DOI: 10.1590/0100-6991e-20181885

Anesthetic therapy for acute pain relief after laparoscopic cholecystectomy: systematic review.

Terapêutica anestésica para o alívio da dor aguda pós-colecistectomia videolaparoscópica: revisão sistemática.

Renato Ribeiro de Jesus[1]; Adebaldo Maia Leite[1]; Simone Soares Leite[1]; Márcio Carneiro Vieira[1]; Nivaldo Ribeiro Villela[1,2]

ABSTRACT

Inappropriate therapy of postoperative pain in laparoscopic cholecystectomy may lead to late mobilization, patient dissatisfaction, delayed hospital discharge, and chronic pain development. Our objective was to identify the best therapeutic strategy available to the anesthesiologist for the acute postoperative pain of patients submitted to elective laparoscopic cholecystectomy. This is a systematic review that included 36 complete articles indexed in the Medline, Scopus, Web of Science and LILACS databases, with a five-year time cut (2012 to 2016), resulting from controlled and randomized studies that were submitted to qualitative analysis. In a proposal for multimodal analgesia, it is important to consider the contraindications, adverse effects, dose and optimal timing of interventions. Non-opioid drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs)/cyclooxygenase-2 (COX-2) inhibitors, gabapentin/pregabalin, N-methyl-D-aspartate (NMDA) receptor antagonists, and others. Opioids may be used at low doses associated with multimodal therapy or are restricted to cases where non-opioid multimodal analgesia is insufficient. We conclude that there is no consensus as to the best analgesic strategy to be implemented in the acute postoperative pain of laparoscopic cholecystectomy, which requires its applicability in an individualized way, based on the scientific evidence found in the literature. As contribution to medical learning and practice, we point out the theoretical enrichment of the analgesic drug options available for the therapy of postoperative pain in patients submitted to elective laparoscopic cholecystectomy, and alert the team to consider the adverse effects of the interventions implemented.

Keywords: Pain, Postoperative. Cholecystectomy, Laparoscopic. Analgesia. Review.

INTRODUCTION

The inadequate treatment of postoperative pain in laparoscopic cholecystectomy (LC) can lead to negative consequences, such as late mobilization, with consequent delay in discharge, development of chronic pain and increased treatment costs[1]. In recent years, multimodal analgesia has been recommended to combine additive and synergistic effects of different analgesics, with less adverse effects and more effective analgesia[1-3]. Systematic reviews of the literature conducted in 2006 and in 2011 highlighted multimodal interventions to relieve pain in LC. One study focused on the preoperative administration of intravenous (IV) dexamethasone (8mg), non-steroidal anti-inflammatory or COX-2 inhibitors and topical bupivacaine, intraoperative use of antiemetic and intraperitoneal bupivacaine in the establishment of pneumoperitoneum and drains[4]. The other study recommended a single preoperative dose of dexamethasone, local anesthetics in the incisions (at the beginning or at the end of the surgery, depending on the anesthesiologist's preference), and continued treatment with non-steroidal anti-inflammatory drugs (NSAIDs)/COX-2 during the first three to four days, reserving the opioids for when other analgesic techniques fail[5].

The objective was to identify the best therapeutic strategy available to the anesthesiologist for treatment of acute postoperative pain of patients submitted to elective laparoscopic cholecystectomy.

METHODS

We carried out the study in June and July 2016 by the main investigator plus one independent

1 - Federal University of Rio de Janeiro, Department of Surgery, Anesthesiology Service, Rio de Janeiro, RJ, Brazil. 2 - State University of Rio de Janeiro, Department of General Surgery, Anesthesiology Service, Center for Teaching and Training in Pain, Rio de Janeiro, RJ, Brazil.

reviewer, following the steps for the design of a systematic review[6]. For the search of the scientific productions, we used the following combination of "Descritores em Ciências da Saúde" (DeCS) and Medical Subject Headings (MeSH) terms, in English, Portuguese and Spanish: "postoperative pain" ("dor pós-operatória", "dolor postoperatorio") AND "laparoscopic cholecystectomy" ("colecistectomia laparoscópica", "colecistectomía laparoscópica") AND analgesia.

The inclusion criteria were papers indexed in the Medical Literature Analysis and Retrieval System Online (Medline), Scopus, Web of Science and Latin American and Caribbean Literature in Health Sciences (LILACS) databases, in the 2012 to 2016 five-year interval, published in Portuguese, English or Spanish, resulting from randomized controlled studies. In addition, we chose studies with adults/elders between 18 and 65 years of age, non-pregnant, submitted to elective laparoscopic cholecystectomy. We excluded works on surgical considerations (instillation of local anesthetics, amount of infused carbon dioxide, etc.), open cholecystectomy, literature reviews, and case reports.

