

COMPARISON OF ANALGESIC EFFECT OF INTRAVENOUS PARACETAMOL VS INTRAVENOUS KETOROLAC ON POST-OPERATIVE PAIN AFTER ABDOMINAL SURGERY

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ABSTRACT

Objective: To compare the analgesic effect of intravenous paracetamol and intravenous ketorolac on post-operative pain after abdominal surgery.

Study Design: Quasi experimental study.

Place and Duration of Study: Surgical department, Combined Military Hospital (CMH) Rawalpindi, from Nov 2018 to May 2019.

Methodology: Two hundred patients undergoing abdominal surgery at a surgical unit of Combined Military Hospital Rawalpindi were recruited in our study. Patients were divided into two equal groups via lottery method. Group A had the patients which received the intravenous paracetamol while group B had the patients which received the intravenous ketorolac after the surgery. Pain was assessed in both the groups via visual analogue scale (VAS) score.

Results: One hundred twenty six patients were males and 74 were females. Mean age of the patients was 39.63 ± 2.545 years. Most common type of surgery was laparoscopic cholecystectomy 61 (30.5%) followed by the hernioplasty 50 (25%). Mean visual analogue scale score in the patients in group A was 4.12 ± 1.121 while in group B was 4.16 ± 1.124 .

Conclusion: Efficacy of intravenous paracetamol was comparable to that of intravenous ketorolac in our target population. Surgeons should keep in mind that increasing the strength and amount of the analgesic will only increase the cost for the patient and add no benefit in pain reduction.

Keywords: Abdominal surgery, Ketorolac, Paracetamol.

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INTRODUCTION

All the surgical centers of the world, may they be in developed or the developing countries perform a huge number of abdominal surgeries throughout the year¹. Usually the complication rate in controlled settings is not very high and wound healing takes place in a week or two with functional recovery of almost all the patients without any pre-morbid factors². Despite these advances still pain remains a common complain among the surgical patients³.

Post-operative pain has been an area of interest for the surgeons as well as pharmaceutical researchers for long. History of pain after the surgery is as old as surgery itself. Various

methods have been tried in this aspect in order to minimize this phenomenon. Oral, intravenous, intramuscular, skin patches, intra thecal, infusion pumps etc are some of the common routes which have been used to administer various classes of analgesics after the surgery^{4,5}. A huge number of drugs have also been tried ranging from paracetamol to opioid analgesics^{6,7}.

Randomized controlled trials involving various groups of drugs have been conducted in order to find the right choice of analgesic after the surgical procedures. A study done in Korea found no difference between the efficacy of paracetamol and ketorolac and concluded that both have been equally effective in controlling the post-operative pain⁸. A randomized controlled trial on the patients undergoing video assisted thoracic surgery revealed the same finding and ketorolac was no superior to

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paracetamol in controlling the pain⁹. However results were different in a study performed on the patients undergoing laparoscopic cholecystectomy and ketorolac emerged as a stronger analgesic as compared to paracetamol¹⁰. There is also marked difference of cost between the two products which makes this debate rational that which should be a preferred option among the two drugs.

Inhibition of synthesis of prostaglandins in response to the tissue damage is the main mechanism by which paracetamol works to control the pain among the individuals.

This study was planned with the rational to compare the analgesic effect of intravenous paracetamol vs intravenous ketorolac on post-operative pain after abdominal surgery at a tertiary care teaching hospital of Pakistan.

METHODOLOGY

This quasi experimental study was planned and conducted at the surgical department of Combined Military Hospital Rawalpindi from November 2018 to May 2019. Sample size was calculated by WHO Sample Size Calculator by using the results of Rawal *et al* and population prevalence proportion of 85%. Non probability Consecutive sampling technique was used to gather the sample. All patients between the age of 18 and 60 years who underwent any type of abdominal surgery either emergency or elective were included in the study. Referred patients from other military, public sector and private hospitals who were undergoing abdominal surgery were also included in the analysis in addition to the patients of own hospital. Exclusion criteria were the patients with less than eighteen year of age or those with any chronic illness like DM, HTN, asthma, RA, recent stroke etc. Patients who were undergoing second surgery in less than one month time were also excluded. Patients with bleeding disorders, leukemia and lymphomas were also part of the exclusion criteria. Immuno-compromised and patients on long term steroids or with autoimmune disorder were also not included.

