ORIGINAL ARTICLE

Factors associated to postoperative pain in the post-anesthetic care unit in patients submitted to laparoscopic gastroplasty*

Fatores associados à dor pós-operatória na recuperação pós-anestésica em pacientes submetidos à gastroplastia laparoscópica

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ABSTRACT

BACKGROUND AND OBJECTIVES: Postoperative pain in obese patients is a noxious event for their recovery delaying hospital discharge and increasing the chance of complications. This study aimed at determining pain frequency in the post-anesthetic care unit and at investigating factors associated to moderate to severe pain in obese patients submitted to gastroplasty, relating them to potential complications.

METHODS: This is an observational and prospective study including 84 patients submitted to general anesthesia with sevoflurane for laparoscopic gastroplasty. Patients were evaluated in the post-anesthetic care unit for pain intensity by the verbal and numerical scale (Ramsay scale), presence of nausea, vomiting and respiratory complications. Logistic regression model was used to determine pain-related independent variables.

RESULTS: There has been no pain at admission to the post-anesthetic care unit in 61.63% of patients. In the multivariate analysis, fentanyl as compared to sufentanil was the only independent factor associated to pain (OR 3.07 – IC95% 1.17 – 6.4). There has been no difference between the type of opioid used and the presence of nausea and vomiting (p>0.05). Ramsay scale scores were not different between opioids used in the intraoperative period (p>0.05).

CONCLUSION: The only independent factor associated to pain in the post-anesthetic care unit was the type of opioid used for anesthetic induction. Postoperative pain is still a frequent event affecting most patients, and analgesic protocols have to be implemented to minimize the effects that undertreated pain may induce.

Keywords: Gastroplasty, Obesity, Pain, Risk.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor pós-operatória em pacientes obesos é um evento prejudicial para sua recuperação, retardando a alta e aumentando a chance de complicações. O objetivo deste estudo foi determinar a frequência de dor na sala de recuperação pós-anestésica e averiguar os fatores associados à ocorrência de dor moderada ou intensa em obesos submetidos a gastroplastia, relacionando-os a possíveis complicações.

MÉTODOS: Estudo observacional prospectivo incluindo 84 pacientes submetidos a anestesia geral com sevoflurano para gastroplastia laparoscópica. Na sala de recuperação pós-anestésica, os pacientes foram avaliados quanto à intensidade da dor pela escala numérica e verbal, sedação (escala de Ramsay), ocorrência de náuseas, vômitos e complicações respiratórias. O modelo de regressão logística foi utilizado para determinar as variáveis independentes associadas à dor.

RESULTADOS: Na sala de recuperação pós-anestésica, a ausência de dor na admissão ocorreu em 61,63% dos pacientes. Na análise multivariada, o uso do opioide fentanil em comparação ao sufentanil foi o único fator independentemente associado à dor (RR 3,07 – IC95% 1,17-6,4). Não houve diferença entre o tipo de opioide utilizado e a ocorrência de náuseas e vômitos (p>0,05). Os escores da escala de Ramsay não diferiram entre os tipos de opioides utilizados no intraoperatório (p>0,05).

CONCLUSÃO: O único fator independentemente associado à dor na sala de recuperação pós-anestésica foi o tipo de opioide utilizado na indução anestésica. A dor pós-operatória ainda é um evento frequente que acomete a maioria dos pacientes e protocolos de analgesia precisam ser implementados para minimizar os efeitos que a dor subtratada pode causar.

Descritores: Dor, Gastroplastia, Obesidade, Risco.

INTRODUCTION

For obese patients, the aim of adequately managing postoperative pain (POP) is providing comfort, early mobilization and improving respiratory function without inducing inadequate sedation and respiratory problems. Obesity pathophysiology, comorbidities and the high prevalence of obstructive sleep apnea in these patients make critical the safe analgesic therapy man-

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agement. This way, pain control after gastroplasty is a major challenge. Notwithstanding several reviews on anesthesia and analgesia for obese patients, there are few evidence-based recommendations.

Anesthesia for morbidly obese patients requires special care, especially with regard to obese patients' physiology and anesthetics pharmacokinetics and pharmacodynamics. In laparoscopic gastroplasty, metabolic aggression and responses of the acute stage to surgical stress are significantly lower. However, postoperative pain, nausea and vomiting are highly incident and contribute for further morbidity and patients' discomfort.

