

## THE BEST THERAPEUTIC STRATEGY FOR ACUTE PAIN AFTER VIDEOLAPAROSCOPIC CHOLESCISTECTOMY: SYSTEMATIC REVIEW

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**Abstract:** Introduction: Late mobilization, delayed discharge, development of chronic pain and increased treatment costs are negative consequences related to inadequate treatment of postoperative pain after laparoscopic cholecystectomy. Several studies propose therapeutic strategies to resolve acute pain after laparoscopic cholecystectomy. Objective: to identify the best therapeutic strategy for acute pain after laparoscopic cholecystectomy, among the available techniques. Methodology: This is a systematic review that included 13 full articles indexed in Medline, Scopus, Web of Science and LILACS databases. Literature review: In a multimodal analgesia proposal, as presented in the postoperative analgesia of videolaparoscopic cholecystectomy, it is important to consider drug interactions, side effects, contraindications, dosage and the ideal moment of interventions. Currently, opioids, non-steroidal anti-inflammatory drugs, selective cyclooxygenase-2 (COX-2) inhibitors, N-methyl-D-aspartate receptor antagonists and the use of gabapentin/pregabalin are mainly used. The particularities of the interactions and the heterogeneity of the presentations make the discussion fragile, but the individualized study of each case must be praised. It is known that opioids are good alternatives for analgesia and recent studies show that the use of oxycodone has shown promise, with a dose of 0.08mg/kg IV 20 minutes before the end of surgery. Conclusion: Although there is no consensus on the best therapeutic strategy, the applicability of the therapy must be individualized based on scientific evidence. The adverse effects of the drugs must be taken into account when choosing the therapy.

**Keywords:** Pain. Postoperative. Cholecystectomy.

## INTRODUCTION

Inappropriate treatment of postoperative pain in laparoscopic cholecystectomy can lead to late mobilization, patient dissatisfaction, delayed hospital discharge and development of chronic pain, considerations that generate negative consequences for the patient. With the advent of videolaparoscopy and the improvement of proposed protocols to minimize discomfort in postoperative patients, such as the ERAS and ACERTO projects, several studies have proposed therapeutic strategies for resolving acute pain after videolaparoscopic cholecystectomy. Multimodal analgesia has been recommended as a basis for the follow-up of patients after videolaparoscopic cholecystectomy. The following review aimed to identify, among the main drug options used to control postoperative pain, the best therapeutic strategy for acute post-cholecystectomy pain.

## METHODS

This systematic review was carried out by the main researcher and four co-authors, students of the Medical Course at the "Universidade Federal do Maranhão, Imperatriz campus at the time of the review, with guidance from a faculty member of the same University, identified as the co-author of this review. The scientific production followed the design steps of a systematic review after extensive research, using complete articles indexed in the LILACS, Medline, Web of Science and Scopus databases, selected after pre-established inclusion and exclusion criteria. For the searches, descriptors in Health Sciences (DeCS) were used from the intersections: laparoscopic cholecystectomy, anesthesiology and postoperative pain therapy. As inclusion criteria, complete articles indexed in the databases of the Medical Literature Analysis and Retrieval System Online (Medline), Scopus, Web of Science and Latin American

and Caribbean Literature in Health Sciences (LILACS) were established, in a clipping 10-year temporal period between 1996 and 2006, based on controlled, randomized studies and considering systematic reviews and cohort studies, published in Portuguese and English. Major drugs from the opioid classes, NSAIDs/COX-2 inhibitors, NMDA receptor antagonists, and GABA analogues were included. As exclusion criteria, case reports, conventional (or open) approach, postoperative evolution to death, use of obsolete anesthetics were used. References were organized to exclude duplications. After eligibility criteria and revisions, 13 (thirteen) articles were evaluated regarding the individual methodology applied, minimizing biases and seeking randomization quality.

## RESULTS

With the modernization of health care and the advent of videolaparoscopy, multimodal analgesia has been recommended by surgeons and anesthesiologists aiming at combining the additive effects of analgesics, considering effective postoperative care and reducing the adverse effects of the medications used. In a multimodal analgesia proposal, as presented in the postoperative analgesia of videolaparoscopic cholecystectomy, it is important to consider drug interactions, side effects, contraindications, dosage and the ideal moment of interventions.

Based on this and considering the current literature, health teams use medications such as simple analgesics, corticosteroids, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), selective cyclooxygenase-2 (COX-2) inhibitors in postoperative pain therapy, opioids and GABA analogues (gabapentin and pregabalin). Its particularities, interactions and sensitivities formulate heterogeneous presentations, motivating broad discussions of efficacy and effectiveness that are considered

in broad levels of evidence, from expert opinions to studies of randomized clinical trials. It was observed that individualization must be praised and in most cases multimodal analgesia has been widely advocated for ensuring better recovery from surgeries such as laparoscopic cholecystectomy.

## **OPIOIDS**

Drugs in this class are among the best options for general analgesia. However, due to its adverse effects and considering chemical dependence after its administration, effective alternatives to its use are proposed in multimodal therapy to optimize its indication for the real need of the patient. Faced with the need to administer opioids after individualization, current literature demonstrates oxycodone as promising in postoperative pain control in patients undergoing videolaparoscopic cholecystectomy. Its use is recommended at a dose of 0.08mg/kg intravenously 20 minutes before the end of the surgery, with less postoperative pain when compared to fentanyl, for example, however, depending on the administered dose, this medication can cause a higher incidence of nausea and vomiting in the immediate postoperative period.

