International Journal of Science and Research Archive, 2020, 01(02), 038–043

International Journal of Science and Research Archive

Cross Ref DOI: 10.30574/ijsra

Journal homepage: https://www.ijsra.net/

(RESEARCH ARTICLE)

Pre-emptive analgesia VS Prophylactic analgesia and its influence on postoperative pain in postoperative laparoscopic cholecystectomy patients

María Fernanda Maya Guerrero [1], Fabiola María Nuccio Giordano [1], Bernardo José Gutiérrez Sougarret [1] and Alejandro Díaz Girón Gidi [2,*]

[1] *Anesthesiology Department. Médica Sur Hospital, Mexico City, México*
[2] *Surgery Department. Hospital Médica Sur, Mexico City, México.*

Publication history: Received on 10 November 2020; revised on 14 December 2020; accepted on 16 December 2020

Article DOI: https://doi.org/10.30574/ijsra.2020.1.2.0029

Abstract

Introduction: There are no studies on the use of dexketoprofen for postoperative pain control in patients undergoing laparoscopic cholecystectomy.

Purpose: To assess if the timing of dexketoprofen administration influences the intensity of postoperative pain in patients undergoing laparoscopic cholecystectomy.

Materials and methods used: Experimental, longitudinal, double-blind, randomized study. 50 mg of dexketoprofen diluted in 50 ml of 0.9% saline was administered to 50 patients divided into two groups: Pre-operative group: the substance was administered one hour before the beginning of surgery. Trans-operative group: the substance was administered at the moment when the gallbladder was separated from the liver base. The Numerical Pain Scale was evaluated and the number of doses and the total dose of tramadol that the patients received as analgesic rescue was quantified.

Results: Administration of dexketoprofen before starting laparoscopic cholecystectomy tends to reduce the intensity of postoperative pain without being statistically significant.

Conclusion: The timing of dexketoprofen administration has no impact on postoperative pain in patients operated for laparoscopic cholecystectomy.

Keywords: Dexketoprofen; Iaparoscopic cholecystectomy; Postoperative pain

1. Introduction

Prophylactic analgesia is an antinociceptive treatment that prevents an altered processing of the afferent entry being established, thus preventing post-operative pain from being amplified (1,2). In prophylactic analgesia, analgesic interventions occur before the surgical incision, to prevent central and peripheral sensitization, as well as the possible evolution to chronic pain. There is another concept called Pre-emptive analgesia; this is applied after the tissue damage, that is, after the beginning of the surgery, when it is very probable that the sensitization mechanisms have already been established (3, 4).

Several schemes of analgesia in patients undergoing laparoscopic cholecystectomy have been proposed; several of these schemes include one, two or more drugs for pain control. Most studies compare the analgesic efficacy of one drug against another for pain control during the postoperative period. Some of the authors, based on the principle of prophylactic analgesia, administer the analgesic drugs during the preoperative phase (5). Others do it once the gallbladder has been removed from the liver base or 30 minutes before the end of the surgical procedure (6), some others administer the

* Corresponding author: Díaz Girón Gidi Alejandro
Surgery Department. Hospital Médica Sur, Mexico City, México.

drugs when the patient is in the recovery area (7). Therefore, when comparing the efficacy of two or more drugs, no one scheme is superior to another; however, differences are observed when the scheme is administered before or after the surgical act.

Among the most widely used drugs to combat nociceptive inflammatory pain in the postoperative period are non-steroidal anti-inflammatory drugs (NSAIDs), whose main mechanism of action is the inhibition of oxygen cycles (COX) and, therefore, of the production of prostaglandins, which are very important in the management of acute pain. Dexketoprofen trometamol belongs to the family of NSAIDs derived from propionic acid; it is an analgesic, anti-inflammatory and antipyretic drug that is defined as the tromethamine salt of S-(+)-2-3- benzoylphenyl propionic acid (8).

