



THE EFFECT OF PRE-EMPTIVE PARACETAMOL ON POSTOPERATIVE ANALGESIC REQUIREMENT IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERY

Anaesthesiology

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ABSTRACT

Background: Pre-emptive use of paracetamol has been shown to reduce the need for postoperative analgesia in many patient groups; however, evidence supporting its role in laparoscopic surgery is lacking. **Aim:** To determine the effect of Pre-emptive paracetamol on post-operative analgesia requirement in patients undergoing laparoscopic surgery. **Materials And Method:** The randomised control trial was conducted at Dr. Kailash Narayan Singh Memorial Institute of Medical Sciences, Barabanki, Uttar Pradesh patients with physical status ASA I or ASA II were randomized into 2 groups. Group 1 received 1 gram of paracetamol intravenously 30 minutes before the operation; Group 2 was the control group and received 100 ml 0.9% normal saline. The VAS pain scores and analgesic needs within 6 hours after operation were compared among the two group. **Results:** Postoperative pain scores remained comparable among the two groups throughout most of the study. Postoperative Tramadol consumption was significantly reduced in groups 1 and compared to group 2. **Conclusion:** Pre-emptive intravenous injection of paracetamol is effective in the treatment of post-operative pain after laparoscopic surgery.

KEYWORDS

Paracetamol, Analgesia, Pre-Emptive, Postoperative, Pain

INTRODUCTION

Gallstone disease is a very common gall bladder disease. Cholecystectomy is the primary treatment for it. Traditionally, cholecystectomy used to be an open surgical procedure, however, since the introduction of laparoscopic cholecystectomy as the minimally invasive procedure, most of the cholecystectomy procedures are being performed through laparoscopic procedures. Today, laparoscopic cholecystectomy has evolved into a gold standard for management of gall stone disease has been quite interesting and evolutionary. Ever since then laparoscopic surgery in general and laparoscopic cholecystectomy in particular has seen tremendous advancements in techniques, equipment and frequency¹.

The increased acceptability of laparoscopy as the gold standard procedure for surgery of benign Gall Bladder disease can be attributed to smaller incision, less intraoperative blood loss, reduced post operative pain, early recovery, short hospital stay and better cosmetic results².

Despite laparoscopic cholecystectomy being successful in substantial reduction of post-operative pain, it still remains to be one of the most important factor affecting the overall patient experience. Post-operative pain also remains to be the most common reason for prolongation of duration of hospital stay. Hence, efforts to reduce the post-operative pain are key considerations while planning a surgical procedure, laparoscopic cholecystectomy is no exception.

Patients undergoing laparoscopic cholecystectomy often complain of pain spreading from back to shoulder region apart from discomforting pain around the port sites. Half of the patients undergoing laparoscopic surgery experience shoulder and sub-diaphragmatic pain. Peak pain intensity is achieved within first few hours after the surgery and lasts till 48 to 72 hours post-operative interval.

Pain after laparoscopic cholecystectomy has multifactorial etiologies¹⁴. Peritoneal insufflation with carbon-dioxide to achieve pneumoperitoneum results in peritoneal stretching and diaphragmatic irritation affective the phrenic nerve that results in post-operative pain¹. Port site pain, on the other hand is somatic in nature

There are three possible strategies to tackle with the problem of post-operative pain among patients undergoing laparoscopic cholecystectomy. These include, preoperative, intraoperative and postoperative interventions. While non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors remain the mainstay of these intervention strategies, other common interventions for post-operative analgesia include use of dexamethasone, local

infiltration of wound anaesthetics and opioids as rescue agents. However, use of these methods for pain relief after laparoscopic cholecystectomy is often reported to be associated with number of lot of side effects. Moreover, they generally do not provide universally similar analgesic effect^{14,15}.

As far as trade-off between safety and efficacy of paracetamol is concerned, a centrally acting drug having capability to inhibit prostaglandin synthesis and COX of nervous system has been shown to have minimal side effects while at the same time it provides excellent relief from pain¹. Commercially too, paracetamol is an easily available, cost-effective alternative to other post-operative analgesics. It's pre-emptive use for post-operative pain management in laparoscopic cholecystectomy may thus reduce the opioid requirements and could hasten the post-operative recovery.

Encouraged by these reports, the present study was planned to study the efficacy of intravenous paracetamol on post-operative analgesia for patients undergoing laparoscopic cholecystectomy.

OBJECTIVES OF THE STUDY:

To determine the effect of Pre-emptive paracetamol on post-operative analgesia requirement in patients undergoing laparoscopic surgery.

MATERIAL AND METHODS

The randomised control trial was conducted at Kailash Narayan Singh Memorial Institute of Medical Sciences, Barabanki, Uttar Pradesh patients with physical status ASA I or ASA II were randomized into 2 groups. Group 1 received 1 gram of paracetamol intravenously 30 minutes before the operation; Group 2 was the control group and received 100 ml 0.9% normal saline. The VAS pain scores and analgesic needs within 6 hours after operation were compared among the two group.