There were 800 articles, 136 in Medline, 306 in Scopus, 349 in Web of Science and nine in LILACS. We performed the search in unpublished, in progress and gray literature data sources through a research in the Clinical Trials website and in the Brazilian Registry of Clinical Trials. We used the terms "postoperative pain" AND "laparoscopic cholecystectomy" and "analgesia", with 46 articles found in Clinical Trials and none in the Brazilian Registry of Clinical Trials. After the search, we sent all references to EndNote® online for organization of study and deletion of duplicates.

There were 846 articles, of which 173 were duplicates, remaining 673 in the first selection. We then read the title and Abstract, prioritizing the sensitivity in detriment of the specificity in order to make a selection of these references[6]. This was done by a pair of reviewers, independently. The article was considered when at least one of the reviewers judged it as eligible. This process resulted in 145 articles that could be submitted to a complete reading. If there was disagreement between the reviewers, these were resolved either by consensus between the reviewers or by consulting a third reviewer.

There were 109 rejected articles and 36 were accepted to compose the definitive set (Figure 1). All articles that met the eligibility criteria for the systematic review had their methodological quality evaluated individually, minimizing biases and maximizing internal and external validity[6]. To that end, we assessed adequate randomization (allocation sequence generation), guaranteed allocation, blinding scheme (participants, team involved in conducting the study, outcome assessors), intention-to-treat analysis, loss of follow-up, as well as other sources of bias, such as early termination of the study due to benefit.

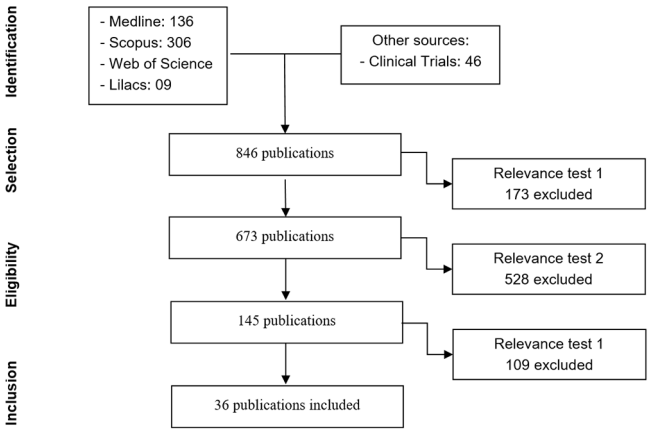

Figure 1. *Flowchart illustrating the article search strategy.*

We organized the articles[1-3,7-38] included in this systematic review and described in table 1. Through the convergence of the findings that answered the question of the study, we grouped the evidence according to the available therapeutic strategies for the control of acute pain after elective LC with the necessary comments to the discussion.

RESULTS AND DISCUSSION

In total, we identified 36 controlled and randomized clinical trials, including 2526 patients (Table 1).

NSAIDs/COX-2 inhibitors

Many studies have been done evaluating the risk-benefit of several NSAIDs/COX-2 inhibitors. The majority of the studies reviewed showed a reduction in the acute pain scores and the need for opioids in the postoperative period of LC, with adverse effects not found and/or not analyzed. There is no substantial superiority between the NSAIDs/COX-2 inhibitors available, and it is up to the anesthesiologist to decide which medication to use, according to the options available. However, their use is recommended as a key element within a

Table 1. *Interventions, evaluation of acute pain, need for postoperative opioid and adverse effects in the included studies.*

First author/year	Number of patients/groups	Intervention	Effects		Adverse effects
			Acute Pain	Need for opioids	
NSAIDs/COX inhibitor					
Anil *et al*., 2016[1]	60/2	Dexketoprofen trometamol (vs. diclofenac)	ǂ	§	ǂ
Fleckenstein *et al*., 2015[7]	103/2	Etoricoxib (vs. placebo)	ǂ	ǂ	ǂ
Shuying *et al*., 2014[8]	120/3	Parecoxib before anesthetic induction (vs. parecoxib after gallbladder removal or vs. placebo)	+	§	ǂ
Gautam *et al*., 2014[9]	120/4	Etoricoxib with methylprednisolone/etoricoxib/ methylprednisolone (vs. placebo)	+	+	ǂ
Kouroukli *et al*., 2013[10]	180/3	Lornoxicam/parecoxib (vs. placebo)	+	ǂ drugs/ § vs. placebo	ǂ
Gousheh *et al*., 2013[11]	30/2	Paracetamol (vs. placebo)	+	ǂ	-
Ureña-Frausto *et al*., 2013[12]	56/4	Ketoprofen and tramadol (vs. ketorolac)	+	§	ǂ
Ekmekci *et al*., 2012[13]	40/2	Tramadol and dexketoprofen (vs. tramadol)	+	§	ǂ
NMDA receptor antagonist					
Ozhan *et al*., 2015[14]	60/2	Ketamine (vs. placebo)	ǂ	§	+
Yadav *et al*., 2015[15]	66/2	Flupirtine (vs. placebo)	+	ǂ	+
Kocman *et al*., 2013[16]	60/3	Magnesium sulfate (vs. placebo)	+	ǂ	ǂ
Leal *et al*., 2013[17]	40/2	Ketamine (vs. placebo)	ǂ	ǂ	ǂ
Karcioglu *et al*., 2013[18]	40/2	Ketamine (vs. placebo)	+	§	+

