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Original Article

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A Multicenter, Retrospective, Real-World Evidence Study to Evaluate the Effectiveness and Safety of Nimesulide-Paracetamol Combination Therapy for the Management of Acute Painful Conditions

Dr. Sandip Dhole [1], Dr. Sandeep Darbastwar [2], Dr. Chittanand Mendhe [3], Dr. Ashwini Shirbhate [4], Dr. Ajitkumar Gondane *[5], Dr. Dattatray Pawar [6], Dr. Akhilesh Sharma [7]

[1]Associate Professor, PMR Department, AIIMS, Bibinagar, Telangana, India.
[2]Consultant Surgeon, Galaxy Centre for Gastrointestinal and Liver Disease, Nanded, Maharashtra, India.
[3]Assistant Professor, Dept. of Orthopaedics, IGGMC Nagpur, Maharashtra, India.
[4]Assistant Professor, VYWS Dental College & Hospital, Amravati, Maharashtra, India.
[5]Medical Advisor, Medical Affairs Division, Alkem Laboratories, Mumbai, Maharashtra, India.
[6]Medical Lead, Medical Affairs Division, Alkem Laboratories, Mumbai, Maharashtra, India.
[7]President & Chief Medical Officer, Medical Division, Alkem Laboratories, Mumbai, Maharashtra, India.

*Corresponding Author: Dr. Ajitkumar Gondane; *ajitkumar.gondane@alkem.com*

Abstract

Introduction: Nimesulide-Paracetamol fixed-dose combination is widely used for managing acute painful conditions, yet real-world evidence remains limited. This study aimed to evaluate its effectiveness and safety in patients presenting with various acute painful conditions in clinical practice. ***Methods:*** This multicenter, retrospective study analyzed records of 1873 adult patients across 528 centers in India who received nimesulide-paracetamol. Pain severity was documented at baseline and follow-up (7 ± 2 days). Statistical analysis included descriptive summaries of patient characteristics and treatment outcomes. ***Results:*** Among 1873 patients (69.6% male; mean age 45.54 ± 21.22 years), common diagnoses included low back pain (33.6%), soft tissue injury (14.5%), myalgia (14.0%), and dental pain (13.2%). At baseline, 8.7% had mild pain, 34.6% moderate, and 56.7% severe pain. Following treatment, 66.8% achieved complete pain relief. Of patients with severe baseline pain (n=1062), 71.7% became pain-free, 20.2% improved to mild, 4.4% to moderate, and 3.7% remained with severe pain. Among those with moderate pain (n=648), 57.4% reported no pain after treatment. No adverse events were reported during the treatment period. ***Conclusion:*** Nimesulide-paracetamol combination therapy demonstrated substantial effectiveness and good tolerability in real-world management of acute painful conditions, achieving significant pain relief with no reported safety concerns.

Keywords: ***Retrospective observational study, Short-term pain management, Analgesic effectiveness.***

Introduction

Pain remains a primary reason for consultations in primary care. Acute pain serves as a protective warning of injury or harmful stimuli and typically subsides with healing. In contrast, chronic pain persists beyond the resolution of the initial injury. Importantly, inadequately treated acute pain may transition into chronic pain [1,2]. Pharmacological management constitutes the fundamental approach to both acute and chronic pain control. In the context of acute pain management, nonsteroidal anti-inflammatory drugs (NSAIDs) represent one of the most commonly utilized analgesic agents [3,4].

NSAIDs comprise a chemically diverse group of drugs sharing anti-inflammatory, analgesic, antipyretic, and, except for Cyclo-oxygenase (COX)-2-selective agents (e.g., Celecoxib, Rofecoxib), platelet-inhibitory effects. They act via opioid-independent inhibition of cyclooxygenase (COX), but their use is limited by dose-dependent side effects [5,6]. Even at therapeutic doses, NSAIDs can cause cerebrovascular and gastrointestinal complications, including ulcers and bleeding. Higher doses increase the risk of cardiotoxicity, nephrotoxicity, and hepatotoxicity [7,8]. Therefore, identifying NSAIDs with improved safety profiles is crucial. Nimesulide, a non-selective NSAID with preferential COX-2 inhibition, demonstrates potent analgesic, anti-inflammatory, and antipyretic effects, with efficacy supported by multiple clinical trials across diverse pain conditions [9]. Over thirty years of clinical use, nimesulide has proven effective in rapidly relieving pain and

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inflammation with a favorable safety profile, notably causing fewer gastrointestinal side effects. However, rare cases of unpredictable hepatic injury have been reported [10]. Nimesulide has the property to inhibit acute inflammation, pain and fever effectively owing to its added benefit over other pain relievers.

