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Research Article





Analgesic Effect of Intraperitoneal Bupivacaine in Laparoscopic Sleeve Gastrectomy: A Matched Case-Control Study and Review of Available Data

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Abstract

Background: Instillation of intraperitoneal local anesthetics (IPLA) has been widely investigated in laparoscopic procedures. Few studies have addressed its efficacy in laparoscopic sleeve gastrectomy (LSG). **Aim**: The aim of this study is to investigate the effectiveness of IPLA instillation in LSG. **Methods**: A matched case-control study was conducted between February 2022 and March 2023. Patients undergoing LSG surgery with instillation of intraperitoneal bupivacaine (Bupivacaine Group) were compared to a historical Control Group undergoing the same procedure without bupivacaine instillation. Patients were matched for age, gender and BMI. The studied outcomes included: quality of emergence from general anaesthesia, postoperative narcotic requirements, pain scores, length of stay in the post anaesthesia care unit (PACU), and postoperative nausea and vomiting (PONV). **Results**: Eighty-four patients were included, 42 patients in each group. Patients in the Bupivacaine Group showed a less agitated emergence from general anaesthesia (9.5% vs 47.6%, p=0.006). Pain scores at admission to PACU were lower in the Bupivacaine Group (Median 2 (IQR 0 – 5)) vs. Control Group (Median 4 (IQR 2 – 7)), p =0.044, as well as morphine needs in PACU [Bupivacaine Group (Median 2 (IQR 0 – 4)) vs. Control Group (Median 6 (IQR 4 – 7)), p =0.007]. Time to discharge from PACU, postoperative narcotic requirements, and incidence of PONV were similar. **Conclusion**: The IPLA in LSG surgery allows better emergence from anaesthesia, reduces narcotics use and pain scores in early postoperative period. Larger randomized controlled trials should be conducted to confirm these results.

Keywords: Bariatric; Intraperitoneal Bupivacaine; Obesity; Postoperative Pain

Introduction

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Obesity is the fifth leading cause of death in the world and has been described as a worldwide pandemic. [1] The rise in the prevalence of obesity is associated with increases in bariatric surgeries that have demonstrated their effectiveness in achieving weight loss and decreasing obesity-related comorbidities such as diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea. [2] Despite that laparoscopic approach is associated with lower pain scores, postoperative pain management remains a major challenge especially in patients with obesity that are more prone to perioperative pulmonary, cardiovascular and thromboembolic complications. [3] Effective analgesia in bariatric patients is therefore crucial, as it promotes better respiration and early ambulation, and thus, improves procedural morbidity and patient outcomes.

pioids are a powerful tool for decreasing pain. Their use is however associated with many side effects, including respiratory depression, excessive sedation, nausea, vomiting and urinary retention. [4,5] The American Society of Anesthesiologists task force on acute pain management developed several strategies for achieving effective pain control in the perioperative setting, while decreasing analgesia-related adverse events. Such techniques included multimodal analgesia, epidural or intrathecal analgesia, patient-controlled analgesia with opioids and regional analgesia with local anesthetics. [6] More recently, intraperitoneal local anesthetics (IPLA) instillation has been proposed as another tool to be added to the analgesic arsenal. It involves infusion a local anesthetic into the abdominal cavity during surgery. This technique has been widely assessed in the setting of laparoscopic cholecystectomy [7,8] and gynecologic procedures [9] with promising results. However, there is still a scarcity of studies focusing on the role of intraperitoneal local anesthetics in bariatric surgery.

The aim of this study is to analyze the analgesic effect of intraperitoneal bupivacaine instillation in patients undergoing laparoscopic sleeve gastrectomy (LSG).

Materiel and Methods

A matched case-control study was conducted between February 2022 and March 2023 at Hotel-Dieu de France University Hospital, comparing a group of patients undergoing LSG with intraperitoneal bupivacaine instillation to a historical control group undergoing the same procedure without intraperitoneal bupivacaine instillation. For the retrospective part of the study (control group), the data were retrieved form the patients' records who already agreed, at time of admission, to share their data for future scientific research. For the prospective group (Bupivacaine group), an informed consent was obtained from all the patients within the group. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the Helsinki declaration of 1975 and its later amendments. Patients over the age of 18 years and undergoing elective LSG were eligible for inclusion in the study. The exclusion criteria were other bariatric procedures, revisional surgeries, past history of previous foregut surgery, allergy to bupivacaine, and patients receiving analgesic drugs 24 hours prior to surgery. The two groups followed the same anesthetic protocol already standardized by the anaesthesia department. Induction of anaesthesia was achieved using propofol 3mg/kg of Lean Body Weight (LBW) and succinvlcholine 1mg/kg of Total Body Weight

