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ORIGINAL ARTICLE

Role of Intervenous Paracetamol as Preemptive Analgesic for Laparoscopic Cholecystectomy

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ABSTRACT

Objective: The purpose of this study was to evaluate the comparative effectiveness of preemptive paracetamol against placebo for laparoscopic cholecystectomy.

Methods: After the approval from Institute review board, this randomized control trial was conducted at Department of Anesthesia, KTH, Peshawar, from 1st August 2020 to 31st January 2021. A total of 60 patients of both gender undergoing laparoscopic cholecystectomy were included in the study. Patients of Group A (n=30) received I.V Paracetamol 10mg/kg (100ml) and Group B (n=30) received 100 ml of Normal saline 10 min before skin incision. Efficacy was noted as per operational definition and noted.

Results: Mean age of patients in group A and B was 34.200±5.56 and 35.900±6.28 years. Mean duration of complain in group A and B was 11.333±3.53 and 10.366±2.51 months. Mean duration of procedure in group A and B was 70.533±10.95 and 72.666±10.58 minutes. Females were predominant in the present study, with 66.7% females in group A while 60% in Group B. 22 of the patients in Group A (73.30%) had success, whereas only 10 of the patients in Group B (33.30%) did so (P= 0.002).

Practical implication: this study will help to demonstrate either paracetamol can be used as analgesic in laparoscopic cholecystectomy

Conclusion: In conclusion, our research shown that paracetamol had an analgesic impact on cholecystectomy patients shortly after surgery.

Keywords: Laparoscopic cholecystectomy, Paracetamol, Placebo, Efficacy

INTRODUCTION

"Pain" is a term used to describe the unpleasant sensory and emotional experience associated with actual or potential tissue damage. Postoperative pain is a potential side effect of undergoing treatment (such as surgery) and can set off a cascade of biochemical and physiological stress responses (1). As a major clinical, social, and economic issue, pain is a global public health crisis (2). Nociceptive pain is the most common type of pain experienced after surgery. Some patients experience chronic postoperative pain after surgery because central and peripheral sensitization and hyperalgesia were induced by the trauma of surgery (3). Both clinicians and patients undergoing surgery place a premium on ensuring that pain is properly managed, especially after the procedure has been completed. Surgical patients frequently inquire about the potential severity of their post-op pain (4). The severity of postoperative pain is associated with an increased risk of complications such as arrhythmias, hyperventilation, decreased alveolar ventilation, chronic pain, poor wound healing, and sleep disturbances, all of which can have a negative effect on a patient's operative outcome, well-being, and satisfaction with medical care. Pain thresholds vary from person to person based on factors like genetics, upbringing, age, and gender (5). The field of modern anesthesiology has expanded beyond the intraoperative period to include the preoperative and postoperative times as well. Effective postoperative pain management is a crucial part of patients' postoperative care (6). Experiencing pain during and after surgery is associated with a greater risk of developing a pain sensitivity, as well as a higher risk of transforming postoperative acute pain into chronic pain (7). Initiating physiotherapy and early ambulation, which speed recovery and decrease hospital length of stay, necessitates effective postoperative pain control (8). Common practice in the field of anesthesia involves the administration of opioid drugs to patients before, during, and after surgery to alleviate their discomfort (9, 10). However, there are drawbacks to taking these drugs, including dizziness, drowsiness, and even respiratory depression. Administering a nonopioid analgesic at the same time as an opioid is recommended for lowering the risk of adverse effects (11). Not knowing whether or not two medications are compatible should never lead to the choice to combine them. Small, concentrated amounts combined in a syringe are more likely to cause incompatibilities than large volumes mixed in an infusion bag (12). Aspirin and acetaminophen are examples of nonsteroidal anti-inflammatory medicines that fall under this category (Paracetamol). The primary mechanism of action of these analgesics is to block the production of cyclooxygenase and prostaglandin, both of which are thought to be crucial environmental factors in preventing hypersensitivity and pain (11). Platelet aggregation, hemostasis, and gastric mucosa protection all rely on cyclooxygenase 1 (COX-1), while pain, inflammation, and fever reduction rely on cyclooxygenase 2 (COX-2). One of the proposed mechanisms for acetaminophen's analgesic effect is its inhibition of the recently discovered cyclooxygenase 3 (COX-3) (13). In most cases, nonsteroidal anti-inflammatory medications are able to alleviate moderate to severe pain. Opioid adjuvants have been shown to be useful for treating moderate to severe pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to be effective for pain control, both when used alone and in combination with opioids (14, 15). Although paracetamol has been used for postoperative pain management (16), the original point of this study was to determine whether or not its use after induction of anesthesia for postoperative pain management was safe. The aim of the study was to compare the efficacy of intravenous paracetamol and placebo as preemptive analgesic for laparoscopic cholecystectomy.

