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Original Research Article

A Comparative Evaluation of Efficacy and Safety of Preemptive Use of Intravenous Paracetamol and Intramuscular Ketorolac for Management of Postoperative Pain after Laparoscopic Cholecystectomy

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Abstract

Aim: The aim of the present study was to compare the efficacy and safety of preemptive use of intravenous paracetamol and intramuscular ketorolac for management of postoperative pain after laparoscopic cholecystectomy.

Methods: The retrospective study was conducted in the Department of Anesthesiology, Government Medical College and Hospital, Bettiah, Bihar , India and included a total of 100 patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia. Age of the patients ranged between 19-59 years with body weight of 50-70 kg. The study was done on patients with American Society of Anesthesiologists grade I and II.

Results: In our study, both the study groups were comparable in terms of mean age, weight, sex ratio and operative time. Baseline heart rate (HR) and mean arterial pressure (MAP) were comparable between the two treatment groups pre- operatively, just after intubation, at 5 min, 15 min, 30 min, 45 min, at the end of surgical procedures as well as at extubation. No statistically significant difference was found between two groups (p-value>0.05). In the paracetamol and ketorolac groups, laparoscopic cholecystectomies were done in a mean operative time of 58.2 and 57.6 minutes respectively (Range 31-108 min). All patients were monitored for VAS in the post-operative period which was found to be persistently higher in paracetamol group as compared to ketorolac group. The Mean VAS scores on the intergroup comparison post- operatively at 30 min, 1 hour, 3 hours and 6 hours were found to be statistically significant (p-value< 0.05), however at 12 and 24 hours the difference was insignificant.

Conclusion: Pre-emptive intramuscular ketorolac (30 mg) is more effective in reducing postoperative pain scores (VAS) after laparoscopic cholecystectomy in the first 6 hours as compared to intravenous paracetamol infusion (1 gm). However both regimes were equally effective in doing so at 12 hours and thereafter. Intramuscular ketorolac is better than paracetamol infusion in reducing the need and prolonging the time for need of a rescue analgesic.

Keywords: Intravenous paracetamol, Intramuscular ketorolac, Postoperative analgesia, preemptive analgesia, Laparoscopic cholecystectomy

Introduction

Laparoscopic cholecystectomy is one of the most frequently performed laparoscopic surgeries nowadays. Since the introduction of diagnostic laparoscopic procedures in the early 1970s and the first laparoscopic cholecystectomy procedures in the late 1980s [1] laparoscopy has expanded impressively both in scope and volume. Increasing success of laparoscopic surgery can be attributed to the fact that it results in multiple benefits compared with open procedures, such as reduced trauma to patient, disturbance of homeostasis, morbidity, mortality, recovery time and hospital stay, with consequent reductions in healthcare costs [2-3] Efforts have been made to use the laparoscopic approach for gastrointestinal (e.g., colonic, gastric, splenic, hepatic surgery), gynecologic (e.g., hysterectomy), urologic (e.g., nephrectomy, prostatectomy), and vascular (e.g., aortic) procedures.

Despite multiple benefits, any laparoscopic surgery

always poses a challenge to its successful anesthetic management, mainly due to significant alteration of hemodynamics, resulting from the combined effects of pneumoperitoneum, patient position, anesthesia, and hypercapnia from the absorbed CO2 that is used to produce pneumoperitoneum. Pneumoperitoneum creation (increased intra-abdominal pressure) is immediately followed by an increased plasma renin activity and increase in plasma levels of norepinephrine and epinephrine [4] The renin–angiotensin–aldosterone system is also activated. All these changes collectively lead to an elevated arterial pressure, increased systemic and pulmonary vascular resistance, and decreased cardiac output. [5] Various agents such as isoflurane, propofol, β-blockers [6] and antihypertensives [7-8] have been used to reduce hemodynamic changes associated with laparoscopic surgery with variable response.