In morbidly obese patients submitted to pneumoperitoneum, diaphragmatic peritoneum inflammation caused by the chemical nature of carbon dioxide and by marked stretching of diaphragmatic muscle fibers by high pressure is a major cause of pain immediately after anesthetic recovery. After laparoscopy, many patients, due to pain, may remain with limited and superficial inbreathing. This leads to decreased tidal volume and perpetuates the maintenance of intraoperative atelectasy determining oxygen desaturation, late post-anesthetic care unit (PACU) discharge and discomfort[1-3].

POP control in the PACU is critical for respiratory system adjustment after pneumoperitoneum deflation and also for a more comfortable, safer and earlier recovery. Anesthetic technique and type of opioid may be important factors for better POP control. However, adverse effects of aggressive analgesic therapy may contribute to increase postoperative complications. Sufentanil has better analgesic potency as compared to fentanyl, but it is not known whether the latter associated to morphine for postoperative analgesia is able to adequately control post-gastroplasty pain in obese patients.

In addition, sufentanil, due to its analgesic potency, may be associated to higher incidence of PACU adverse effects, such as deep sedation, hypoxemia, respiratory depression and nausea. Factors such as gender, age and surgical duration are also possible factors influencing PACU pain control[3]. So, this study aimed at determining pain frequency in the PACU and at evaluating factors associated to moderate or severe pain in obese patients submitted to gastroplasty, relating them to potential complications.

METHODS

This was an observational, analytical and prospective study carried out by the Department of Anesthesiology, Hospital São Luiz/Clinical Anesthesiology CMA (ITAIM unit), São Paulo-SP.

Sample was made up of 84 sequential patients receiving general anesthesia for laparoscopic gastroplasty from October 2012 to January 2013. All patients were evaluated during preanesthetic consultation, moment when data related to weight (kg) and height (cm) were collected. Body mass index (BMI) was calculated dividing weight in kilograms by the square of height in meters according to World Health Organization (WHO) definitions. BMI was classified in obesity (BMI≤40 kg/m^2) and morbid obesity (BMI>40 kg/m^2).

Before being referred to the operating center, all patients were premedicated with intramuscular midazolam (7.5mg). Anesthetic technique was general inhalational anesthesia with sevoflurane. Before the procedure, all patients received parecoxib (40mg), pantoprazol (40mg) and dexamethasone (0.1mg.kg^{-1}) of corrected body weight (CBW) to the maximum of 10mg.

Monitoring in the operating room consisted of: electrocardioscope, pulse oximeter, non-invasive automatic blood pressure with adequate cuff and coverage of 75 to 100% of the arm, and capnograph with inspiratory and expiratory gases analyzer. All patients received pharmacological and mechanical prevention against venous thromboembolism during the procedure and in the postoperative period (low molecular weight heparin, compression stockings and pneumatic bag). Anesthesia was induced after peripheral venous puncture and oxygenation with 100% O_2.

Controlled ventilation was achieved with closed system and 2L.min^{-1}, tidal volume of 8 to 10mL.kg^{-1} (CBW), FiO_2 0.5 and enough respiratory rate to maintain end tidal CO_2 around 35 to 40mmHg. Opioid for induction was chosen according to anesthesiologists' preference and was not influenced by the study protocol. Opioid doses for induction were determined in 1µg.kg^{-1} (real weight) for sufentanil or 5µg.kg^{-1} (real weight) for fentanyl. Propofol (2-3µg.kg^{-1}) (real weight) and neuromuscular blocker chosen by the assistant anesthesiologist were also used for anesthetic induction.

During surgery, remifentanil continuous infusion was used in doses enough to maintain adequate and tailored anesthesia for each case (0.1 to 0.3µg.kg.min^{-1}) without bolus of other opioids used for anesthetic induction. Sevoflurane at 2% was administered in mixture of oxygen and compressed air (1:1). Close to procedure completion (20 minutes before), all patients received dipirone (2000mg), dihydrate ondansentron hydrochloride (0.1mg.kg^{-1}) from CBW to the dose of 8mg, and morphine in the dose of 50µg.kg^{-1} of CBW. Before anesthetic induction all patients were previously hydrated with 10mL.kg^{-1} lactated Ringer's solution. In the intraoperative period, fluid infusion was 5.0mL.kg^{-1}.h.

