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Original Research Article

Prospective Randomized Comparative Clinical Assessment of the Diclofenac with Different Preparation of Paracetamol for Post-Operative Analgesia Following Laparoscopic Cholecystectomy

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Abstract

Aim: To evaluate the efficacy of postoperative pain control by diclofenac with Paracetamol 100 mL infusion (P) and diclofenac with Paracetamol 2 mL stat (PL).

Material & Methods: The proposed study was carried out in the department of Surgery, JNKTCH, Madhepura, Bihar, India, over a period of one year.120 patients were included in the study. They were divided into two groups with 60 patients in each group: Group DP and Group DF.

Results: The demographic data showed that the mean age group was 35 years, weight was 60.5 kg, height was 160 cm and a sex ratio of female: male=51:49 in either group. VAS taken for post-operative pain assessment was same in both the age groups over equal time interval without significant difference.

Conclusion: Comparing both the formulations of these paracetamol in combination with diclofenac in laparascopic surgeries and we did not find any significant difference between these two in terms of demography, VAS, VRS and any other side effects. However, the major difference in the cost between these two formulations makes a significant impact in the economic burden.

Keywords Diclofenac; Paracetamol; Cysteine hydrochloride monohydrate; Lignocaine hydrochloride; Benzyl alcohol; Laparoscopic cholecystectomy; Postoperative pain

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. [1] Postoperative pain, is typically associated with neuro-endocrine stress response that is proportional to pain intensity. Many patients, however, continues to experience inadequate pain relief. [2] Despite improvements in analgesic delivery, several recent surveys have found that up to 80% of patients report moderate to severe pain after surgery. [3-5] After laparoscopic cholecystectomy parental opioid and NSAIDS are commonly used for postoperative analgesia. [6-7] Opioid remain the agents of choice for severe pain; however, this class of analgesics is associated with dose-dependent adverse effects such as nausea vomiting, ileus,

sedation and respiratory depression and prolongs the time to readiness for discharge. [8-9]

Laparoscopic cholecystectomy is the treatment of choice for cholelithiasis as it has got several advantages like smaller and more cosmetic incision, reduced blood loss, reduced post-operative stay, low post-operative complications and early mobilization. But postoperative pain is one of the major drawbacks of this procedure. Hence adequate analgesia must be given to the patient both intra and postoperatively in order to make the patient pain free. Both diclofenac and paracetamol play very important role in pain management following laparoscopic cholecystectomy. Paracetamol is available in two forms either Paracetamol 100 mL solution for infusion (P), containing paracetamol, cysteine hydrochloride monohydrate, disodium phosphate dihydrate, hydrocholoric acid, mannitol and sodium hydroxide [PERFALGAN, marketed by Bristol-Myers Squibb India private limited] or Paracetamol and lignocaine 2 mL injection (PL), containing paracetamol, lignocaine hydrochloride and benzyl alcohol. [10] Thus we aim to evaluate the efficacy of postoperative pain control by diclofenac with Paracetamol 100 mL infusion (P) and diclofenac with Paracetamol 2 mL stat (PL).

Material & Methods:

The proposed study was carried out in the department of Surgery, JNKTCH, Madhepura, Bihar, India, over a period of one year. 120 patients were included in the study. They were divided into two groups with 60 patients in each group,

Group DP: Patients received Diclofenac with Paracetamol P (100 ml infusion)

Group DF: Patients received Diclofenac with Paracetamol PL (2 ml stat)

Selected patients were from either sex, age group between 20-to-50-year, average weight, belonging to ASA grade I and II posted for laparoscopic cholecystectomy. Patients with history of drug allergy, bleeding disorders [11-12], asthma, gastrointestinal system bleeding, renal insufficiency, etc. were excluded from the study.

Methodology

Patient was taken into the pre-operative preparation room where intravenous (I.V) cannula was secured and 1 mg midazolam was given slow I.V. Then patient was shifted to the operation theatre and standard monitors ECG, NIBP and pulse oximeter were attached. All the patients were given injection 0.2 mg glycopyrolate I.V, 1 mg/kg body weight ondansetron I.V, 2 mg/kg fentanyl I.V as premedication. Induction was performed with 2 mcg/kg propofol I.V and after loss of consciousness 0.1 mg/kg vecuronium bromide I.V was given for muscle relaxation.

