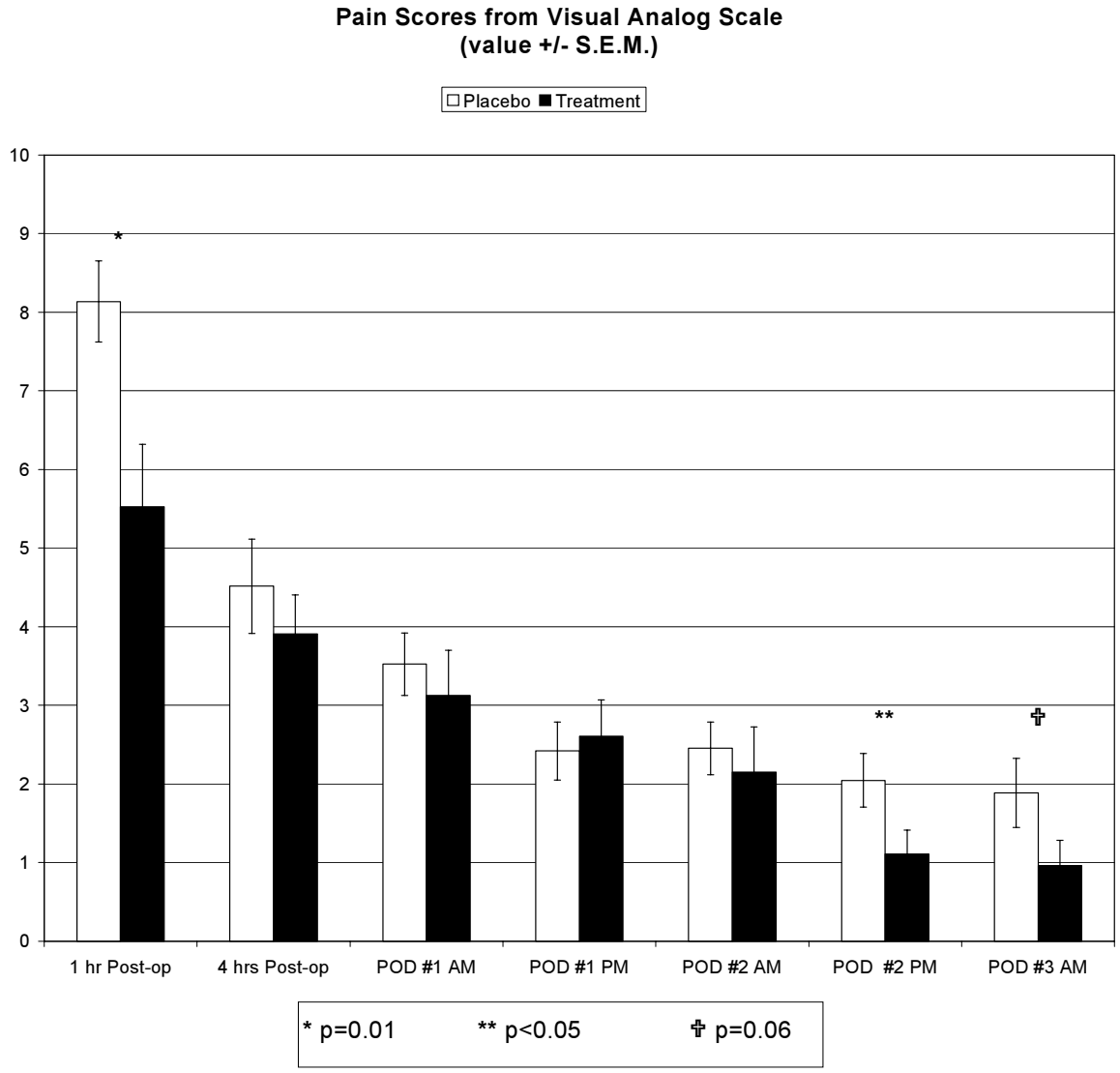

Fig. 1. Recorded VAS pain scores over time (mean ± SEM).