The fixed drug combination (FDC) of Nimesulide and Paracetamol is employed for pain relief across various medical contexts. It effectively mitigates pain associated with conditions such as headache, mild migraine, muscle pain, dental pain, rheumatoid arthritis, etc. Tiwaskar et. al performed a clinical study which aimed to evaluate the efficacy and safety of nimesulide/paracetamol (100 mg + 325 mg) fixed-dose combination twice a day for 2 weeks in the management of acute pain in Indian population. Analysis of liver function tests (LFTs) revealed only a slight elevation which did not exceed the normal range. Only one out of every 500 patients reported adverse events (AEs) and an impressive improvement of 96.6% was noted in the patient global assessment scale (GAS), while physicians observed a 97.2% enhancement in their assessment according to the GAS [11].

Despite of all this, there is very less data is available pertaining to effectiveness and safety of Nimesulide-Paracetamol FDC. So, due to the limited real-world Indian data available on the nimesulide/paracetamol FDC, an open-label retrospective multicentric study was conducted to evaluate the safety and effectiveness of Nimesulide-Paracetamol FDC in the management of acute painful conditions in real-world settings. Also, this study aims to provide valuable insights into the effectiveness and safety profile of this pharmacological combination, thereby informing clinical decision-making and optimizing patient care strategies.

Methods

Study design and population

This single-arm, multicentre, retrospective real-world study utilized medical records from 1873 patients with acute painful conditions (low back pain, soft tissue injury, myalgia, dental pain, generalized pain, sprain, arthralgia, headache etc) who presented to outpatient departments and received nimesulide-paracetamol combination therapy. Eligible participants were adults aged 18 years with documented clinical diagnosis and treatment outcomes (at least one post treatment follow-up visit data at 7±3 days) following Nimesulide-Paracetamol therapy. Only those patients with complete medical record is included in the analysis. Exclusion criteria comprised patients under 18 years of age, those not prescribed co-amoxiclav as primary or adjunct therapy, and individuals with incomplete medical documentation.

Data collection

Study investigators and site personnel identified eligible patients through a thorough review of existing medical records at each participating centre, applying predefined selection criteria. Individual prescriptions and laboratory reports were screened, and relevant data was systematically recorded in a standardized reporting system. Each patient record was assigned a unique identification number, starting from 001 for each investigator site. The baseline visit was defined as the initiation of co-amoxiclav therapy, with data collection occurring at baseline (Day 0) and during a follow-up visit.

The primary endpoints included therapeutic effectiveness and safety outcomes. At baseline, comprehensive demographic data-including age, gender, and medical diagnosis-were collected for all participants. The therapeutic response was assessed and stratified as decrease in pain severity as mild, moderate, or severe. Safety was monitored through documentation of any adverse events occurring during the treatment period. Follow-up assessments were conducted approximately 7 ± 2 days after treatment initiation.

Statistical Analyses

Statistical analysis was performed using descriptive statistics to summarize sample characteristics, including means, standard deviations, and frequencies for categorical variables. This approach facilitated the understanding of symptom distribution, treatment responses, and demographic patterns within the sample, enabling nuanced interpretation of the study findings. The paired t-test was employed to evaluate changes in key clinical parameters between baseline and follow-up. All analyses were conducted using SPSS software, with statistical significance defined at a 95% confidence interval (CI).

Ethical Considerations

The study protocol was reviewed and approved by a registered Institutional Ethics Committee (IEC) before commencement. This research complied with the Ethical Guidelines for Biomedical Research on Human Participants as established by the Indian Council of Medical Research (ICMR). Informed consent was waived due to the retrospective nature of the study, which utilized anonymized patient data extracted from medical records of individuals previously treated with co-amoxiclav. Patient confidentiality was maintained rigorously throughout the study.