In PACU, all patients were monitored with electrocardioscope, pulse oximeter and non-invasive automatic blood pressure. Patients were evaluated in four different moments with 15-minute intervals: M1 – PACU admission; M2 – 15 min after admission; M3 – 30 min after admission and M4 – 45 min after admission. In all moments, patients' pain intensity was evaluated by the verbal numerical scale. In all moments, nausea and vomiting, pulse oximetry, blood pressure, heart rate and urinary output were evaluated. All patients were able to answer the question about their pain in any evaluated moment.

At PACU admission, patients were evaluated for the need for supplementary oxygen. M1 has evaluated pulse oximetry without supplementary oxygen. All patients with oximetry below 93% have received supplementary oxygen by facial mask with oxygen flow (5L.min^{-1}). Rescue morphine dose in

case of pain in PACU was 30-50μg.kg^{-1}, according to PACU assistant anesthesiologist evaluation. Patients with nausea and vomiting in the PACU have received 50mg dimenhydrinate.

Still in the intraoperative period, surgical duration was evaluated considering the period from incision until procedure completion and the type of surgical technique (gastroplasty – "Sleeve" technique or gastroplasty with "Roux-en-Y" intestinal bypass). The study has not included chronic opioid users, reoperations, drug addicts, surgeries combined with other surgical procedures in addition to gastroplasty, other surgical techniques different from those specified and emergency surgeries.

Statistical analysis used the Stata/SE 9.0 for Windows (Stata Corporation, College Station, Texas, USA) computer program. Categorical variables were presented as absolute and percentage values, and numerical variables were represented as mean and standard deviation or median and percentiles, when appropriate. Histograms and Shapiro-Wilk test were used to verify data distribution symmetry. Comparisons between groups by pain scores and Ramsay scale were performed by non-parametric Kruskal-Wallis test for continuous variables, followed by Dun test of multiple posterior comparisons if p value was below 0.05.

Chi-square test was used for categorical variables and Chi-square partition was adopted with $p<0.05$. Mann-Whitney test was used to compare oxygen saturation by pulse oximetry per type of opioid used for anesthetic induction in analyzed moments. Logistic Regression model was used to adjust risks according to misleading factors. For such, independent variables, which in the univariate model were associated to the dependent variable pain in PACU ($p<0.20$) were inserted in the multivariate model. Dependent variable pain in PACU was considered whenever patients referred pain score above 3 in the numerical scale. Logistic regression was performed with the stepwise with forward elimination technique. In the final adjusted model, significance criteria was $p<0.05$ and confidence interval was 95%.

This study was approved by the Ethics Committee/CMA process 002/2012. All participants have signed the Free and Informed Consent Term (FICT).

RESULTS

Patients mean age was 35.54±10.31 years. Most were females (73.26%). Mean BMI was 41.95±5.13kg/m^2. Most patients have received sufentanil for anesthetic induction (55.81%). Mean surgical duration was 121.01±41.36 min. "Roux-en-Y" technique was used in 87.21% of patients and "Sleeve" technique was used in 12.79%.

No pain at PACU admission was observed in 61.63% of patients. In M3 and M4 there have been more patients with mild pain as compared to M1 and M2. Other verbal scale categories did not differ among studied moments (Table 1). There has been no statistically significant difference in pain score medians by the numerical scale in all studied moments (Figure 1).

Table 1. Relation between verbal pain scale and evaluation moments in the post-anesthetic care unit (PACU)

Verbal scale	Moments (PACU)			
	M1 – Admission	M2 - 15 min	M3 – 30 min	M4 – 45min
No pain	53 (61.63)	43(50)	35(40.70)	38(44.19)
Mild	03 (3.49)	08(9.3)	16(18.70)*	17(19.77)*
Moderate	23(26.74)	12(31.41)	23(26.75)	23(26.74)
Severe	07(8.14)	08(9.3)	12(13.96)	08(9.30)

Values in absolute figures (%). Chi-square test (p=0.01). *Partition test: M3 and M4 > M1 and M2 for mild pain.