Then patient was pre-oxygenated for 3 minutes and adequate size of I-gel was secured for ventilation. After confirming the proper placement of I-gel, anaesthesia was maintained with 1 liter of oxygen and 2 liters of nitrous oxide followed by propofol infusion. Stomach was decompressed with 10 Fr size of orogastric tube via side port of I-gel. Tidal volume and respiratory rate were adjusted to maintain the $EtCO_2$ between 35-45 mm Hg. After 10 minutes of starting of surgery patients of DP group received 75 mg of diclofenac sodium aqueous I.V over a period of 10-15 minutes followed by paracetamol infusion (P) 15 mg/kg. DF group received diclofenac sodium I.V of same dose given over same period and paracetamol (PL) in same dose. After completion of surgery the muscle relaxant was reversed with injection neostigmine 0.05 mg/kg and glycopyrolate 0.01 mg/kg I.V. Once the patient gained full onsciousness then shifted to post-operative care unit, where the patient was monitored for next 6 hours. The anaesthesiologist who was blinded for the study was asked

to visit the patient at 30 minutes, 1 hour, 2 hour, 4 hour and 6 hour. He was also asked to keep the record of VAS score:

- Fair control
- Good control
- Excellent control

The rescue analgesia was given only on patient demand, in the form of injection pentazocine 30 mg slow I.V. over 10 minutes and the patient was monitored for the next 30 minutes for respiratory depression and sedation. Total requirement of rescue analgesia was noted in both the groups. Statistical analysis was conducted using SPSS 13 software and comparisons among the groups were analyzed by using Chi-square test. All the measurements were expressed as mean + standard deviation with P value.

Results:

The demographic data showed that the mean age group was 35 years, weight was 60.5 kg, height was 160 cm and a sex ratio of female: male=51:49 in either group. The mean duration of operation was 30.11 ± 30 minutes and the mean duration of analgesia was 105.1 ± 9.4 minutes (Table 1).

VAS taken for post-operative pain assessment was same in both the age groups over equal time interval without significant difference (Table 2).

The requirements of rescue analgesia were also same in both the groups. The patient satisfaction at 6 hour was assessed by taking verbal rating scale, which was same in both the age groups (Table 3).

There was no significant difference in incidence of side effect among both the groups (Table 4).

Table 1: Demographic data

Demographic data	Group DP	Group DF	P value
Age (in years)	34.1 ± 7.9	36.1 ± 8.3	>0.05
Sex (M/F)	51 %	49 %	>0.05
Weight (kg)	60.5 ± 10.6	62.5 ± 3.4	>0.05
Height (cm)	157.9 ± 10.3	151.6 ± 3.7	>0.05
Duration of Operation (in min)	30.11 ± 30	31.4 ± 35	>0.05
Duration of Analgesia (in min)	105.1 ± 9.4	101.4 ± 10.7	>0.05

Table 2: VAS pain score (n=60 in each group)

Time	Group DP	Group DF	P value
30 min	5.12 ± 1.7	5.72 ± 1.15	>0.05
1 hour	4.71 ± 1.3	5.2 ± 1.4	>0.05
2 hour	4.44 ± 1.3	4.7 ± 1.2	>0.05
4 hour	4.63 ± 1.2	4.3 ± 1.1	>0.05
6 hour	3.30 ± 1.1	3.2 ± 1.0	>0.05

Table 3: Patient satisfaction at 6 hour of operation using Verbal Rating Scale

Verbal rating scale	Group DP	Group DF	P value
Poor 1	3	4	>0.05
Fair 2	10	12	>0.05
Good 3	16	18	>0.05
Excellent 4	5	3	>0.05

Table 4: Incidence of side effects (n=60 in each group)

Side effects	Group DP	Group DF	P value
Nausea and Vomiting	4	2	>0.05
Sedation	0	0	>0.05
Headache	2	2	>0.05
Restlessness	1	0	>0.05
Dizziness	1	1	>0.05
Rashes	0	0	>0.05

Discussion:

NSAIDS are helpful in management of the postoperative pain after laparoscopic cholecystectomy which is mainly visceral experienced due to rapid distension of peritoneum because of CO2 insufflation which leads to traumatic traction of nerves and causes release of inflammatory mediators which cause pain. [13] This visceral pain occurs early in the postoperative period and its intensity decreases after first 24 h. NSAIDS are the best agents for pain relief after laparoscopic cholecystectomy may be because the pain in this surgery is mostly dependent on the release of inflammatory mediators. [13] Preemptive analgesia prevents the onset of the noxious stimulus and prevents central sensitization.

After laparoscopic cholecystectomy, parentral acetaminophen, opioid and NSAIDS are commonly used for postoperative analgesia. Besides showing individual variation in intensity and duration, the pain is often unpredictable. It may even remain severe throughout the first week in 18% of the patients. [14] Although laparoscopic cholecystectomy is less invasive procedure than classical open surgical approach, many laparoscopic patients suffer considerable postoperative pain. [15]

Agarwal et al. also reported that oral pregabalin 150 mg administered before the operation was effective in reducing postoperative pain and the postoperative patient-controlled fentanyl requirement in patients undergoing laparoscopic cholecystectomy. [16]

Paech et al. found that no better pain relief than placebo and an increase in side effects, after a single preoperative dose of pregabalin 100 mg in patients have day-case uterine surgery. [17]

These results were partially consistent with Peng et al. who reported that multiple doses of pregabalin resulted in superior analgesia only in the first 90 min over placebo. Pregabalin 75 mg offered better analgesia compared with pregabalin 50 mg. However, pregabalin did not result in a reduction in opioid consumption, clinical meaningful side effects or an improvement in quality of recovery. [18]

Montgomery et al used paracetamol 1500 mg alone, diclofenac 100 mg alone and paracetamol 1500 mg in addition to diclofenac 100 mg single rectal dose given before surgery with 24 hours of observation following elective gynecological surgery. He found pain intensity to be positive and higher percentage of nausea and vomiting, which could be due to morphine used in higher doses [19]. Munishankar et al also found same result as Montgomery et al [20]. Riad et al carried out a study in children undergoing inguinal hernia surgery and they used diclofenac 1 mg/kg, paracetamol 40 mg/kg and a combination of diclofenac 1 mg/kg with paracetamol 40 mg/kg, in which all drugs were given rectally 1 hour before surgery. They found pain intensity

to be lesser in combination of drug [21, 22].

