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ORIGINAL ARTICLE

Comparison of Post-operative Mean Pain Score with Intravenous Ketorolac Versus Ibuprofen Infusion in Patients Undergoing Open Cholecystectomy Under General Anesthesia

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ABSTRACT

Background: Postoperative pain management is a key to enhanced recovery after surgery. Ketorolac and ibuprofen are both recommended by food and drug administration for this purpose, however; it is unclear, if there is any difference in the effectiveness of these drugs.

Objective: To compare the post-operative mean pain score with intravenous ketorolac versus ibuprofen infusion in patients undergoing open cholecystectomy under general anesthesia.

Study Design: Randomized controlled trial.

Place and Duration of Study: Shaikh Zayed Hospital, Lahore from 12th January 2021 till 11th July 2021.

Methodology: One hundred patients who met the inclusion criteria and assigned them randomly into two groups, each comprising 50 individuals. Before the surgery, patients in group A received IV ketorolac, while those in group B received IV ibuprofen, after which cholecystectomy was performed. We evaluated the postoperative VAS pain scores at 6 hours and analyzed the results statistically.

Results: The average age of patients in the IV ketorolac group was 40±9.85 years, while those in the IV ibuprofen group had an average age of 41±9.95 years. The mean VAS pain score 6 hours after surgery was 3±0.57 for the IV ketorolac group and 4±0.91 for the IV ibuprofen group (p=0.007).

Conclusion: Patients who underwent open cholecystectomy, preoperative IV administration of ketorolac resulted in a significantly greater reduction in postoperative pain scores compared to IV ibuprofen.

Keywords: Analgesia, Cholecystectomy, Gallbladder

INTRODUCTION

In developed nations, cholecystectomy stands as the most prevalent abdominal surgical procedure. This operation can be performed through either open surgery or laparoscopy. A multitude of factors contribute to the pain experienced by patients undergoing such procedures, including phrenic nerve irritation, abdominal distension, surgical incisions, and trauma associated with gallbladder removal.[1] Postoperative pain, marked by acute sensations and inflammation stemming from surgical trauma, diminishes as tissues heal.[2] Effective postoperative pain management plays a pivotal role in averting numerous adverse effects related to pain, such as impaired breathing, heightened cardiovascular strain, delayed mobilization with an increased risk of thromboembolism, and activation of the sympathetic nervous system. Moreover, postoperative pain significantly impacts clinical outcomes, including recovery time and hospital stay duration.[3]

The World Health Organization (WHO) has underscored pain and its management as a pressing healthcare concern.[4] Given the alarming rates of opioid abuse in many developed countries, there is a critical need to prioritize non-opioid medications during the perioperative period. To enhance pain management, emerging evidence advocates for a multimodal approach that incorporates opioid-sparing agents to facilitate swift recovery and minimize adverse effects.[5] In this context, non-steroidal anti-inflammatory drugs (NSAIDs) have been employed to manage pain and inflammation. These agents work by inhibiting pain receptors' response to injury, impeding the conversion of arachidonic acid into prostaglandins.[6]

In 2009, the FDA approved two drugs, ketorolac and ibuprofen, for this purpose.[6] Intravenous ketorolac has been employed for acute postoperative pain management, boasting high bioavailability (around 80-100%) and a rapid onset of action, with peak plasma concentrations achieved within 30 to 60 minutes. The perioperative use of intravenous ketorolac has been associated with adverse events, including increased intraoperative and postoperative bleeding. However, intravenous ibuprofen is an attractive alternative for postoperative pain management since it is well-tolerated when given both before and after surgical procedures and does not require dose adjustment for high-risk populations, such as the elderly.[7]

One study by Dwarica et al[8] compared intravenous ketorolac and intravenous ibuprofen during a surgical intervention. The researchers discovered that the average pain score 24 hours after surgery was 2.30±2.10 for the ketorolac group and 2.68±2.34 for the ibuprofen group; however, this difference was not statistically significant (p=0.20). Another study by Wajekar et al[9] compared the efficacy of commonly prescribed drugs (acetaminophen, ibuprofen, and ketorolac) in relieving orthodontic pain in patients who underwent initial aligning arch wire.[2] They found that the mean pain scores in both groups were 49.01±5.80 and 50.13±7.61 at 24 hours after the procedure, respectively, with no statistically significant difference at 24 hours (p=0.2087). At 6 hours after the procedure, the mean pain scores in the ketorolac group were 15.50±4.16, compared to 27.30±6.31 in the ibuprofen group (p<0.001).

