International Clinical and Medical Case Reports Journal
Original Research Article (ISSN: 2832-5788)

Single Intramuscular Injection of Diclofenac Sodium in Adult Febrile Patients

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Citation: *Dhiman P, Grewal R, Issar NK, Prasad AS, Jain R, Singh S, et al. Single Intramuscular Injection of Diclofenac Sodium in Adult Febrile Patients. Int Clinc Med Case Rep Jour. 2024;3(6):1-7.*

Received Date: 22 June, 2024; **Accepted Date:** 30 June, 2024; **Published Date:** 02 July, 2024

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1. ABSTRACT

1.1. Introduction: There is not much data and studies till date on the use and efficacy of use of intramuscular injection diclofenac as an adjunct or sole antipyretic agent in adult febrile patients. This study reports the use, efficacy and adverse effects of a single IM injection of diclofenac sodium in adult patients with and without concomitant use of acetaminophen.

1.2. Materials and Methods

1.2.1. Type of study: Retrospective observational study

1.2.2. Population: Data of the adult patients presenting at Fever clinic and admitted during the period January 2022 to January 2024 with diagnosed and undiagnosed causes of fever were analyzed. Study subjects included adult patients with fever which was defined as an axillary temperature of 38 °C or higher. Patients having previous co morbidity like CAD, Diabetes mellitus, patients with sepsis requiring ionotropes and vasopressors or mechanical ventilator support, having kidney impairment in form of AKI or preexisting CKD, patients with CLD, having altered sensorium, patients on Corticosteroids and those having history of adverse reaction to any NSAID's were excluded from the study. Data of total of 1102 patients were analyzed.

1.2.3. Protocol: Body temperature was measured at 30 min to 60 min intervals following Diclofenac sodium injection. Patients who were not on any antipyretic and who did not respond to usual dose of Acetaminophen (15 mg/kg - 30 mg/kg of the body weight in divided doses) were included in the analysis. Intramuscular Diclofenac sodium Dose 75 mg was given to patients presenting with fever with and without concomitant use of other anti-pyretic or NSAID's.

1.3. Results: Fever alleviation could be achieved in 1058 out of 1102 patients by use of Diclofenac. The average time taken for antipyretic effect following administration of intramuscular diclofenac sodium was 39.1 min ±

23.8 min. The average time taken for antipyretic action was 33 min + 15.7 min for patients on concomitant antipyretics which was significantly less than 39.3 min + 17.2 min for those not on any antipyretics p value < 0.01. The average temperature reduction after 1 h was 1.2 ℃ ± 1.1 ℃ being greater for patients on antipyretics as compared to patients not on any other antipyretic being 1.1 ℃ ± 0.9 ℃. During the period of study and at end of 7 days, minor GI side effects were the most common and there were no reported major side effects.

1.4. Conclusion: A single dose of Intramuscular injection of diclofenac sodium provided effective antipyretic in the study population of the febrile adult patients. Diclofenac may be used alone or as an adjunct with antipyretics. No serious side effects were observed.

2. Keywords: Fever; Adults; NSAID's; Antipyretics; Injection diclofenac

3. INTRODUCTION

Fever is one of the most common symptoms resulting in OPD visits and admission to hospital. There is scanty evidence that high fever may cause serious complications like cognitive dysfunction in adults [1]. Antipyretics such as acetaminophen and ibuprofen are widely used, but many patients present with fever which may not be alleviated by these oral medications. Alternative methods for fever control include tepid sponging, parenteral fluid administration and use of Intramuscular (IM) or Intravenous (IV) injection antipyretics. A single IM antipyretic injection of Diclofenac sodium is used widely in paediatric population [2]. There are very few reports on the effectiveness and safety of IM antipyretic injections in adult patients. This study reports the efficacy and adverse effects of a single IM injection of diclofenac sodium in adult patients.

4. MATERIALS AND METHODS

This was a retrospective study in which data of adult patients presenting to the outpatient department, Fever clinic was analyzed. This study was approved by the Institutional Ethical committee.

4.1. Study Population

Subjects included adult patients presenting with symptoms of fever which was defined as an axillary temperature of 38 ℃ or higher. We analyzed records of total of 1102 patients during the period September 2019 to September 2020. It was observed that the number of patients with fever have increased since the COVID 19 pandemic. Average number of patients reporting daily to fever clinic being 28 + 17 during the September 2019 to March 2020 as compared to 39 + 19 during April 2020 to September 2020 p value < 0.01. Medical records of patients who received diclofenac sodium were analyzed for side effects like allergic reaction and any other side effect for next 7 days. Note was made of patients who were already on anti-pyeretics and who were not.