First author/year	Number of patients/groups	Intervention	Effects		Adverse effects
			Acute Pain	Need for opioids	
Singh *et al*., 2013[19]	80/4	Ketamine (vs. placebo)	+	§	+
Nesek-Adam *et al*., 2012[20]	80/2	Ketamine and diclofenac (vs. placebo)	+	ǂ	ǂ
Olgun *et al*., 2012[21]	60/2	Magnesium sulfate (vs. placebo)	+	§	+
Gabapentin/Pregabalin					
Gurunathan *et al*., 2015[22]	100/4	Pregabalin/celecoxib/pregabalin and celecoxib (vs. placebo)	ǂ	ǂ	+
Bekawi *et al*., 2014[23]	90/3	Pregabalin (vs. Gabapentin or vs. placebo)	+	§	+
Sarakatsianou *et al*., 2013[24]	50/3	Pregabalin (vs. placebo)	+	§	+
Balaban *et al*., 2012[25]	90/3	Pregabalin (vs. diclofenac)	+	§	+
Miscellaneous					
Bakan *et al*., 2015[2]	80/2	Dexmedetomidine and lidocaine (vs. remifentanyl)	+	ǂ	+
Dereli *et al*., 2015[26]	60/4	Esmolol (vs. placebo)	+	§	+
Delfino *et al*., 2015[27]	50/2	Phenylephrine (vs. placebo)	ǂ	§	ǂ
Akelma *et al*., 2014[28]	48/3	Esmolol/ lidocaine (vs. remifentanyl)	+	§	ǂ
Ortiz *et al*., 2014[3]	80/4	Propofol (vs. isoflurane, vs. desflurane and vs. sevoflurane)	ǂ	ǂ	-
Lee *et al*., 2013[29]	90/3	Nefopam and fentanyl (vs. fentanyl)	+	ǂ	-
Park *et al*., 2012[30]	42/2	Dexmedetomidine (vs. placebo)	+	ǂ	-
Lopez-Alvarez *et al*., 2012[31]	60/2	Esmolol (vs. ketamine and remifentanyl)	+	§	ǂ
Peripheral blockades					
Elamin *et al*., 2015[32]	80/2	TAP block (vs. no blockade)	+	ǂ	ǂ
Basaran, 2015[33]	76/2	TAP block (vs. no blockade)	+	§	ǂ
Pandey *et al*., 2015[34]	60/2	Epidural blockade with levobupivacaine and clonidine (vs. ropivacaine and clonidine)	+	ǂ	+
Bathia *et al*., 2014[35]	60/3	Subcostal TAP block (vs. posterior TAP block)	+	§	ǂ
Petersen *et al*., 2012[36]	80/2	TAP block with ropivacaine (vs. placebo TAP block)	+	§	ǂ
Opioids					
Choi *et al*., 2015[37]	54/2	Oxycodone (vs. fentanyl)	+	ǂ	ǂ
Hwang *et al*., 2014[38]	81/2	Oxycodone (vs. fentanyl)	+	ǂ	+

Legends: - Not investigated; + Significant effect in the treated group; ǂ Non-significant effect in the treated group; § Opioid reduction in the postoperative period. Studies of degree of recommendation A - level of evidence 1B.

multimodal therapy, mainly because of its analgesic benefits and the rarity and low importance of its adverse effects. Some options are presented in the text and serve as a scientific basis for conduct.

Intravenous (IV) parecoxib 40mg used 30-45 minutes prior to anesthetic induction was associated with less postoperative pain and opioid consumption when compared with its administration after gallbladder removal or with placebo[8]. The use of oral (VO) lornoxicam 8mg showed analgesic efficacy similar to parecoxib 40mg IV and better than placebo when given in three doses (30 minutes before surgery and 12 and 24 hours after). The need for opioids in the postoperative period was similar between lornoxicam and parecoxib[10].

The administration of methylprednisolone 125mg IV and etoricoxib 120mg VO one hour before surgery was more effective in reducing the consumption of opioids, without a higher incidence of adverse effects. However, only the associated use showed better postoperative pain scores[9]. The use of etoricoxib 120mg VO on the morning of surgery and for three days after surgery did not show superiority to placebo in reducing the cumulative dose of opioid after LC or in perioperative pain scores[7].