To far, no comparable comparative study has been carried out in Pakistan, despite a plethora of worldwide research comparing intravenous ketorolac and ibuprofen in patients undergoing various surgical operations.[10,11] Therefore, the goal of this study is to evaluate the mean pain scores of patients receiving intravenous ibuprofen infusion versus intravenous ketorolac infusion during open cholecystectomy under general anesthesia. The findings of this study will be very helpful in helping Pakistani anesthesiologist select an analgesic drug that will best relieve postoperative pain, improving patient satisfaction and lowering problems associated with pain.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Shaikh Zayed Hospital, Lahore from 12th January 2021 till 11th July 2021. A total of 100 patients were included in the sample, with 50 individuals allocated to each group. This calculation was based on a 95% confidence interval, a 5% margin of error, and anticipated mean

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postoperative pain scores of 15.5±4.16 in the intravenous ketorolac group and 27.3±6.312 in the ibuprofen group. Enrolled were all patients, male or female, ASA status I or II, admitted for elective open cholecystectomy, and aged 18 to 60. Exclusions from the study included patients with a history of gastrointestinal bleeding or ulceration, inflammatory bowel disease, asthma, significant anemia, congestive heart failure, cognitive impairment (such as dementia), known allergies to hydromorphone or nonsteroidal anti-inflammatory drugs (NSAIDs), renal dysfunction, or a documented history of chronic NSAID or opioid usage.

Every patient had a physical examination, a clinical history, and demographic data collected; the results were entered onto a pre-made form. In order to establish baseline data, various tests were carried out, such as serum electrolytes, CBC, RFTS, LFTS, hepatitis screening, and chest X-rays. Every patient was evaluated by the researcher to see if they were candidates for anesthesia. The patients were then divided into two groups at random, each consisting of fifty patients.

Individuals in Group B got two intravenous doses of 800 mg ibuprofen, whereas patients in Group A received a single intravenous dosage of 30 mg ketorolac. Both groups received the same anesthetic and perioperative drug regimes. Midazolam was given intravenously at a dosage of 0.03–0.09 mg/kg as part of the pre-induction regimen. Intravenous lidocaine (1 mg/kg) and propofol (2 mg/kg) were used to induce anesthesia. Sevoflurane was then used to maintain the anesthesia in a combination of oxygen and air. An intraoperative fentanyl dosage of 1.0 mcg/kg was administered. To further reduce nausea and vomiting during surgery, 4–8 mg of intravenous dexamethasone and 4 mg of ondansetron were administered.

After the procedure, Group A received an intravenous dosage of 30 mg of ketorolac, while Group B received an intravenous dose of 800 mg of ibuprofen given in two doses: the first dose was given just before to the procedure, and the second dose was given four hours later. Six hours following surgery, all patients' pain levels were measured using the Visual Analog Scale in accordance with the established operational criteria. The outcomes were entered using the same form, and statistical analysis was performed.

Data analysis was performed using SPSS version 24.0. The data were stratified based on age, gender, ASA grade, and BMI. Post-stratification T-tests were conducted, and a p-value of ≤0.05 was considered statistically significant. For the comparison of mean postoperative pain scores at six hours, independent T-tests were applied, and a p-value of ≤0.05 was considered statistically significant.

RESULTS

Patients receiving intravenous ketorolac had an average age of 40±9.85 years, whereas those receiving intravenous ibuprofen had an average age of 41±9.95 years. The average age of all patients was 40.8±9.63 years (Table 1). Six hours following the procedure, patients receiving IV ketorolac scored 3±0.57, those receiving IV ibuprofen scored 4±0.91, and the overall mean VAS pain score was 3.6±0.78 (Table 2).

As the mean VAS pain score was compared between the two groups six hours postoperatively, the IV ketorolac group scored 3±0.57 and the IV ibuprofen group scored 4±0.91. With a p-value of 0.007, this difference was statistically significant. There were 28% men and 22% women in the intravenous ketorolac group and 30% men and 20% women in the intravenous ibuprofen group. The data was subsequently divided into groups according to BMI, ASA grade, age, and gender. The mean VAS pain scores six hours postoperatively for males, those between the ages of 36 and 60, those with ASA grade I, and those with a BMI more than 30 kg/m^2 were substantially different in the IV ketorolac and IV ibuprofen groups. Tables 3 show that the p-value for these effect modifiers was less than 0.05.