In several surgical models, the analgesic efficacy of dexketoprofen trometamol, administered intramuscularly and intravenously, was evaluated in the treatment of moderate to severe pain. The results of these models show that the beginning of the analgesic effect was fast, with a maximum effect reached during the first 45 minutes. In addition, the duration of the analgesic effect after the administration of 50 mg of dexketoprofen has been proven to be normally 8 hours (8).

The anesthesia documentation includes five studies in which dexketoprofen has been used for postoperative pain control in patients undergoing laparoscopic cholecystectomy. In one of them dexketoprofen was used before and after the incision (9); in another it was given as a post-operative Rescue (10) and the remaining three were administered 15 to 30 minutes before the end of the surgery (11). None of these studies compare pre-surgery versus post-surgery administration.

The present study uses the same analgesia scheme with dexketoprofen, but administered at different times during the surgical act (12-14). The purpose is to evaluate whether the time at which dexketoprofen is administered influences the intensity of pain during the postoperative period in patients undergoing laparoscopic cholecystectomy.

2. Material and methods

This study was carried out with the authorization of the Ethics Research Committee of Hospital Médica Sur. It was an experimental, longitudinal, double-blind, randomized study; it began in June 2017 and ended in June 2018. A total of 50 patients selected consecutively and randomly assigned to one of two groups were studied.

The inclusion criteria were a) patients older than 18 years and younger than 70 years, b) patients scheduled for laparoscopic cholecystectomy under general anesthesia and c) ASA I, II, III patients. Exclusion criteria are listed as follows: a) patients allergic to dexketoprofen or any drug included in the study, b) patients who had contraindication for the administration of an NSAID such as chronic renal failure, platelet dysfunction or history of gastrointestinal tract bleeding, c) pregnant patients, d) patients who did not wish to participate in the study and e) patients with mental retardation or cognitive dysfunction. The elimination criteria considered was that the surgery be converted to open cholecystectomy.

The 50 patients were assigned to one of the experimental groups by sealed envelopes, using a table of random numbers. The sealed envelopes contained a sheet with the working model of group 1 or group 2, respectively. Group 1 (preoperative NSAID) was given 50 mg of dexketoprofen diluted in 50 ml of 0.9% saline for 10 minutes, one hour before the beginning of surgery. In addition, at the time the gallbladder was separated from the liver base, 50 ml of 0.9% saline was administered for 10 minutes. On the other hand, group 2 (trans-operative NSAID) was given 50 ml of 0.9% saline for 10 minutes, one hour before the beginning of the surgery; while at the time of separation of the gallbladder from the liver bed, 50 mg of dexketoprofen diluted in 50 ml of 0.9% saline for 10 minutes.

The sealed envelope was given to the preoperative nurse, who prepared the substances to be administered. Only the nurse knew which of the two preparations contained the dexketoprofen; they were then given to the anesthesiologist responsible for the case, so that they could be administered to the patient at the assigned time, according to the experimental group (double-blind study). Neither the patient nor the researcher knew the treatment sequence received.

Once the surgical intervention was finished, the anesthesiologist evaluated the VAS, according to the number that the patient selected to describe his condition (0 is the absence and 10 is the highest pain intensity). The evaluation was made upon arrival at the post-anesthesia care unit, upon going to the room and 8, 12 and 24 hours after the end of the surgery. Also, in case the patient indicated VAS >4, the number of doses and the total dose of tramadol he received as analgesia Rescue from his admission to the post-anesthesia care unit and up to 24 hours after surgery was quantified.

3. Results and discussion

Results were analyzed using measures of central tendency and dispersion (average or middle and standard deviation or interquartile interval) of pain intensity, depending on the distribution of the data (normal or not). Comparison of VAS in both groups was made by student T-test or U-Mann Whitney test; and number of Rescues by chi-square or Fisher exact test, depending on data distribution. A $p < 0.05$ was considered statistically significant.