Ketorolac 1mg/kg IV on induction *bolus* showed worse scores of acute pain and greater need for rescue opioids compared with groups in which drugs were given 60 minutes before surgery in continuous infusion. These groups were ketoprofen 100mg IV followed by 2mg/kg/24h; ketoprofen 50mg IV associated with tramadol 50mg IV, followed by 1mg/kg/24h and 0.1mg/kg/h, respectively, in addition to one group using twice the dose of attack and maintenance of the previous group. The latter group receiving ketoprofen 100mg IV associated with tramadol 100mg IV with maintenance of 2mg/kg/24h and 0.2mg/kg/h, respectively, needed less opioids in the postoperative period in relation to the other groups[12].

Single dose administration of dexcetoprofen trometamol 50mg IV 30 minutes before the end of surgery presented postoperative pain scores similar to the use of diclofenac sodium 75mg IV in patients submitted to LC. However, opioid consumption was higher in the dexketoprofen trometamol group compared with the diclofenac sodium group. There was no increase in adverse effects[1]. The use of dexcetoprofen trometamol 100mg IV associated with tramadol 600mg IV, via patient controlled analgesia, when used in physiological solution 0.9% of 100ml with 3ml *bolus*, interval between doses of 15 minutes and 15ml limit in four hours, showed lower analgesic consumption in the postoperative period without increase in adverse effects when compared with the use of tramadol 600mg IV[13].

The administration of paracetamol 1g IV immediately after induction of anesthesia reduced pain significantly compared with placebo, but without reduction in opioid consumption after LC procedures[11].

NMDA receptor antagonists (N-methyl-D-aspartate)

Regarding NMDA receptor antagonists, a large part of the studies reported lower scores of acute pain and opioid need in the postoperative period of LC. However, they indicated significant adverse effects depending on the intervention used. The anesthesiologist should take this into consideration when opting for its use within the multimodal therapy, since it will influence the anesthetic and perioperative dynamics.

The use of ketamine 1mg/kg IV on induction *bolus*, followed by 25mcg/kg/min IV until the end of surgery, used as supplementary form to propofol and alfentanyl in total venous anesthesia, produces lower postoperative pain scores and decreases opioid consumption compared with placebo. However, there was longer time to extubation and discharge from the post-anesthetic recovery room[18]. When

administered at a dose of 5mcg/kg/min IV, with changes in its dosage according to hemodynamic parameters, at the time of induction until the end of surgery, it did not alter the intensity of postoperative pain and the need for opioid in the LC postoperative period[17]. At the 0.25mg/kg IV *bolus* dose two minutes before induction, it reduced postoperative acute pain and opioid need scores over placebo. However, Aldrete scores were lower, with higher sedation due to Ramsay scores, as well as loss of verbal response and orientation after extubation[14].

Ketamine at the dose of 0.5-1mg/kg IV given 30 minutes before induction was effective in controlling acute pain and opioid need in the postoperative period of LC compared with placebo. As a side effect, increased heart rate (HR) and presence of hallucinations were observed[19]. At a dose of 0.15mg/kg before the surgical incision, associated with diclofenac sodium 1mg/kg IV 20 minutes before induction of anesthesia, it reduced postoperative pain scores, but not opioid consumption. However, the individual use of ketamine did not display these findings and the isolated use of diclofenac sodium did not spare opioid postoperatively[20].

The administration of magnesium sulphate 40mg/kg IV before induction, followed by intraoperative 10mg/kg/h, showed lower pain scores and opioid requirement in the postoperative period. Nevertheless, it led to inadequate breathing and delayed recovery, as demonstrated by a decreased Aldrete score[21]. Its administration prior to anesthetic induction of 5.0mg/kg and 7.5mg/kg reduced postoperative acute pain after LC compared with placebo. However, 7.5mg/kg were more effective. There was no difference in postoperative adverse effects and opioid consumption[16].

The use of flupirtine 200mg VO two hours before surgery was superior to placebo for acute postoperative pain, but there was no difference in opioid consumption. Nonetheless, there was a higher incidence of sedation in the group studied[15].

Gabapentin/Pregabalin

In general, the use of gabapentin/pregabalin in patients undergoing LC also showed lower scores of acute pain and need for opioid in the postoperative period, but several studies have shown adverse effects that may limit their use, such as sedation, delayed extubation and dizziness. Administration of pregabalin 150mg or 300 mg VO an hour before surgery decreased pain intensity and opioid consumption after LC compared with placebo. There was a higher degree of sedation on the Ramsay scale in the 300mg pregabalin group[25]. This dose, on the night before surgery and one hour before surgery, when compared with placebo, also obtained these positive analgesic results, albeit associated with delayed extubation time, as well as with increased incidence of post- operative dizziness[24].

