

Evaluation of the Analgesic Efficacy of two Doses of Oral Ibuprofen in Patients Presenting to the Emergency Department Complaining of Severe Pain

MUHAMMAD SAQIB HABIB¹, SAQIB KHALIL², ABDUL AZEEM³, SAMEER AHMED⁴, AMANAT ALI⁵, FAYAZ AHMED MEMON⁶

¹Assistant Professor of Medicine, Islamic International Medical College and Trust Islamabad

²Assistant Professor women medical college Abbottabad Consultant neurosurgeon Jinnah International hospital Abbottabad

³Assistant Professor Department of Pharmacology Watim Medical and Dental College, Rawat, Rawalpindi

⁴Assistant Professor Pharmacology HBS Medical and Dental College, Islamabad

⁵Associate Professor Pharmacology HBS Medical and Dental College, Islamabad

⁶Professor Department of Medicine Muhammed Medical College & Hospital, Mirpurkhas, Sindh

Corresponding author: Saqib Khalil, Email: drskjadoon1980@gmail.com

ABSTRACT

Objective: The purpose of this study is to examine the relative effectiveness of two different oral dosages of ibuprofen in relieving pain in patients presenting to the emergency department complaining of sudden, severe discomfort.

Study Design: Randomized, Double-blind trial

Place and Duration: Islamic International Medical College and Trust Islamabad, during from January 2021 to June 2021.

Methods: Total 180 patients of both genders with ages 20-75 years had acute pain were presented. After obtaining participants' informed consent, demographic data such as age, sex, BMI, and residence were collected from those who participated. Causes of pain among all cases were also recorded. Single doze 400mg was given to 90 patients in group I and doze of 800mg was given to group II. Visual analogue scale was used for measurement of pain score among both groups. SPSS 22.0 was used to analyze all data.

Results: There were majority males 112 (62.2%) and 68 (37.8%) females in this study. Among 180 patients, 80 (44.4%) had age 21-30 years, 60 (33.3%) had age 31-40 years and 50 (27.8%) had age >40 years. Majority was from urban areas 105 (58.3%). Most common cause of acute pain was fallen, RTA, sports and knife abuse among all cases. We found no any significant difference in pain score at 2, 4 and 6 hours among both groups and both doses were effective among all cases in reduction of pain with p value <0.005. Post-treatment side effects were dizziness, nausea and diarrhea among both groups but there was also no any significant difference observed.

Conclusion: We concluded in this study the oral ibuprofen (400mg, 800mg) was an effective and useful in reduction of pain score among patients admitted to ED because of injury. No any significant difference was observed between efficacy and as well as in side effects.

Keywords: Acute Pain, ED, VAS, Ibuprofen, Side Effects

INTRODUCTION

Ibuprofen (eg, Advil, Motrin) and other oral analgesics are often used in the ED to treat mild to moderate pain either alone or in combination with acetaminophen, and severe pain either alone or in combination with opioid analgesics. This drug is a nonselective NSAID since it blocks the action of both cyclooxygenase-1 (constitutive) and cyclooxygenase-2 (inducible), preventing the production of prostaglandins and thromboxanes. The analgesic, antipyretic, and anti-inflammatory ibuprofen may be administered in a variety of ways, including orally, rectally, intravenously, or topically. Many people go to the emergency department because they are experiencing severe pain at the moment.[1] This might range from musculoskeletal pain to dental pain to tension headaches to dysmenorrhea. The half-life of ibuprofen is short 2 to 2.5 hours since it is mostly metabolised by the liver and subsequently eliminated by the kidneys. [2] Inhibition of cyclooxygenase, leading to decreased glomerular filtration, or competitive displacement of the second drug from protein-binding sites are two examples of the various drug-drug interactions in which it is involved. Lithium enhances the toxicity of ibuprofen, while diuretics and angiotensin-converting enzyme inhibitors raise the risk of systolic blood pressure and decrease renal functions. The combination of ibuprofen and warfarin increases the risk of gastrointestinal bleeding. [3- 5]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are cyclooxygenase inhibitors with anti-inflammatory, analgesic, antipyretic, and platelet-aggregation-inhibiting properties [6, 7]. Since non-steroidal anti-inflammatory medicines do not slow breathing or impede digestion, they are not controlled substances and do not carry the risk of addiction [7,8]. Patients with a predisposition to bronchospasm should avoid them since they trigger the release of histamine. In addition, they may aggravate renal and cardiac failure and irritate the gastrointestinal mucosa, leading to indigestion or ulcers. The danger of adverse effects, however, has

been demonstrated to be minimal at moderate dosages by several investigations.

