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THE EFFECTIVENESS OF KETOROLAC AS AN ANALGESIC FOR CONTROLLING PRIMARY HEADACHE IN EMERGENCY DEPARTMENTS

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Abstract:
Objective: *One of the Nonsteroidal Anti-inflammatory Drugs (NSAIDs) called ketorolac is often used to relieve acute pain. This study was conducted to measure the effectiveness of ketorolac as an analgesic for controlling primary headache in emergency departments.*
Place and Duration: *This study was conducted in the Emergency Medicine department of Services Hospital, Lahore for six duration from November 2019 to April 2020.*
Methods: *In this study, 50 patients with 50 headaches, receiving 60 mg of ketorolac intravenously by slow infusion over approximately 10 minutes, were included in the study. Pain ratings were assessed on arrival as well as 1 hour and 2 hours after infusion of ketorolac using a visual analogue scale (VAS). To assess differences in VAS pain scores, statistical analysis of data collected using Wilcoxon and Mann-Whitney tests was performed.*
Results: *The result of study shows decreasing of the VAS more than 3 points from the arrival until 1 hour ($P < 0.001$), and more than 5 points from the arrival until 2 hours after ketorolac administration ($P < 0.001$) were seen. Those with history of analgesic use before admission in emergency department in comparison with the others did not accompany with more decline in pain score after 1 hour ($P = 0.34$) or 2 hours ($P = 0.92$).*
Conclusion: *Ketorolac appears to be a safe and well-tolerated means of controlling pain in patients with primary headache in emergency departments. Based on the results obtained in this study, ketorolac has a pronounced effect that is even more pronounced within 1 hour after application and 2 hours later.*
Key words: *Ketorolac, Headache, Pain management, Emergency Medicine.*

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INTRODUCTION:

Headache is a ubiquitous disease with a 90% incidence. There are several types of headaches, so 150 diagnostic pain categories have been identified. Most patients who come to the emergency room with severe headaches require a quick and effective relief of symptoms. There are common guidelines for the treatment of acute headaches, often recommended by several different agents such as dihydroergotamine, triptans, phenothiazines, opioids or nonsteroidal anti-inflammatory drugs (NSAIDs). Ketorolac is one of the NSAIDs that has been tested many times in randomized clinical trials and is recommended as an effective remedy for painful patients. However, the search continues. Ketorolac was considered an alternative to nonsteroidal painkillers and opioids to relieve moderate to severe pain. About twenty years ago, it was thought that ketorolac had restrictions on use, such as rapid abortion pain in the emergency department, although it had a serious analgesic effect. Others believed that this drug could be considered an alternative to a useful adjuvant or opioid for people with moderate to severe pain. Given that different headaches contain the same inflammatory component in their pathophysiology, ketorolac is expected to be effective. This agent is an effective non-narcotic analgesic with an indirect anti-inflammatory effect. Therefore, consider this as the preferred option for treating pain in various cases of primary headache reported to the emergency room. This study was conducted to measure the effectiveness of ketorolac as a non-hunting anti-inflammatory analgesic to control primary headache in emergency patients with any type of primary headache.

METHODS:

This Prospective study was held in the Emergency Medicine department of Services Hospital, Lahore for six duration from November 2019 to April 2020. Patients with any type of primary headache were enrolled for the study.

All patients between 18 and 60 years of age who suffered from moderate to severe headache (pain rating> 5) showing intravenous treatment were included.

Patients with a positive history of any of the following are excluded: breastfeeding, pregnancy, active peptic ulcer, coagulopathy, inflammatory bowel disease, renal insufficiency or liver failure.
Pain results were recorded on arrival using a visual analog scale (VAS), and subjects who received a score above 5 were given intravenous 60 mg of ketorolac by slow infusion over approximately 10 minutes. They are all considered possible side effects such as irritability, itching, injection pain, hypertension, tachycardia, nausea and / or vomiting. If something happened, the process had to stop. One and two hours after the injection, the patients were again asked to assess the pain. Dropping more than 3 points on the pain scale was accepted as an appropriate response.

The SPSS version 22 was used for statistical analysis. The mean, median, interquartile range and standard deviation were used to define continuous variables. Mann-Whitney U and Wilcoxon tests were used to analyze differences in registered pain points. Frequency and percentage are used to define qualitative variables. $P \leq 0.05$ was considered significant.

