

## COMPARATIVE EFFECTS OF IV INJECTION OF KETOPROFEN AND PARACETAMOL IN THE TREATMENT OF TENSION-TYPE HEADACHE

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### Abstract

**Background:** Headaches are one of the commonly reported issues throughout the world population. Globally, Tension-type headache is a more common problem. Individuals facing long occurring and more severe headaches may go for care from the medical facility. However, most of the individuals do not do so which usually consequences in inappropriate and inadequate management of this problem.

**Objective:** The aim of the present study is to compare the effectiveness of ketoprofen IV injection and paracetamol IV injection in the treatment of tension-type headache.

**Methodology:** A validated questionnaire was designed to conduct this study. Certain inclusion and exclusion criteria were established to select the participants. Patients having the age between 20 to 40 years were treated with paracetamol and ketoprofen and their responses were recorded and evaluated.

**Results:** Our results suggest that paracetamol has more vital signs stability when compared with ketoprofen and is safer in terms of drug-induced allergic reaction and injection site reaction. However, ketoprofen has a faster onset of action when compared with paracetamol.

**Conclusion:** Management of tension-type headache is neglected most of the time which affects the quality of life and productivity in the affected population. Development and update of existing guidelines for tension-type headache are essential in managing this issue. Both ketoprofen and paracetamol are effective in treating this issue but both have some side effects. Future studies are still desired to further evaluate their effects.

**Keywords:** *Tension-type headache, Headache, analgesics, Ketoprofen, Paracetamol*

### Introduction:

Headaches are one of the commonly reported issues throughout the world population. In the general adult population, its annual occurrence rate is estimated to be 46 percent [1], and its lifetime prevalence rate is estimated to be higher than 90 percent [2]. Discrepancies in the reported occurrence can be due to the variation in the population, design of the study, probable genetic factors, environmental and cultural factors, overlap with the possible migraine, or exclusion and inclusion of occasional episodic tension-type headache [3]. If compare with migraine, Tension-type headache is more common globally and this finding is replicated throughout the world [4].

The care and management of the person facing headaches are highly neglected [2] and can be uneven due to the participation of practitioners from diverse medical specialties such as psychiatry, ophthalmology, ENT (ear, nose, and throat), and neurology. Clinicians from different subspeciality may have a different approach to treating this issue. Headache is rarely life-risking and most of the time headache pain intensity is usually mild to moderate. That's

why individuals mostly use the medication on their own and do not go for formal medical care services [5].

Headache can be categorized into two types. In the primary type, there is no evident underlying cause while in the secondary type, it can be occurred due to other underlying local and systemic issues [6]. Tension-type headache is considered to be from primary headaches and is observed in about one-third of the population having headaches. This large affected population puts a considerable burden on the healthcare services [1]. Usually, tension-type headache episodes are self-limiting and their intensity is mild to moderate and self-limiting. However, a small number of patients may have this issue in the severe and disabling form [6]. Individuals facing long occurring and more severe headaches may go for care from the medical facility. However, most individuals do not do so which usually consequences in inappropriate and inadequate management of this problem [7]. According to the community survey conducted through telephone to evaluate the medication pattern of 274 people with commonly occurring headaches, it is shown that only one percent of the patients were using prescribed medication. A large number of individuals from this survey reported that they are using over-the-counter

medicines such as aspirin (15%) and paracetamol (56%), and the apparent efficacy of these medicines was about seven on zero to ten scale [8]. The tendency to develop analgesic abuse is high in individuals who are self-medicating with over-the-counter medicine to cure the frequently occurring tension-type headache.

Due to that reason, It is highly advisable to develop management guidelines and treatment strategies that can bring sustained and substantial pain relief with no and minimum side effects.

Managerial Strategies of tension-type headache have been typically derived from already existing for migraine. The world health organization essential drug list does not contain indications for tension-type headache management [9].

European Federation of Neurological Societies and British Association for the Study of Headache in 2010 restructured and published the guidelines on tension-type headache management [10]. Similarly, Austrian and German guidance is existing [11]. These guidelines show the continuous systemic struggle to abridge the gap between clinical practice and clinical trial evidence with the purpose to make practice more efficient.

The present study aims to compare the effectiveness of ketoprofen IV injection and paracetamol IV injection to treat the tension-type headache.

### Methodology:

For this research, a cross-sectional study was performed. A validated questionnaire was designed to collect the response. Participants of this research were selected by considering the following criteria.

The age limit for the participants was set at 20 to 40 years. All the selected participants were visiting ER department with the complaint of recurrent severe tension-type headache. There was no previous history of any other chronic medical conditions. Headache severity was reported on a scale of 0 to 10 where needed.

Patients who were visiting ER department for the first time with the complaint of headache were excluded from this study. Similarly, the patients with no previous history of headache were also excluded from this study. Moreover, adults having the age more than 40 years, children, individuals with a chronic medical history, with the previous complaint of cluster headache and migraine headache were also part of the exclusion criteria.

Considering the upper criteria, 102 headache patients native to Jordan were selected. Only 75 of them continued to follow up for two days and their response was collected for further analysis.

