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ORIGINAL CONTRIBUTIONS

Comparison of Intravenous Ibuprofen and Paracetamol for Postoperative Pain Management after Laparoscopic Sleeve Gastrectomy. A Randomized Controlled Study

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Abstract

Background Laparoscopic sleeve gastrectomy (LSG) is defined as the first-step bariatric surgery for the treatment of obesity. Opioid analgesics are often preferred for pain management because of their strong analgesic potentials. However, opioids have undesirable adverse effects.

Objectives The objective of this study is to evaluate and compare the influence of IV forms of ibuprofen and paracetamol on pain management and opioid consumption on patients undergoing LSG surgery.

Setting This study was conducted at Istanbul Medipol University Hospital.

Methods Patients were stratified into three groups. Group I (group ibuprofen, $n = 30$) was administered 800 mg of IV ibuprofen, group P (group paracetamol, $n = 30$) was administered 1000 mg of IV paracetamol, and group C (control group, $n = 30$) was given 100 ml of saline solution. We evaluated opioid consumption and VAS scores postoperatively.

Results This study included 90 patients who underwent LSG. The use of rescue medication in group I was statistically lower than the other groups. VAS scores in group I and group P at recovery and at 2, 4, 8, 12, and 24 h were lower than those in group C. In particular, the VAS scores in group I at the first 2 h postoperatively were significantly lower than those in group P ($p < 0.05$). Opioid consumption in group C was significantly higher than the other groups ($p < 0.05$).

Conclusion Our study suggested that IV ibuprofen resulted in lower pain scores compared to paracetamol by reducing postoperative opioid use in the first 24 h in patients undergoing LSG surgery.

Keywords Laparoscopic sleeve gastrectomy · Analgesia · Ibuprofeny

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Introduction

Bariatric surgery has been widely used in the treatment of obesity in recent years. It has been shown to be effective in reaching the ideal weight and reducing obesity-induced co-morbidities [1]. Laparoscopic sleeve gastrectomy (LSG) is defined as the first-step bariatric surgery for patients in the high surgical risk group [2]. It has been shown that the laparoscopic approach has lower complication rates, shorter hospital stays, and earlier mobilization compared to open surgery [3]. However, postoperative pain management is very important because it might cause major morbidity, especially pulmonary complications in the early postoperative period [4].

General recommendations for bariatric surgery include multimodal analgesia without sedatives, local analgesic infiltration, and early mobilization [5]. Opioid analgesics are often preferred for pain management because of their strong analgesic potentials. However, opioids have undesirable adverse effects such as sedation, dizziness, constipation, nausea, vomiting, physical dependence and addiction, hyperalgesia, immunologic and hormonal dysfunction, muscle rigidity, tolerance, and respiratory depression [6]. The morbidly obese patients treated with opioids experience an increased risk for adverse effects such as atelectasis, which causes postoperative pulmonary complications, and obstructive sleep apnea, which causes hypoxemia, postoperative ileus, and longer hospital stay due to nausea and vomiting [7–10]. For this reason, in 2006, the American Society of Anesthesiologists (ASA) suggested minimizing or avoiding opioids during perioperative and/or postoperative pain management to the bariatric patients. Therefore, ASA recommends the use of multimodal analgesia including local anesthesia, regional anesthesia, and nonsteroidal anti-inflammatory drugs (NSAIDs) [11].

NSAIDs have long been used in the treatment of pain and inflammation. These agents prevent the pain receptors from responding to injury by blocking the transformation of arachidonic acid to prostaglandins [12]. Ibuprofen is a propionic acid derivative that has anti-inflammatory, antipyretic, and analgesic effects similar to other NSAIDs [13]. The oral form of ibuprofen has been used safely for a long time and is one of the most preferred NSAIDs. The intravenous (IV) form of ibuprofen has been used in the pain treatment since 2009. Although there are insufficient studies about IV ibuprofen, it has been shown to be effective, safe, and with less adverse effects in the treatment of postoperative pain [14–17]. There are not still any data about the use of IV ibuprofen for LSG surgery.