Results

A total of 1873 patients were included in this multicentre, retrospective, real-world evidence study. Of these, 1303 (69.6%) were male and 570 (30.4%) were female. The mean (±SD) age of the cohort was 45.54 ± 21.22 years, and the mean (±SD) body weight was 72.67 ± 19.08 kg.

Baseline Diagnoses

The distribution of acute painful conditions leading to treatment with the nimesulide-paracetamol combination is presented in Figure 1. The most frequent diagnosis was low back pain (n=630; 33.6%), followed by soft tissue injury (n=271; 14.5%) and myalgia (n=262; 14.0%). Other indications included dental pain (n=248; 13.2%), generalized pain (n=202; 10.8%), sprain (n=94; 5.0%), arthralgia (n=82; 4.4%), headache (n=50; 2.7%), and various other conditions (n=34; 1.8%).

Duration of Illness and Treatment

The majority of patients (n=1725; 92.0%) reported a duration of illness of up to 15 days, while 148 patients (8.0%) had symptoms persisting for more than 15 days as depicted in table 1. Regarding treatment duration with nimesulide-paracetamol combination, 707 patients (37.7%) received therapy for up to 5 days, 563 patients (30.1%) for 6-7 days, and 603 patients (32.2%) for 8-10 days.

Decrease in pain intensity after treatment

Pain severity was evaluated as mild, moderate or severe at baseline and after treatment. At baseline, 8.7% of patients (n = 163) reported mild pain, 34.6% (n = 648) reported moderate pain, and 56.7% (n = 1,062) reported severe pain. Among patients with mild pain at baseline (n = 163), 72.4% (n = 118) reported no pain after treatment, 22.1% (n = 36) continued to have mild pain, 4.3% (n = 7) progressed to moderate pain, and 1.2% (n = 2) progressed to severe pain. Among those with moderate pain at baseline (n = 648), 57.4% (n = 372) reported no pain following treatment, 35.5% (n = 230) improved to mild pain, 6.8% (n = 44) remained at moderate pain, and 0.3% (n = 2) experienced worsening to severe pain. Of the patients with severe

pain at baseline (n = 1,062), 71.7% (n = 761) reported no pain after treatment, 20.2% (n = 215) improved to mild pain, 4.4% (n = 47) improved to moderate pain, and 3.7% (n = 39) continued to have severe pain.

So, as depicted in figure 2 overall improvement in pain relief was observed in 72.39% of patients with mild pain, 92.90% of patients with moderate pain, and 96.33% of patients with severe pain following treatment.

Also, no adverse effects were reported in the study during treatment period.

In summary, treatment with the nimesulide-paracetamol combination resulted in substantial reduction in pain intensity across all baseline severities, with over 90% of patients with moderate or severe pain achieving pain relief. Which underscores the effectiveness of this combination in acute painful condition in real world scenario.