Statistical Analysis:

The data was entered in an MS-Excel 2013 worksheet. Data analysis was performed using IBM SPSS Stats 21.0 version. Chi-square test and Independent samples 't'-test were used to compare the data. A 'p' value less than 0.05 was considered as statistically significant.

RESULTS

Patients were randomly divided into two equal groups with the help of Computer generated random number tables. Out of the total 60 patients enrolled in the study, a total of 30 (50%) patients received i.v. 1g Paracetamol infusion in 100 ml NS over 30 min pre-operatively comprised Group 1 of the study while remaining 30 (50%) patients received i.v. 100 ml NS 30 min prior to surgery comprised Group 2 of the study. Mean age of patients in Groups 1 and 2 was 37.57±9.70 and

41.50±12.29 years respectively. Statistically, there was no significant difference between two groups with respect to mean age (p=0.174). Majority of cases in both the groups were females (70%). The sex-profile of both the groups was identical (p=1). Mean body weight of the patients in Group 1 was 58.77±8.49 kg and that in Group 2 was 60.27±7.39 kg. Statistically, there was no significant difference between two groups with respect to mean body weight (p=0.469). In Group 1, there were 19 (63.3%) ASA I and 11 (36.7%) ASA II patients whereas in Group 2, there were 15 (50.0%) ASA I and 15 (50.0%) ASA II patients. Statistically, there was no significant difference between two groups with respect to ASA grade (0.297).

During the post-operative follow-up period, mean VAS scores for pain ranged from 0.00±0.00 (0 min) to 2.43±1.14 (6 hr) in Group 1 and from 0.37±0.49 (0 min) to 2.33±1.23 (6 hr) in Group 2. VAS scores for pain were significantly lower in Group 1 as compared to Group 2 at all the follow up from 0m to 3h. Pain scores of both the groups were comparable at follow up at 4h, 5h and 6h. (p<0.05) as depicted in Table 1 and Fig.1.

Table 1: “Comparison Of Post-operative VAS Scores For Pain Between The Two Groups”

SN	Time interval	“Group 1 (n=30)”		“Group 2 (n=30)”		“Statistical Significance”	
		Mean	SD	Mean	SD	't'	'p'
1.	0 min	0.00	0.00	0.37	0.49	-4.097	<0.001
2.	30 min	0.03	0.18	1.20	0.76	-8.164	<0.001
3.	1 hr	0.10	0.55	2.33	1.06	-10.242	<0.001
4.	2 hr	0.60	0.81	2.63	1.33	-7.160	<0.001
5.	3 hr	0.73	0.69	1.77	1.52	-3.382	0.001
6.	4 hr	1.47	0.82	1.63	1.22	-0.622	0.536
7.	5 hr	2.10	1.06	1.93	1.28	0.548	0.586
8.	6 hr	2.43	1.14	2.33	1.24	0.326	0.746

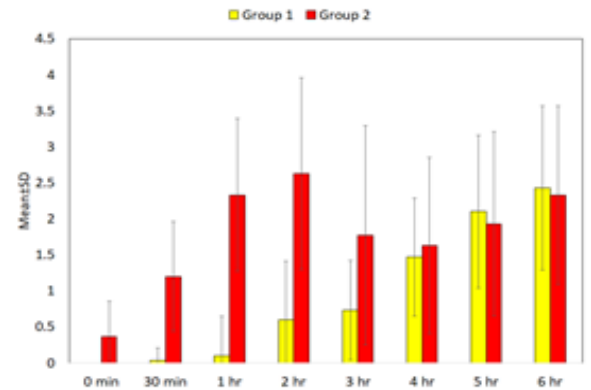


Fig. 1: “Comparison of post-operative VAS scores for pain between the two groups”

In Group 1, 20/30 (66.7%) and in Group 2, 3/30 (10.0%) patients did not require rescue analgesia. In Group 1, 10 (33.3%) patients required only one dose and none (0.0%) required two dosages. Compared to this, 22 (73.3%) in Group 2 required one dose, 5 (16.7%) required two dosages. On comparing the data statistically, the difference between two groups was found to be significant (p<0.001) as depicted in Table 2 and Fig.2.