Effects of α2-adrenergic agonist clonidine have also been studied widely. [9-10] Dexmedetomidine is alpha-2 adrenergic receptor agonist that modulates the hemodynamic changes by inhibiting the release of catecholamines and vasopressin. [11] Esmolol, an ultrashort-acting cardio selective beta-1 antagonist, has also been used to control tachycardia and hypertension. [12] Hence, we performed this study so as to compare the efficacy of these two agents and also to compare the safety of these drugs [13] It has been reported in studies that there is a 10–30% reduction in cardiac output during pneumoperitoneum. [14] Increases in arterial pressure can pose a risk for adverse cardiovascular events in patients with pre-existing essential hypertension, ischemic heart disease, or increased intracranial pressure. [15] Hypercapnia and pneumoperitoneum stimulate sympathetic nervous system, causing catecholamine and vasopressin release [16]

The aim of the present study was to compare the efficacy and safety of preemptive use of intravenous paracetamol and intramuscular ketorolac for management of postoperative pain after laparoscopic cholecystectomy.

Materials and Methods

The retrospective study was conducted in the Department of Anesthesiology, Government Medical College and Hospital, Bettiah, Bihar , India from February 2021 to January 2022 and included a total of 100 patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia. Age of the patients ranged between 19-59 years with body weight of 50-70 kg. The study was done on patients with American Society of Anesthesiologists grade I and II. Enrolled patients were divided into two equal groups (A and B) of 60 each by computer generated randomization. Exclusion criteria included acid peptic disease, pregnancy and lactation, known allergy to paracetamol or ketorolac, chronic analgesic dependency, significant coronary artery disease or ischemic myocardial disease, drug or alcohol abuse, chronic pulmonary disease, renal failure, hepatic dysfunction, hemorrhagic disorder, psychological disorder and those with acute cholecystitis. Group A (n=60) comprised of patients who received intravenous paracetamol infusion (1g) and group B (n=60) patients received intramuscular ketorolac (30 mg) 15 min before surgery. A day before surgery all the patients were explained details of Visual Analogue Scale (VAS of 0- 100). Tab alprazolam 0.5 mg and tab. pantoprazole 40 mg were given orally night before surgery. In the operation theatre, intravenous line was established with 18G cannula and Ringer Lactate solution was started at the rate of 60-80 ml/h. Preoperative recording of heart rate (HR),noninvasive blood pressure (Systolic/Diastolic/Mean) and arterial oxygen saturation (SpO2) was carried out. All patients were premedicated intravenously with, midazolam (0.02 mg/kg). After being preoxygenated with100% oxygen for 3 minutes, patients were induced with intravenous propofol (1%) in dose of 2 mg/kg followed by atracurium 0.5 mg/ kg to facilitate the laryngoscopy and tracheal intubation. In addition to above mentioned monitoring end tidal carbon dioxide (ETCO2) monitoring was done intraoperatively. Anesthesia was maintained with isoflurane, nitrous oxide 60% in oxygen, and Atracurium in incremental dosages of 0.02 mg/kg when needed. Laparoscopic cholecystectomy was done using four standard ports at conventional sites (Umbilical 10mm, Epigastric 10mm, Right subcostal 5mm and Right lumbar 5mm). Surgery was completed in all the patients. A small 14 Fr tube drain was placed in sub-hepatic region in all the patients. Ports were removed under vision and port sites closed. A few minutes before the completion of surgery, inj. ondansetron 0.1mg/kg was given to patient for prevention of PONV. At the conclusion of surgery residual muscle paralysis was reversed with inj. neostigmine 50 µg/kg and inj. glycopyrrolate 10 µg/ kg intravenously. The patients were extubated following return of regular, rhythmic respiration when reasonably awake, after a gentle oral suction. Patients were transferred to post anesthesia care unit to monitor hemodynamic parameters, and any other adverse events such as nausea, vomiting and bleeding. Pain intensity was measured based on a 10-point Visual Analogue Scale (VAS; 0-10 cm; 0= no pain and 10= worst imaginable pain) at 30 minutes, 1 hour, 3 hours, 6 hours, 12 hours and 24 hours post-operatively. Initial dose of analgesic (Paracetamol intravenous infusion 1gm or intramuscular Ketorolac 30 mg) was given to the patients in the postoperative period when the pain