The isolated use of pregabalin 150mg VO or in combination with celecoxib 400mg one hour before surgery did not provide lower pain scores or need for opioid when compared with placebo. The pregabalin group presented more dizziness and somnolence[22]. The use of gabapentin 1200mg VO two hours before surgery, followed by the same dose 12 hours postoperatively and every eight hours for two days, and pregabalin 150mg VO in the same administration scheme, reduced the need for opioids in patients undergoing LC when compared with placebo. The pregabalin group showed lower pain scores when compared with the other groups. Non-placebo interventions resulted in a greater degree of dizziness and drowsiness[23].

Miscellaneous

Interventions that could not be amassed in the previous groups were considered miscellaneous. These showed satisfactory results in the fight against acute pain and opioid need in the postoperative period of LC. However, several of their adverse

effects were not highlighted in the studies or were not evaluated. In conducting the case, the anesthesiologist should always consider the risk-benefit of such interventions.

The infusion of dexmedetomidine 1mg/kg/min IV before induction followed by 0.5mcg/kg/h showed a reduction in postoperative pain scores only in the first hour compared with placebo. There was no difference in the need for opioid in the postoperative period. The intervention group showed lower values of bispectral index (BIS), systolic blood pressure (SBP) and heart rate (HR)[30].

Opioid-free total venous anesthesia with propofol, dexmedetomidine 0.6mcg/kg IV followed by 0.3mcg/kg/h and lidocaine 1.5mg/kg IV and 2mg/kg/h intraoperatively is associated with lower opioid consumption and postoperative pain scores compared with total venous anesthesia with remifentanyl and propofol. Greater hypertensive events and longer recovery time were observed in the opioid-free group[2].

The use of esmolol 1mg/kg followed by 10mcg/kg/min IV after induction of anesthesia until the end of surgery, whether associated with propofol and remifentanyl or with desflurane and remifentanyl, decreased the need for opioid and postoperative pain when compared with its non-use. As adverse effects, there was a greater reduction in HR, but the mean arterial pressure remained the same[26]. Esmolol 0.5mcg/kg IV, when used at induction followed by 5-15mcg/kg/min until the end of surgery, reduced the need for opioid and improved postoperative analgesia when compared with the group receiving ketamine 0.5mg/kg IV at induction[31].

The infusion of esmolol 1mg/kg IV before induction followed by 50mcg/kg/min until the end of surgery and/or lidocaine 2mg/kg/min, followed by 2mg/kg/min in the same manner, showed lower opioid consumption in the post-anesthetic recovery room. The use of esmolol resulted in a decrease in the use of opioids extending up to 24 hours postoperatively. There was no reduction in postoperative pain scores[28].

The use of intravenous phenylephrine to maintain SBP 20-30% above baseline reduced opioid consumption and pain scores after LC when compared with maintenance of SBP 20-30% below baseline. There was no change in postoperative hemodynamic parameters. In this study, according to the author, it was not possible to distinguish whether this analgesic effect resulted from the increase in SBP or from the direct effect of phenylephrine as a pain modulator[27].

Administration of nefopam 20mg or 40mg IV with fentanyl 50mcg IV at the end of surgery reduced postoperative pain and side effects of opioid when compared with the single use of fentanyl. There was no evaluation of the need for opioid in the postoperative period[29]. Maintaining general anesthesia with propofol compared with isoflurane, desflurane or sevoflurane did not result in minor pain scores and opioid consumption after LC. No adverse effects of the medications used were evaluated[27].

Peripheral blockade

In the majority of studies, the use of peripheral blockade in the analgesia of patients submitted to LC reduced the postoperative acute pain and opioid need scores. However, some studies have discouraged its routine use because of adverse effects, which, although rare, do not justify its use in this type of surgery. It is up to the professional anesthesiologist to know the anesthetic options available in the hospital in question and suited to be used in the patient to assemble his/her analgesic arsenal.

Patients who received ultrasound-guided transverse abdominal plane block (TAP block) after

LC had reduced pain scores when coughing, but not at rest, when compared with those who did not receive the block. Postoperative opioid consumption was lower[36]. Another similar study showed reduction of postoperative acute pain, but the reduction in the need for opioids in the postoperative period was not evaluated[32].

An oblique subcostal approach in the use of a single-injection TAP block was effective in the control of LC postoperative pain and decreased opioid consumption[33]. This block showed lower postoperative pain and opioid need scores in comparison to the posterior TAP block or no blockade[35]. When two groups undergoing epidural block were compared in a LC surgery, the associated use of clonidine with levobupivacaine resulted in less analgesic need in the treatment of shoulder pain compared with clonidine with ropivacaine, but both groups had a high decline in blood pressure, requiring vasopressors[34].