RESULTS:

50 patients with an average age of 30.14 ± 11.4 years participated. 22 (44%) participants are men and 28 (56%) are women. It should be noted that 28 (56%) patients did not use any painkillers before arriving at the emergency room. Almost all other 22 patients (44%) who have already taken another drug have used acetaminophen or various types of NSAIDs. The mean time of standard deviation when taking other drugs for ketorolac administration was 2.77 ± 1.9 hours. The median VAS decreased significantly from 8.0 ± 2.0 to 5.0 ± 4.0 after 1 hour and 3.0 ± 2.0 after 2 hours (Fig. 1).

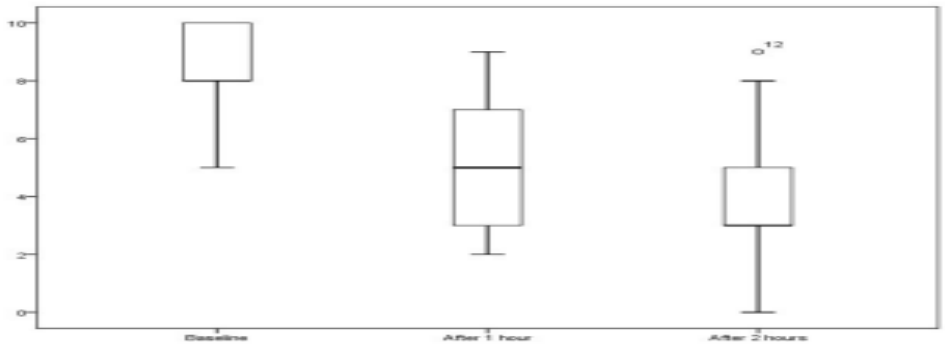

Figure 1. Minimum, maximum, median and interquartile range of visual analogue scale at baseline, 1 hour and 2 hours after ketorolac intravenous infusion.

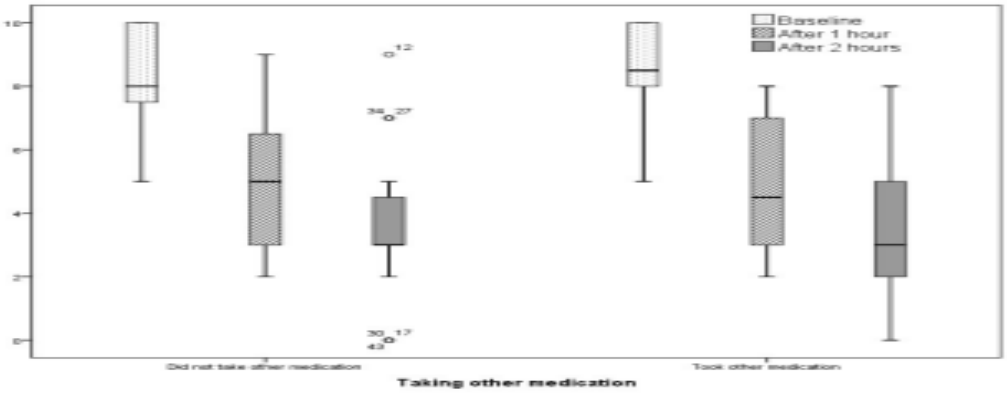

Figure 2. Minimum, maximum, median and interquartile range of visual analogue scale at baseline, one hour and two hours after ketorolac intravenous infusion for patients who took analgesic before arrival and those who did not.

A significant decrease in VAS value (> 3 points,> 35%) was recorded from the initial value to 1 hour after administration of ketorolac (Wilcoxon test Z = -6.1; P <0.001). An hour later, another reduction (> 6 points,> 60%) was observed (Wilcoxon Z test Z = -6.1; P <0.001). There was a statistically significant difference between VAS 1 hour and 2 hours after drug administration (Wilcoxon test Z = -4.2; P <0.001).

To assess the possible effects of drug use before arriving at ED, registered patients were divided into 2 groups based on whether they had previously taken the drug. Statistical analysis did not reveal significant differences between the groups. Initially, after administration of ketorolac, 1 hour and 2 hours later, the P values associated with comparing VAS between the two groups were 0.51, 0.62 and 0.69, respectively. There was no statistically significant difference between the groups in terms of VAS reduced by 1 hour (P = 0.34) and 2 hours (P = 0.92) after ketorolac (Fig. 2).