Table 1 Demographic variables

	Preoperative NSAID	**Trans-operative NSAID**	**Value of p**
Age (years)	43.9 ± 15.5	49.1 ± 15.9	0.129
Gender (F/M %)	62/38	53/47	0.579
BMI	28.0 ±3.8	26.3 ±3.6	0.861
ASA (I/II/III %)	50/47/3	40/55/5	0.785
Comorbidities (yes/no %)	57/43	55/45	0.882
Total of Narcotic Dose	278.1 ± 87.7	294.5 ± 100.3	0.252
Port infiltration with local anesthetic (yes/no %)	53/47	60/40	0.658
Duration of surgery (hours)	1:03:48 ± 0:19:18	1:11:18 ± 0:22:14	0.214
Length of anesthesia (hours)	1:27:04 ± 0:22:37	1:30:45 ± 0:29:34	0.623

Values are expressed as averages ± standard deviation or percentages.

The patients were distributed in 62% women and 38% men, with an average age of 43.9 years, they integrated the group that received dexketoprofen in the preoperative. The group that received dexketoprofen in the trans-operative was formed by 53% women and 47% men, with an average age of 49.1 years, and a non-significant statistical p. Of the patients belonging to the preoperative NSAID group, 57% presented some comorbidity; this percentage was 55% for the trans-operative NSAID group (Table 1).

In the preoperative NSAID group the average time for anesthesia was 1:27:04 hours and for surgery was 1:03:48 hours; of this group only 53% of the patients were infiltrated with local anesthetic at the surgical incision site, and the average consumption of fentanyl was 278.1 mcg. The trans-operative NSAID group had an average anesthesia time of 1:30:45 hours and surgery time of 1:11:18 hours; of these patients, 60% were infiltrated with local anesthetic at the surgical incision site and had an average fentanyl consumption of 294.5 mcg. The comparison of the two groups did not show any statistically significant differences (Table 1).

Table 2 VAS values during the first 24 hours

Timing of the VAS assessment	**Pre-operative NSAIDs**	**Trans-operative NSAID**	**Value of p**
Entry into recovery	2.9 ± 3.3	2.6 ± 2.5	0.894
Discharge from recovery	0.4 ± 1.5	1.3 ± 2.5	0.258
8 hours after surgery	1.5 ± 2.3	2.0 ± 2.2	0.339
12 hours after surgery	0.1 ± 0.7	1.1 ± 2.2	0.203
24 hours after surgery	0.0 ± 0	± 0.4	0.768

The results are expressed as an average ± standard deviation.

If we compare the averages of the VAS that patients expressed at different times during the postoperative period, some differences are observed (Figure A), particularly at the time of discharge from recovery (preoperative NSAID group= 0.4 vs. trans-operative NSAID group= 1.3). However, the p=0.258, that is, statistically not significant (Table 2).

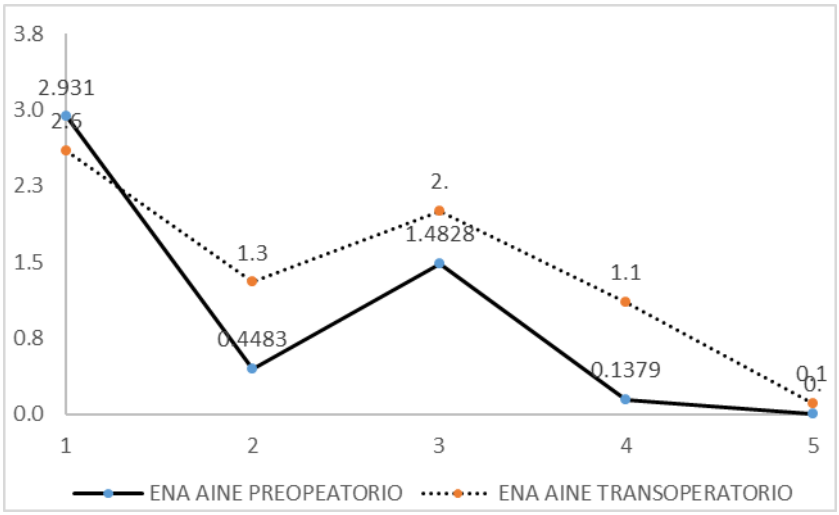

Figure A Postoperative evolution of pain (VAS scale), according to whether preparatory or trans-operative NSAIDs were received.