4.2. Body Temperature Measurement

Baseline body temperature was measured using the Infra-red thermometer and as well as axillary temperature using the mercury thermometer. The temperature was then measured at 30 min to 60 min intervals following diclofenac sodium injection.

4.3. Data Analysis

Time at Onset of effect of the antipyretic was defined as time taken for the temperature fall by 1 ℃ below the baseline temperature at presentation. Temperature change was defined as the change in temperature 1 h following injection of Diclofenac sodium. For data analysis SPSS statistics 20.0 was used. A multiple linear

regression analysis was performed to identify factors affecting the antipyretic effects. The Mann-Whitney U test was performed to compare antipyretic effect. The level of significance was considered if a P value < 0.05.

4.4. Results

The number of adult patients who received diclofenac sodium was 1102 during the study period. By inclusion criteria, a total of 1102 subjects were included, of which 631 were males (Min age 18 years and Max age 76 years and 7 months with Mean age 31 ± 17 years, mean weight 63.3 kg ± 11.6 kg) and 471 were females (Min age 18 years and max age 61 years 5 months, Mean age being 30 ± 18.3 years and mean weight 56.3 kg ± 9.6 kg). The average dose of diclofenac sodium injected was 75 mg, Dose was required to be repeated for 19 subjects. Out of 1102 subjects 236 were already on anti-pyeretics. The average temperature on presentation to the emergency department was 38.6 ℃ ± 0.9 ℃. Fever was alleviated in 1058/1102 patients after Diclofenac injection. 19/1058 patients required two dosages of Inj Diclofenac. The diagnosis of fever included: Respiratory infections (374), Urinary tract Infection (197), Malaria(23), Dengue fever (11), undiagnosed fever at presentation(42), acute pharyngitis (76), acute tonsillitis (73), gastroenteritis (67), Pneumonia(57), Enteric fever(56), Skin infection incl abcess(25), liver abcess(27), Epididymo orchitis(17), Scrub typhus(03), COVID infection (54), etc. (Table 1 to Table 3).

4.5. Adverse Effect profile of Inj Diclofenac

There were no reported adverse reactions. A total of 23 patients in the study group had a history of nasobronchial allergy and asthma but no bronchospasm occurred during the observation period in this subset of patients. 37 out of 1102 patients reported mild burning epigastrium which subsided on its own in next 48 hours. On follow up for 07 days no adverse effects were noted.

4.6. Changes in Body Temperature 1 h Following Injection

The average temperature on presentation to the emergency department was 38.6 ℃ ± 0.9 ℃. The average temperature reduction after 1 h was 1.1 ℃ ± 0.8 ℃.

4.7. Factors Affecting Antipyresis

Association of onset of antipyretic effect with variables were analyzed by multiple linear regression analyses. It was found that the mean time to effect was significantly less in the patient who were on other anti pyeretics. The concomitant use of the NSAID seems to be having an additive effect. The time taken for anti-pyretic action following injection Diclofenac was significantly less being 33 min + 15.7 min in the group who were already on other anti pyeretics NSAID as compared to 39.3 min + 17.2 min for those who received only Injection Diclofenac sodium $p < 0.01$. The change in temperature 1 h following injection was higher in group already on anti pyeretics than those patients who were not on any anti pyeretics 1.2 ℃ + 1.1℃ *vs* 1.1 + 0.9 ℃.

4.8. Comparison between Male and Female patients and response to Age

There was no difference in response and time to the anti-pyretic effect between the male and female patients. We also did not find any difference of response depending on age.

Table 1: Demographics and clinical data of patients.

Characteristics, n= 1102		
Male n = 631	Mean Age 31 ± 17 yrs	Mean weight 63.3 ± 11.6 kg
Female n = 471	Mean Age 30 ± 18.3 yrs	Mean weight 56.3 ± 9.6 kg

Table 2: Causes of fever in study population.