Analysis of variance was also performed for the morphine equivalent narcotic use for each of the two study groups.

Results

No patient experienced any pulmonary, hemorrhagic, or other complications. One patient from each of the two groups was discharged on the evening of POD 2, after the 6–8 PM data collection. The remaining 18 patients went home after the 6–8 AM data collection on the morning of POD 3. There were no cases of oversedation or any other adverse drug reactions.

Members of the two groups were statistically similar with respect to mean age (40 vs 43.9 years), mean BMI (49.8 vs 52.3 kg/m^2), mean incision length (18.1 vs 20 cm), and mean operative time (186 vs 200 min) for the placebo versus treatment groups, respectively. The gender composition of the two groups was similar as well (placebo group, nine women and one man; treatment group, seven women and three men). Three patients in the treatment group each had additional surgical procedures (one cholecystectomy and two umbilical hernia repairs). The timing of the operations was similar for both groups of patients. The average ending times for the morning cases were 12:23 PM for the placebo group (n = 6) and 12:32 PM for the treatment group (n = 5), and those for the afternoon cases were 6:00 PM for the placebo group (n = 4) and 6:57 PM for the treatment group (n = 5).

Pain scores were lower in the treatment group 1 hour after completion of surgery (8.1 ± 0.5 vs 5.5 ± 0.8; P = .01) and in the evening of POD 2 (2.1 ± 0.3 vs 1.1 ± 0.3; P = .03) (Fig. 1). Morphine equivalent use was significantly higher in the placebo group on the day of surgery and POD 1 than on POD 2 ($P < .01$), whereas the treatment group

had similar use on each postoperative day (P = not significant [NS]). The placebo group used significantly more narcotic pain medication than the treatment group on the day of surgery (42.1 ± 6.8 vs 20.6 ± 3.3; $P = .01$) and on POD 1 (42.3 ± 6.9 vs 23.5 ± 5.1; $P = .02$), with similar use on POD 2 (15.44 ± 3.4 vs 15.57 ± 6.3; P = NS). Comparing the morning and afternoon surgical patients, those operated on in the afternoon had significantly lower VAS scores at both data collection times on POD 1. This was true for both the placebo and treatment groups. Comparing morning and afternoon surgical patients from the placebo group with their counterparts in the treatment group showed no significant VAS differences. Narcotic use was higher in the morning and afternoon placebo group patients than in the morning and afternoon treatment group patients on both the day of surgery and POD 1. Because the present study was not designed to specifically evaluate these subgroups, statistical significance was achieved only for the difference in narcotics use between the morning placebo and morning treatment groups for the day of surgery (50.1 ± 8.7 vs 23.2 ± 6.0; $P = .02$).

Discussion

The present study appears to be the first prospective randomized trial of combined preemptive and preventive analgesia in morbidly obese patients. Our study preliminarily demonstrates that a combined preemptive/preventive regimen reduces self-reported pain and the use of narcotic medications after open gastric bypass surgery.

Conceptually, if one were to view the surgical trauma (ie, incision, manipulation of viscera, and closure) as the noxious stimulus, then a pain-control regimen could be initiated before the procedure (preemptive), during, or after the procedure (preventive), or at combinations of any or all three points in time. Patients routinely receive some form of pain control during surgery and postoperatively. The results of our small study of severely obese patients, in agreement with numerous studies of preemptive analgesia in other patient populations [14,15] indicate that administration of pain-blocking medications before surgery is beneficial. Activation of pain pathways can be broken down into four distinct processes: transduction, transmission, modulation, and perception. Hyperexcitability of dorsal horn neurons, a sign of acute pain perception, has been shown to be attenuated in experimental models if the afferent impulse is prevented from reaching the central nervous system by preinjury blockade [16–18]. We chose multiple agents known for their combined effectiveness in blocking the pain pathway at multiple locations. Ketoralac, a nonsteroidal anti-inflammatory agent, has an attenuating effect on pain transduction. Bupivacaine, a local anesthetic agent, has an attenuating effect on pain transmission, whereas parenteral morphine and fentanyl, both injectable opiates, as well as propofol, a general anesthetic, have attenuating effects on pain perception centrally [11].