Opioids

Opioids are the best option for analgesia. However, due to their potential for chemical dependence and adverse effects, several other drugs appear on the market every day. Currently, the combination of drugs is recommended to approximate the analgesic quality of opioids, a therapy known as multimodal. Researches involving opioids aim for greater efficacy with the fewest possible adverse effects. In this sense, the use of oxycodone has been shown to be promising in patients submitted to LC[37].

Oxycodone 0.08mg/kg IV 20 minutes before the end of surgery relieved immediate postoperative pain when compared with fentanyl 1mcg/kg, and was not associated with an increase in side effects in patients submitted to LC. The need for additional doses was similar between groups[37]. Regarding its use by patient-controlled analgesia, oxycodone 1mg IV per *bolus* showed similar effects for pain relief compared with fentanyl 10mcg IV, but showed a higher incidence of postoperative nausea and vomiting[38].

Despite the viability of the various strategies for acute pain relief in patients undergoing LC, some studies have not investigated the adverse effects of interventions, only efficacy in postoperative analgesia and the need for opioids. This can be explained by the rarity of their occurrences, difficulty in evaluation, or because they were not the objective of these studies[4].

The heterogeneity of the review studies may have led to weaknesses in the discussion. Nevertheless, this systematic review of the literature has contributed to teaching and professional practice with the theoretical enrichment of the analgesic tools available for LC therapy, as well as to alert the team to consider the adverse effects of the implemented interventions. Our study did not consider surgical strategies in the treatment of acute pain relief of patients undergoing LC, but these should be valued in the search for a better analgesic strategy.

CONCLUSION

There is no consensus as to the best analgesic strategy to be implemented in the acute postoperative pain of laparoscopic cholecystectomy, which requires its applicability in an individualized way, based on the scientific evidence found in the literature.

R E S U M O

A terapêutica inadequada da dor pós-operatória em colecistectomia videolaparoscópica pode levar a mobilização tardia, insatisfação do paciente, atraso na alta hospitalar e desenvolvimento de dor crônica. Objetivou-se identificar qual a melhor estratégia terapêutica disponível ao anestesiologista na terapia da dor aguda pós-operatória de pacientes submetidos à colecistectomia videolaparoscópica eletiva. Trata-se de revisão sistemática que incluiu 36 artigos completos indexados nas bases de dados Medline, Scopus, Web of Science e LILACS, com recorte temporal de cinco anos (2012 a 2016), resultantes de estudos controlados e randomizados que foram submetidos à análise qualitativa. Em uma proposta de analgesia multimodal, é importante considerar as contraindicações, os efeitos adversos, a dose e o momento ideal das intervenções. Utiliza-se fármacos não opioides, como anti-inflamatórios não esteroides (AINES)/inibidores da ciclo-oxigenase-2 (COX-2), gabapentina/pregabalina, antagonistas dos receptores N-methyl-D-aspartato (NMDA), entre outras. Os opioides podem ser utilizados em doses baixas associadas ou não a terapia multimodal e/ou ficarem restritos aos casos em que a analgesia multimodal não opioide for insuficiente. Conclui-se que não há consenso sobre qual a melhor estratégia analgésica a ser implementada na dor aguda pós-operatória da colecistectomia videolaparoscópica, o que requer sua aplicabilidade de forma individualizada, com base nas evidências científicas encontradas na literatura. Aponta-se como contribuições para o ensino e a prática profissional o enriquecimento teórico das opções medicamentosas analgésicas disponíveis para a terapêutica da dor pós-operatória de pacientes submetidos à colecistectomia videolaparoscópica eletiva, além de alertar a equipe para considerar os efeitos adversos das intervenções implementadas.

Descritores: *Dor Pós-Operatória. Colecistectomia Laparoscópica. Analgesia. Revisão.*