(TBW). Maintenance of anaesthesia was achieved with a target controlled IV infusion of remifentanil set at around 2 to 5 ng/ml, and sevoflurane in a gas mixture air/oxygen (0.6). Bispectral index goals varied between 40 and 60. Muscular relaxation was achieved using rocuronium 0.6 mg/kg followed by reinjections according to neuromuscular transmission (NMT) measurements.

Forty-two patients were prospectively included in the Bupivacaine Group. The same surgeon using the same surgical technique performed all LSGs. At the end of the procedure, and before the discontinuation of the pneumoperitoneum, 20 mL of bupivacaine 0.25 % mixed with 0.1 mg of epinephrin were sprayed into the peritoneal cavity, over the diaphragmatic area, in the hepato-diaphragmatic and spleno-diaphragmatic spaces. The surgeon, under direct visualization, administered the solution. All patients received 1g of paracetamol, 20 mg of nefopam, 100 mg of ketoprofen and morphine 0.1mg/kg of ideal weight 30 minutes prior to extubation. All patients were extubated in the operation room and transferred to the postanaesthesia care unit (PACU) for routine surveillance.

Forty-two patients in the Control Group were retrospectively selected among patients having undergone the same type of surgery, by the same surgeon but without instillation of IP Bupivacaine, in a period of time preceding the beginning of the current study. Patients in the Control Group were therefore selected to match the demographic properties (age, gender, weight, BMI) of patients in the Bupivacaine Group.

Study data were recorded for the Bupivacaine Group and collected retrospectively from patients' records for the Control Group. One should note that patients in the Control Group had undergone the same general anaesthesia protocols as well as the same analgesia protocols administered prior to extubation, at PACU and postoperatively. These protocols are standardized and are systematically used by the anaesthesia department, even outside the research settings.

Depending on the patient status, quality of emergence from general anaesthesia is routinely noted as quiet or agitated on the anaesthesia sheet. Accordingly, this information was recorded in the Bupivacaine Group and collected retrospectively from the anaesthesia sheet for the Control Group.

During their stay in the PACU, all the patients received IV morphine titration for analgesia, according to the standardized protocol used by the anaesthesia department: 2 mg of morphine with evaluation of the visual analog pain scale score (VAS) at admission to PACU and every 7 minutes until a (VAS) $\leq 3/10$ was reached. VAS scores are then evaluated every hour and at discharge from the PACU.

VAS scores were noted for all patients in the Bupivacaine Group upon their admission to the PACU, 30 min, one-hour, two hours postoperatively, and/or at discharge from PACU whatever occurs before. For patients who stayed less than 2 hours in the PACU, VAS value at discharge from PACU (which occurred between 1h and 2 hours) was considered as VAS at 2-hourtime point. In the Control Group, corresponding data were collected from the anaesthesia record sheet.

Outcome variables included the quality of emergence from anaesthesia, VAS scores in PACU, length of stay in PACU, occurrence of postoperative nausea and vomiting (PONV) during PACU stay (defined by Yes=presence or No=absence) and postoperative narcotic use. Narcotic prescription on the ward included tramadol administered intravenously as rescue analgesia and leaved to the surgeon's discretion.

Statistical analysis was performed using the SPSS[®] software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 28. Armonk, NY: IBM Corp.). Qualitative variables were defined by numbers and percentage of cases, and compared using chi-square test, with Fisher exact test when applicable. Quantitative

variables not departing from normality were described as mean and standard deviation, and analyzed using a two-tailed t-test. Quantitative variables departing from normality were expressed as median with its interquartile range (IQR). Baseline VAS scores were compared using the Mann-Whitney U test. Repeated VAS measures were compared inside each group using the Friedman's non-parametric analysis of variance for repeated measures: For each group, there are 4 measurements for VAS, namely at baseline, at 30 minutes, at 1 hour and at 2 hours. To account for the repeated within-subjects measurements and for the ordinal nature of VAS, the Friedman nonparametric repeated measures ANOVA was used for each group, testing whether all 4 VAS measurements are equal inside each group.