Ibuprofen is often regarded as the least dangerous NSAID on the market due to its lack of major adverse effects [9,10]. It is widely used in the first treatment of soft tissue injuries in emergency rooms all around the globe.

When it comes to relieving pain, many doctors believe that the NSAIDs are superior than paracetamol, despite paracetamol being a safe and inexpensive option [11]. There is no strong evidence that NSAIDs are more beneficial than paracetamol in treating acute musculoskeletal disorders, as noted by a Cochrane clinical review in 2000 [12]. These data represented the state-of-the-art as at the time this research was conceived.

When evaluating the clinical effectiveness of analgesics for acute postoperative pain, numbers required to treat (NNT) are often utilised [13]. It has been argued that utilising NNT values as proof of pain alleviation across procedures is deceptive, despite their apparent usefulness. Integration of data from trials with potential confounding variables, such as a range of pain modalities and intensities [14], a wide age range, and a diverse range of ethnicities among patients, means that they may not be typical of all forms of postoperative pain [15]. As a one-dimensional impact metric, NNT values ignore time-related factors, as well as patient-reported outcome measures, when evaluating analgesics (PROM). The purpose of this research was to examine the analgesic efficacy and potential adverse effects of ibuprofen doses of 400 mg, 800 mg, and a combination of these two doses for the treatment of soft tissue injury.

MATERIAL AND METHODS

This Randomized, Double-blind trial was conducted at Islamic International Medical College and Trust Islamabad, during from January 2021 to June 2021 and comprised of 180 patients had acute pain. After obtaining participants' informed consent,

demographic data such as age, sex, BMI, and residence were collected from those who participated. Patients who did not give informed consent, those who had an allergy to the treatment, women who were pregnant, and those who suffered from cardiovascular illness or lung disease were not included.

Included patients were aged between 22-70 years. Blood pressure of all the patients was noted. All the patients were divided in two groups. Causes of pain among all cases were also recorded. Single doze 400mg was given to 90 patients in group I and doze of 800mg was given to group II. The Visual Analogue Scale for Pain (VAS) was used to measure pain after medication administration, and the results were compared between the two groups. Both groups' medication-related side effects and patients' levels of satisfaction were evaluated and compared.

SPSS 20.0 was used to analyze all of the data collected. Calculations involving the mean and standard deviation were made. There were tabular representations of the frequencies and percentages. The pain scale, adverse effects, and patient satisfaction were compared using a chi-square test.

RESULTS

There were majority males 112 (62.2%) and 68 (37.8%) females in this study. 140 (77.8%) patients had BMI <25kg/m² and 40 (22.2%) cases had BMI >25kg/m². Most common cause of acute pain was fallen, RTA, sports and knife abuse among all cases.(table 2)

Table-1: Included patients with detailed demographics

Variables	Frequency	Percentage
Gender		
Male	112	62.2
Female	68	37.8
BMI		
<25kg/m ²	140	77.8
>25kg/m ²	40	22.2
Cause of Acute Pain		
Fallen	70	38.9
RTA	50	27.8
Sports	35	19.4
knife abuse	25	13.9

Among 180 patients, 80 (44.4%) had age 21-30 years, 60 (33.3%) had age 31-40 years and 50 (27.8%) had age >40 years.(figure 1)

