

RESEARCH ARTICLE

COMPARATIVE EFFECTIVENESS OF MEFENAMIC ACID, PARACETAMOL,
AND IBUPROFEN IN THE MANAGEMENT OF PRIMARY HEADACHE AMONG
MEDICAL STUDENTS

(*PERBANDINGAN EFEKTIVITAS ASAM MEFENAMAT, PARASETAMOL, DAN
IBUPROFEN DALAM PENGELOLAAN NYERI KEPALA PRIMER PADA
MAHASISWA KEDOKTERAN*)

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ABSTRACT

Primary headache is a common neurological complaint among medical students, often associated with academic stress, sleep deprivation, and unhealthy lifestyle patterns. Over-the-counter analgesics such as mefenamic acid, paracetamol, and ibuprofen are frequently used for self-medication; however, comparative data regarding their effectiveness in this population remain limited. This study aimed to compare the effectiveness of these three drugs in the management of primary headache among medical students. This study employed an analytical cross-sectional design involving 73 students from the Faculty of Medicine, Universitas Jenderal Achmad Yani, class of 2024. Data were collected using questionnaires assessing the type of analgesic used, onset of action, and duration of effect, and were analyzed using the Kruskal–Wallis test. Most respondents were classified as having probable migraine (61.7%) based on the HSQ. Paracetamol was the most commonly used analgesic (75.3%), followed by ibuprofen (9.9%) and mefenamic acid (4.9%). The fastest onset of action (<30 minutes) was most frequently reported with mefenamic acid (75%), while the longest duration of effect (>8 hours) was mainly observed with ibuprofen and mefenamic acid (25% each). However, no statistically significant differences were found in onset of action ($p = 0.472$) or duration of effect ($p = 0.060$) among the three drugs. These findings indicate that the three analgesics demonstrate comparable effectiveness in relieving primary headache among medical students. The observed differences appear to represent clinical tendencies rather than statistically significant variations.

Keywords: ibuprofen, medical student, mefenamic acid, paracetamol, primary headache

ABSTRAK

Nyeri kepala primer merupakan keluhan neurologis yang umum dialami mahasiswa kedokteran akibat stres akademik, kurang tidur, dan gaya hidup yang kurang sehat. Analgesik bebas seperti asam mefenamat, parasetamol, dan ibuprofen sering digunakan untuk swamedikasi, namun perbandingan efektivitas ketiganya pada populasi mahasiswa masih terbatas. Penelitian ini bertujuan membandingkan efektivitas ketiga obat tersebut dalam penanganan nyeri kepala primer. Penelitian ini menggunakan desain analitik potong lintang pada 73 mahasiswa Fakultas Kedokteran Universitas Jenderal Achmad Yani angkatan 2024. Data dikumpulkan menggunakan kuesioner terkait jenis analgesik, onset kerja, dan durasi efek obat, kemudian dianalisis dengan uji Kruskal–Wallis. Sebagian besar responden mengalami migrain probable (61,7%). Parasetamol merupakan obat yang paling banyak digunakan (75,3%), diikuti ibuprofen (9,9%) dan asam mefenamat (4,9%). Onset kerja tercepat (<30 menit) paling sering dilaporkan pada asam mefenamat (75%), sedangkan durasi efek terlama (>8 jam) terutama ditemukan pada ibuprofen dan asam mefenamat (masing-masing 25%). Namun, tidak terdapat perbedaan signifikan pada onset kerja ($p = 0,472$) maupun durasi efek ($p = 0,060$). Hasil ini menunjukkan bahwa secara statistik ketiga analgesik memiliki efektivitas yang sebanding dalam meredakan nyeri kepala primer pada mahasiswa kedokteran.

Kata kunci: asam mefenamat, ibuprofen, mahasiswa kedokteran, nyeri kepala primer, paracetamol

INTRODUCTION

Primary headaches are among the most prevalent neurological disorders worldwide and are a major contributor to reduced productivity and impaired daily functioning.^{1,2} The World Health Organization (WHO) estimates that more than half of the global adult population experiences at least one episode of headache annually.¹ In Indonesia, headache ranks among the top ten most frequent complaints encountered in primary healthcare and constitutes a substantial proportion of visits to neurology clinics.²

Medical students are considered a population at higher risk for primary headaches due to the demanding academic environment, psychological stress, irregular sleep patterns, and lifestyle factors such as

excessive caffeine consumption.³⁻⁵

Previous studies have reported that the prevalence of primary headaches among medical students can exceed 50%, with symptoms often interfering with learning processes, concentration, and overall academic performance.^{3,4} These circumstances frequently lead students to self-medicate using over-the-counter analgesics as an immediate strategy to relieve symptoms.⁶⁻⁸