This study was conducted during the period between May to November 2020 at Amman Surgical Hospital (Private) Amman, Jordan.

All intravenous medication was performed under sterilized conditions using aseptic techniques. Patients selected for this study were not receiving any analgesic medication prior to ER department visit. Two groups were formed on the basis of treatment, one received Paracetamol IV injection and another was administered Ketoprofen IV injection. Follow-up on the second day was performed to be sure that the headache was not overestimated and to make sure it was a tension headache. The daily assessment was carried out on a phone call by a nurse for 3 days. Doctor follow-up was on day 2 after medication (Day +2).

A total of thirteen multiple-choice questions were part of this survey, and these questions, along with options, were as following;

1. The number of patients with each medication type.
  - a. Paracetamol IV
  - b. Ketoprofen IV
2. Age group.
  - a. 20 to 25 years
  - b. 26 to 30 years
  - c. 31 to 35 years
  - d. 36 to 40 years
3. Gender of patients
  - a. Male
  - b. Female
4. Gender.
  - a. Male
  - b. Female
5. In paracetamol-treated patients, the appearance of irritation signs on injection site during ER visit and day after administration.
  - a. On the day of administration (D 0)
  - b. 1 day post-administration (D +1)
  - c. 2 day post-administration (D +2)
6. In Ketoprofen treated patients, the appearance of irritation signs on injection site during ER visit and day after administration.
  - a. On the day of administration (D 0)
  - b. 1 day post-administration (D +1)
  - c. 2 day post-administration (D +2)
7. Decrease in headache severity or cured of headache with paracetamol treatment
  - a. On the day of administration (D 0)
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all
  - b. 1 day post-administration (D +1)
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all
  - c. 2 days post-administration (D +2)
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all

8. Decrease in headache severity or cured of headache with Ketoprofen treatment
  - a. On the day of administration
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all
  - b. 1 day post-administration (D +1)
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all
  - c. 2 days post-administration (D +2)
    - i. Number of patients cured
    - ii. A decrease in severity from (more than 7/10) to (less than 3/10)
    - iii. No effect at all
9. Number of patients having an allergic reaction due to medication
  - a. Paracetamol
    - i. On the day of administration (D 0)
    - ii. 1 day post-administration (D +1)
    - iii. 2 day post-administration (D +2)
  - b. Ketoprofen
    - i. On the day of administration (D 0)
    - ii. 1 day post-administration (D +1)
    - iii. 2 day post-administration (D +2)
10. The onset of medication action
  - a. Paracetamol IV
  - b. Ketoprofen IV
11. Number of the patient who needs extra analgesic medication
  - a. Paracetamol IV
    - i. On the day of administration (D 0), the addition of NSAID after 45 minutes as a patient ask for more analgesia
    - ii. 1 day post-administration (D +1)
    - iii. 2 day post-administration (D +2)
  - b. Paracetamol IV
    - i. On the day of administration (D 0), the addition of paracetamol after 60 minutes as a patient ask for more analgesia
    - ii. 1 day post-administration (D +1)
    - iii. 2 day post-administration (D +2)
12. Effect of medication on vital signs after the administration of the drug
  - a. Paracetamol IV
  - b. Ketoprofen IV
13. Duration of stay in ER department after consultation with the physician
  - a. Paracetamol IV
  - b. Ketoprofen IV

### Ethical Considerations

Prior approval by the research ethics committee of the institute was obtained to conduct this study. Participants participated in this study as a volunteer, and all participants signed written informed consent. This study's questionnaire

was filled by the participants anonymously, and all the collected information was kept secure and confidential.

### Results:

Out of 102 selected patients, only 75 continued to follow up for two days and their response was collected for further analysis.

Among these participants of the study, 40 percent of patients were male and 60 percent of patients were female. Participants of this study formed four groups i.e. 20 to 25, 26 to 30, 31 to 35, and 36 to 40 years old and these groups have 33, 20, 14, and 33 percent patients respectively. Two groups were formed on the basis of treatment, one group received Paracetamol IV injection, and another was administered Ketoprofen IV injection. Paracetamol IV injection was given to 35 (47 percent) patients and the remaining 40 (53 percent) patients received Ketoprofen IV. None of the patients in the paracetamol treated group showed any sign of irritation at the injection site or no redness, itching, or extravasation signs were noted during the follow-up. However, 5 percent of patients in the Ketoprofen treated group has shown sign irritation at the injection site during the stay at ER department. On day 1 and day 2 post medication, no irritation signs were present in this group.

Regarding the effectiveness of medication in treating tension-type headache, ketoprofen has illustrated relief in a greater number of patients at ER department.

During staying at ER department, Paracetamol IV injection cured 43 percent of the participants of this group, while 43 percent of participants of this group reported reduced severity of the headache from 7/10 to 3/10 on a scale of 0 to 10. However, 14 percent of patients of this group did not show any improvement and ask for more analgesia. On day 1 post medication, 94 percent of patients were cured and on day 2 post medication, all patients were cured. During the follow up two patients reported recurrent attacks of headache.