Pregnant women, diagnosed psychiatric patients and illicit drug users were also not approached to participate in the study or were excluded at the first step. Patients with serious complications during the surgery and those with known hypersensitivity to paracetamol or ketorolac were also not included in our trial.

Patients who underwent any type of abdominal surgery at surgical unit of CMH Rwp fulfilling the above mentioned inclusion and exclusion criteria were included in the study. Institutional review board of our hospital approved the study and IRB letter number was 28-5-19. Patients with both emergency and elective surgeries were included. Patients were divided into two equal groups via lottery method. Group A had the patients with standard adult dose of paracetamol which was given in IV form TDS post-operatively. As the population was adult, so weight difference did not markedly change the results after the surgical procedure. Group B had the patients with intravenous ketorolac in standard adult dose which was given in IV form TDS post-operatively. Patients were given paracetamol and ketorolac till 48 hours in the standard dosage which is according to the half life of the drug. Both drugs are given TDS post-op and their efficacy was assessed after 48hrs. It was not one time administration of drug in 48 hours. It was done in TDS in standard forms. VAS score was applied to assess the post-operative pain around the wound after 48 hours of the surgery. A special proforma was designed for this study which included the record of sociodemographic profile and the VAS score 48 hours after the surgeries. Our study was double blind as the patient and the person who administered the drug both were unaware about the type of drug administered to the patients. Same brand of both the medications were used in all the patients included in the study. Parenteral diclofenac or nalbuphine was rescue analgesia depending upon choice and clinical condition of patient. Patients who left the hospital before 48 hours or against the medical advice were

considered as drop outs and were not made part of the final analysis.

All statistical analysis was performed by using the SPSS-24. Frequency and percentages for gender, and all the type of surgeries performed during the study were calculated. Mean and standard deviation for age and VAS score 48 hours after the surgery were also calculated for the study participants. Student t test was applied to look for the difference between the mean VAS score of both the groups. The *p*-value ≤ 0.05 was considered as significant to ascertain the association in this analysis.

RESULTS

A total of 216 patients were initially approached to get them included in the analysis. Five had uncontrolled DM, two had history of illicit substance use, two were pregnant and

Table-I: Characteristics of study participants (n=200).

	n (%)
Gender	
Male	126 (63.4%)
Female	74 (36.6%)
Age (years)	
Mean \pm SD	39.63 \pm 2.545
Range (min-max)	19-60 years
Surgeries Performed	
Laparoscopic cholecystectomy	61 (30.5%)
Hernioplasty	50 (25%)
Appendectomy	35 (17.5%)
Exploratory Laparotomy	29 (14.5%)
Open cholecystectomy	12 (6%)
Others	10 (5%)
Emergency surgeries	39 (19.5%)
Elective surgeries	161 (80.5%)

Table-II: Comparison of Visual analogue scale (VAS) score in both the groups (n=100).

	Group A	Group B	<i>p</i> -value
Mean visual analogue scale score	4.12 \pm 1.121	4.16 \pm 2.224	0.221

seven dropped out from the study and left the hospital in less than 48 hours after the surgical procedure. Two hundred patients divided into two groups A and B were included in the final

analysis. A total of 126 (63%) were males and 74 (27%) were females. Mean age of patients who underwent abdominal surgery was 39.63 \pm 2.545 years. Most of the patients included in the study underwent laparoscopic cholecystectomy followed by hernioplasty. Other characteristics of study population have been summarized in table-I. Mean VAS score of the patients in group A was 4.12 \pm 1.121 while in group B was 4.16 \pm 1.224. A *p*-value of 0.221 indicated that there was no statistical difference between the two groups as shown in table-II.

DISCUSSION

Ketorolac is non-steroidal anti-inflammatory drug and works by inhibiting the cyclooxygenase systems¹¹. Inhibition of synthesis of prost-aglandins in response to the tissue damage is the main mechanism by which paracetamol works to control the pain among the individuals. In addition to this, it has also been believed that it affects the serotonergic pathway and has central mechanism as well for inhibition of pain transmission¹². Ineffective pain control, long stay in hospital and more time to recovery pose the burden on individual as well as overall health care budget and that becomes extremely important in case of country like ours where both individual and government resources are usually limited¹³⁻¹⁶.