METHODOLOGY

After the approval from Institute review board, this randomized control trial was conducted at Department of Anesthesia, KTH, Peshawar, from 1st August 2020 to 31st January 2021. Patients between 20-50 years of both Gender with gallstones ≤ 4 in numbers (size ≤ 2cm) on ultrasound for > 6 months and undergoing laparoscopic cholecystectomy were included in the present study. Patients those having contraindications to paracetamol (allergy, liver disease) and other comorbidities or the Patients those on treatment by steroids, NSAIDs, or opioids before surgery were excluded from the study. 60 patients fulfilling the inclusion criteria were included in the study and were divided into

two groups randomly, Group A(n=30), Group B(n=30). Patients of Group A (n=30) received I.V Paracetamol 10mg/kg (100ml) and Group B (n=30) received 100 ml of Normal saline 10 min before skin incision. All of the patients had a 3-minute session of pre-oxygenation with 100% oxygen utilising Bain's circuit. All patients were given intravenous (IV) injections of thiopentone (5 mg/kg), fentanyl (2 µg/kg), and vecuronium (0.1 mg/kg), and their tracheas were intubated using an endotracheal tube (ETT) of the appropriate size. After intubation, isoflurane in 40:60 oxygen:nitrous oxide was provided to keep the patient under general anaesthesia, with further doses of 0.01 mg/kg vecuronium given as needed. After complete reversal with 0.01 mg/kg of glycopyrrolate and 0.05 mg/kg of neostigmine and adequate suctioning, patients were extubated. Postoperative pain was assessed using a visual analogue scale (VAS) from 0 to 10, with 0 indicating no pain and 10 representing the greatest possible pain, in the post anaesthesia care unit. In the postoperative period, pain levels were tracked at 15min, 30min, 1-, 2-, and 6-hour intervals. If the patient's VAS score was more than three, 50 mg of tramadol was administered intravenously as a rescue analgesic. Notes on effectiveness were recorded on a custom-made proforma based on the operational definition of success (Annexure-I).

SPSS version 26 was used for the statistical analysis. Proportions of people in both Group A and Group B were analyzed. Quantitative characteristics like gender and effectiveness have their frequencies and percentages calculated. Quantitative factors such as age, duration of complaint, and procedure length were provided as mean±S.D. The effectiveness of each group was compared using a chi-square test, with a p-value of ≤0.05 being considered statistically significant. Age, gender, complaint length, and procedure time were used as stratification criteria to examine their impact on success rates. After dividing participants into two groups, the chi-square test was used to determine which ones were statistically different.

RESULTS

Demographic characteristics of the patients in both groups were presented in Table 1. Mean age of patients in group A and B was 34.200±5.56 and 35.900±6.28 years. Mean duration of complain in group A and B was 11.333±3.53 and 10.366±2.51 months. Mean duration of procedure in group A and B was 70.533±10.95 and 72.666±10.58 minutes. Females were predominant in the present study, with 66.7% females in group A while 60% in Group B. According to Table 2, 22 of the patients in Group A (73.30%) had success, whereas only 10 of the patients in Group B (33.30%) did so (P= 0.002). Tables 3, 4, 5, and 6 illustrate the effectiveness stratification in both groups according to age, gender, length of complaint, and duration of procedure.

Table 1: Demographic and clinical parameters of the patients in both groups

Parameters	Group A (n=30)	Group B (n=30)
Age (years)	34.200±5.56	35.900±6.28
Female n (%)	10 (33.3%)	12 (40%)
Male n (%)	20 (66.7%)	18 (60%)
Duration of complain (months)	11.333±3.53	10.366±2.51
Duration of procedure (mins)	70.533±10.95	72.666±10.58

Table 2: Comparison of efficacy in both groups

Efficacy	Group A (n=30)	Group B (n=30)	P Value
Yes	22 (73.3%)	10 (33.3%)	0.002
No	8 (26.7%)	20 (66.7%)	

Table 3: Stratification of efficacy with respect to age in both groups

Age Group	Efficacy	Group A	Group B	P Value
20-35 years	Yes	15(75%)	8(53.3%)	0.181
	No	5 (25%)	7 (46.7%)	
36-50 years	Yes	7(70%)	3 (30%)	0.004
	N0	2 (13.3%)	13 (86.7%)	

Table 4: Stratification of efficacy with respect to gender in both groups

Gender	Efficacy	Group A	Group B	P Value
Male	Yes	30 (100%)	28 (93.3%)	0.176
	No	0	2 (16.7%)	
Female	Yes	12(60%)	8 (40%)	0.000
	No	0	30 (100%)	