Results

Eighty-four patients were included in the study, 42 patients in each group. The demographic characteristics between the participants of the two groups were similar. Intraoperative opioid needs were also identical between the 2 groups (Table 1). There were no cases needing conversion to a laparotomy approach.

	Bupivacaine group (N=42)	Control group (N=42)	p value					
Age (y) Gender	36.86 ± 11.88	35.81 ± 11.08	0.769					
Male (%)	4 (9.5%)	4 (9.5%)	0.999					
Female (%)	38 (90.5%)	38 (90.5%)	1					
Weight (kg)	106.66 ± 12.19	102.71 ± 11.50	0.287					
Height (cm)	165.61 ± 11.26	163.14 ± 7.10	0.399					
BMI	39.10 ± 4.08	38.58 ± 2.57	0.624					
OSA Yes (n)	0	0	1					
No (n)	42	42	1					
Conversion to Open surgery	0	0	1					
Intraoperative opioid use Remifentanyl (μg)	2061.80 ± 631.58	2007.14 ± 293.80	0.722					
Morphine (mg)	5.57 ± 0.97	5.66 ± 1.77	0.831					
Operative time (min)	120.1 ± 31.58	$118.50 \pm 32,62$	0.719					
Quantitative data are expressed in mean \pm standard deviation.								

P values show no statistical difference.

BMI, body mass index; OSA, obstructive sleep apnea.

 Table 1: Demographic characteristics of participants and operative data.

In the Bupivacaine Group, 9.5 % of the patients showed an agitated emergence from anaesthesia as compared to 47.6 % in the Control Group (p = 0.006, Table 2). Morphine use in PACU was lower in the study group [Bupivacaine Group (Median 2 (IQR 0 – 4)) vs. Control Group (Median 6 (IQR 4 – 7)), p = 0.007]. The median length of stay in the PACU was not different between the 2 groups [Bupivacaine Group (Median 120 min (IQR 90 min – 130 min) vs. Control Group (Median 120 min (IQR 120 min – 150 min), p=0.093] as depicted in Table 2. No differences were noted for the total doses of narcotics used for postoperative analgesia during the entire hospital stay (Table 2). Postoperative analgesic requirements peaked between day 0 and day 1 and declined later on.

	Bupivacaine group (N=42)	Control group (N=42)	p value						
Quality of emergence from general anaesthesia									
Quiet (n)	38	22	0.006						
Agitated (n)	4	20							
Postoperative narcotics needs*									
Dose of morphine in PACU (mg)	2 (0 – 4)	6 (4 – 7)	0.007						
Total dose of tramadol (mg)	100 (75 – 200)	200 (100 - 200)	0.563						
Length of stay in PACU (min)	120 (90 - 130)	120 (120 - 150)	0.093						
PONV									
Yes (n)	10 (23.8)	6 (14.3)	0.697						
No (n)	32 (76.2)	36 (85.7)							
p < 0.05 is considered statistically significant.	p < 0.05 is considered statistically significant.								

* Described as median (1st Ouartile – 3rd Ouartile)

PACU, post anaesthesia care unit; PONV, post-operative nausea and vomiting.

Table 2: Differences in efficacy endpoints between groups.

Visual Analog pain scores were significantly lower in the Bupivacaine Group at the time of admission to the PACU (p=0.044) and remained low and unchanged (Friedman's p = 0.604), while the VAS scores peaked at 30 minutes in the Control Group and decreased gradually until the second hour (Friedman's p value < 0.001) as showed in Table 3 and Figure 1.

	GRO	P value*		
	Bupivacaine	Control		
VAS at the admission to PACU	2 (0 – 5)	4 (2 – 7)	0.044	
VAS at 30 min	2 (2 – 5)	4 (3 – 8)	0.026	
VAS at H1	2 (2 – 3)	3 (2 – 4)	NS	
VAS at H2	2 (2 – 3)	2 (0 – 2)	NS	
p-value**	0.604	<0.001		

(*) VAS values at the admission to PACU were compared using the Mann-Whitney U test.

(**) The Friedman nonparametric repeated measures ANOVA was used for each group: for each group, there are 4 measurements for VAS, namely at baseline, at 30 minutes, at 1 hour and at 2 hours. To account for the repeated within-subjects measurements and for the ordinal nature of VAS, the Friedman nonparametric repeated measures ANOVA was used for each group, testing whether all 4 VAS measurements are equal inside each group.

Table 3: Median VAS values at different times in PACU.