The objective of the present study is to evaluate and compare the influence of IV forms of ibuprofen and paracetamol on pain management and opioid consumption on patients undergoing LSG surgery.

Materials and Methods

The study was approved by the ethics committee of the Istanbul Medipol University. Ninety patients aged between 18 and 60 years, with body mass index (BMI) ≥ 35 kg/m^2 and hospitalization period of at least 24 h, and who have planned for LSG surgery were included in this randomized, prospective, double-blind, placebo-controlled study. Informed consent was obtained from all individual participants included in the study. This article does not contain any studies with human participants or animals performed by any of the authors.

All LSG operations were performed laparoscopically by the same surgical team using the same technique. Data collected included age, height (cm), weight (kg), BMI, gender, ASA score, duration of operation (minutes), and duration of anesthesia (minutes).

Patients graded above ASA 3, with a history of renal, hepatic, and cardiovascular disease, gastrointestinal bleeding history, known study drug or paracetamol allergy, long-term NSAID and opioid use, history of oral anticoagulant drug use, platelet count < 80.000, neuropathic diseases, inability to use a patient-controlled analgesia (PCA) device, and those discontinued the medication required in the study for any reason and those who are pregnant were excluded from the study.

Patients were evaluated 1 day before the operation. The study protocol was described, and information about the visual analogue scale (VAS; pain scale) and patient-controlled analgesia device (PCA) was explained. Patients were stratified into three groups by a randomizing computer program. Group I (group ibuprofen, $n = 30$) was administered 800 mg of IV ibuprofen, group P (group paracetamol, $n = 30$) was administered 1000 mg of IV paracetamol, and group C (control group, $n = 30$) was given 100 ml of saline solution and after intubation. The study drugs were administered in 100 ml saline solution. No one in the operation room was aware of the randomization. General anesthesia included propofol (2.0–3.0 mg/kg), rocuronium (0.6 mg/kg), and fentanyl (75–100 mcg). Anesthesia was maintained with sevoflurane 2% in an oxygen–air mixture (40% O_2/60% air). Remifentanil 0.25 μg/kg/min was used for intraoperative analgesia. Meperidine (0.25 mg/kg) was administered to all patients about 30 min before the end of the surgery.

Postoperative Analgesia Management

Patients in all groups received their medications every 8 h for the first 24-h period postoperatively. They were attached to a PCA device in the recovery room. The PCA device prepared with fentanyl was programmed to a 10 mcq concentration, 10-min lockout, and 25 mcq bolus dose with no basal infusion, maintained for 24 h. Postoperative patient evaluation was performed by an anesthetist blinded to the drugs used and groups.

Postoperative analgesia was evaluated using a VAS score (VAS 0 = no pain and VAS 10 = the most severe pain). Meperidine (0.25 mg/kg) was given to patients with a VAS score of 4 or above for rescue analgesia. This was repeated after 5 min if necessary.

All patients received IV pantoprazole 1 × 40 mg for gastric protection during 48 h at the postoperative period. After discharge from the hospital, oral anti-acid suspension (including calcium carbonate and magnesium carbonate) 4 × 1 and ibuprofen oral suspension 3 × 400 mg were prescribed to all patients. There were no readmissions during 30 days.

The adverse effects of opioids and ibuprofen were recorded. The presence of nausea, vomiting, itching, and allergic reactions associated with the protocol drugs was analyzed.

Statistical Analysis

IBM SPSS 20.0 software program was used to perform the statistical analysis. The power of the study was analyzed according to the total fentanyl consumption variable. The sample size was 95.28 in the 95% confidence interval and the power was 0.99. This shows that the size of the study is sufficient. Data were analyzed by using the Kolmogorov–Smirnov test. Pearson's χ^2 test was used to compare the categorical data between groups. Differences between groups were controlled by using the one-way ANOVA at the significance level of 5%. Descriptive statistics were explained as mean ± SD.