REFERENCES

1. Anil A, Kaya FN, Yavascaoglu B, Mercanoğlu Efe E, Türker G, Demirci A. Comparison of postoperative analgesic efficacy of intraoperative single-dose intravenous administration of dexketoprofen trometamol and diclofenac sodium in laparoscopic cholecystectomy. J Clin Anesth. 2016;32:127-33.
2. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H, et al. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Rev Bras Anestesiol. 2015;65(3):191-9. Portuguese.
3. Ortiz J, Chang LC, Tolpin DA, Minard CG, Scott BG, Rivers JM. Randomized, controlled trial comparing the effects of anesthesia with propofol, isoflurane, desflurane and sevoflurane on pain after laparoscopic cholecystectomy. Rev Braz Anesthesiol. 2014;64(3):145-51.
4. Ahn Y, Woods J, Connor S. A systematic review of interventions to facilitate ambulatory laparoscopic cholecystectomy. HPB (Oxford). 2011;13(10):677-86.
5. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment of the evidence. Anesthesiology. 2006;104(4):835-46.
6. Galvão TF, Pansani TSA, Harrad D. Principais itens para relatar revisões sistemáticas e meta-análises: a recomendação PRISMA. Epidemiol Serv Saúde. 2015;24(2):335-42.
7. Fleckenstein J, Kohls N, Evtouchenko E, Lehmeyer L, Kramer S, Lang PM, et al. No effect of the cyclooxygenase-2 inhibitor etoricoxib on pre-emptive and post-operative analgesia in visceral surgery: results of a randomized controlled trial. Eur J Pain. 2016;20(2):186-95.
8. Shuying L, Xiao W, Peng L, Tao Z, Ziying L, Liang Z. Preoperative intravenous parecoxib reduces length of stay on ambulatory laparoscopic cholecystectomy. Int J Surg. 2014;12(5):464-8.
9. Gautam S, Agarwal A, Das PK, Agarwal A, Kumar S, Khuba S. Evaluation of the efficacy of methylprednisolone, etoricoxib and a combination of the two substances to attenuate postoperative pain and PONV in patients undergoing laparoscopic cholecystectomy: a prospective, randomized, placebo-controlled trial. Korean J Pain. 2014;27(3):278-84.
10. Kouroukli I, Zompolas V, Tsekoura V, Papazoglou I, Louizos A, Panaretou V. Comparison between lornoxicam quick-release and parecoxib for post-operative analgesia after laparoscopic cholecystectomy: a prospective randomized, placebo-controlled trial. J Anaesthesiol Clin Pharmacol. 2013;29(4):485-90.
11. Gousheh SM, Nesioonpour S, Javaher Foroosh F, Akhondzadeh R, Sahafi SA, Alizadeh Z. Intravenous paracetamol for postoperative analgesia in laparoscopic cholecystectomy. Anesth Pain Med. 2013;3(1):214-8.

12. Ureña-Frausto CA, Plancarte-Sánchez R, Reyes-Torres JI, Ramírez-Aranda JM. Infusional therapy: an alternative for shouder pain post-laparoscopy. Cir Cir. 2013;81(3):187-95. Spanish.
13. Ekmekçi P, Kazak Bengisun Z, Kazbek BK, Özis SE, Tastan H, Süer AH. The efficacy of adding dexketoprofen trometamol to tramadol with patient controlled analgesia technique in post-laparoscopic cholecystectomy pain treatment. Agri. 2012;24(2):63-8.
14. Ozhan Y, Bakan N, Karaoren GY, Tomruk SG, Topaç Z. Effects of subanesthetic ketamine on pain and cognitive functions in TIVA. J Clin Anal Med. 2015;6(4):452-7.
15. Yadav G, Behera SS, Das SK, Jain G, Choupoo S, Raj J. Role of flupirtine as a preemptive analgesic in patients undergoing laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol. 2015;31(2):169-73.
16. Kocman IB, Krobot R, Premuzić J, Kocman I, Stare R, Katalinić L, et al. The effect of preemptive intravenous low-dose magnesium sulfate on early postoperative pain after laparoscopic cholecystectomy. Acta Clin Croat. 2013;52(3):289-94.
17. Leal PC, Sakata RK, Salomão R, Sadatsune EJ, Issy AM. Assessment of the effect of ketamine in combination with remifentanil on postoperative pain. Braz J Anesthesiol. 2013;63(2):178-82.
18. Karcioglu M, Davarci I, Tuzcu K, Bozdogan YB, Turhanoglu S, Aydogan A, et al. Addition of ketamine to propofol-alfentanil anesthesia may reduce postoperative pain in laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech. 2013;23(2):197-202.
19. Singh H, Kundra S, Singh RM, Grewal A, Kaul TK, Sood D. Preemptive analgesia with Ketamine for Laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol. 2013;29(4):478-84.
20. Nesek-Adam V, Grizelj-Stojčić E, Mršić V, Rašić Z, Schwarz D. Preemptive use of diclofenac in combination with ketamine in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. Surg Laparosc Endosc Percutan Tech. 2012;22(3):232-8.
21. Olgun B, Oguz G, Kaya M, Savli S, Eskiçirak HE, Güney I, et al. The effects of magnesium sulphate on desflurane requirement, early recovery and postoperative analgesia in laparascopic cholecystectomy. Magnes Res. 2012;25(2):72-8.
22. Gurunathan U, Rapchuk IL, King G, Barnett AG, Fraser JF. The effect of pregabalin and celecoxib on the analgesic requirements after laparoscopic cholecystectomy: a randomized controlled trial. J Anesth. 2016;30(1):64-71.
23. Bekawi MS, El Wakeel LM, Al Taher WM, Mageed WM. Clinical study evaluating pregabalin efficacy and tolerability for pain management in patients undergoing laparoscopic cholecystectomy. Clin J Pain. 2014;30(11):944-52.
24. Sarakatsianou C, Theodorou E, Georgopoulou S, Stamatiou G, Tzovaras G. Effect of pre-emptive pregabalin on pain intensity and postoperative morphine consumption after laparoscopic cholecystectomy. Surg Endosc. 2013;27(7):2504-11.
25. Balaban F, Yagar S, Özgök A, Koç M, Güllapoglu H. A randomized, placebo-controlled study of pregabalin for postoperative pain intensity after laparoscopic cholecystectomy. J Clin Anesth. 2012;24(3):175-8.
26. Dereli N, Tutal ZB, Babayigit M, Kurtay A, Sahap M, Horasanli E. Effect of intraoperative esmolol infusion on anesthetic, analgesic requirements and postoperative nausea-vomitting in a group of laparoscopic cholecystectomy patients. Rev Bras Anestesiol. 2015;65(2):141-6. Portuguese.
27. Delfino AE, de la Fuente N, Echevarría GC, Altermatt FR, Cortinez LI. Effect of acute arterial hypertension on morphine requirements and postsurgical pain. J Clin Anesth. 2015;27(3):226-32.
28. Akelma FK, Ergil J, Özkan D, Akinci M, Özmen M, Gümüs J. A comparison of the effects of intraoperative esmolol and lidocaine infusions on postoperative analgesia. Anestezi Dergisi. 2014;22(1):25-31.
29. Lee JH, Kim JH, Cheong YK. The analgesic effect of nefopam with fentanyl at the end of laparoscopic cholecystectomy. Korean J Pain. 2013;26(4):361-7.
30. Park JK, Cheong SH, Lee KM, Lim SH, Lee JH, Cho K, et al. Does dexmedetomidine reduce postoperative pain after laparoscopic cholecystectomy with multimodal analgesia? Korean J Anesthesiol. 2012;63(5):436-40.