Figure 1: Visual Analog Pain scores (VAS) at different times in PACU. Boxplots of visual analog pain scores (VAS) at admission to the PACU, 30 min, 1 hour and 2 hours later. Significant difference was seen at the time of admission (p=0.044) and at 30 min (p=0.026) in favor of Bupivacaine. VAS median values remained stable low until H2 (Friedman's p-value = 0.604) in the Bupivacaine group. VAS median values decreased gradually in the control group (Friedman's p-value < 0.001)

The occurrence of nausea and vomiting in the postoperative period was similar in the two groups (Table 2). No postoperative complications were noted in this study. Monitored complications included surgical complications such as anastomotic leakage, fever, hemorrhage... as well as local anesthetics related toxicity including central nervous and cardiovascular system side effects".

All patients were discharged from hospital on postoperative day 2.

Discussion

The emergence of laparoscopic surgery has revolutionized patient care and lead to decreased postoperative pain scores and earlier recovery and hospital discharge.[10] Controlling the remaining pain is however crucial, especially in patients with obesity undergoing laparoscopic bariatric surgery.[3] In addition to discomfort at incision and surgical dissection sites, pain during laparoscopy has been linked to stretching of intraabdominal cavity, peritoneal inflammation, diaphragmatic irritation and retention of insufflated CO2 in the abdomen after surgery.[11,12] Kahokehr et al. evoked a "two-wound" model of pain after abdominal surgery, which includes a parietal and a visceral component, the latter being responsible of a diffuse, poorly localized and referred nociceptive sensation.[13] In addition, visceral irritation can generate autonomic reflexes resulting in nausea and vomiting.[14]

In theory, local anesthetics administered intraperitoneally allow reversible blocking of visceral afferent signaling. Moreover, via their anti-inflammatory properties, they might inhibit the proinflammatory cytokine cascade that modulates visceral afferents in the vagus nerve. [15] The application of local anesthetics in the peritoneal cavity has been the subject of many randomized clinical trials. Their effectiveness has been mainly demonstrated in laparoscopic cholecystectomy [7,8] and gynecologic procedures, [9] with an overall reduction in pain intensity scores and opioid consumption, a decreased incidence of referred shoulder pain, and a reduced hospital length of stay. Like cholecystectomies and gynecologic interventions, bariatric procedures are intraperitoneal, inducing presumably a similar visceral pain, and thus, might benefit from intraperitoneal analgesia. However, fewer studies have addressed to date the effectiveness of IPLA in the setting of laparoscopic bariatric surgery (Table 4).

The first study evaluating intraperitoneal bupivacaine in LRYGB (Laparoscopic Roux-en-Y Gastric Bypass) surgery was published in 2007 by Symons et al. [16] The authors found in their randomized placebo-controlled double-blinded trial of 133 patients a statistically significant decrease in oral hydrocodone/ acetaminophen use at day one, in favour of the bupivacaine group. Other outcomes variables including VAS rating, hydromorphone patient-controlled analgesia (PCA) use, hospital length of stay (LOS), antiemetic use, and pulmonary function evaluated with incentive spirometer volumes showed no differences [1]. Postoperative VAS scores were significantly decreased after IPLA instillation in seven subsequent trials, [17-24] but a reduced opioid use was noted in only four trials.[19,20,22,23] Hospital LOS was assessed in four trials with contradictory results.[16,17,20,22] In only one study, IPLA through its opioid-sparing effect and its antiinflammatory characteristics improved bowl function, and lead to an earlier fluids intake.[20] Enhanced respiratory effort after

surgery was reported in two studies, with results in favor of IPLA found in one [24]. Finally, one of the most common adverse effects of abdominal surgery under general anaesthesia is postoperative nausea and vomiting (PONV). Overall, six articles reported on PONV, with 2 studies showing a decreased incidence in the study group (IPLA), [17,20] while the other 4 demonstrated no difference between treatment and control groups. [16,21,24,25] A literature review of IPLA in bariatric surgery is shown in table 4.

In the present study, IPLA group (bupivacaine Group) had statistically significant less agitated emergence from general anaesthesia and a short-term reduction in VAS pain scores (at arrival to PACU and at 30 minutes). This calm emergence from anaesthesia might be of particular benefit in obese patients, it enhances patients' cooperation and help to maintain them in adequate position, allowing deep and regular respiration before and after extubation. Analgesia was then similar between the 2 groups (VAS at one hour and at 2 hours showed no statistically significant difference) but this analgesia was achieved in the control group using significantly

higher dose of morphine titration at PACU. Finally, other studied outcome variables (length of stay in PACU, total postoperative narcotics requirement, occurrence of nausea and vomiting) were comparable between the two studied groups.