## **NONSTEROIDAL ANTI-INFLAMMATORY DRUGS/COX-2 INHIBITORS.**

The applicability of multimodal therapy considers essential the use of NSAIDs/COX-2 inhibitors as postoperative analgesia, considering low rates of adverse effects and high efficacy in most patients. With regard to simple analgesics, the use of 1g intravenous paracetamol immediately after anesthetic induction substantially reduced pain compared to placebo, without showing a reduction in opioid consumption after videolaparoscopic gallbladder surgeries.

Studies including the use of NSAIDs/COX-2 inhibitors in the postoperative period of laparoscopic cholecystectomy showed a reduction in the association of opioids in the treatment of patients, without identifying superiority among the available options, leaving the physician and anesthesiologist to make the best decision available considering individualities of the patient, experience, efficiency, effectiveness and considering the cost of the proposed treatment, characteristics that are particularized according to the region.

Regarding the other NSAID options available, intravenous parecoxib at a dose of 40mg 30 minutes before anesthetic induction stands out, and as an oral route of administration, lornoxicam at a dose of 8mg 30 minutes before surgery followed by additional doses 12 hours and 24 hours after the procedure. Both showed positive effects on postoperative control when compared to placebo. As for the worst postoperative pain control scores, the use of ketorolac at a dosage of 1mg/kg intravenously in anesthetic induction is evidenced, with a greater need for the association of opioids in the follow-up. Comparatively, groups with NSAIDs/COX-2 inhibitors with continuous infusion were superior to ketorolac. These groups included intravenous ketoprofen 100mg in association with intravenous tramadol hydrochloride 50mg in bolus with additional doses of 1mg/kg and 0.1mg/kg in 24h, respectively, and initial intravenous ketoprofen 100mg followed by 2mg/kg/24h, with lower needs of postoperative opioid use.

The administration of a single dose of intravenous dexketoprofen trometamol 50mg 30 minutes before the end of the surgery had a similar result to the administration of intravenous diclofenac sodium 75mg in patients undergoing videolaparoscopic cholecystectomy, but the consumption of opioids was higher in the use of trometamol

compared to diclofenac. In association with intravenous tramadol at a dose of 600mg, dexketoprofen trometamol showed lower postoperative analgesic consumption when compared to the isolated use of tramadol.

### **CORTICOSTEROID**

The associated administration of corticosteroids, in the studied study with the use of intravenous methylprednisolone 125mg associated with etoricoxib 120mg orally 1 hour before surgery, was more effective in reducing the consumption of opioids, with no higher incidence of adverse effects. It is important to consider that methyl-D-aspartate receptor antagonists.

The use of this class of drugs demonstrated greater control of acute pain and less need for opioids in the postoperative period of laparoscopic cholecystectomies, however, its use demonstrated a higher rate of significant adverse effects, depending on the dose, with increased heart rate and hallucinations, a factor which must be taken into account when choosing a combination of multimodal therapy. The administration of ketamine at a dose of 1mg/kg intravenously at anesthetic induction followed by 25mcg/kg/min intravenously until the end of the surgery demonstrated less postoperative pain and lower consumption of opioids compared to placebo, but increased extubation time and hospital discharge. of anesthetic recovery. The same drug in alternative doses according to the patient's hemodynamics did not change the intensity of pain after the surgical procedure. After reviewing anesthetic scores, this drug may impair verbal response and orientation after intubation, factors that must be taken into account when choosing this drug in multimodal therapy.

### **GABAPENTIN/PREGABALIN**

In general, GABA analogues such as

gabapentin/pregabalin can be used in patients undergoing video cholecystectomy. In patients who received these drugs, there was a lower rate of acute pain and need for postoperative opioids, but the proportion of adverse effects arising from these medications, such as excessive sedation, dizziness and delay in extubation also reinforce the individualization of their use. There was a decrease in the use of opioids in the postoperative period with the use of oral pregabalin 150mg or 300mg 1 hour before surgery compared to placebo, as well as a decrease in acute pain in the postoperative period. Lower doses of pregabalin have been studied in association with celecoxib, the latter without considerable effect in reducing acute pain or decreasing the need for opioids, with a higher rate of side effects. On the other hand, oral gabapentin doses above 1200mg 2 hours before surgery followed by the same dose 12 hours later demonstrated better postoperative pain control and less need for opioids in patients undergoing videolaparoscopic cholecystectomy when compared with placebo.

### **DISCUSSION**

Given the wide availability of drugs and interactions, considering the particularities of patients and their sensitivity, as well as variable adverse effects, several multimodal therapy strategies are currently used to control postoperative pain, including procedures such as videolaparoscopic cholecystectomies.

In this scenario, most available studies aim to investigate medications for the applicability of interventions, fundamentally based on the effectiveness of the proposed analgesia and the need for the use of opioids. However, the wide possibility of adverse effects characteristic of each drug is not characterized in most studies, as they are considered rare events, however, the existence of these effects must be taken into account when choosing the best drug

indication for patients.

In addition, the heterogeneous scenario considering specialists and a particular approach to patient care allow broad discussions about the same therapeutic indication, without an exact definition of the best proposal for multimodal therapy applied to patients in postoperative recovery. The individualized study persists as the best approach to the patient without establishing a consensus on the best therapeutic approach.

## CONCLUSION

Although there is no consensus on the best therapeutic strategy, the applicability of the therapy must be individualized based on scientific evidence. The adverse effects of the drugs must be taken into account when choosing the therapy.

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