Table 3 Additional analgesia

	Pre-operative NSAID	**Trans-operative NSAID**	**Value of p**
Received Rescues (yes/no %)	50/50	80/20	0.034
Tramadol dosage (milligrams)	56.89 ± 74	68.0 ± 72.6	0.605

The results are expressed as an average ± standard deviation.

Finally, it should be noted that in the preoperative NSAID group only 50% of patients expressed VAS >4 and received tramadol Rescues, with an average of 56.8 mg; while in the trans-operative NSAID group 80% of patients received tramadol rescues, with an average of 68 mg, this with a p= 0.034 (Table 3).

4. Discussion

For laparoscopic cholecystectomy, prophylactic vs. postoperative analgesia, both with ketorolac, have been compared and it has been found that the average postoperative ANE was lower for the prophylactic analgesia group; the rescue dose was necessary in 7% of the patients in the preventive analgesia group and 53% in the postoperative analgesia group (13). There is another study in which, for this same intervention, diclofenac was administered preventively and diclofenac non-preventively, concluding that preventive administration prevents postoperative pain from appearing (15).

When comparing the results of these and other studies with the results obtained in the one presented here, it can be seen that prophylactic analgesia has some advantages in the control of postoperative pain. This becomes evident when analyzing the decrease in pain scale scores, as well as the reduction in the number of patients needing analgesic rescue (15,16).

In the specific case of dexketoprofen, evaluations have been made on its efficacy in patients operated for laparoscopic cholecystectomy. One study evaluates two groups, one of them was given 600 mg tramadol with 100 mg dexketoprofen trometamol, and the other 600 mg tramadol with saline solution for post-operative PCA. The results show that the addition of dexketoprofen trometamol in the analgesia lowers VAS scores, increases patient satisfaction, and decreases opioid consumption (9).

Another study compared the effects of a single intravenous dose of dexketoprofen trometamol and diclofenac sodium. While, 30 minutes before the end of surgery, one group of patients received 50 mg of dexketoprofen trometamol, the

other was given 75 mg of diclofenac sodium intravenously. It was concluded that VAS scores were similar in the follow-up periods, but opioid consumption was significantly lower in the group receiving dexketoprofeno (11).

The results of the study developed here are in line with the above-mentioned works. It is shown that the administration of the NSAID dexketoprofen before starting the laparoscopic cholecystectomy tends to reduce the intensity of postoperative pain, but without being statistically significant, and therefore requiring less rescue dose of opioid, which was statistically significant. However, the total dose of this rescue was not statistically significant.

5. Conclusion

The timing of dexketoprofen administration has no effect on postoperative pain in patients operated for laparoscopic cholecystectomy. Likewise, the time of administration of dexketoprofen does not influence the total dose of opioid used as a rescue to control the pain of patients undergoing this surgery.

The observed results have implications for general and future studies of analgesia, since the difference between prophylactic and preventive analgesia probably has no clinical implications, despite the theoretical evidence on the subject. In addition, it would be important to analyze whether the use of prophylactic analgesia or Pre-emptive analgesia with NSAIDs has any effect on the development of chronic pain.

Compliance with ethical standards

Disclosure of conflict of interest

There are no conflicts of interest.

Statement of ethical approval

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Jørgen B. Dahl. Steen Møiniche. Pre-emptive analgesia. British Medical Bulletin. 2005; 71(1): 13-27.

[2] Kissin Igor. Preemptive Analgesia. Anesthesiology. 2000; 93(4): 1138-1143.

[3] Pogatzki-Zahn EM, Zahn PK. From pre-emptive to preventive analgesia. Current Opi-nion in Anaesthesiology 2006; 19(5): 551–555.