Results

Each group in this study included 30 patients. Baseline demographics, duration of anesthesia, and duration of the operation were similar between the groups, showing no statistical difference ($p > 0.05$) (Table 1).

The use of rescue medication in group I was statistically lower than the other groups (Table 2). Pain scores (VAS) in group I and group P at recovery and at 2, 4, 8, 12, and 24 h were lower than those in group C. In particular, the VAS scores in group I at the first 2 h postoperatively were significantly lower than those in group P ($p < 0.05$) (Table 2). Opioid consumption in group C was significantly higher than the other groups ($p < 0.05$) (Table 2).

The incidence of nausea and itching in group I was lower than the other groups ($p < 0.05$). The adverse effects are shown in Table 3. No statistical difference was seen between the groups in terms of the other adverse effects (Table 3).

Discussion

This study demonstrated that the intravenous form of ibuprofen reduced the 24-h opioid consumption and was effective, which is evident from the lower pain scores in the postoperative period compared to paracetamol. In addition, IV ibuprofen significantly reduced rescue analgesic use.

Opioids are widely used analgesic agents. Parenteral opioids are preferred for the treatment of acute postoperative pain after surgery [18]. Even though opioids are very important for acute postoperative pain management, they may cause opioid-related adverse events (ORAE) such as nausea, vomiting, constipation, addiction, pruritus, sedation, respiratory depression, and postoperative ileus [19]. Obesity is related to pharynx abnormalities associated with airway collapse, and these patients have anatomical and physiological features such as increased intra-abdominal pressure, reduced chest wall compliance, and impaired hepatic drug clearance that predisposes ORAE [20, 21]. Systemically administered opioids may cause hypoxia and hypercapnia by reducing the respiratory rate, level of consciousness and the supraglottic airway muscle tone [21]. Therefore, the use of postoperative opioids in obese patients after LSG surgery should be kept at a minimum [22]. This is the reason clinicians need alternative analgesic agents.

Postoperative pain can ideally be treated with a combination of analgesics acting on different pathways of the pain mechanism. This technique is called multimodal analgesia. Multimodal analgesia reduces doses and adverse effects of analgesics; thus, it provides safer pain treatment, improves analgesia quality, and results in better functional outcomes [23]. The World Health Organization, American Pain Society, American Society of Anesthesiologists, American Society of Regional Analgesia and Pain Medicine, and the Joint Commission recommend multimodal analgesia for pain management [24]. Therefore, NSAIDs can be used in combination with opioids for postoperative multimodal pain management.

Ibuprofen is a well-known NSAID that has analgesic, anti-inflammatory, and antipyretic effects. The analgesic efficacy of ibuprofen is associated with cyclooxygenase enzyme inhibition (COX-1 and COX-2 isoenzymes). COX-2 inhibition is responsible for the analgesic, antipyretic, and anti-inflammatory effects. COX-1 inhibition causes undesirable side effects. The inhibition rate of COX-1 to COX 2 of ibuprofen is 2.5:1, whereas other NSAIDs, for example ketorolac, have an inhibition ratio of 330:1, a reason for a high risk of adverse effects. Therefore, ibuprofen has a lower risk of bleeding or gastrointestinal problems [25]. The IV form of ibuprofen has been evaluated in patients undergoing orthopedic surgery, abdominal hysterectomy, or laparoscopic cholecystectomy; it is reported to be quite safe and effective [14–17]. There is no literature study about the efficacy of IV ibuprofen in patients undergoing obesity surgery. Paracetamol is one of the most commonly used analgesics. Studies about the use of paracetamol in patients undergoing LSG report that paracetamol is effective for this type of surgery [26–29]. The anti-inflammatory mechanism of paracetamol is complex:

Table 1 Comparison of demographic data

	Group C (*n*, 30)	Group P (*n*, 30)	Group I (*n*,30)	*p* value
Age (years) (mean ± SD)	43.93 ± 8.58	48.10 ± 16.01	50.16 ± 14.46	0.192[a]
Weight (kg) (mean ± SD)	72.76 ± 9.89	76.43 ± 14.71	72.50 ± 12.19	0.395[a]
Height (cm) (mean ± SD)	164.43 ± 8.56	163.03 ± 9.55	162.40 ± 8.43	0.663[a]
BMI	26.90 ± 3.51	28.56 ± 5.59	27.40 ± 3.83	0.329[a]
Gender (%) (M/F)	50.0/50.0	26.6/74.4	43.3/457.7	0.164[b]
ASA (I/II/III)	18/12/0	14/16/0	10/18/2	0.112[b]
Duration of anesthesia (mean ± SD)	60.26 ± 6.90	60.86 ± 6.35	57.56 ± 5.19	0.095[a]
Duration of the operation (mean ± SD)	46.50 ± 6.45	48.63 ± 8.93	45.63 ± 6.04	0.263[a]

Values are expressed as mean ± standard deviation; *ASA*, American Society of Anesthesiologists; *BMI*, body mass index

[a] $p > 0.05$ one-way ANOVA between groups

[b] $p > 0.05$ chi-square test between groups

paracetamol affects both the peripheral (COX inhibition) and central pathways [30]. In a meta-analysis comparing the efficacy of oral ibuprofen and paracetamol in acute and chronic pain syndromes, Moore et al. reported that paracetamol is the first choice for pain management but emphasized that ibuprofen is generally superior to paracetamol at standard doses [31]. In our study, we evaluated the efficacy of the IV form of ibuprofen compared to paracetamol. In a study evaluating the efficacy of IV ibuprofen and paracetamol, Çelik et al. performed a single preemptive dose of drugs for rhinoplasty surgery and reported that IV ibuprofen was superior to paracetamol in providing effective postoperative analgesia [32]. In another study, Gozeler et al. performed a single preemptive dose IV ibuprofen 800 mg for septorhinoplasty surgery and reported that it resulted in lower postoperative pain scores [33]. In our study, we continued to give the drugs at every 8 h postoperatively. We found that IV ibuprofen provides effective analgesia in the first 24 h postoperatively and reduces opioid consumption compared to paracetamol. In addition, the analgesic effect with IV ibuprofen is more effective than paracetamol especially in the first 2 h postoperatively. Therefore, we recommend that IV ibuprofen may be used as an alternative drug in multimodal analgesia.

Adverse effects such as nausea and itching were higher in the control and paracetamol groups because of the higher opioid use. The use of rescue analgesic was lower in the ibuprofen group compared to the other groups. We observed that ibuprofen reduced ORAE by reducing the opioid requirement.

There are some limitations to this study. Firstly, the drug has two forms, 400 and 800 mg; however, we used only the 800 mg dose, irrespective of patient weight. Different results and different adverse effect profiles might have been obtained with 400 mg. The second limitation is that the 800 mg dose was used with a 3 × 1 dosage during 24 h postoperatively. We can use a 4 × 1 dosage at 24 h period. The aim was to keep the dosage lower and the time interval longer. Third, no local anesthetic injection was administered to the port site incisions. Pain scores might have been reduced further with port site injection. Finally, the sample size was determined on the basis of opioid requirement comparing ibuprofen and paracetamol after LSG surgery, the primary aim. Further studies with a larger sample size may be needed to evaluate IV ibuprofen-related side effects.

Table 2 Comparison of VAS scores, fentanyl consumption doses of PCA, and rescue analgesic use

VAS (mean ± SD)	Group C (*n*,50)	Group P (*n*,50)	Group I (*n*,50)	*p* value
VAS recovery	6.93 ± 1.46	4.56 ± 1.16[a]	3.40 ± 1.24[a,b]	< 0.001
VAS 2nd hour	4.43 ± 0.85	2.90 ± 0.92[a]	2.06 ± 1.17[a,b]	< 0.001
VAS 4th hour	3.43 ± 0.81	2.33 ± 0.95[a]	1.80 ± 1.44[a]	< 0.001
VAS 8th hour	3.96 ± 1.29	2.16 ± 1.28[a]	1.46 ± 0.97[a]	< 0.001
VAS 12th hour	3.06 ± 1.33	1.43 ± 0.93[a]	0.83 ± 0.79[a]	< 0.001
VAS 24th hour	1.70 ± 0.65	0.76 ± 0.72[a]	0.36 ± 0.55[a]	< 0.001
Fentanyl consumption	568.33 ± 131.30	276.00 ± 88.10[a]	226.66 ± 133.73[a]	< 0.001
Rescue analgesia	63.3/37.7	13.3/86.7[a]	3.3/96.3[a,b]	< 0.001