The role of IPLA in laparoscopic bariatric surgery is still controversial. Reasons for these contradictory findings are not clear. This may be due to studies heterogeneity. Moreover, comparison between published trials is difficult due to disparities in surgical procedures (laparoscopic Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding), timing of infusion of local anesthetics (after pneumoperitoneum versus before wound closure), instillation sites, and type/dose/duration of local anesthetics (bypivacaine versus ropivacaine/ statim versus continuous administration). One should also note that only a small number of good quality trials have been conducted, and even those have insufficient methodologies such as small sample size and different outcomes and evaluation methodology (Table 4).

First Author	Year	Study type	Sample size	Procedure	Timing of infu- sion*	Infusion site	Injected solu- tion	VAS	Postop nar- cotic use	Postop re- spiratory function	Hospital LOS	PONV	Bowel function	Conclusions
Zheng [24]	2023	RCT	110	LSG	Post	Left crus dis- sected area	10 ml ropiva- caine 0.7%	Decreased within the first 24h after surgery	Decreased	Enhanced respira- tory effort from 6h after surgery	N/A	No difference	N/A	IP ropiv is safe, re- duces postoperative pain, and enhances the recovery of respiratory effort
Safari [23]	2020	RCT	106	LSG, MGB or LRYGB	Post	Site of anas- tomosis and the stitches on stomach and intestine	50 ml of 0.2% Bupivacaine (vs. saline 0.9%)	Decreased at 1, 4, 8, and 24 hours after surgery	Decreased	N/A	N/A	N/A	N/A	Intraperitoneal lavage with bupiva- caine is an effective approach to control postoperative pain in obese patients undergoing lapa- roscopic bariatric surgery
Alamdari [17]	2018	PCS	120	LSG	Post	Above the stomach, under the diaphrag, the bed of the spleen	0.25% bupiv 30 cm3 (vs. no IPLA)	Decreased	NA	N/A	Tend to decrease (p=0.06)	Decreased	N/A	IP bupiv is safe and effective in reducing postop pain, nausea, and vomiting
Ruiz-Tovar [20]	2016	RCT	110	LSG or LRYGB	Post	N/S	300 mg of ropiv in 200 mL (vs. NS)	Decreased	Decreased	N/A	Decreased	Tend to decrease (p=0.056)	earlier fluids in- take	IP ropiv is associ- ated with a reduc- tion in postop pain, morphine needs, earlier mobilization and fluids intake, and shorter LOS
Symons [16]	2007	RCT	133	LSG or LRYGB	Pre	Esophageal hiatus	0.5% bupiv 15 mL (vs. NS)	No difference	Decreased†	No differ- ence	No differ- ence	No difference	No dif- ference	IP bupiv can limit or prevent peritoneal irritation and reduce narcotic use.
Alkhamesi [18]	2008	RCT	50	LAGB or LRYGB	Post	N/S	Aerosolized 0.5% bupiv 10 mL (vs. NS)	Decreased at 24h	Decreased PCA usage (p = 0.52)	N/A	N/A	N/A	N/A	IP bupiv is safe use and helps reducing postop pain.
Cohen [22]	2013	RR	207	LRYGB‡	Post	N/S	of 0.375% bu- piv, continu- ous infusion for 48h (4 to 7 mL/h) (vs. no IPLA)	No difference	Decreased	N/A	No differ- ence	N/A	N/A	IP bupiv may decrease postop opi- oid, with no differ- ences in VAS scores or hospital LOS
Sherwin- ter[21]	2008	RCT	30	LAGB	Post	Site of maximal dissection	0.375% bupiv, continuous infusion for 48h (7.5 mg/h) § (vs. NS)	Decreased	No difference	N/A	N/A	No difference	N/A	Continuous IP bupiv reduces postop pain
Rodriguez [19]	2011	RCT	46	Laparoscopic bariatric surgery	Post	N/S	0.25% levo- bupiv 30 mL (vs. NS)	Decreased at 24h and 48h	Decreased at 24h and 48h	N/A	N/A	N/A	N/A	IP bupiv is as- sociated better postop pain control in the first 48h and reduces morphine consumption
Cottam [25]	2007	PCS	40	LRYGB	Post	Subxiphoid, radiating in both directions caudally	ON-Q bupiv pain pump (vs. no IPLA)	No difference	Decreased leaving the PACU to 6h	N/A	N/A	No difference	N/A	Continuous IP bupiv dramatically reduc- es the use of opioids postoperatively by eliminating PCA.