[4] Crile GW. Austin A, Man – An Adaptive Mechanism. The Macmillan Company. 1916.

[5] Medina-Vera AJ, Novoa LM. Reduced anaesthetic requirements and postoperative analgesics in patients undergoing laparoscopic cholecystectomy: premedication with intravenous paracetamol versus ketorolac, a double blind and randomised clinical trial. Revista Española de Anestesiología y Reanimación. 2017; 64(2): 64-70.

[6] Jensen K, Kehlet H, Lund CM. Post-operative recovery profile after laparoscopic cholecystectomy: a prospective, observational study of a multimodal anaesthetic regi-me. Acta Anaesthesiologica Scandinavica. 2007; 51(4): 464–471.

[7] Echevarría Hernández Ana Teresa. Preemptive analgesia versus analgesia preventiva. Revista Cubana de Anestesiología y Reanimación. 2012; 11(1): 37-47.

[8] Leman P, Kapadia Y, Herrington J. Randomised controlled trial of the onset of anal-gesic efficacy of dexketoprofen and diclofenac in lower limb injury. Emergency Medical Journal. 2003; 20(6): 511-513.

[9] Ekmekçi P, Kazak Bengisun Z, Kazbek BK, Öziş SE, Taştan H, Süer AH. The efficacy of adding dexketoprofen trometamol to tramadol with patient controlled analgesia techni-que in post-laparoscopic cholecystectomy pain treatment. Agri. The journal of the Tur-kish Society of Algology. 2012; 24(2): 63-8.

[10] Gülsüm Altuntaş Ömer Taylan Akkaya, Derya Özkan, Mehmet Murat Sayın, Şener Balas, Elif Özlü. Comparison of Intraabdominal and Trocar Site Local Anaesthetic Infiltra-tion on Postoperative Analgesia After Laparoscopic Cholecystectomy. Turkish Journal of Anaesthesiology and Reanimation. 2016; 44(6): 306-311.

[11] Anıl A, Kaya FN, Yavaşcaoğlu B, Mercanoğlu Efe E, Türker G, Demirci A. Comparison of postoperative analgesic efficacy of intraoperative single-dose intravenous adminis-tration of dexketoprofen trometamol and diclofenac sodium in laparoscopic cholecys-tectomy. Journal of clinical anesthesia. 2016; 32: 127-133.

[12] Forse A, El Beheiry H, Butler PO, Pace RF. Indomethacin and ketorolac given preoperatively are equally effective in reducing early postoperative pain after laparos-copic cholecystectomy. Canadian Journal of Surgery. 1996; 39(1): 26-30.

[13] Camacho Meneses, Martha, Mello de la Cruz, Patricia. Dolor postoperatorio: analge-sia preventiva versus analgesia postoperatoria con ketorolaco en colecistectomía video-laparoscópica. Universidad Nacional Mayor de San Marcos. Repositorio de Tesis - UNMSM.

[14] Figueroa Balderas Lorena, Franco López Francisco, Flores Álvarez Efrén, López Ro-dríguez Jorge Luis, Vázquez García José Antonio, Barba-Valadez Claudia Teresa. Reduc-tion of omalgia in laparoscopic cholecystectomy: compairson between ketorolac and acetazolamide. Cirujía y Cirujanos. 2013; 81(5): 346-9.

[15] Perdomo Fernández Isabel, Martínez Bazán Yacnira, Tornes Salgado Carlos, Ortiz Sánchez Yurisnel. Preventive analgesia with Diclofenac in the post-operative pain after the videolaparoscopic cholecystectomy. Multimed. 2015; 19(6).

[16] Fanelli A, Ghisi D, Pergolotti B, Martinetti M, Fanelli G, Danelli G. Pilot double-blinded study to assess efficacy and tolerability of morphine sulphate oral solution (Oramorph) given preoperatively as ad don therapy within a multimodal postoperative pain approach in patients undergoing laparoscopic cholecystectomy. Minerva Aneste-siologica. 2014; 80(1): 66-75.