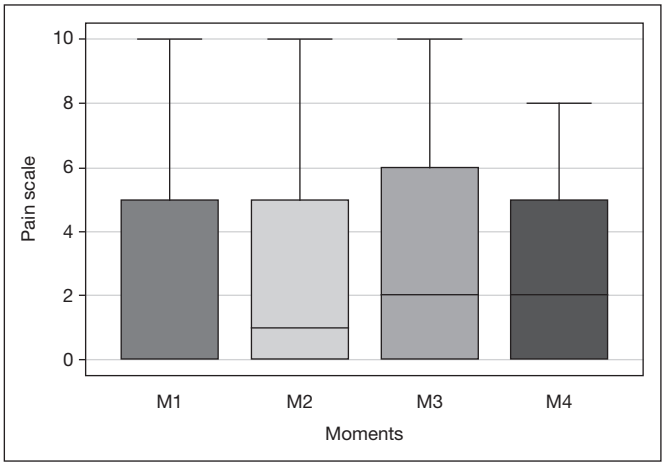

Figure 1. Pain score (numerical scale) in studied moments

M1 – Admission; M2-15min; M3-30 min; M4-45 min. Values in medians and percentiles (25-75%). Kruskal-Wallis analysis of variance: p=0.22.

The frequency of moderate to severe pain in some PACU moment has corresponded to 56.98% of analyzed patients. In univariate analysis, gender and type of intraoperative opioid were factors associated to PACU pain (Table 2). In multivariate analysis, fentanyl as compared to sufentanil was the only independent factor associated to PACU pain (Table 3). Morphine rescue was used for 45.35% of PACU patients, being that 25.53% of patients with pain scores above 3 have not received morphine rescue.

The highest frequency of PONV was observed at PACU admission (11.63%), without difference among analyzed moments. There has been statistically significant difference in Ramsay scale scores in analyzed moments, being that patients were more alert and cooperative in the last two PACU moments (Table 4). There has been no statistically significant relationship between pain (score higher than 3) and incidence of PONV in any analyzed moment. There has been no difference between the type of opioid and the presence of PONV ($p>0.05$). Ramsay scale scores in the PACU have not differed with regard to type of intraoperative opioids ($p>0.05$).

Pulse oximetry frequency below 90% in patients with oxygen supplementation was 22.09% with no relationship with the type of intraoperative opioid in any moment ($p<0.05$) (Fig-

Table 2. Factors associated to moderate to severe pain in the post-anesthetic care unit (PACU)

Dependent variable	PACU moderate to severe pain			
	f(%)	RR	CI 95%	P value
Gender				0,04
Male	9 (18.37)	1.0		
Female	40 (81.63)	2.7	(1.01-7.22)	
Morbid obesity				0.98
No	16(32.65)	1.0		
Yes	33(67.35)	0.99	(0.39-2.46)	
Age				0.69
<30 years	17(34.69)	1.0		
30 to 39 years	19(38.78)	0.67	(0.23-1.92)	
40 to 49 years	8(16.33)	0.60	(0.16-2.21)	
>50 to 59 years	5(10.20)	0.44	(0.10-1.85)	
Surgery duration				0.48
<120 min	34(69.39)	1.0		
≥120 min	15(30.61)	1.02	(0.49-1.72)	
Surgical technique				0.07
"Roux-en-Y"	40(81.63)	1.0		
"Sleeve"	9(18.37)	0.93	(0.79-2.19)	
IO Opioid				0.005
Sufentanil	21(42.86)	1.0		
Fentanyl	28(57.14)	3.6	(1.43-5.6)	

Univariate analysis, IO: intraoperative.

Table 3. Factors associated to moderate to severe pain in the post-anesthetic care unit (PACU)

Dependent variable	PACU moderate to severe pain		
	Adjusted RR	CI 95%	p
Gender			0.19
Male	1.0		
Female	1.98	(0.69-5.62)	
Surgical technique			0.12
Bypass	1.0		
Sleeve	1.07	(0.70-3.96)	
Intraoperative opioid			0.02
Sufentanil	1.0		
Fentanyl	3.07	(1.17-6.4)	

Multivariate analysis.

ure 2). Pulse oximetry below 80% with oxygen supplementation was observed in 0.01% of patients (1 morbidly obese patient who received sufentanil citrate for induction), with improvement after ventilation under mask with 100% oxygen and respiratory physiotherapy in the PACU. No patient was referred to the intensive care unit or presented surgical complications while staying in the PACU. Mean recovery time in PACU was 78±24.9 min and has not differed with regard to opioids used for anesthetic induction.