*Data are described in relation of infusion to surgical dissection.

†for oral as needed hydrocodone/acetaminophen after 12h, but not for IV PCA.

‡with some conversions to open surgery.

 $\$ and 0.5% bupiv 20 mL for of surgical wounds $\,$ infiltration (for both study groups).

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bupiv: bupivacaine; IP: intraperitoneal; PCS, prospective constructed study; PONV, Post-operative nausea and vomiting; RCT, randomized controlled trial; ropiv: ropivacaine; RR, retrospective review; LAGB: Laparoscopic adjustable gastric banding; LOS, length of stay; LRYGB: Laparoscopic Roux-en-Y gastric bypass; LSG: laparoscopic sleeve gastrectomy; MGB: Mini gastric bypass; N/A, not assessed; NS, normal saline; N/S, not specified; Postop, postoperative; VAS, visual analog scale

Table 4: Literature review of intraperitoneal local anesthetics (IPLA) infusion in bariatric surgery.

The technical methods for IPLA instillation might have influenced our study results. Some protocols administer the anesthetics on the site of maximal dissection, others on the esophageal hiatus, or above the stomach and under the diaphragm [16,17,21] In our study, bupivacaine was sprayed in the peritoneal cavity, over the diaphragmatic area, in the hepato-diaphragmatic and spleno-diaphragmatic spaces. The optimal timing of infusion of IPLA (before dissection or afterwards) is also a controversial issue. Many authors defend the pre-emptive IPLA as it allows blocking afferent pain signals before surgical trauma. [26,27] Pasqualucci et al. reported reduced glucose and cortisol levels when infusing IPLA immediately after peritoneal insufflation compared with IPLA done at the end of a cholecystectomy. [28] The most comprehensive literature review to date including 12 trials and 798 patients undergoing elective laparoscopic cholecystectomy randomized to different methods of IPLA instillation, concluded that the currently available evidence is inadequate to determine superiority of one instillation method. [29]

Bupivacaine is a local anesthetic of the amino-amid type, with a half-life of about 6 hours, and so should be the presumed duration of analgesia after its instillation intraperitoneally. This fact meets in part the results of our study, in terms of reduction in immediate postoperative VAS scores and Morphine needs, unfortunately limited to a short period of time. This leads to the assumption that continuous infusion of bupivacaine in the postoperative period could enable a better postoperative pain management, of longer duration, along with a more prominent opioid-sparing effect. Sherwinter et al. tested this hypothesis in 2008, and demonstrated that a continuous infusion of intraperitoneal bupivacaine 0.375% with an On-Q pump lead to a significant decrease in VAS until the end of the study (48 h), compared with the control group. [21] Moreover, Cohen et al. showed that a continuous infusion of bupivacaine lowered morphine needs over the entire postoperative period of 72

h. [22] In addition, Cottam et al. concluded that the use of bupivacaine pain pumps placed in the subxiphoid region dramatically reduces the use of opioids postoperatively in all bariatric patients by eliminating the use of PCA. [25] This change could potentially reduce the incidence of respiratory failure from over sedation, common in such population, while offering the same levels of pain control.

Finally, bupivacaine was mixed with 0.1 mg of epinephrine with the perspective of prolonging the effect of the IPLA. Although such outcome could not be demonstrated with this study design, Narchi et al. concluded that adding epinephrine to intraperitoneal lidocaine resulted in decreased serum levels of the drug and an extended duration of effect. [30] Another logical alternative for augmenting IPLA effect is lowering concentration and augmenting the volume of the infused solution, in order to maximize the covered surface area.

Although, opioids are largely used as major postoperative analgesics, their side effects limit their routine usage and motivate the search for a better analgesic method. A multimodal analgesic regimen is often required to assure an optimal postoperative pain management. In this study, paracetamol, nefopam and NSAIDs were associated with IPLA; in a previous study done by our team NSAIDs seemed to be associated with better analgesia without increased incidence of complications [31].