31. López-Álvarez S, Mayo-Moldes M, Zaballos M, Iglesias BG, Blanco-Dávila R. Esmolol versus ketamine-remifentanil combination for early postoperative analgesia after laparoscopic cholecystectomy: a randomized controlled trial. Can J Anaesth. 2012;59(5):442-8.
32. Elamin G, Waters PS, Hamid H, O'Keeffe HM, Waldron RM, Duggan M, et al. Efficacy of a laparoscopically delivered transversus abdominis plane block technique during elective laparoscopic cholecystectomy: a prospective, double-blind randomized trial. J Am Coll Surg. 2015;221(2):335-44.
33. Basaran B, Basaran A, Kozanhan B, Kasdogan E, Eryilmaz MA, Ozmen S. Analgesia and respiratory function after laparoscopic cholecystectomy in patients receiving ultrasound-guided bilateral oblique subcostal transversus abdominis plane block: a randomized double-blind study. Med Sci Monit. 2015;21:1304-12.
34. Pandey A, Kumar R, Kang CLS, Agarwal M. Comparative study between levobupivacaine with clonidine and ropivacaine with clonidine in thoracic epidural block for laparoscopic cholecystectomy. J Evolution Med Dent Sci. 2015;4(9):1457-65.
35. Bhatia N, Arora S, Jyotsna W, Kaur G. Comparison of posterior and subcostal approach to ultrasound-guided transverse abdominis plane block for postoperative analgesia in laparoscopic cholecystectomy. J Clin Anesth. 2014;26(4):294-9.
36. Petersen PL, Stjernholm P, Kristiansen VB, Torup H, Hansen EG, Mitchell AU, et al. The beneficial effect of transversus abdominis plane block after laparoscopic cholecystectomy in day-case surgery: a randomized clinical trial. Anesth Analg. 2012;115(3):527-33.
37. Choi YJ, Park SW, Kwon HJ, Choi JM, Lee YM. Efficacy of early intravenous bolus oxycodone or fentanyl in emergence from general anaesthesia and postoperative analgesia following laparoscopic cholecystectomy: a randomized trial. J Int Med Res. 2015;43(6):809-18.
38. Hwang BY, Kwon JY, Kim E, Lee DW, Kim TK, Kim HK. Oxycodone vs. fentanyl patient-controlled analgesia after laparoscopic cholecystectomy. Int J Med Sci. 2014;11(7):658-62.

Received in: 04/02/2018
Accepted for publication: 05/17/2018
Conflict of interest: none.
Source of funding: none.

Mailing address: Renato Ribeiro de Jesus
E-mail: renatordejesus@gmail.com
ok.renato@hotmail.com