Among the analgesics commonly used for headache management, mefenamic acid, paracetamol, and ibuprofen remain widely accessible and frequently selected for self-treatment.^{6,7,9,10} These medications produce analgesic effects primarily through the inhibition of cyclooxygenase (COX) enzymes, thereby reducing prostaglandin

synthesis involved in pain pathways.^{11–13} Despite their shared mechanism of action, the three drugs differ in their pharmacokinetic behavior and effect profiles.^{11,14–16} Mefenamic acid and ibuprofen, both classified as nonsteroidal anti-inflammatory drugs (NSAIDs), provide anti-inflammatory benefits but carry a risk of gastrointestinal irritation.^{9,11,13,16,17} In contrast, paracetamol is generally associated with a more favorable safety profile, particularly for the gastrointestinal tract, and is often preferred for its tolerability.^{12,18} Several studies have compared these three analgesics across various pain conditions, but the findings have been inconsistent.^{10,18–20} Some studies report that ibuprofen has a longer duration of action, whereas paracetamol demonstrates a faster onset and better tolerability.^{15,18–20} However, evidence regarding the effectiveness of these analgesics specifically for primary headaches particularly among medical students in Indonesia remains very limited.^{3,4}

METHODS

This study employed a descriptive-analytic cross-sectional design conducted at the Faculty of Medicine, Universitas Jenderal Achmad Yani, from September 30 to October 3, 2025.

The study population consisted of medical students from the 2024 cohort. The inclusion criteria were students who experienced probable primary headache within the last 5–7 days based on the Headache Screening Questionnaire (HSQ). The HSQ was used to identify probable primary headache and does not replace clinical diagnosis by a physician. Participants must have used only one type of analgesic (mefenamic acid, paracetamol, or ibuprofen) during their most recent headache episode and provided informed consent. No age restriction was applied, as all respondents belonged to the same academic cohort.

The exclusion criteria included students diagnosed with secondary headache or those with medical conditions that may indicate secondary causes of headache. Respondents who used combination analgesic therapy during a single headache episode were excluded to ensure clear group classification. Students with a history of chronic neurological disorders were also excluded. Incomplete questionnaire responses were excluded from the final analysis.

The sample size was calculated using Slovin's formula with a 10% margin of error, resulting in a minimum required sample of 72 participants. Consecutive sampling was applied, and data collection

was closed once the required sample size had been achieved.

Data were collected using a validated and reliable structured questionnaire (Headache Screening Questionnaire/HSQ) administered online via Google Forms. The survey link was distributed through the official WhatsApp group of the 2024 medical student cohort. The questionnaire was self-administered and completed anonymously.

Electronic informed consent was provided at the beginning of the questionnaire. Participants were required to indicate agreement before proceeding. The consent form explained the study objectives, voluntary participation, confidentiality, and the right to withdraw at any time without consequences. No personal identifying information was collected. Participants received a small token of appreciation after completing the questionnaire.

Analgesic use was identified through predefined multiple-choice options (mefenamic acid, paracetamol, ibuprofen). Respondents selecting other medications were excluded from the analysis. Analgesic use was self-reported and limited to the most recent headache episode. The study focused on commonly used standard single doses (mefenamic acid 500 mg, ibuprofen 400 mg, and paracetamol 500 mg). Dosage

and frequency were not independently verified.

Onset of action was measured using predefined categories (<30 minutes, 30–60 minutes, and >60 minutes) and was operationally defined as the time interval between analgesic intake and the initial reduction or disappearance of headache symptoms. Duration of analgesic effect was measured using predefined categories (<4 hours, 4–8 hours, and >8 hours) and was defined as the time interval between analgesic intake and recurrence of headache symptoms. Both measurements were based on respondent self-perception.

To minimize recall bias, respondents were instructed to report data based only on their most recent headache episode within the previous 5–7 days. The short recall period was selected to improve the accuracy of self-reported information.

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Jenderal Achmad Yani (Ethical Approval No. 048/UM1.09/2025) on September 24, 2025.

RESULTS AND DISCUSSION

The study was conducted at the Faculty of Medicine, Universitas Jenderal Achmad Yani, from September 30 to October 3, 2025. Of the 81 medical students from the 2024 cohort who initially participated, 8 met the exclusion criteria, resulting in a

final sample of 73 respondents included in the analysis.

Data were collected online using the Headache Screening Questionnaire (HSQ) along with an additional structured questionnaire regarding analgesic use for primary headache. The collected data were processed and analyzed to determine the distribution of respondent characteristics, types of primary headache experienced, distribution of analgesic use, onset of action, and duration of analgesic effect. The findings are presented systematically according to the study objectives and are

followed by an in-depth discussion integrating relevant literature to interpret the observed patterns.