We recognize some limitations in our study. They include small number of participants and lack of randomization. The limited infusion time could also have influenced the results. Further confirmatory prospective randomized double-blinded studies are warranted to assess the safety and efficacy of IPLA, and should they be confirmed, continuous IPLA instillation for prolonged analgesia could be an option for future

studies; comparing IPLA to intraoperative IV lidocaïne infusion could be another one [32].

Conclusion

Intraperitoneal instillation of bupivacaine following laparoscopic sleeve gastrectomy seems to improve the quality of emergence from anesthesia and reduce opioid consumption in PACU together with VAS scores until one hour postoperatively. However, its effect on reducing postoperative narcotics requirements and the length of hospital stay showed no significant difference. While the results of the current trial point toward IPLA utility in laparoscopic bariatric surgery, more randomized controlled trials are needed to better assess its efficacy and safety in these settings. At a further stage, studies evaluating continuous instillation of intraperitoneal local anesthetics would be interesting in this context.

References

- Ng M, Fleming T, Robinson M, Thomson B, Graetz N et al. (2014) Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 384(9945): 766-81.
- Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, et al. (2004) Bariatric surgery: a systematic review and meta-analysis. JAMA. 292(14): 1724-37.
- Adolfo Z. Fernandez J. (2004) Multivariate Analysis of Risk Factors for Death Following Gastric Bypass for Treatment of Morbid Obesity. Ann Surg 239(5): 698-702.
- De Boer HD, Detriche O, Forget P (2017) Opioid-related side effects: Postoperative ileus, urinary retention, nausea and vomiting, and shivering. A review of the literature. Best Pract Res Clin Anaesthesiol 31(4): 499-504.
- Nagappa M, Weingarten TN, Montandon G, Sprung J, Chung F (2017) Opioids, respiratory depression, and sleep-disordered breathing. Best Pract Res Clin Anaesthesiol 31(4): 469-485.
- (2012) American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology 116(2): 248-273.
- Boddy AP, Mehta S, Rhodes M (2006) The Effect of Intraperitoneal Local Anesthesia in Laparoscopic Cholecystectomy: A Systematic Review and Meta-Analysis: Anesth Analg. 103(3): 682-8.
- Choi GJ, Kang H, Baek CW, Jung YH, Kim DR (2015) Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy. World J Gastroenterol. 21(47): 13386-13395.
- Marks JL, Ata B, Tulandi T (2012) Systematic Review and Metaanalysis of Intraperitoneal Instillation of Local Anesthetics for Reduction of Pain After Gynecologic Laparoscopy. J Minim Invasive Gynecol 19(5): 545–53.
- Carr BM, Lyon JA, Romeiser J, Talamini M, Shroyer ALW (2018) Laparoscopic versus open surgery: a systematic review evaluating Cochrane systematic reviews. Surg Endosc. 24; 1-17.
- 11. Jackson SA, Laurence AS, Hill JC (1996) Does post-laparoscopy pain relate to residual carbon dioxide? Anaesthesia 51(5): 485-7.

