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Comparison of Intraoperative Intravenous Ibuprofen versus Intravenous Paracetamol for Post-Operative Pain Relief in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To compare intraoperative intravenous Ibuprofen versus intravenous Paracetamol for post-operative pain relief in patients undergoing laparoscopic cholecystectomy.

Study Design: Quasi-experimental study.

Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Feb to Nov 2021.

Methodology: The study was conducted on 400 patients who underwent laparoscopic cholecystectomy during the study period. Patients were randomized into two groups. Group A received intravenous Ibuprofen, while Group B received intravenous Paracetamol during the surgical procedure. The pain at the surgical site was recorded on the visual analog scale (VAS) at 2 hours and 6 hours after the surgical procedure. The difference in post-operative pain and the requirement of opioid analgesia was compared in both groups via the chi-square test.

Results: Out of 400 patients randomized into two groups, 198(49.5%) were categorized into Group A, and 202(50.5%) were categorized into Group B. 290(72.5%) were female, while 110(27.5%) were male. The mean age of patients who underwent laparoscopic surgery in our study was 40.24±7.69 years. Patients who received intravenous Ibuprofen had more chances of not having significant postoperative pain at 02 and 06 hours after the surgery as compared to those who received intravenous Paracetamol (p-value<0.05).

Conclusion: The Use of intravenous Ibuprofen during laparoscopic surgery emerged as better management for early post-operative pain as compared to the use of intravenous Paracetamol. There was no difference in the use of opioid analgesia in the early postoperative period in both groups.

Keywords: Ibuprofen, Laparoscopic Cholecystectomy, Paracetamol.

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INTRODUCTION

Gallbladder surgeries have been a staple of general surgeons worldwide. Post-operative pain has been a problem for surgical teams. Trained professionals work in a team, and both surgeons and anesthetists collaborate closely to minimize the adverse effects related to surgery, especially post-operative pain.[1,2] Pakistan is a developing country with limited healthcare facilities and emerging new specialties.[3,4] Anaesthetists and medical specialists have been pursuing careers in pain medicine, seeking to introduce innovative methods for alleviating pain, particularly after various surgical procedures.[5] Ibuprofen has been used for decades as a painkiller for various conditions, but its intravenous use is a relatively new development and is still under trial for various indications.[6]

Multiple methods have been used for years to reduce the post-operative pain among the patients undergoing laparoscopic surgeries. A recent study concluded that this combined form of analgesia was effective in reducing post-operative pain and the need for opioid painkillers.[7] Effects of single-dose pre-emptive intravenous Ibuprofen on postoperative opioid consumption and acute pain after laparoscopic cholecystectomy were studied by Ahiskalioglu *et al.* It was revealed that a pre-emptive single dose of IV Ibuprofen in laparoscopic cholecystectomy reduced postoperative opioid consumption in the 1st 24 hours by 45%. It generated lower pain scores in the postoperative period compared with the placebo.[8] Ekinci *et al.*, (2020) published an RCT regarding the efficacy of intravenous Ibuprofen and Paracetamol in postoperative pain after laparoscopic cholecystectomy. They revealed that IV Ibuprofen resulted in lower pain scores and reduced opioid use compared with acetaminophen postoperatively in the first 24 hours in patients undergoing laparoscopic cholecystectomy surgery.[9]

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Pain has long been a concern for patients, particularly those undergoing any surgical procedure. Pain has affective, mechanical, physical, and physiological components, and then the threshold is different for each patient. Newer modalities or new routes for existing medications have always been interesting choices for physicians and researchers. A recent local study compared Paracetamol and intravenous ketorolac for pain relief among patients undergoing abdominal surgical procedures.[10] Limited local data have been available regarding the use of intravenous Ibuprofen for this purpose, and it would be helpful to gather data in this regard to provide patients with the best possible pain relief. This study was planned with the rationale of comparing intra-operative intravenous Ibuprofen versus intravenous Paracetamol for post-operative pain relief in patients undergoing laparoscopic cholecystectomy.

METHODOLOGY

The Quasi-experimental study was conducted at the Anesthesia/Surgical Department of the Combined Military Hospital, Rawalpindi Pakistan, from Feb to Nov 2021. The sample size was calculated using the WHO Sample Size Calculator, which utilized the population prevalence proportion of pain after laparoscopic cholecystectomy of 12%.[11] Non-probability consecutive sampling technique was used to gather the sample.