Table 2: Comparison Of Time To Rescue Analgesia Free Time Between The Two Groups

SN	Time interval	“Group 1 (n=30)”		“Group 2 (n=30)”	
		No.	%	No.	%
1.	Upto 1 h	0	0.0	4	13.3
2.	1-3 hours	1	3.3	17	56.7
3.	3h-5h	4	13.3	4	13.3
4.	6h	25	83.3	5	16.7
$\chi^2=31.556$; $p<0.001$					
Mean rescue analgesia free time $\pm$ SD		342.00 $\pm$ 50.20		178.00 $\pm$ 97.75	
$t=8.175$; $p<0.001$					

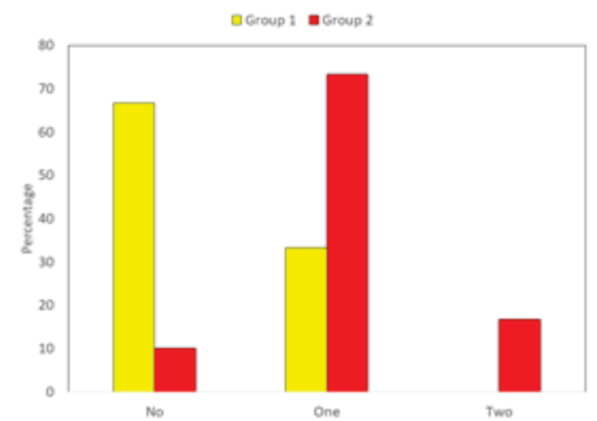


Fig. 2: “Comparison of Rescue Analgesia Need between two study groups”

None of the patient had Bradycardia, hypotension, hypertension, respiratory depression.

In significantly higher proportion of Group 2 patients as compared to Group 1 complaints of nausea (66.7% vs. 23.3%), Vomiting (43.3% vs. 13.3%) and Tachycardia (76.7%) were observed.

Headache and shivering were reported by 2 (6.7%) and 1 (3.3%) of Group 1 patient and none of the Group 2 patients. This difference was not found to be significant statistically.

DISCUSSION

Recent studies have shown the efficacy of pre-emptive (I.V) paracetamol in reducing postoperative pain and decreasing the need for additional analgesics. Patients receiving (I.V) paracetamol pre-emptively report lower pain scores and reduced opioid consumption postoperatively, which minimizes opioid-related side effects and enhances patient recovery and satisfaction. Additionally, paracetamol's favourable safety profile, with minimal gastrointestinal, renal, or cardiovascular risks, makes it suitable for a broad range of patients, including those with comorbidities³⁵.

With this background the present study was undertaken to determine the effect of pre-emptive paracetamol on post-operative analgesia requirement in patients undergoing laparoscopic surgery.

For this purpose, a prospective randomized clinical trial was carried out that included a total of 60 ASA I/II patients scheduled to undergo laparoscopic cholecystectomy under general anaesthesia were randomly allocated to receive either intravenous 1g Paracetamol in 100 ml normal saline, 30 min prior to surgery (Case group; n=30) or intravenous 100 ml normal saline, 30 min prior to surgery (Control group; n=30).

In the present study, patients in the two study groups had mean age of 37.57±9.70 and 41.50±12.29 years and had a dominance of females (70%). As such laparoscopic cholecystectomy is generally recommended in cases experiencing cholelithiasis which is known to middle aged women. Similar to the present study, most of the other workers also reported the mean age of patients in 35 to 45 years range and a dominance of females^{42,45,46,53-58}. Though some studies, especially those from abroad had reported the mean age of patients to be more than 50 years⁵ and some showing dominance of males^{43,51}. Thus, the age and sex profile of patients in the present study was comparable to most of the contemporary studies. Moreover, there was no statistically significant difference between the two groups for age, sex, ASA grade and baseline heart rate, mean arterial pressure and respiratory rates, thereby showing that there was no confounding effect of these factors due to random allocation of patients in two groups.

In the present study, we found mean VAS scores for pain to be significantly lower in PCM group as compared to control group at 0, 30 min, 1 hr, 2 hr and 3 hr postoperative intervals. Simultaneously, mean time to rescue analgesia was also significantly longer in PCM group (342±50.2 min) as compared to that in control group (178±97.75 min). Rescue analgesic need was also significantly lower in PCM (66.7%) as compared to that in control group (90%). Moreover, none of the PCM

group patients required two dosages of rescue analgesia as compared to 16.7% of control group patients who required two dosages of rescue analgesia.

These findings suggest that PCM performed extremely well as compared to control in post-operative pain and post-operative rescue analgesic reduction. Reza *et al.*⁵⁰ in their study also documented that preoperative intravenous paracetamol when compared to control group was helpful in increasing the duration of analgesic requirement and reduction in postoperative opioid consumption in LC patients. However, Patel and Patel⁵³ while comparing pre-emptive paracetamol against controls found mean VAS scores to be lower in PCM as compared to control group at 15 min post-operative interval only but found the postoperative rescue analgesic need to be significantly lower in PCM as compared to control group as seen in the present study

CONCLUSION

The findings of the study showed that pre-emptive use of intravenous paracetamol was effective in controlling the post-operative pain. It was also found to be safe and instrumental in reducing the post-operative nausea, vomiting and other adverse effects. Further studies on a larger sample size are recommended.