- 12. Joris J, Thiry E, Paris P, Weerts J, Lamy M (1995) Pain after laparoscopic cho lecystectomy: characteristics and effect of intraperitoneal bupivacaine. Anesth Analg 81(2): 379-84.
- Kahokehr A, Sammour T, Zargar Shoshtari K, Taylor M, Hill AG (2011) Intraperitoneal local anesthetic improves recovery after colon resection: a double-blinded randomized controlled trial. Ann Surg 254(1): 28-38.
- 14. Cervero F, Laird JM (1999) Visceral pain. Lancet Lond Engl 353(9170): 2145-8.
- Martinsson T, Oda T, Fernvik E, Roempke K, Dalsgaard CJ et al. (1997) Ropivacaine inhibits leukocyte rolling, adhesion and CD11b/ CD18 expression. J Pharmacol Exp Ther. 283(1): 59-65.
- Symons JL, Kemmeter PR, Davis AT, Foote JA, Baker RS, et al. (2007) A Double-Blinded, Prospective Randomized Controlled Trial of Intraperitoneal Bupivacaine in Laparoscopic Roux-en-Y Gastric Bypass. J Am Coll Surg 204(3): 392-8.
- Alamdari NM, Bakhtiyari M, Gholizadeh B, Shariati C (2018) Analgesic Effect of Intraperitoneal Bupivacaine Hydrochloride After Laparoscopic Sleeve Gastrectomy: a Randomized Clinical Trial. J Gastrointest Surg 22(3): 396-401.
- Alkhamesi NA, Kane JM, Guske PJ, Wallace JW, Rantis PC (2008) Intraperitoneal aerosolization of bupivacaine is a safe and effective method in controlling postoperative pain in laparoscopic Roux-en-Y gastric bypass. J Pain Res 1: 9.
- Rodriguez LM, Barreiro PC, Gonzalez CA, Sanduende OY, Taboada BMR et al. (2011) Intraperitoneal analgesia compared with levobupivacaine 0.25% versus saline in laparoscopic bariatric surgery: 14AP5-11. Eur J Anaesthesiol EJA 28: 203.
- Ruiz-Tovar J, Gonzalez J, Garcia A, Cruz C, Rivas S, et al. (2016) Intraperitoneal Ropivacaine Irrigation in Patients Undergoing Bariatric Surgery: a Prospective Randomized Clinical Trial. Obes Surg 26(11): 2616-21.
- Sherwinter DA, Ghaznavi AM, Spinner D, Savel RH, Macura JM, et al. (2008) Continuous Infusion of Intraperitoneal Bupivacaine after Laparoscopic Surgery: A Randomized Controlled Trial. Obes Surg 18(12): 1581-6.
- 22. Cohen AR, Smith AN, Henriksen BS (2013) Postoperative Opioid Requirements Following Roux-en-Y Gastric Bypass in Patients Receiving Continuous Bupivacaine Through a Pump System: A Retrospective Review. Hosp Pharm 48(6): 479.
- Safari S, Rokhtabnak F, Djalali Motlagh S, Ghanbari Garkani M, Pournajafian A (2020) Effect of intraperitoneal bupivacaine on postoperative pain in laparoscopic bariatric surgeries. Surg Obes Relat Dis Off J Am Soc Bariatr Surg 16(2): 299-305.
- Zheng LQ, Kosai NR, Ani MFC, Maaya M (2023) The Impact of Laparoscopic Intraperitoneal Instillation of Ropivacaine in Enhancing Respiratory Recovery and Reducing Acute Postoperative Pain in Laparoscopic Sleeve Gastrectomy: a Double-Blinded Randomised Control; RELiEVE Trial. Obes Surg 33(10): 3141-6.
- Cottam DR, Fisher B, Atkinson J, Link D, Volk P, et al. (2007) A randomized trial of bupivicaine pain pumps to eliminate the need for patient controlled analgesia pumps in primary laparoscopic Roux-en-Y gastric bypass. Obes Surg 17(5): 595-600.
- Gupta A. (2005) Local anaesthesia for pain relief after laparoscopic cholecystectomy—a systematic review. Best Pract Res Clin Anaesthesiol 19(2): 275-92.
- 27. Pappas-Gogos G, Tsimogiannis KE, Zikos N, Nikas K, Manataki A, et al. (2008) Preincisional and intraperitoneal ropivacaine plus normal saline infusion for postoperative pain relief after laparoscopic cholecystectomy: a randomized double-blind controlled trial. Surg Endosc 22(9): 2036-45.

- Pasqualucci A, Contardo R, Da Broi U, Colo F, Terrosu G, et al. (1994) The effects of intraperitoneal local anesthetic on analgesic requirements and endocrine response after laparoscopic cholecystectomy: a randomized double-blind controlled study. J Laparoendosc Surg 4(6): 405-12.
- Abou Zeid H, Kallab R, Najm MA, Jabbour H, Noun R, et al. (2019) Safety and Efficacy of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Used for Analgesia After Bariatric Surgery: A Retrospective Case-Control Study. Obes Surg 29(3): 911-6.
- Sakata RK, De Lima RC, Valadão JA, Leal PC, Moura EC, et al. (2020) Randomized, Double-Blind Study of the Effect of Intraoperative Intravenous Lidocaine on the Opioid Consumption and Criteria for Hospital Discharge After Bariatric Surgery. Obes Surg 30(4): 1189-93.
- Gurusamy KS, Nagendran M, Toon CD, Guerrini GP, Zinnuroglu M, et al. (2014) Methods of intraperitoneal local anaesthetic instillation for laparoscopic cholecystectomy. Cochrane Database Syst Rev 25;(3): CD009060.
- Narchi P, Benhamou D, Bouaziz H, Fernandez H, Mazoit JX. (1992) Serum concentrations of local anaesthetics following intraperitoneal administration during laparoscopy. Eur J Clin Pharmacol 42(2): 223-5.