intensity, as observed on the VAS, showed a score >4. Thereafter, Paracetamol 1g intravenous infusion or Ketorolac 30 mg intramuscular was given every 6 hours. If the VAS score was >4, rescue analgesia wit intravenous tramadol 2mg/kg body weight was given to the patients. At the end of 24 hours, the total amount of patients requiring rescue analgesic and its timing in each group was noted. At the end of the study the data was collected and analyzed statistically. Chi-square test was used as a test of significance for data and a p-value of <0.05 was considered significant.

Results

Table 1: Demographic characteristics of patients in two groups

Parameter	PCM Infusion	Intramuscular Ketorolac	P-value
Mean Age (Years)	42.81	40.97	0.7631
Sex Ratio (M: F)	22:28	20:30	0.5645
Mean Weight (Kg)	59.85	61.03	0.8769
Mean Operative Time (Minutes)	58.20	57.66	0.6892

In our study, both the study groups were comparable in terms of mean age, weight, sex ratio and operative time.

Table 2: Preoperative and Intraoperative hemodynamic parameters

Time	CM Infusion (n=50)	Intramuscular Ketorolac (n=60)	p-Value	CM Infusion (n=60)	Ketorolac IM(n=50)	p-Value
Preoperative	81	83	0.9192	85	87	0.8987
Intubation	101	103	0.9223	105	106	0.9982
5 minutes	102	105	0.8768	100	101	0.9991
15 minutes	93	91	0.8665	92	93	0.9879
30 minutes	87	86	0.9811	87	86	0.9811
45 minutes	82	81	0.8874	86	85	0.9781
Extubation	109	112	0.8183	106	104	0.9541

Baseline heart rate (HR) and mean arterial pressure (MAP) were comparable between the two treatment groups pre- operatively, just after intubation, at 5 min, 15 min, 30 min, 45 min, at the end of surgical procedures as well as at extubation. No statistically significant difference was found between two groups (p-value>0.05). In the paracetamol and ketorolac groups, laparoscopic cholecystectomies were done in a mean operative time of 58.2 and 57.6 minutes respectively (Range 31-108 min).

Table 3: Mean Visual analogue scale (VAS) pain scores in the two groups undergoing Laparoscopic Cholecystectomy

Post-Op Time	Mean VAS (PCM Infusion)	Mean VAS (Intramuscular Ketorolac)	P-value
30 minutes	3.2	1.5	< 0.0001
1 hour	4.6	2.1	< 0.0001
3 hours	4.5	2.8	< 0.0001
6 hours	2.8	2.5	0.0393
12 hours	1.1	0.8	0.7291
24 hours	0.6	0.5	0.5631

All patients were monitored for VAS in the post-operative period which was found to be persistently higher in paracetamol group as compared to ketorolac group. The Mean VAS scores on the intergroup comparison post- operatively at 30 min, 1 hour, 3 hours and 6 hours were found to be statistically significant (p-value< 0.05), however at 12 and 24 hours the difference was insignificant.

Discussion

Laparoscopic cholecystectomy is the current gold standard for the treatment of gall stone disease. [17] Laparoscopic surgery has displayed advantages over open surgery, including less postoperative pain, smaller incisions, shorter postoperative ileus, reduced blood loss, reduced length of hospital stay, faster recovery, as well as earlier return to preoperative activity and work. [18,19] Studies have shown that laparoscopic surgery too causes postoperative pain in at least one-third of the patients and these patients have been seen taking more analgesics to alleviate pain. [20]