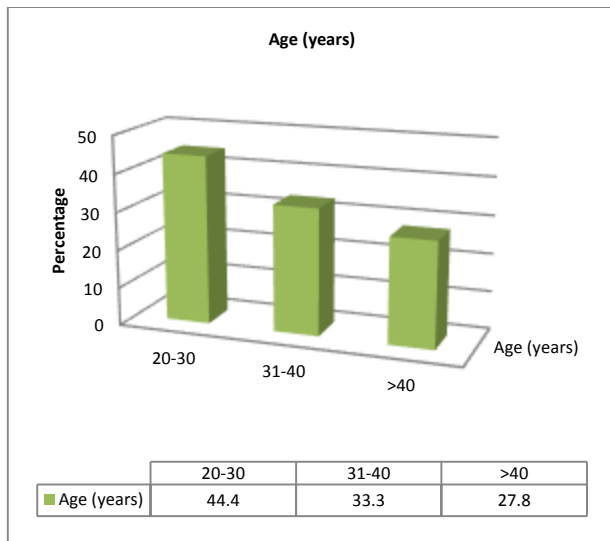


Figure-1: Included patients with age distribution

We found no any significant difference in pain score at 2, 4 and 6 hours among both groups and both doses were effective among all cases in reduction of pain with p value <0.005.(table 2)

Table-2: Outcomes among both groups by using VAS

Variables	Group I	Group II
Pain Score (VAS)		
Baseline	9.14±3.09	9.12±4.17
2 (hours)	5.11±8.11	5.3±14.9
4 (hours)	3.2±8.17	3.8±11.8
6 (hours)	1.4±0.8	1.1±0.02

Post-treatment side effects were dizziness, nausea and diarrhea among both groups but there was also no any significant difference observed.(table 3)

Table-3: Comparison of side effects among both groups

Variables	Group I	Group II
Side Effects		
dizziness	9 (10%)	13 (14.4%)
nausea	10 (11.1%)	8 (8.95)
diarrhea	6 (6.7%)	7 (7.8%)

We found among all 180 patients, satisfaction rate was higher 170 (94.4%).(figure 2)

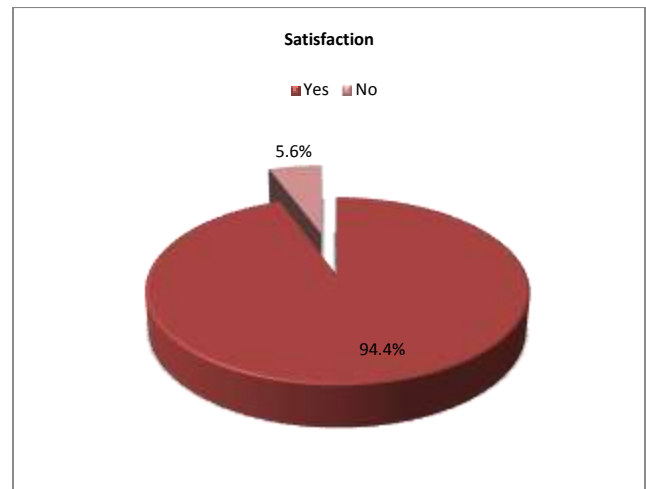


Figure-2: Post-treatment satisfaction among all cases

DISCUSSION

In both hospital and outpatient settings, ibuprofen is often used to alleviate pain. As a first-line analgesic (alone or in combination with acetaminophen) for a broad variety of acute traumatic, non-traumatic, and chronic pain issues in the ED due to its anti-inflammatory, anti-pain, and parenteral/enteral/topical availability. In the emergency room, ibuprofen doses well beyond the amount shown to provide any pain relief are routinely given out. For acute pain, however, even the maximum daily dosage of ibuprofen (400 mg) is effective in reducing pain and inflammation. The only difference between the analgesic ceiling dosage of ibuprofen and the higher doses may be the duration of analgesia due to the linear kinetic pattern followed by NSAIDs. [16,17]

In this research 180 patients had acute pain were presented. There were majority males 112 (62.2%) and 68 (37.8%) females in this study. 140 (77.8%) patients had BMI <25kg/m² and 40 (22.2%) cases had BMI >25kg/m². Most common cause of acute pain was fallen, RTA, sports and knife abuse among all cases. These were comparable to the previous studies.[18,19] Among 180 patients, 80 (44.4%) had age 21-30 years, 60 (33.3%) had age 31-40 years and 50 (27.8%) had age >40 years.[20] We found no any significant difference in pain score at 2, 4 and 6 hours among both groups and both doses were effective among all cases in reduction of pain with p value <0.005.[18-20]