REFERENCES

1. McSherry CK. Open Cholecystectomy. *Am J Surg* 1993; 165: 435-39.
2. Rosen M, Ponsky J. Minimally invasive surgery. *Endoscopy* 2001; 33: 358-66.
3. Duron JJ, Hay JM, Msika S, Gaschard D, Domergue J, Gainant A, Fingerhut A. Prevalence and mechanisms of small intestinal obstruction following laparoscopic abdominal surgery: A retrospective multicentre study. *Arch Surg* 2000; 135: 208-12.
4. Squirrel DM, Majeed AW, Troy G, Peacock JE, Nicholl JP, Johnson AG. A randomized, prospective, blinded comparison of postoperative pain, metabolic response, and perceived health after laparoscopic and small incision cholecystectomy. *Surgery*, 1998; 123 (5): 485-495. Link
5. Shukla A, Seth S, Ranjan A. A comparative study between laparoscopic and open cholecystectomy in cases of cholecystitis with cholelithiasis: one year experience in tertiary care center. *Int Surg J*. 2017 Mar;4(3):903-907. Link
6. Kim SS, Kim SH, Mun SP. Should subcostal and lateral trocars be used in laparoscopic cholecystectomy? A randomized, prospective study. *Journal of Laparoendoscopic & Advanced Surgical Techniques*. 2009; 19(6): 749-753.
7. Gould J. Laparoscopic versus open inguinal hernia repair. *Surg Clin North Am*. 2008;88:1073-1081.
8. Talpur KAH, Malik AM, Sangrasi AK, Memon AI, Leghari AZ, Qureshi JN. Comparative study of conventional open versus laparoscopic cholecystectomy for symptomatic cholelithiasis. *Pak J Med Sci* 2011;27(1):33-37. Link
9. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. *Eur J Surg*. 2001;167(2):84-96. Link
10. Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Factors determining convalescence after uncomplicated laparoscopic cholecystectomy. *Arch Surg*. 2001;136:917-21. Link
11. Morsy KM, Abdalla EEM. Postoperative pain relief after laparoscopic cholecystectomy: intraperitoneal lidocaine versus nalbuphine. *Ain-Shams J Anaesthesiol*. 2014;7:40. Link
12. Alkhamesi N, Peck D, Lomax D, Darzi A. Intraperitoneal aerosolization of bupivacaine reduces postoperative pain in laparoscopic surgery: a randomized prospective controlled double-blinded clinical trial. *Surg Endosc*. 2007;21:602-6. Link
13. Gupta R, Bogra J, Kothari N, Kohli M. Postoperative analgesia with intraperitoneal fentanyl and bupivacaine: a randomized control trial. *Can J Med*. 2010;1:1-11. Link
14. Wallace DH, Serpell MG, Basxter JN, O'Dwyer PJ. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. *Br J Surg*. 1997;84:455-8. Link
15. Tsimoyiannis EC, Siakas P, Tassis A, Lekkas ET, Tzourou H, Kambili M. Intraperitoneal normal saline infusion for postoperative pain after laparoscopic cholecystectomy. *World J Surg*. 1998;22:824-28. Link
16. Wills V, Hunt D. Pain after laparoscopic cholecystectomy. *Br J Surg*. 2000;87:273-84. Link
17. Barazanchi AWH, MacFater WS, Rahiri JL, Tutone S, Hill AG, Joshi GP; PROSPECT collaboration. Evidence-based management of pain after laparoscopic cholecystectomy: a PROSPECT review update. *Br J Anaesth*. 2018;121(4):787-803. Link
18. Kucuk C, Kadiogullari N, Canoler O, Savlı S. A placebo-controlled comparison of bupivacaine and ropivacaine instillation for preventing postoperative pain after laparoscopic cholecystectomy. *Surg Today*. 2007;37:396-400. Link
19. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh P, Singh U. Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. *Br J Anaesth*. 2008;101:700-4. Link
20. Vejdani SA, Khosravi M, Naseh G. Post Laparoscopic Pain Control Using Local Anesthesia through laparoscopic port sites. *Novelty in Biomedicine*. 2014;2:102-6. Link
21. Bonnefont J, Courade JP, Alloui A, Eschaliere A. Antinociceptive mechanism of action of paracetamol. *Drugs*. 2003;63:1-4. Link
22. Pini LA, Vitale G, Ottani A, Sandrini M. Naloxone-reversible antinociception by paracetamol in the rat. *J Pharmacol Exp Ther*. 1997;280:934-40. Link
23. Wininger SJ, Miller H, Minkowitz HS, Royal MA, Ang RY, Breitmeyer JB, Singla NK. A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two intravenous acetaminophen dosing regimens for the treatment of pain after abdominal laparoscopic surgery. *Clin Ther*. 2010;32(14):2348-69.