Inclusion Criteria: All patients between the ages of 18 and 65 years undergoing cholecystectomy via laparoscopic method in our hospital for any reason were included. Patients referred from another hospital for the same purpose were also included.

Exclusion Criteria: Patients with uncontrolled or poorly controlled comorbid illness or those whose age did not fall in inclusion were excluded. Those with any gallbladder, biliary tract, or other neoplastic conditions were also excluded. Patients who had undergone redo surgeries or exhibited immediate signs of surgical complications, including infection, were also excluded from this study. Patients suffering from any chronic pain disorder or any psychiatric condition or using any illicit substance were also excluded from the study. Patients who were allergic to Ibuprofen or Paracetamol were not included, along with patients who had difficult gall bladder or conversion of laparoscopic cholecystectomy to open cholecystectomy.

After obtaining approval from the Ethical Review Board Committee (IREB Letter No: 225/12/21), the research team recruited patients who fulfilled the laid-down criteria. Routine antibiotics and pre-anesthetic medication were administered to all patients, regardless of the assigned group. Patients were randomly assigned to two groups using a lottery method. Group A received intravenous Ibuprofen, while Group B received intravenous Paracetamol during the surgical procedure (Figure). The pain at the surgical site was recorded on the visual analog scale (VAS) at 2 hours and 6 hours after the surgical procedure. To blind the health professional who assessed the pain, the person assessing the data was unaware of the patient's Group and the details of the mode used for pain score assessment. Patients were also unaware of this information. A score of greater than 6 was used as a cut-off to classify significant pain.

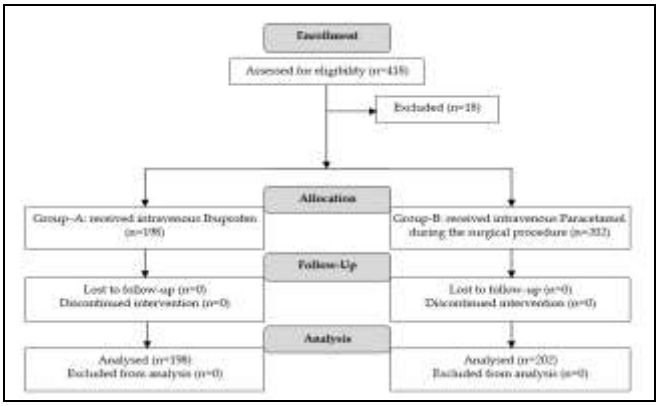

Figure: Patient Flow Diagram (n=400)

The consultant laparoscopic surgeon did a Cholecystectomy as per protocol.[12] Intravenous Paracetamol was given as 1g in 100ml of 0.9% NaCl immediately after induction of anesthesia over 15 minutes.[13] Intravenous Ibuprofen was given in the dose of 400mg intravenously in 100 ml saline over half an hour.[14] Pain and requirement of opioid analgesia was checked by consultant anesthetist at 02 and 06 hours after the surgery in both the groups.

All statistical workup for the study and application of relevant tests was conducted using the Statistical Package for the Social Sciences (SPSS) version 24. Frequency and percentages were calculated for all qualitative variables included in the study. The mean and standard deviation for age were also calculated for the study participants in both groups. The Pearson Chi-square test was applied to examine the association between the presence of significant pain and the requirement for analgesia with the type of analgesic agent used intraoperatively.

An association was established if the *p*-value after applying the chi-square test was ≤0.05.

RESULTS

A total of 400 patients who underwent laparoscopic cholecystectomy during the study period were included in the study. Out of 400 patients randomized into two groups, 198(49.5%) were assigned to Group A, and 202(50.5%) were assigned to Group B. 290(72.5%) were female, while 110(27.5%) were male. Table-I summarizes the general characteristics of study participants. The mean age of patients who underwent laparoscopic surgery in our study was 40.24±7.69 years. 292(73%) had no significant pain at two hours, while 108(27%) had significant pain at 02 hours after the surgery. At 06 hours after the surgery, 324(81%) did not report significant pain, while 76(19%) did report significant pain. Table-II summarizes the results of the statistical analysis. Patients who received intravenous Ibuprofen had a higher chance of not experiencing significant postoperative pain at 2 hours (*p*-value <0.001) and 6 hours (*p*-value =0.003) after surgery compared to those who received intravenous Paracetamol. The requirement of opiate analgesia for pain relief after the surgery at 02 hours (*p*-value-0.121) and 6 hours (*p*-value-0.954) was not statistically significantly different in patients who received intravenous Ibuprofen or intravenous Paracetamol.