Our protocol was designed to incorporate interventions at all three time periods relative to the noxious stimulus (ie, before, during, and after surgery). A critical step in the protocol was the administration of a rectus sheath block before fascial closure. This was specifically intended to preempt the pain associated with the placement and tying of the running fascial closure sutures.

Scientific investigations have inherent strengths and weaknesses, and the present study is no exception. Standardization provides uniformity and consistency. A single operation performed by a single experienced surgeon under uniform conditions with the same equipment and routine clinical pathways was the ideal setting for testing our hypothesis. Randomization of patients can sometimes introduce variables not taken into consideration during the study design. For example, variations in pain sensitivity for women at various stages of their menstrual cycle or differences in body fat composition between men and women with similar BMIs could result in an otherwise well-designed study becoming underpowered. Due to the small sample size approved for investigation by our Institutional Review Board, associated comorbid medical conditions were not expected to be statistically uniform between the two groups of patients, and thus data on these were not collected as part of the study. While analyzing our data, we noticed that all patients needing additional procedures performed at the time of their surgery belonged to the treatment group. One might speculate that this incurred a disadvantage to our treatment group and that the differences in narcotic use might have otherwise been greater than they were.

The present study was designed to test the difference between a combined preemptive and preventive analgesia technique against a placebo. Had we wished to evaluate the individual components of preemptive analgesia versus preventive analgesia versus placebo, then we would have needed to add another group of patients receiving no preoperative interventions and only a rectus sheath block.

With regard to our choice of drugs used for this study, Ketorolac is an excellent drug that has achieved notoriety due to reports of complications associated with its misuse. When used according to accepted guidelines (ie, 30 mg fixed dose IV every 6 hours, not to exceed 5 days) the drug is extremely effective and as safe as any other NSAID agent. The dose is not adjusted according to patient BMI. Because the first dose is given before surgery, some may raise the possibility of increased risk of intraoperative bleeding complications, especially when combined with medical deep venous thrombosis prophylaxis initiated before surgery. This is not the case, however. There is nothing better than meticulous hemostasis achieved by operating with loupes for preventing bleeding complications.

The intraoperative dosage of fentanyl was at the discretion of the anesthesiologist based on his judgment of the

patient's pain perception (based on electrocardiography, heart rate, and blood pressure findings). The anesthesiologist was blinded from knowing whether the patient was receiving treatment medications or placebo. The anesthesiologist felt that he was able to determine whether or not a patient had received treatment based on the patient's physiological response to the surgery and the smaller amount of fentanyl needed. This could certainly make for an interesting review of the data, but it was not part of the initial Internal Review Board application. Perhaps this would provide an opportunity to provide more proof of the protocol's effectiveness as a separate study.

An unanticipated finding was noted when each group of patients was divided into morning and afternoon surgery groups. For reasons unclear to us, the VAS pain perception recorded on POD 1 was lower for patients operated on in the afternoon. This was true for both the treatment and placebo groups. One might want to speculate that for the treatment group, the rectus sheath block was still acting, but there would be no such explanation for the placebo group. If one were to propose further study, then larger groups of patients would be required in each of the morning and afternoon subgroups.

Conclusion

The data collected in this study clearly demonstrate the effectiveness of using a combined preemptive and preventive analgesia regimen in morbidly obese patients undergoing open gastric bypass surgery. In the present study, narcotic use in these patients was approximately half that in a nontreated group of matched patients for the initial 48-hour postoperative period. This reduction in narcotic requirement came without sacrifice of patient comfort. Large follow-up studies implementing this protocol are needed to determine overall patient safety.

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