Values are expressed as mean ± standard deviation; VAS, visual analog scale

[a] $p < 0.05$ one-way ANOVA compared with group C

[b] $p < 0.05$ one-way ANOVA compared with group P

Table 3 Comparison of the incidence of adverse events

	Group C ($n = 30$)	Group P ($n = 30$)	Group I ($n = 30$)	p value
Nausea	10	6^b	1^a	0.012
Vomiting	5	7	3	0.383*
Itching	9	7^b	1^a	0.023
Allergic reactions	2	0	0	0.129*

Values are expressed as mean ± standard deviation

*$p > 0.05$

[a] $p < 0.05$ one-way ANOVA compared with group C

[b] $p < 0.001$ one-way ANOVA compared with group I

In conclusion, IV ibuprofen resulted in lower pain scores compared to paracetamol by reducing postoperative opioid use in the first 24 h in patients undergoing LSG surgery. It also reduced rescue analgesic use in the postoperative period and ORAE such as nausea and vomiting. IV ibuprofen may have a more potent analgesic effect than IV paracetamol in the postoperative pain management according to our results. Larger studies are needed to evaluate the efficacy and use of ibuprofen in patients undergoing LSG surgery.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Bray GA. Medical consequences of obesity. J Clin Endocrinol Metab. 2004;89:2583–9.
2. Cottam D, Qureshi FG, Mattar SG, et al. Laparoscopic sleeve gastrectomy as an initial weight-loss procedure for high-risk patients with morbid obesity. Surg Endosc. 2006;20:859–63.
3. Bisgaard T, Klarskow B, Kristiansen BV, et al. Multiregional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: a randomized double-blind placebo controlled study. Anesth Analg. 1999;89:1017–8.
4. Cantore F, Boni L, Di Giuseppe M, et al. Pre-incisional local infiltration with levobupivacaine reduces pain and analgesic consumption after laparoscopic cholecystectomy: a new device for day-case procedure. Int J Surg. 2008;6:89–92.
5. Schug SA, Raymann A. Postoperative pain management of the obese patient. Best Pract Res Clin Anaesthesiol. 2011;25:73–81.
6. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. Pain Physician. 2008;11(2 Suppl l):S105.
7. Gallagher SF, Haines KL, Osterlund LG, et al. Postoperative hypoxemia: common, undetected, and unsuspected after bariatric surgery. J Surg Res. 2010;159:622–6.
8. Block M, Jacobson LB, Rabkin RA. Heart block in patients after bariatric surgery accompanying sleep apnea. Obes Surg. 2001;11:627–30.
9. Augestad KM, Delaney CP. Postoperative ileus: impact of pharmacological treatment, laparoscopic surgery and enhanced recovery pathways. World J Gastroenterol. 2010;16:2067–74.
10. Moussa AA, Oregan PJ. Prevention of postoperative nausea and vomiting in patients undergoing laparoscopic bariatric surgerydgranisetron alone vs granisetron combined with dexamethasone/droperidol. Middle East J Anesthesiol. 2007;19:357.
11. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an update report by the American Society of Anesthesiologist Task Force on acute pain management. Anesthesiology. 2012;116:248.
12. Svensson CI, Yaksh TL. The spinal phospholipase-cyclooxygenase-prostanoid cascade in nociceptive processing. Annu Rev Pharmacol Toxicol. 2002;42:553–83.
13. Scott LJ. Intravenous ibuprofen: in adults for pain and fever. Drugs. 2012;72:1099–109.
14. Martínez AG, Rodriguez BE, Roca AP, et al. Intravenous ibuprofen for treatment of post-operative pain: a multicenter, double blind, placebo-controlled, randomized clinical trial. PloS one. 2016;11(5):e0154004.
15. Kroll PB, Meadows L, Rock A, et al. A multicenter, randomized, double-blind, placebo-controlled trial of intravenous ibuprofen (IV-ibuprofen) in the management of postoperative pain following abdominal hysterectomy. Pain Pract. 2011;11:23–32.
16. Singla N, Rock A, Pavliv L. A multi-center, randomized, double-blind placebo-controlled trial of intravenous-ibuprofen (IV-ibuprofen) for treatment of pain in post-operative orthopedic adult patients. Pain Med. 2010;11(8):1284–93.
17. Ahiskalioglu EO, MD AA, Aydin P, et al. Effects of single-dose preemptive intravenous ibuprofen on postoperative opioid consumption and acute pain after laparoscopic cholecystectomy. Medicine. 2017;96(8):e6200.
18. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. Pain Physician. 2008;11(Suppl 2):S105–20.
19. Levi D, Goodman ER, Patel M, et al. Critical care of the obese and bariatric surgical patient. Crit Care Clin. 2003;19(1):11–32.
20. Littleton SW. Impact of obesity on respiratory function. Respirology. 2012;17(1):43–9. https://doi.org/10.1111/j.1440-1843.2011.02096.x.
21. Frey WC, Pilcher J. Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. Obes Surg. 2003;13(5):676–83. https://doi.org/10.1381/096089203322509228.
22. White PF. Multimodal analgesia: its role in preventing postoperative pain. Curr Opin Investig Drugs. 2008;9:76–82.
23. American Society of Anesthesiologist Task Force. Practice guidelines for acute pain management in the perioperative setting. Anesthesiology. 2012;116:248–73.
24. Kroll PB. Intravenous ibuprofen for postoperative pain. Pain Manag. 2012;2:47–54. https://doi.org/10.2217/pmt.11.68.
25. Song K, Melroy MJ, Whipple OC. Optimizing multimodal analgesia with intravenous acetaminophen and opioids in postoperative