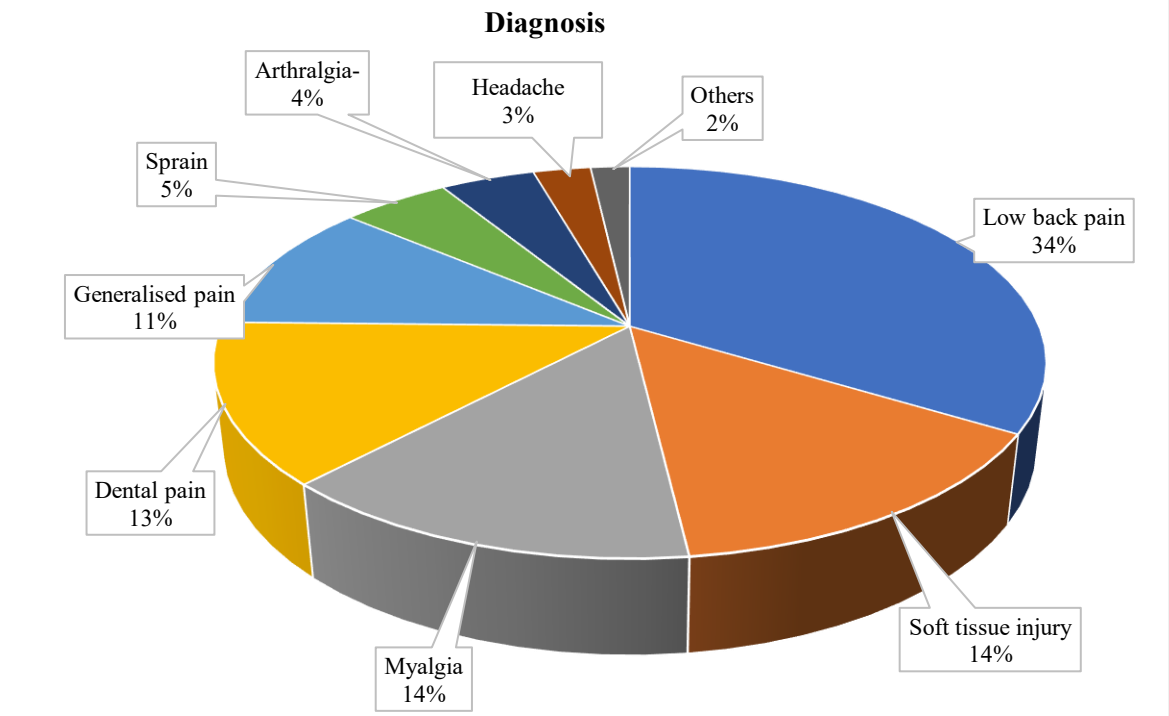

Figure 1: Distribution of acute painful conditions

Table 1: Duration of illness and treatment

Duration of Illness		Duration of Treatment	
Duration	**Number of patients (%)**	**Duration**	**Number of patients (%)**
Up to 15 days	1725 (92.0%)	**Up to 5 days**	707 (37.7%)
More than 15 days	148 (8.0%)	**6-7 days**	563 (30.1%)
		8-10 days	603 (32.2%)