Table 4. Ramsay scale and incidence of postoperative nausea and vomiting in the post-anesthetic care unit (PACU)

	Moments (PACU)			
	M1 – Admission	M2 - 15 min	M3 – 30 min	M4 – 45min
Ramsay scale *				
Median	3	3	2	2
Percentiles (25-75%)	(3-3)	(2-3)	(2-3)	(2-3)
PONV				
No	76(88.37)	80(93.2)	82(95.35)	83(96.51)
Yes	10(11.63)	6(6.98)	4(4.65)	3(3.49)

* Kruskal-Wallis analysis of variance: p=0.01 – after Dunn test: m1 > M3, M1 > M4m M2 > M4. PONV: postoperative nausea and vomiting. Values in absolute figures (%). Chi-square: p=0.14.

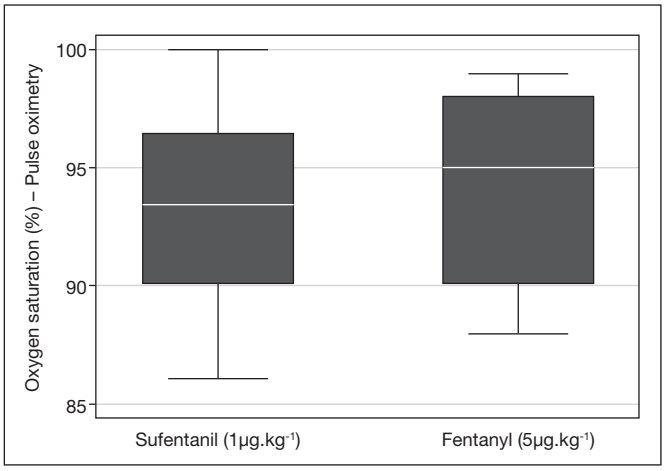

Figure 2. Oxygen saturation by pulse oximetry at post-anesthetic care unit admission, by type of opioid used for anesthetic induction.
Values in median and 25-75% percentiles. Mann-Whitney test: p=0.28.

DISCUSSION

This study has adopted multimodal analgesia with non-steroid anti-inflammatory drugs and opioids. This practice is effective and safe. However, it is difficult to standardize an analgesic protocol due to the uniqueness of pain management in obese patients[3,5]. The polymorphism of the gene involved in opioids pharmacokinetics and pharmacodynamics may be a factor justifying a tailored pain therapy and may explain different pain scores in obese patients receiving the same analgesic therapy.

A study[6] has identified 3 types of polymorphisms in the mu opioid receptor without difference between genders. In our study, patients anesthetized with fentanyl citrate had higher pain scores even receiving morphine at surgery completion. Patients receiving sufentanil citrate had lower pain scores. However, there was still a high incidence of pain regardless of the choice of opioids. Due to this tailored response to opioids, a systematized and effective evaluation is critical in the PACU to early identify patients more sensitive to pain, thus

avoiding analgesic overdose for those with more effective response to opioids.

Although results have shown a higher incidence of pain among females, this was not confirmed by the multivariate analysis, confirming a study[6] where it does not seem to be a predominance of polymorphism variation of opioid receptors by gender.

Some studies have shown that genotype changes may explain the less effective analgesic effect of fentanyl in some patients. Patients with allele G in OPRM1 gene have less analgesic effectiveness with fentanyl as compared to those who have the allele A[7]. However, the frequency of this genotype has not been determined in general population and its relationship with the use of sufentanil has not been studied. In the future, genetic sequencing may be a major tool to better tailor analgesic therapy for surgical patients.