During staying at ER department, Ketoprofen IV injection cured 63 percent of the participants of this group, while 32 percent of participants of this group reported reduced severity of the headache from 7/10 to 3/10 on a scale of 0 to 10. However, 5 percent of patients of this group did not show any improvement and ask for more analgesia. On day 1 and day 2 post medication, all patients were cured. Overall, Ketoprofen IV injection was more effective in treating the headache.

In the comparison of allergic reaction toward the medication, Paracetamol was found safer than Ketoprofen. In paracetamol, no allergic reaction occurred in any patient while in the ketoprofen group 5 percent of patients exhibited allergic reaction along with skin rashes and nausea. However, these allergic signs subsided on day 1 and day 2 post medication.

During the initial 20 minutes, Ketoprofen IV injection reduces the headache severity in more patients as compare to Paracetamol treated group. 43 percent of patients in the paracetamol treated group shown signs of relief during the

early 20 minutes while 75 percent of patients from the Ketoprofen group exhibited signs of relief within 20 minutes of injection.

In the paracetamol group, 14 percent of patients ask for more analgesia after 45 minutes at ER department. But on day 1 and day 2 post medication, 6 percent and 3 percent of the patients ask for painkillers respectively.

In the Ketoprofen group, 5 percent of patients ask for more analgesia after 45 minutes at ER department. But on day 1 and day 2 post medication, 5 percent and 3 percent of the patients ask for painkillers respectively.

Paracetamol injection affected the vital signs in 14 percent of the group patients. These patients showed tachycardia with a heart rate of 100 to 120 bpm which returned to the normal (60 to 100) after 30 minutes. A considerable number (30) of patients of this group were discharged from ER within 60 minutes.

On the other hand, ketoprofen injection affected the vital signs in more number (20 percent) of the group patients. These patients showed tachycardia with a heart rate of 100 to 130 bpm and 15 percent of them returned to the normal (60 to 100) after 30 minutes while the remaining 5 percent took one hour to be with normal vital signs. 37 patients of this group were discharged from ER within 90 minutes as the medication took over 45 minutes to act and produced the effect.

### Discussion:

Headaches are one of the commonly reported issues throughout the world population and among them, tension-type headache is more common. Its management is highly neglected and it can be uneven due to the participation of the practitioners from diverse medical specialties. Headache is rarely life-risking and most of the time headache pain intensity is usually mild to moderate. That's why individuals mostly use the medication on their own and do not go for formal medical care services [5]. It is highly recommended to evaluate the effect of commonly used medications which can be useful in developing the guideline for the patient with tension-type headache.

In the present study, Paracetamol IV injection and Paracetamol IV injection were used to treat tension like a headache. Some studies have already been performed to evaluate the efficacy of these medications [12, 13].

Results from our study are in accord with previous studies which has shown that ketoprofen paracetamol and ibuprofen were better than placebo in treating the tension-type headache [14, 15]. Moreover, our results are also supported by the existing EFNS guidelines where paracetamol or aspirin is recommended in treating tension-type headache [10].

According to our finding, paracetamol was found to be safer than ketoprofen in terms of injection site irritation and associated signs. In the paracetamol treated group, no patient showed irritation signs while in the case of ketoprofen injection 5 percent of patients illustrated signs of irritation at the injection site. Our results are comparable with a previous study [16] where Intravenous

dexketoprofen was compared with racemic ketoprofen for inducing injection pain and dexketoprofen induced less pain as compared to racemic pain.

Regarding the efficacy of medication to treat tension-type headache, ketoprofen has illustrated relief in a higher number of patients at ER department when compared with paracetamol. Our results are supported by a previous study by [13] where it has been shown that ketoprofen has a more quick onset of analgesia as compared to acetaminophen (paracetamol) in treating headaches.

In terms of a drug-induced allergic reaction, Paracetamol was found safer than Ketoprofen. However, some studies [17, 18] have already demonstrated the hypersensitivity to paracetamol in patients. Similarly, ketoprofen allergy is also described in a report by [19].

Our data shows that ketoprofen has rapid onset action and it reduced the intensity of pain in more patients within 20 minutes when compared with paracetamol. Our results are supported by a previous study by [13] where it has been shown that ketoprofen has a more quick onset of analgesia as compared to acetaminophen (paracetamol) in treating headaches.

Our study shows that paracetamol has more vital signs stability when compared with ketoprofen. A previous study [20] also supports that vital signs are less affected with the use of paracetamol. However, their research was to compare with remifentanyl and morphine.

### Conclusion:

Management of tension-type headache is neglected most of the time which affects the quality of life and productivity in the affected population. Its better management can prevent the over and ab-use of the over-the-counter analgesic drug. Development and update of existing guidelines for tension-type headache are essential in managing this issue. Our study suggests that paracetamol has more vital signs stability when compared with ketoprofen and is safer in terms of drug-induced allergic reaction and injection site reaction. However, ketoprofen has a faster onset of action when compared with paracetamol. Both ketoprofen and paracetamol are effective in treating this issue but both have some side effects. Future studies are still desired to further evaluate their effects.

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