In a study comparing 400 mg and 800 mg of ibuprofen for dental surgery-related pain, Winter et al. found no significant difference [21]. Subsequently, pain models very comparable to

ours [22] discovered a distinct ibuprofen dosage response, with a maximum effect shown at 400 mg. However, no differences were found between the medication dosages in two dental surgery models with varying degrees of pain (mild to severe) that tested ibuprofen 400 mg, 600 mg, and 800 mg [23], and models with varying degrees of pain (30 mm VAS) that tested ibuprofen 200 mg, 400 mg, and 600 mg [24]. There was no difference in pain relief between the 400 mg, 600 mg, and 800 mg in a non-dental pain model with a greater baseline pain level (emergency room pain > 6 NRS) [25]. Our findings with an initial pain level of moderate pain support these findings and strongly imply that ibuprofen achieves its analgesic ceiling at a dosage of roughly 400 mg, irrespective of starting pain level or acute pain type.

Ibuprofen was shown to be significantly better than paracetamol across several situations in a prior meta-analysis [26]. This was shown most clearly in studies of chronic pain caused by osteoarthritis, migraines, and other forms of headaches. The use of fast-acting versions of ibuprofen has been shown to give much superior analgesia than regular ibuprofen, with a greater reduction in pain intensity immediately following administration and less need for further treatment [27]. Fast-acting ibuprofen formulations have not yet been shown effective in our study population, thus more research is needed. While we were limited in our ability to evaluate the safety of two different oral ibuprofen doses and to compare the duration of analgesia between the two groups beyond the duration of the study, we believe that our findings support the analgesic efficacy of 400 mg of ibuprofen per dose for managing acute pain in the ED.

Single doses of 400, 600, or even 800 mg of ibuprofen do not cause acute toxicity or substantial side effects. Greater ibuprofen dose resulted in greater analgesia for longer periods of time due to the drug's linear kinetic pattern. [28] Ibuprofen's maximum daily dose for anti-inflammatory effects is 2,400 to 3,200 mg/day, which is significantly greater than the maximum amount for relieving pain. [29]

CONCLUSION

We concluded in this study the oral ibuprofen (400mg, 800mg) was an effective and useful in reduction of pain score among patients admitted to ED because of injury. No any significant difference was observed between efficacy and as well as in side effects.