Table-I: Characteristics of Study Participants (n=400)

Study Parameters	n(%)
Age (years)	
Mean±SD	40.24±7.69
Range (min-max)	21 - 60
Gender	
Female	290(72.5%)
Male	110(27.5%)
Type of medication	
Intravenous Ibuprofen	198(49.5%)
Intravenous Paracetamol	202(50.5%)
Significant pain at 02 hours	
No	292(73%)
Yes	108(27%)
Significant pain at 06 hours	
No	324(81%)
Yes	76(19%)

DISCUSSION

Pain medicine is a complex specialty and a challenging task for the team, especially when it comes to post-operative pain. Surgeons and anesthesiologists work hand in hand to make the procedure as minimally painful as possible for the patients. New agents have been introduced, but still, conventional painkillers have not been obsolete. The route via which an analgesic is administered is also very important. Intravenous administration of NSAIDs was less in practice in the last few decades, but recent studies have shown promising results for intravenous use of conventional NSAIDs like Ibuprofen. We, therefore, conducted this study to compare intraoperative intravenous Ibuprofen versus intravenous Paracetamol for postoperative pain relief in patients undergoing laparoscopic cholecystectomy.

Table-II: Difference in Presence of Significant Postoperative Pain and other Parameters in the Study Groups (n=400)

Time interval	Intravenous Ibuprofen	Intravenous Paracetamol	*p*-value
Significant pain at 02 hours			
No	160(80.8%)	132(65.3%)	<0.001
Yes	38(19.2%)	70(34.7%)	
Significant pain at 06 hours			
No	172(86.8%)	152(75.2%)	0.003
Yes	26(13.2%)	50(24.8%)	
Requirement of Opioid analgesia within 2 hours			
No	177(89.3%)	170(84.1%)	
Yes	21(10.7%)	32(15.9%)	0.121
Requirement of Opioid analgesia within 6 hours			
No	169(85.3%)	172(85.1%)	
Yes	29(14.7%)	30(14.9%)	<0.954

Lee *et al.,* (2021) compared two different types of analgesic methods for pain relief after hernia surgery in children.[15] They concluded that combination analgesia involving Ibuprofen and Paracetamol was more effective in pain relief in children undergoing a laparoscopic procedure for hernia repair. Although our study design differed slightly, the efficacy of intravenous Ibuprofen over Paracetamol was established.

Celik *et al.,* (2018) conducted a study on postoperative pain relief after septorhinoplasty. They revealed that the short-term results (for the first 12 hours) were better in the Group administered intravenous Ibuprofen compared to the Group administered intravenous Paracetamol.[16] After 12 hours, both groups had no statistically significant difference in terms of pain relief. Our results supported their findings, but we only studied short-term pain relief, which was also a limitation of our study.

A randomized controlled study was published by Ciftci *et al.,*[17] in 2019 regarding a comparison of intravenous Ibuprofen and Paracetamol for postoperative pain management after laparoscopic

sleeve gastrectomy. They came up with the findings that IV Ibuprofen resulted in lower pain scores compared to Paracetamol by reducing postoperative opioid use in the first 24 hours. We did not study for the first 24 hours, but in the first two and six hours' patients who received Ibuprofen had lesser chances of having significant pain as compared to those who received Paracetamol.

Kayhan *et al.*, 2018 compared intravenous Ibuprofen and acetaminophen for postoperative multimodal pain management in bariatric surgery. They found that the severity of pain had no relationship with the analgesic used. However, the use of opioid analgesia was significantly reduced in patients who received intravenous Ibuprofen.[18] In our study, the presence of significant pain was less in patients who got Ibuprofen, but the need for opioid analgesia was not statistically different in both groups.

Several limitations in the methodology of our study reduce the generalizability of the results. Everyone has a pain threshold; therefore, subjective assessment of pain cannot be used to generate generalizable results for an entire population. Adverse events in both groups were not recorded; therefore, the effectiveness of the medication cannot be ascertained. Randomized controlled trials in this regard studying both efficacy and adverse effects can generate better results.

CONCLUSION

The use of intravenous Ibuprofen during laparoscopic surgery emerged as better management for early post-operative pain as compared to the use of intravenous Paracetamol. There was no difference in the use of opioid analgesia in the early postoperative period in both groups.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WT & AS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

AR & MASK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HBT & KB: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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