The incidence of POP immediately after gastroplasty was similar to that found in case series with surgical patients in the first postoperative day (approximately 54% in the first postoperative day)[8]. However, in the PACU, the frequency of rescue morphine was below expected for the incidence of pain that has been observed. Approximately one fourth of patients with moderate to severe pain have not received rescue morphine. This shows that pain rescue for gastroplasty in the PACU has to be improved with the adoption of a more effective system to evaluate and manage pain.

Studies with non obese patients submitted to laparoscopic procedures have shown that age, gender and marital status are more associated to further need for analgesics for painful patients. However, we have not found association between age, gender and severe pain scores (numerical scale above 7) in the postoperative period[9].

Our results have shown a low incidence of respiratory complications, below of what was found in the literature. This low incidence may be justified by the ability of the teams in performing gastroplasty in a reference center and with shorter surgical duration, which assures lower morbidity of laparoscopic procedures in obese patients[10]. In our sample, surgical duration was predominantly 120 minutes with standard deviation of 40 minutes, not being related to PACU postoperative pain.

Sufentanil, synthetic and highly liposoluble opioid, is approximately 10 times more potent than fentanyl. Its fast distribution half-life (T1/2) is 1.4 minutes producing fast induction and being rapidly excreted by the body (T/12) in 2.7 hours. With regard to plasma excretion half-life (T½ß) sufentanil has an intermediate position (148-164 min) between fentanyl (185-219 min) and alfentanil (70-98 min). Thanks to higher binding rate with plasma proteins, it has lower distribution volume as compared to fentanyl and its plasma clearance is the highest among opioids[11]. It provides deep analgesia and lower hormonal response to stress, however it may induce respiratory depression, bradycardia, histamine release, muscle stiffness, pruritus, urinary retention, decreased bowel movements, nausea and vomiting[12].

Sufentanil analgesic potential is higher than fentanyl, but there is no evidence in the literature contemplating which induction opioid would bring more benefits in terms of postoperative analgesia and, at the same time, without increasing the incidence of adverse events, such as respiratory depression, hypoxemia and sleepiness in obese patients. In our study, sufentanil has shown better profile to control PACU pain and has not increased the incidence of adverse events. Oxygen desaturation, hypoxemia, PONV and sedation scale were not different between both opioids. Even in morbidly obese patients, sufentanil was safe with regard to respiratory complications and was effective to control pain.

There has been one case of transient respiratory depression in a patient receiving sufentanil. This complication was easily resolved with ventilation under facial mask with 100% O_2, with no need for reversion with naloxone. However, one has to be prepared for this type of intercurrence, especially when the intraoperative opioid is of high potency and intermediate duration, especially in morbidly obese patients. Despite this case, the incidence of respiratory complications with sufentanil is low[13].

Better postoperative analgesic quality with lower analgesic consumption in the postoperative period provided by sufentanil as compared to other opioids has assured better pain control with the use of this drug. And notwithstanding sufentanil potential to prolong emergence and induce sleepiness and sedation during anesthetic recovery, the low consumption of morphine rescue in the PACU due to good pain control has allowed recovery time to be similar to fentanyl with further comfort to patients[12,14].

In addition, in a study with patients submitted to cardiac surgery, even when fentanyl residual plasma concentration was within the therapeutic range in the first postoperative day, there is no correlation with pain scales. This might be due to individual pain intensity variation and response to opioids, which is especially true with lower analgesic potency opioids such as fentanyl[15,16].

A limitation of this study was opioid dose restriction to standardize the approach and the analysis. Higher fentanyl doses not routinely used in short lasting anesthesia for gastroplasty in this institution could lead to decreased pain scores. However, such opioid, for having a pharmacological profile with higher distribution volume and longer excretion half-life could increase the risk of complications in morbidly obese patients even after PACU discharge, when patients would no longer be under direct care of the anesthetic team.

CONCLUSION

The only independent factor associated to PACU pain in patients submitted to gastroplasty was the type of opioid used for anesthetic induction. Fentanyl citrate has increased the chance of PACU pain as compared to sufentanil citrate as anesthetic induction opioid. Sufentanil as anesthetic induction opioid in morbidly obese patients was not associated to respiratory complications, to decreased oxygen saturation in pulse oximetry and to the incidence of PONV in the PACU. Postoperative pain is still a frequent event affecting most patients and analgesic protocols have to be implemented to minimize the effects of undertreated pain.

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