bariatric patients. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2014;34(S1):14S–21S.
26. Ng JJ et al. A multimodal analgesic protocol reduces opioid-related adverse events and improves patient outcomes in laparoscopic sleeve gastrectomy. Obes Surg. 2017;27(12):3075–81.
27. Gonzalez MA et al. Intravenous acetaminophen in bariatric surgery: effects on opioid requirements. J Surg Res. 2015;195(1):99–104.
28. Wininger SJ, Miller H, Minkowitz HS, et al. A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two intravenous acetaminophen dosing regimens for the treatment of pain after abdominal laparoscopic surgery. Clin Ther. 2010;32(14):2348–69.
29. Bebenista MJ, Paracetamol NJZ. Mechanism of action, applications and safety concern. Acta Pol Pharm Drug Res. 2014;71(1):11–23.
30. Moore RA, Derry S, Wiffen PJ, et al. Overview review: comparative efficacy of oral ibuprofen and paracetamol (acetaminophen) across acute and chronic pain conditions. Eur J Pain. 2015;19: 1213–23.
31. Gazal G, Al-Samadani KH. Comparison of paracetamol, ibuprofen, and diclofenac potassium for pain relief following dental extractions and deep cavity preparations. Saudi Med J. 2017;38:284–91.
32. Çelik EC, Kara D, Koc E, et al. The comparison of single-dose preemptive intravenous ibuprofen and paracetamol on postoperative pain scores and opioid consumption after open septorhinoplasty: a randomized controlled study. Eur Arch Otorhinolaryngol. 2018;275:2259–63. https://doi.org/10.1007/s00405-018-5065-6.
33. Gozeler MS, Sakat MS, Kilic K, et al. Does a single-dose preemptive intravenous ibuprofen have an effect on postoperative pain relief after septorhinoplasty? Am J Otolaryngol. 2018;39:726–30.