DISCUSSION:

Based on the findings of this study, a significant reduction in pain scores from the onset to 1 hour and 2 hours after ketorolac administration was observed. This improvement was achieved in almost all cases, except for two patients in whom VAS did not improve even after 2 hours. Intravenous ketorolac was associated with significant success, which resulted in a reduction of VAS by more than 3 points by the hour and over 5 hours by 2 hours.

All patients were observed for possible short-term adverse effects and headaches for approximately 6 hours after drug administration. Fortunately, patients did not experience such complications that could confirm the safety and efficacy of intravenous ketorolac. In this study, results should be interpreted cautiously according to the inclusion and exclusion criteria in patient selection.

Parenteral ketorolac is often used for moderate to severe headache abortion. Like NSAIDs, the mechanism of action of ketorolac is to inhibit prostaglandin synthesis by non-selective inhibition of the cyclooxygenase enzyme.

Ketorolac has been used in several studies, which is why comments of support and objection were proposed. In a pilot study, 60 mg of intramuscular ketorolac was administered to twelve patients with a headache attack. All patients showed statistically significant improvement in the McGill pain questionnaires, and the authors recommended this drug as a potentially useful agent in the treatment of such patients.

In a prospective double-blind study in patients with migraine headaches, intravenous ketorolac was compared with nasal administration. The authors reported that intravenous ketorolac is more effective in this context than nasal sumatriptan, although both drugs significantly reduce pain.

In a controlled study, intramuscular ketorolac was compared with meperidine plus promethazine, as well as normal saline and placebo in tension-related headaches. The authors reported that ketorolac was better than placebo after 0.5 and 1 hour, and meperidine after 2 hours. Interestingly, these authors did the same study 2 years ago about acute attacks of headache and reported that using all three options can lead to significant pain control, but their number does not differ between them.

In a non-random, non-invasive analgesic study, intramuscular ketorolac and oral ibuprofen were compared. The authors of the above-mentioned study found that both options provide similar pain relief when treating acute ED pain. They believed that ketorolac is no better than ibuprofen for this purpose.

Another study in migraine patients showed that injecting a dose of ketorolac can lead to a significant reduction in headache symptoms after 1 hour in most participants.

In a randomized trial comparing the efficacy of intravenous ketorolac, metoclopramide and sodium valproate in the treatment of acute migraine, it was found that ketorolac is better than sodium valproate but less effective than metoclopramide.

Intravenous ketorolac has also been compared with intravenous diphenhydramine and metoclopramide in the treatment of some primary headaches. The study found that intravenous diphenhydramine plus metoclopramide was more effective than intravenous ketorolac in adults reporting an emergency migraine or primary headache without clumping.

The use of a standard measuring tool, such as VAS, and the selection of a suitable patient can be considered as strengths for this study. On the other hand, the short observation time is one of the limitations. Considering the control group, it is proposed that future studies increase the dose, increase the population and identify patients who do not respond to ketorolac.

CONCLUSION:

Ketorolac appears to be a safe and well-tolerated means of controlling pain in patients with primary headache in the emergency department. Based on the results obtained in this study, ketorolac has a pronounced effect that is even more pronounced within 1 hour after application, 2 hours later.

REFERENCES:

1. Umer, Muhammad, Farrukh Saleem Shah, and Sajid Rahim. "EFFICACY OF IITRAVENOUS KETOROLAC IN POST ELETRRO-CONVULSIVE THERAPY (ECT) HEADACHE." *Pakistan Armed Forces Medical Journal* 70, no. 1 (2020): 236-39.
2. Khazaei, Mojtaba, Nahid Hosseini Nejad Mir, Fateme Yadranji Aghdam, Mohammad Taheri, and Soudeh Ghafouri-Fard. "Effectiveness of intravenous dexamethasone, metoclopramide, ketorolac, and chlorpromazine for pain relief and prevention of recurrence in the migraine headache: a prospective double-blind randomized clinical trial." *Neurological Sciences* 40, no. 5 (2019): 1029-1033.
3. Engel, Emily Rubenstein, and Joshua Cheng. "IM ketorolac vs diclofenac potassium powder for oral solution for the acute treatment of severe migraine: a randomized controlled trial." *Neurological Sciences* (2020): 1-6.
4. Golikhatir, Iraj, Hamed Cheraghmakani, Farzad Bozorgi, Fatemeh Jahanian, Mohammad Sazgar, and Seyed Hosein Montazer. "The Efficacy and Safety of Prochlorperazine in Patients With Acute Migraine: A Systematic Review and Meta-Analysis." *Headache: The Journal of Head and Face Pain* 59, no. 5 (2019): 682-700.
5. Sotoodehnia, Mehran, Mozhgan Farmahini-Farahani, Arash Safaie, Fatemeh Rasooli, and Alireza Baratloo. "Low-dose intravenous ketamine versus intravenous ketorolac in pain control in patients with acute renal colic in an emergency setting: a double-blind randomized clinical trial." *The Korean Journal of Pain* 32, no. 2 (2019): 97.
6. Martins, Luciana-Dorochenko, Márcia Rezende, Alessandro D. Loguercio, Marcelo-Carlos Bortoluzzi, and Alessandra Reis. "Analgesic efficacy of ketorolac associated with a tramadol/acetaminophen combination after third molar surgery-a randomized, triple-blind clinical trial." *Medicina oral, patologia oral y cirugia bucal* 24, no. 1 (2019): e96.
7. Talebian, Mohammad-Taghi, Sahar Mirbaha, Elnaz Davarinezhad-Moghadam, and Pooya Payandemehr. "Comparing the Therapeutic Effects of Dexamethasone-Metoclopramide with Ketorolac in Relieving Headache in Patients with Acute Migraine Attacks Presenting to the Emergency Department." *Advanced journal of emergency medicine* 3, no. 2 (2019).
8. Jagarlamudi, Anup, E. Anushree, Soma Harika, K. Kavya Sri, and Ch Rohit. "A simple randomized comparative study to evaluate the

efficacy of 0.7% w/v Olopatadine hydrochloride ophthalmic solution and the Fixed Dose Combination of 0.1% w/v Olopatadine hydrochloride and 0.4% w/v Ketorolac tromethamine ophthalmic solution for the." *Journal of Drug Delivery and Therapeutics* 9, no. 3 (2019): 279-285.

9. McCoy, Jessica J., Kim Aldy, Elizabeth Arnall, and Joshua Petersen. "Treatment of Headache in the Emergency Department: Haloperidol in the Acute Setting (THE-HA Study): A Randomized Clinical Trial." *The Journal of Emergency Medicine* (2020).
10. Watts, Kathryn, Stephen Balzer, Melissa Drum, John Nusstein, Al Reader, Sara Fowler, and Mike Beck. "Ibuprofen and acetaminophen versus intranasal ketorolac (Sprix) in an untreated endodontic pain model: a randomized, double-blind investigation." *Journal of endodontics* 45, no. 2 (2019): 94-98.
11. McNicol, Ewan D., McKenzie C. Ferguson, Sean Gallagher, and Roman Schumann. "Single-dose intravenous ketorolac for acute postoperative pain in adults." *The Cochrane Database of Systematic Reviews* 2019, no. 2 (2019).
12. Heard, Kennon, Vikhyat S. Bebarta, Jason A. Hoppe, and Andrew A. Monte. "Does administration of haloperidol or ketorolac decrease opioid administration for abdominal pain patients? A retrospective study." *The American journal of emergency medicine* 38, no. 3 (2020): 517-520.
13. Long, Brit, Alex Koyfman, and Michael Gottlieb. "Prochlorperazine for treatment of acute migraines in adults." *Academic Emergency Medicine* 27, no. 3 (2020): 243-244.
14. Mazhar, Heena, Ratna Samudrawar, Prashant Tamgadge, Rashmi Wasekar, Rahul Vinay Chandra Tiwari, and Heena Tiwari. "Preemptive Oral Ketorolac with Local Tramadol Versus Oral Ketorolac in Third Molar Surgery: A Comparative Clinical Trial." *Journal of Maxillofacial and Oral Surgery* (2020): 1-8.
15. Zangouei, Amirsadra, Seyed Ali Hossein Zahraei, Amir Sabertanha, Ali Nademi, Zahra Golafshan, and Malihe Zangoue. "Effect of low-dose intravenous ketamine on prevention of headache after spinal anesthesia in patients undergoing elective cesarean section: A double-blind clinical trial study." *Anesthesiology and Pain Medicine* 9, no. 6 (2019).