Causes of fever in the study population, n = 1102	
Respiratory infection	374
Urinary tract Infection	197
Acute pharyngitis	76
Acute tonsillitis	73
Acute gastroenteritis	67
Pneumonia	57
Enteric fever	56
COVID infection	54
Liver abscess	27
Skin infection incl abscess	25
Malaria	23
Epididymo-orchitis	17
Dengue fever	11
Scrub typhus	3
Undiagnosed fever at presentation	42

Table 3: Time at Onset of Antipyretic effect and change in temperature following Inj Diclofenac.

Parameter	
Mean Temp at presentation	38.6 ℃ ± 0.9 ℃
Onset of antipyretic action in study population (n= 1102)	39.1 min +28.9 min
Onset of antipyretic in patients with concomitant NSAID use (n = 236)	33 min + 15.7 min
Temperature change in patients with concomitant NSAID use (n = 236)	1.2 ℃ + 1.1℃
Onset of antipyretic in Diclofenac group	39.3 min + 17.2 min
Temperature change in Diclofenac group	1.1 ℃ + 0.9 ℃

5. DISCUSSION

Diclofenac sodium is a chemical derivative of phenylacetic acid. Though the mechanism of its action is poorly understood it likely acts like other NSAIDs inhibiting the prostaglandin synthesis. Hence it is classified as a Nonsteroidal Anti-Inflammatory Drug (NSAID) having both the analgesic as well as antipyretic effects [3]. When administered orally, rectally, or intramuscularly, the drug has rapid absorption and reaches peak plasma concentrations in about 10 min to 30 min [4,5]. The main metabolite being 4 - hydroxydiclofenac which is primarily eliminated from the body by urine and biliary excretion [6-8]. Diclofenac sodium is having been used widely to treat inflammatory diseases like Arthritis, Gout, Rheumatoid arthritis and for controlling associated pain with ureteric calculi etc [9-12]. In children also diclofenac sodium has been successfully and safely for conditions such as juvenile rheumatoid arthritis, fever and postoperative pain relief [13,14]. Gastrointestinal symptoms such as nausea, vomiting, and gastric upset are the most frequent reported side effects. Allergic reactions resulting in symptoms such as rash or dizziness have also been reported [15]. Diclofenac sodium is an effective antipyretic agent. Studies have documented antipyretic effect after oral or rectal administration in children, and an approximately 1.5 °C temperature reduction was observed within 2 h of injection of a 0.25 mg/kg or 0.5 mg/kg dose [16,17]. An accurate antipyretic dose is not established for paediatrics or adult patients. There are scanty reports on the antipyretic effects after IM injection in children and adults [17]. In the current study, we used 75 mg diclofenac sodium of standard preparation which was administered as a single IM injection. The patients were then observed for 1 h - 2 h and the antipyretic effects during the first hour and there after following injection Diclofenac and the time at which the temperature was reduced by at least 1°C were noted and analyzed. Any immediate and delayed adverse effects of diclofenac sodium were also noted. In our study, the only adverse effect directly associated with the administration of diclofenac sodium was local pain at injection site and mild gastritis which were self-resolving. Hypothermia which is a theoretical possibility with concomitant use of anti pyeretics however was did not observe hypothermia in any patient in our study. Nonsteroidal anti-inflammatory drugs may cause bronchospasm or exacerbate asthmatic symptoms in patients with history of Asthma and nasal polyp and nasobronchial allergy [18-19]. In our study we did not observe such adverse effects following injection even in patients having preexisting history. The average time taken for antipyresis in our study was lesser in patients on concomitant NSAID use as compared to Diclefenac alone. Effective antipyresis was achieved in 1058/ 1102 after a single IM injection of 75 mg of Diclofenac sodium. No serious side effects were not observed in our study. Use of concurrent antipyretics was observed to be having an additive effect in our study. As this was not a controlled study, we could not determine the duration of antipyretic effects. The limitation of this study was that because of retrospective study design incomplete and inaccurate data cannot be ruled out. The result of the current study does however indicate that diclofenac sodium is an effective antipyretic. But the further study will be required about desired effects and any side effect for widespread use and recommendation in adult patients.

7. CONCLUSION

A single dose of diclofenac sodium provided effective antipyresis in adult patients. Antipyresis occurred more rapidly in patients with concurrent NSAID use. No serious side effects were observed.

8. ACKNOWLEDGMENT

The authors received no financial support for the research and/or authorship of this article.

9. CONFLICT OF INTEREST

Nil

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