In our study, both the study groups were comparable in terms of mean age, weight, sex ratio and operative time. Baseline heart rate (HR) and mean arterial pressure (MAP) were comparable between the two treatment groups pre- operatively, just after intubation, at 5 min, 15 min, 30 min, 45 min, at the end of surgical procedures as well as at extubation. No statistically significant difference

was found between two groups (p-value>0.05). In the paracetamol and ketorolac groups, laparoscopic cholecystectomies were done in a mean operative time of 58.2 and 57.6 minutes respectively (Range 31-108 min). All patients were monitored for VAS in the post-operative period which was found to be persistently higher in paracetamol group as compared to ketorolac group. The Mean VAS scores on the intergroup comparison post-operatively at 30 min, 1 hour, 3 hours and 6 hours were found to be statistically significant (p-value< 0.05), however at 12 and 24 hours the difference was insignificant. Clinically, paracetamol has analgesic efficacy comparable to aspirin but it is less effective than other NSAIDs. [21] Rastogi B et al [22] compared the efficacy of preemptive intravenous paracetamol versus intravenous ketorolac for post-operative analgesia after laparoscopic cholecystectomy and concluded that ketorolac exerted superior postoperative analgesia in comparison to paracetamol without any significant side effect. These results are consistent with our study even though the route of ketorolac administration in our study was intramuscular and that in study by Rastogi B et al [22] was intravenous. The reason for this consistent analgesic effect despite the different route of its administration is that ketorolac is highly protein bound, has a limited volume of distribution, and has a terminal half-life of approximately 5-6 hours regardless of the route of administration. [23]

Khan MR et al[24] studied the effect of preemptive dose of ketorolac, diclofenac and tramadol in laparoscopic cholecystectomy patients for postoperative pain and hemodynamic changes. They concluded that postoperative pain can be managed by preemptive use of diclofenac, ketorolac, and tramadol for the first 24 hours with little or no supplementation of low dose intravenous pethidine. The analgesic efficacy of ketorolac and tramadol is same and better than diclofenac. There was no significant complication in using the drugs. Boccara et al[25] compared preemptive use of proparacetamol and ketoprofen for providing analgesia after laparoscopic cholecystectomy and concluded that preoperative administration of NSAIDS such as ketoprofen has better postoperative analgesia after laparoscopic cholecystectomy as compared to proparacetamol and postoperative use of both these drugs.

Conclusion

Pre-emptive intramuscular ketorolac (30 mg) is more effective in reducing postoperative pain scores (VAS) after laparoscopic cholecystectomy in the first 6 hours as compared to intravenous paracetamol infusion (1 gm). However both regimes were equally effective in doing so at 12 hours and thereafter. Intramuscular ketorolac is better than paracetamol infusion in reducing the need and prolonging the time for need of a rescue analgesic.

References

1. Sain AH. Laparoscopic cholecystectomy is the current" gold standard" for the treatment of gallstone disease. Annals of surgery. 1996 Nov ;224(5):689.
2. Buanes T, Mjåland O. Complications in laparoscopic and open cholecystectomy: a prospective comparative trial. Surgical Laparoscopy Endoscopy & Percutaneous Techniques. 1996 Aug 1;6(4):266-72.
3. Mendoza-Sagaon M, Hanly EJ, Talamini MA, Kutka MF, Gitzelmann CA, Herreman-Suquet K, Poulose BF, Paidas CN, De Maio A. Comparison of the stress response after laparoscopic and open cholecystectomy. Surgical endoscopy. 2000 Dec;14:1136-41.
4. Ure BM, Troidl H, Spangenberger W, Dietrich A, Lefering R, Neugebauer E. Pain after laparoscopic cholecystectomy: intensity and localization of pain and analysis of predictors in preoperative symptoms and intraoperative events. Surgical endoscopy. 1994 Feb;8:90-6.
5. Joris J, Cigarini I, Legrand M, Jacquet N, De Groote D, Franchimont P, Lamy M. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. BJA: British Journal of Anaesthesia. 1992 Oct 1;69(4):341-5.
6. Rastogi B, Singh VP, Gupta K, Jain M, Singh M, Singh I. Postoperative analgesia after laparoscopic cholecystectomy by preemptive use of intravenous paracetamol or ketorolac: A comparative study. Indian Journal of Pain. 2016 Jan 1;30(1):29-33.
7. Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. The Lancet Global Health. 2015 Apr 27;3:S13-20.
8. Simões CM, Carmona MJ, Hajjar LA, Vincent JL, Landoni G, Belletti A, Vieira JE, de Almeida JP, de Almeida EP, Ribeiro U, Kauling AL. Predictors of major complications after elective abdominal surgery in cancer patients. BMC anesthesiology. 2018 Dec;18:1-8.
9. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. Journal of pain research. 2017 Sep 25:2287-98
10. Borys M, Zyzak K, Hanych A, Domagała M, Gałkin P, Gałaszkiewicz K, Kłaput A, Wróblewski K, Miękina J, Onichimowski D, Czuczwar M. Survey of postoperative pain control in different types of hospitals: a multicenter observational study. BMC anesthesiology. 2018 Dec;18:1-9.

11. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg 2013; 26(3): 191-96
12. Luo J, Min S. Postoperative pain management in the postanesthesia care unit: an update. Journal of pain research. 2017 Nov 16:2687-98.
13. Campagna S, Antonielli D'Oulx MD, Paradiso R, Perretta L, Re Viglietti S, Berchialla P, Dimonte V. Postoperative pain, an unmet problem in day or overnight Italian surgery patients: a prospective study. Pain Research and Management. 2016;2016(1):6104383.
14. Morgan GE, Mikhall MS & Murray MJ, Clinical anaesthesiology, Lange Medical Books/McGraw-Hill, 2006; 361
15. Dahl JB, Møiniche S. Pre-emptive analgesia. British Medical Bulletin. 2005 Jan 1;71(1):13-27.
16. Bonnefont J, Courade JP, Alloui A, Eschalier A. Antinociceptive mechanism of action of paracetamol. Drugs. 2003 Jan 1;63:1-4.
17. A H Sain. Laparoscopic cholecystectomy is the current "gold standard" for the treatment of gallstone disease.Ann Surg. 1996 Nov; 224(5): 689–690.
18. Buanes T, Mjåland O. Complications in laparoscopic and open cholecystectomy: a prospective comparative trial. Surg Laparoscopy Endosc 1996; 6: 266-72.
19. Mendoza-Sagaon M, Hanly E, Talamini M, Kutka M, Gitzelmann C, Herreman-Suquet K, et al. Comparison of the stress response after laparoscopic and open cholecystectomy. Surg Endosc 2000; 14: 1136-41.
20. Ure BM, Troidl H, Spangberger W, Dietrich A, Lefering R, Neugebauer E. Painafter laparoscopic cholecystectomy. Surgical Endoscopy. 1994;8(2):90-96.
21. Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: Therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacology2013; 21: 201-32.
22. Bhawana Rastogi, VP Singh, Kumkum Gupta et al. Postoperative analgesia after laparoscopic cholecystectomy by preemptive use of intravenous paracetamol or ketorolac: A comparative study. Indian Journal of Pain. 20 16; 30(1): 29-33.
23. Gillis JC, Brogden RN. Ketorolac A Reappraisal of its Pharmacodynamic and Pharmacokinetic properties and therapeutic use in pain management. Drugs 1997;53: 139-188.
24. Khan MR, Islam MZ, Hossain MS, Aziz L, Choudhury SS. Comparison of Pre-emptive use of diclofenac, ketorolac and tramadol for post-operative pain in laparoscopic cholecystectomy. J Bangladesh Soc Anaesthesiol2007; 20: 24-9.
25. Boccara G, Chaumeron A, Pouzeratte Y, Mann C. The preoperative administration of ketoprofen improves analgesia after laparoscopic cholecystectomy in comparison with propacetamol or postoperative ketopro fen. Br J Anaesth2005; 94: 347-51.