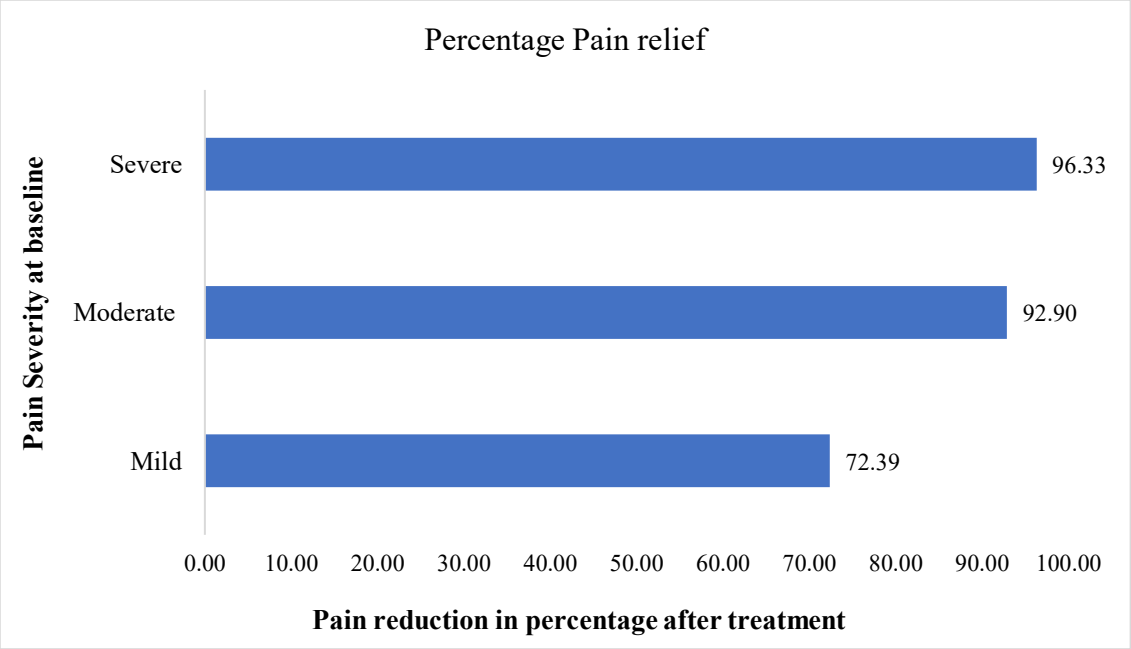

Figure 2: Percentage pain relief following treatment

Discussion

In this retrospective study, conducted using medical records of patients treated with the nimesulide-paracetamol combination for acute painful conditions, substantial pain relief was observed across the cohort, particularly among those with moderate and severe pain at baseline. The findings suggest that while many patients achieved effective pain control within a few days, a significant proportion needed longer treatment, indicating variability in pain resolution among individuals. Notably, despite differences in treatment duration, the therapy was well-tolerated, with no adverse events reported during the study period. This underscores the potential of the nimesulide-paracetamol combination as an effective and safe option for managing acute painful conditions in diverse patient populations.

We have observed that the treatment duration for the acute pain management is up to 10 days depending upon the pain severity and treatment duration varied, with 37.7% of patients receiving therapy for up to 5 days, 30.1% treated for 6-7 days, and 32.2% requiring 8-10 days of medication. These treatment durations reflect real-world clinical practice, where the intensity and persistence of pain dictate therapy length. In an expert opinion by Alberto Magni et al, on adequate duration of NSAID therapy it is stated that the duration of NSAID should be as minimum as possible and duration should be tailored to the patient profile [13]. Usually, the treatment duration is at least 7-10 days, considering the time required to achieve the analgesic action. Furthermore, a study examining the usage and prescribing preferences of NSAIDs reported that the majority of physicians (72.6%) typically prescribed NSAIDs for a duration of up to 7 days in clinical practice [14]. A similar treatment duration was reported in an observational study by Patil et al., where physicians prescribed Nimesulide, diclofenac, or aceclofenac in combination with paracetamol for a maximum of up to 10 days, based on their clinical discretion [15].

In our study we have observed that there was substantial decrease in pain intensity after nimesulide paracetamol combination. Overall 87.21% of patients experience decrease in pain intensity by at least 1 grade. Similar findings were observed in studies by Tiwaskar et al and Patil et, where pain intensity was decreased significantly after treatment with nimesulide paracetamol combination [15,16]. Our findings on the reduction in pain intensity are further supported by a study conducted by Bianca et al., which demonstrated that nimesulide treatment led to significant decreases in pain intensity on the first, second, and third days of therapy in patients experiencing postoperative pain [17]. This evidence of decreased pain intensity supports the results of our study, as the effectiveness of nimesulide has also been demonstrated in patients with gout, where it provided faster pain relief and a greater reduction in pain intensity compared to diclofenac [18]. Furthermore, evidence for pain management is reinforced by a recent prospective study demonstrating that nimesulide provides more effective relief of both pain and fever [19].

This study has certain limitations, as pain is inherently subjective and, without standardized tools like the VAS or NRS, the assessment of effectiveness may lack precision. Additionally, other medications, comorbidities, or lifestyle factors could have influenced pain control outcomes. Being retrospective, the data may also underreport mild or transient side effects, potentially underestimating safety concerns.

This retrospective study provides valuable real-world evidence regarding the effectiveness and safety of the fixed-dose combination of nimesulide and paracetamol in managing a variety of acute painful conditions. The analysis demonstrates that this combination offers significant pain relief across different clinical scenarios, supporting its role as an effective therapeutic option. Importantly, the large patient sample size and the inclusion of data from multiple diverse centers enhance the robustness and generalizability of these findings. Moreover, no major safety concerns emerged during the study period, suggesting that the combination is generally well tolerated. However, further prospective studies are warranted to confirm these observations and to explore long-term safety and effectiveness in broader patient populations.

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Declarations

Conflict of interest declaration

Authors AG, DP, and AS are full-time employees of the Medical Affairs Department, Alkem Laboratories Ltd., Mumbai, India.

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Contributors/Authors

Dr. Ajitkumar Gondane, Dr. Dattatray Pawar, Dr. Akhilesh Sharma

Ethical Clearance

Reviewed and approved by a registered Independent Ethics Committee (EC).

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