Pain management is emerging as a new specialty in all parts of the world. This specialty is still at toddler stage in our set up¹⁷. Usually it is the surgeon or the anesthetist who have to adjust the analgesic for the surgical patient after the surgery instead of pain management expert. Therefore adequate knowledge is must for the surgeons and anesthetists regarding the effectiveness and safety of routine analgesia. Patient is usually unaware of the surgical skill mastery which surgeon has demonstrated during the surgery; rather he is more interested in good postoperative reduction of symptoms and a smooth recovery with minimum pain and discomfort. Pain free recovery is associated with lesser number of complications and reduced

hospital stay³. This study was planned with this rationale to find the difference in efficacy of the two routinely used analgesics in our population.

Male female ratio of patients in our study was 1.7:1 clearly highlighting the male predominance among surgical patients. Ahmed *et al* did a study in our part of the world and produced similar results clearly showing the male predominance in the sample of patients undergoing the abdominal surgeries¹⁵. Reasons for this could be multiple, it might be that female patients have lesser chance of getting abdominal pathology requiring the surgery in our part of the world or they may have lesser access to tertiary care service in a third world country like ours. Our sample was also a bit biased as it was from a military hospital and our military mostly comprised of male volunteers so automatically chances of females get reduced to get enrolled in our study. More research was required to ascertain the difference in pain perception and effect of medication to reduce the pain in both the genders.

There were variable results reported in the past literature regarding the difference in efficacy of paracetamol and ketorolac. Paracetamol works by prostaglandin synthesis inhibition and also acts on serotonergic system while ketorolac is an NSAID which works by inhibiting the cyclooxygenase system. These were postulated by Graham *et al* and Russo *et al* in 2005 and 2017 respectively^{11,12}. Cost of both the medications is also different. Difference in efficacy has also been expected which was the basis to plan this randomized control trial. Results were different from these expectations and there was no statistical difference between the two agents in terms of efficacy to reduce the post-operative pain after the abdominal surgery. This was a very interesting finding highlighting the fact that as per pain management guidelines paracetamol should be the first line drug but few surgeons prefer ketorolac or other NSAIDs contrary to the existing evidence. They use the plea that ketorolac on the basis of its mechanism of action is better analgesic and superior in reducing post-

operative pain in the surgical patients. Evidence generated by this RCT has clearly declared that paracetamol is equally effective and surgeons should not be extravagant in this regard. Similar results have already been documented in other studies as well done by Jahagiri *et al* and Rastogi *et al* in recent past. In both these studies p -value >0.05 indicated no marked difference in both groups with regard to post-surgical pain control^{8,9}.

Laparoscopic cholecystectomy was the commonest abdominal surgery patients underwent in this study followed by the hernioplasty. Similar results have been generated in the past as well by a study published in 2015 by Golzarri-Moreno *et al*¹⁸. The intensity of pain which the patients perceive usually depends upon the type of surgery as well. Therefore a holistic approach should be practiced in order to understand the phenomenon of pain among the surgical patients and treat them effectively.

Strengths of this study includes the strict inclusion criteria especially regarding comorbidities. Therefore the results reflect the effect of both drugs on the pain management in both the groups. Complex and re-do surgeries were also not included to ascertain the relationship of prescribed drugs only with the control of post-operative pain.

In addition to the strengths, there were few limitations as well. The major limitation of our study was the lack of generalizability as patients were not recruited from the general population or public hospitals. One hospital with military setup was selected to gather the sample which raises the issue of selection bias and reduces the generalizability of our study. Comparison was not made for each type of surgery which again is a limitation to generalize and compare the results. Patients were not followed up for long term after the discharge so final outcome regarding the long term management of pain could not be determined. Type of anesthesia used and pre-anesthetic medications should also have been controlled for both the groups in order to

clearly observe the effect of the drugs under study. Larger studies with a more representative sample size should be planned with long term follow up and record of adverse effects may serve the purpose in a much better way.

CONCLUSION

Efficacy of intravenous paracetamol was comparable to that of intravenous ketorolac in our target population. Surgeons should keep in mind that increasing the strength and amount of the analgesic will only increase the cost for the patient and add no benefit in pain reduction. Paracetamol intravenous infusion still remains the first line of pain relief treatment after the abdominal surgery.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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