Table 5: Stratification of efficacy with respect to complaint time in both groups

Complaint Time	Efficacy	Group A	Group B	P Value
6-12 months	Yes	12 (63.2%)	7 (36.8%)	0.059
	NO	7 (33.3%)	14 (66.7%)	
>12 months	Yes	10(90.9%)	3 (33.3%)	0.007
	NO	1 (9.1%)	6 (66.7%)	

Table 6: Stratification of efficacy with respect to procedure time in both groups

Procedure Length	Efficacy	Group A	Group B	P Value
≤60 minutes	Yes	5 (100%)	1 (20%)	0.008
	NO	0	4 (80%)	
> 60 minutes	Yes	17(68%)	9 (36%)	0.024
	NO	8 (32%)	16 (64%)	

DISCUSSION

Twenty-two patients in group A (73.30%) showed efficacy, while only ten patients in group B (33.30%) did (P= 0.002). Intervenors paracetamol was found to be more effective as a preemptive analgesic for laparoscopic cholecystectomy (92% vs. 20% with placebo) in a study by Reza S, et al (17). Sreenivasulu A et al. found that, as a preemptive analgesic for laparoscopic cholecystectomy, intervenous paracetamol was 74.19 percent effective, while placebo was only 35.48 percent effective (18). As this research shows, cholecystectomy patients who receive paracetamol after surgery fare better than those who receive placebo. Its analgesic impact was not sufficient as a solo agent, while it did reduce overall opioid intake over a 24-hour period and lengthen the time before first analgesic usage. The findings of controlled clinical investigations indicated that the prescribed therapeutic dosages of intravenous paracetamol are safe and well tolerated, with a profile that supports the high reliability comparable to placebo. Unlike opioids and NSAIDs, paracetamol does not cause the same gastrointestinal and central nervous system side effects, so it is widely considered a safe drug (18). Numerous studies have shown that oral paracetamol is an effective and well-tolerated agent in a variety of surgical procedures (19). After surgery, however, paracetamol can only be taken by mouth so much. Patients having surgical treatments want effective and rapid commencing eradication of pain. Compared to oral paracetamol, the effects of parenteral paracetamol are felt sooner and last longer (20). Similar to the analgesic effects of diclofenac (75 mg), ketorolac (30 mg), and morphine (10 mg) after surgery, intravenous 1 g of paracetamol has been shown to be effective in relieving moderate to severe pain (21). It has been established in a double-blind, placebo-controlled trial that administering both intravenous paracetamol and ketoprofen during the first 48 hours after surgery reduces post-operative pain and cumulative opiate intake (22, 23). Further evidence was shown that intravenous paracetamol may reduce opioid use. There is an increase in patient satisfaction and a decrease in the patient's need for opioids of 24-46%(24). A meta-analysis conducted by Remy et al.(25) found that paracetamol decreases post-operative morphine use. It has been reported that giving patients with moderate pain after major orthopaedic procedures 1g of paracetamol every six hours for 24 hours results in rapid and effective analgesia, decreases the need for morphine, and increases the time before the patient requests analgesia for the first time (26). The effectiveness of intravenous paracetamol was studied by Fijalkowska et al. (27) in 92 patients undergoing laparotomy or laparoscopy. Only 16.3% of patients undergoing laparoscopy required additional morphine, while 71.4% of those undergoing laparotomy did so. To sum up, they reported that paracetamol lessens the requirement for opioid analgesics, but that a multimodal approach is required for major

surgeries. Based on the findings of a study by Guner et al. (28), which compared paracetamol and tramadol, we know that both medications can help reduce the need for opioids following major abdominal surgeries, but that neither can provide sufficient pain relief on their own. Furthermore, our study found that patients in group B required more analgesics than those in group A. We agree that a multimodal analgesic approach, including paracetamol to lessen the need for opioids, would be preferable during major surgical procedures. Paracetamol 1 g iv preoperatively, intraoperatively, and every 6 h for 24 h for continued infusions of 1 g in patients scheduled for lumbar discectomy surgery may provide a better post-operative analgesia compared to the control group, will delay the time of the post-operative first morphine request, and will reduce post-operative use of total morphine, as reported by Toygar et al.(29). Further research may be necessary on the topic stated, but preoperative paracetamol application does not have a preventative analgesic effect.

CONCLUSION

In conclusion, our research shown that paracetamol had an analgesic impact on cholecystectomy patients shortly after surgery. Paracetamol may be taken without risk after surgery since it reduces the need for opioids while producing fewer negative effects.

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