REFERENCES

- Nalamachu S, Pergolizzi JV, Raffa RB, et al. Acute pain management in the emergency department: emphasis on NSAIDs. *Emerg Med.* 2013;4:1000171.
- Jones SF, O'Donnell AM. Clinical pharmacology: traditional NSAIDs and selective COX-2 inhibitors. In: Macintyre PE, Walker SM, Rowbotham DJ, et al, eds. *Clinical Pain Management (Acute Pain)*. 2nd ed. London, England: Hodder & Stoughton Limited; 2008:79.
- Moore N, Pollack C, Butkerait P. Adverse drug reactions and drug-drug interactions with over-the-counter NSAIDs. *Clin Risk Manag.* 2015;11:1061-1075.
- McDonald TM, Wei L. Effect of ibuprofen on cardioprotective effect of aspirin. *Lancet.* 2003;361:573-574.
- Hernández-Díaz S, García-Rodríguez LA. Epidemiologic assessment of the safety of conventional nonsteroidal anti-inflammatory drugs. *Am J Med.* 2001;110(Suppl 3A):20S-27S
- Ferreira SH. Prostaglandins, aspirin-like drugs, and analgesia. *Nature* 1972;240(102):200-3.
- Benedetti C, Butler SH. Systemic analgesics. In Bonica JJ (Ed): *The Management of Pain*, ed 2. Philadelphia, Lee and Febiger, 1990:1640-1675.
- Griffin MR, Piper JM, Daugherty JR, Snowden M, Ray WA. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. *Annals of Internal Medicine.* 1991;114(4):257-63. PMID:1987872
- García Rodríguez LA, Jick K. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. *Lancet* 1994;343(8900):769-72. PMID:7907735
- Owen PR. Prostaglandin synthetase inhibitors in the treatment of primary dysmenorrhea: outcome trials reviewed. *American Journal of Obstetrics and Gynecology.* 1984;148(1):96-103. PMID:6419611
- Göttsche PC. Non-steroidal anti-inflammatory drugs. *BMJ: British Medical Journal.* 2000;320(7241):1058. PMID:10764369
- Collins S, Moore RA, McQuay HJ, Wiffen PJ, Rees J, Derry S. Single dose oral ibuprofen for acute postoperative pain in adults. *The Cochrane Library*; 2000
- Moore RA, Derry S, Aldington D, Wiffen PJ (2015) Single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews*, Issue 9. Art. No.: CD008659.
- Tramèr MR, Walder B (2005) Number needed to treat (or harm). *World J Surg* 29:576-581
- Wyatt R (2013) Pain and ethnicity. *Am Med Assoc J Ethics* 15:449-454.
- Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain. *Cochrane Database Syst Rev.* 2013;6:CD010210.
- Nalamachu S. An overview of pain management: the clinical efficacy and value of treatment. *Am J Manag Care.* 2013;19(14 suppl):s261-s266
- FARRUKH ADEEL1 , GHAZALA YASMEEN2 , QAMAR ZAMAN3 , SHAISTA KHADIM4 , FAISAL MASOOD5 , SOHAIB ASGHAR. Comparison of the Analgesic Efficacy of Oral Ibuprofen at two Different Doses in Patients Presented with Acute Pain. *P J M H S Vol. 14, NO. 4, OCT - DEC 2020*
- Motov S, Masoudi A, Drapkin J, Sotomayor C, Kim S, Butt M, Likourezos A, Fassassi C, Hossain R, Brady J, Rothberger N, Flom P, Marshall J. Comparison of Oral Ibuprofen at Three Single-Dose Regimens for Treating Acute Pain in the Emergency Department: A Randomized Controlled Trial. *Ann Emerg Med.* 2019 Oct;74(4):530-537.
- Yngstad, G., Skjelbred, P., Swanson, D.M. et al. Analgesic effect of oral ibuprofen 400, 600, and 800 mg; paracetamol 500 and 1000 mg; and paracetamol 1000 mg plus 60 mg codeine in acute postoperative pain: a single-dose, randomized, placebo-controlled, and double-blind study. *Eur J Clin Pharmacol* 77, 1843-1852 (2021).
- Winter L Jr, Bass E, Recant B, Cahaly JF (1978) Analgesic activity of ibuprofen (Motrin) in postoperative oral surgical pain. *Oral Surg Oral Med Oral Pathol* 45:159-166
- Schou S, Nielsen H, Nattestad A, Hillerup S, Ritzau M, Branbjerg PE et al (1998) Analgesic dose-response relationship of ibuprofen 50, 100, 200, and 400 mg after surgical removal of third molars: a single-dose, randomized, placebo-controlled, and double-blind study of 304 patients. *J Clin Pharmacol* 38:447-454.
- Laska EM, Sunshine A, Marrero I, Olson N, Siegel C, McCormick N (1986) The correlation between blood levels of ibuprofen and clinical analgesic response. *Clin Pharmacol Ther* 40:1-7
- Seymour RA, Ward-Booth P, Kelly PJ (1996) Evaluation of different doses of soluble ibuprofen and ibuprofen tablets in postoperative dental pain. *Br J Oral Maxillofac Surg* 34:110-114.
- Motov S, Masoudi A, Drapkin J, Sotomayor C, Kim S, Butt M et al (2019) Comparison of oral ibuprofen at three single-dose regimens for treating acute pain in the emergency department: a randomized controlled trial. *Ann Emerg Med* 74:530-537.
- Moore RA, Derry S, Aldington D, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults—an overview of Cochrane reviews. *Cochrane Database Syst Rev.* 2015;(9):CD008659. PMID:26414123
- Bondarsky EE, Domingo AT, Matuza NM, Taylor MB, Thode HC, Singer AJ. Ibuprofen vs acetaminophen vs their combination in the relief of musculoskeletal pain in the ED: a randomized, controlled trial. *The American Journal of Emergency Medicine.* 2013;31(9):1357-60. PMID:23896011
- Bijur PE. Validation of a verbally administered numerical rating scale of acute pain for use in the emergency department. *Acad Emerg Med.* 2003;10:390-392.
- Davies NM. Clinical pharmacokinetics of ibuprofen. The first 30 years. *Clin Pharmacokinet.* 1998; 34:101-154.