Table 1: Frequency of age and gender (n=100)

Variable	IV Ketorolac group	IV Ibuprofen group	Total
Age (years)	40±9.85	41±9.95	40.8±9.63
Gender			
Male	28 (28%)	30 (30%)	58 (58%)
Female	22 (22%)	20 (20%	42 (42%)
Mean Vas Pain Score 6 hours postoperatively	3±0.57	4±0.91	3.6±0.78

Table 2: Comparison of Ketorolac and Ibuprofen Groups

Group	Mean±SD	P-value
IV Ketorolac group	3±0.57	0.007
IV Ibuprofen group	4±0.91	

Table 3: Stratification of mean vas pain score at 6 hours postoperatively with respect to age, gender, BMI and ASA physical status

Variables	Category	Groups	No.	Mean VAS Pain Score	P value
Age (years)	18 - 35	IV Ketorolac	16	3.3±0.6	0.152
		IV Ibuprofen	12	3.7±0.96	
	36 -60	IV Ketorolac	34	3.5±0.56	0.03
		IV Ibuprofen	38	3.9±0.89	
Gender	Male	IV Ketorolac	28	3.4±0.62	0.004
		IV Ibuprofen	30	4±0.89	
	Female	IV Ketorolac	22	3.5±0.51	0.501
		IV Ibuprofen	20	3.7±0.92	
ASA Physical Status	Grade I	IV Ketorolac	24	3.4±0.58	0.023
		IV Ibuprofen	23	4±0.95	
	Grade II	IV Ketorolac	26	3.4±0.58	0.122
		IV Ibuprofen	27	3.7±0.86	
Body mass index	20-30 kg/m^2	IV Ketorolac	8	3.4±0.74	0.07
		IV Ibuprofen	11	4.1±0.83	
	>30 kg/m^2	IV Ketorolac	42	3.4±0.55	0.044
		IV Ibuprofen	39	3.8±0.92	

DISCUSSION

The traditional method of using opioids for pain treatment is losing favor with patients and doctors due to worries about side effects such as addiction and delayed discharge.[12] This is the rationale behind the preference for non-steroidal anti-inflammatory medicines (NSAIDs), which can also be taken in addition to opioids. As such, NSAIDs are regarded as an essential part of multimodal postoperative pain management techniques.[13]

By preventing prostaglandin formation, NSAIDs regulate the inflammatory response locally. COX-1 is recognized for manufacturing prostaglandins that protect the gastrointestinal mucosa, whereas COX-2 is upregulated at sites of inflammation and is in charge of making prostaglandins that mediate inflammation and pain. As a result, COX-2 inhibition appears to be mostly in charge of the NSAIDs' anti-inflammatory and analgesic properties, but COX-1 inhibition may negatively impact the

gastrointestinal mucosa and raise the possibility of serious consequences.[14-16]

According to the present study, the mean VAS pain score six hours after surgery was 3±0.57 for the IV ketorolac group and 4±0.91 for the IV ibuprofen was noted. This difference was statistically significant. In a research evaluating the effectiveness of two routinely given medications, ketorolac and ibuprofen, Zhou et al[17] discovered that, six hours after the surgery, the mean pain ratings were 27.30±6.31 in the ibuprofen group and 15.50±4.16 in the ketorolac group ($p<0.001$). In a different study, the clinical effects of intraoperative IV NSAIDs on postoperative pain relief in patients undergoing laparoscopic cholecystectomy were evaluated. The results showed that the group receiving ibuprofen had a significantly higher mean postoperative pain score (mean of 5.09 versus 4.61, $p=0.027$) when measured immediately in the recovery room. These trials confirm our results that IV ketorolac, as opposed to IV ibuprofen, is more effective in controlling postoperative pain six hours after surgery.[18,19] But in a research comparing the postoperative analgesic effects of intravenous ketorolac and ibuprofen, Abdelbaser et al[20] found that both groups' pain levels were comparable. It's important to note that our study concentrated on adults, whereas theirs included youngsters, and that the kind of surgical technique employed differed between the two. Consequently, our results contradict those of Abdelbaser et al[20] reported hat IV ketorolac worked better than IV ibuprofen.

CONCLUSION

It is concluded that patients who underwent open cholecystectomy, preoperative IV administration of ketorolac resulted in a significantly greater reduction in postoperative pain scores compared to IV ibuprofen.

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