Conclusion:

Comparing both the formulations of these paracetamol in combination with diclofenac in laparascopic surgeries and we did not find any significant difference between these two in terms of demography, VAS, VRS and any other side effects. However, the major difference in the cost between these two formulations makes a significant impact in the economic burden.

References:

1. Morgan GE, Mikhall MS & Murray MJ, In: Clinical anaesthesiology', Lange Medical Books/Mc Graw-Hill, 2006; 361.
2. Dahl JL, Gordon D, Ward S. Institutionalizing pain management: The postoperative pain management quality improvement Project. J Pain 2003; 4: 361-71.
3. Warfield CA, Kahn CH. Acute pain management programs in U.S. Hospitals and experiences and attitudes among U.S adults. Anaesthesiology 1995; 83: 1090-94.
4. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. P Troil H, Spangenberger W, Langen R, aljaostoperative pain experience: Results from a national survey suggests postoperative pain continues to be undermanaged. Anesth ANALG 2003; 97: 534-40.
5. Huang N, Cunninggham F, Laurito CE, Chen C: Can we do better with postoperative pain management. Am J Surg 2001; 182: 440-8.
6. Elia N, Lyskowski C, Tramer MR. Does multimodal analgesia with acetaminophen, nonsteroidal anti-inflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient –controlled analgesia morphine offer advantages over morphine alone? Meta analyses of ramdomized trials. Anesthesiol. 2005; 103(6):1296-304.
7. Schug SA, Manopis A. Update on the role of nonopioids for postoperative pain treatment. Best Pract Res Clin Anaesthesiol. 2007; 21(1):15-30.
8. Amjad A, Chohan U, AtiqF. Intravenous tramadol vs ketorolac in laparoscopic dye test. JCPSP 2005; 16: 3-6.
9. Dubos F, Icard P, Berthelot G, Levard H. Coelioscopic Cholecystectomy. Ann Surg 1990;2(11):60-2.
10. Shashi Prakash, Sandeep Loha, Rajesh Kumar Meena, Anil Kumar Paswan, Arvind Bhalekar and Yashpal Singh. A Comparative Study of the Diclofenac with Different Preparation of Paracetamol for Post-Operative Analgesia Following Laparoscopic Cholecystectomy. J Anesth Clin Res. 2016; 7:7.
11. Moote C. Efficacy of Non-Steroidalanti-Inflammatory Drugs in Management of Post-operative pain. 1992; 44:14-29.
12. Fredman B, Olsfranger D, Jedkin R. A comparative study of Ketorolac and Diclofenac on post laparoscopic cholecystectomy pain. Euro J Anaesthesiology. 1995; 12:501-4.
13. Alexander JI. Pain after laparoscopy. Br J Anaesth 1997; 79:369-78.
14. Bisgard T, Klarskov B, Kehlet H, Rosenberg J. Characteristics and prediction of early pain after laparoscopic cholecystectomy. Pain 2001; 90:261-9.
15. Cliffod JW & Mun SC, 'Preemptive analgesia- Treating postoperative pain by preventing the establishment of central sensitization', Anaesthesia Analgesia,1999;13:445-8.
16. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, 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.
17. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A

randomized, placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. Anesth Analg 2007; 105:1449-53.
18. Peng PW, Li C, Farcas E, Haley A, Wong W, Bender J, et al. Use of low dose pregabalin in patients undergoing laparoscopic cholecystectomy. Br J Anaesth 2010; 105:155-61.
19. Montgomery JE, Sutherland CJ, Kestin IG, Sneyd JR. Morphine consumption in patients receiving rectal Paracetamol and Diclofenac alone or in combination. British Journal of Anaesthesia. 1996; 77:445-447.
20. Munishankar, Fetters P, Moore C, McLeod GA. A double blind randomised controlled trial of Paracetamol, Diclofenac or the combination for the pain relief after caesarean section. International Journal of Obstetric Anesthesia. 2008;17: 9-14.
21. Riad W, Moussa A. Pre-operative analgesic with rectal Diclofenac and/or paracetamol in children undergoing inguinal hernia repair. Anaesthesia. 2007; 62:1241-1245.
22. Saccomanni, B. Some words about fractures of radial head. Journal of Medical Research and Health Sciences, 2020:3(10), 1106–1108.