Participant Characteristics

Sex and Academic Semester

This study involved 73 third-semester medical students from the Faculty of Medicine, Universitas Jenderal Achmad Yani. The majority of respondents were female (71.2%), while 28.8% were male. These demographic characteristics provide an overview of the study population included in the analysis.

the most commonly experienced type of primary headache was probable migraine (61.7%), followed by probable tension-type headache (35.8%), and mixed headache (2.5%). These findings indicate that pulsating-type headaches (migraine) were more predominant than tension-type headaches (TTH).^{4,10,21}

Table 1 Research subjects by gender

Characteristics	N	%
Male	21	28,8%
Female	52	71,2%

Proportion of Primary Headache Types Among Medical Students

Based on the classification of the Headache Screening Questionnaire (HSQ),

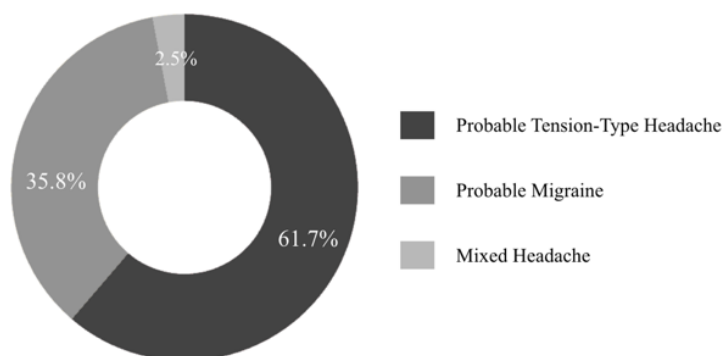


Figure 1 Proportion of primary headache types among medical student.

These findings indicate that migraine is the most common type of primary headache among young adults, particularly medical students.^{4,21} Contributing factors include academic stress, irregular sleep patterns, fatigue, and excessive caffeine intake.³⁻⁵ Most respondents experienced probable migraine, characterized by moderate to severe pulsating pain often accompanied by nausea, photophobia, or phonophobia.²¹ Meanwhile, probable tension-type headache (TTH) is marked by bilateral, pressure-like pain described as a tight band around the head, commonly associated with muscle tension resulting from poor study posture or chronic stress.^{5,21} The relatively high proportion of TTH (35.8%) in this study also supports existing evidence that

TTH is the most prevalent type of headache in the general population, with incidence rates reaching 40–60% (WHO, 2020).²¹

The presence of a small number of mixed headache cases indicates that some individuals experience overlapping symptoms of migraine and tension-type headache. In contrast, the unclassified headache category may reflect symptom variations that do not fully meet the HSQ diagnostic criteria.^{1,21}

Distribution of Analgesic Use

Figure 2 illustrates the distribution of analgesic use among respondents. A total of 4 respondents (4.9%) used mefenamic acid, 61 respondents (75.3%) used paracetamol, and eight respondents (9.9%) used ibuprofen.

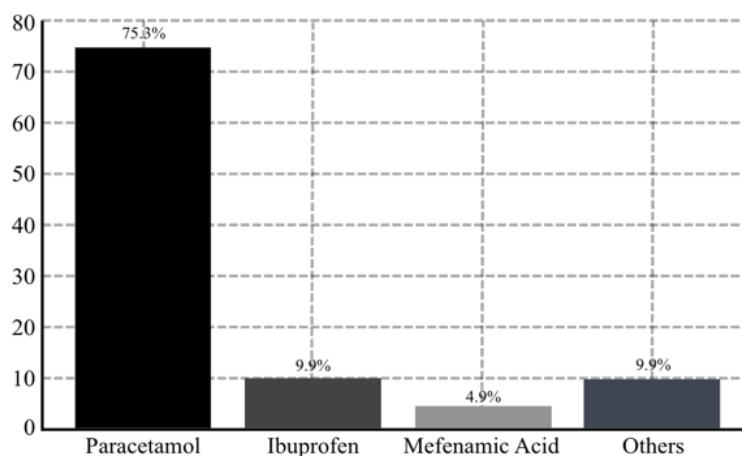


Figure 2 Distribution of analgesic use

The majority of respondents used paracetamol (75.3%), followed by ibuprofen (9.9%) and mefenamic acid (4.9%). These results indicate a tendency to

choose medications with better safety profiles and availability. Additionally, 9.9% of respondents reported not using any of

these three analgesics or using other medications outside this group.

Comparison of Analgesic Effectiveness on Onset and Duration of Primary Headache

As shown in Tables 2 and 3, no statistically significant differences were observed ($p = 0.472$ and $p = 0.060$,

respectively). These results suggest that mefenamic acid, paracetamol, and ibuprofen have comparable effectiveness in managing primary headaches among medical students. No significant differences were found in either the onset of action or the duration of analgesic effect among the three medications

Table 2 Comparison of analgesic effectiveness on the onset of primary headache

Onset of Action	Mefenamic Acid	Paracetamol	Ibuprofen	Total
< 30 minutes	3 (75,0%)	27 (44,3%)	4 (50,0%)	34 (46,6%)
30–60 minutes	1 (25,0%)	31 (50,8%)	2 (25,0%)	34 (46,6%)
> 60 minutes	0 (0,0%)	3 (4,9%)	2 (25,0%)	5 (6,8%)
p-value				0,472

No statistically significant difference in onset of action was observed among the three analgesics ($p = 0.472$).

Table 3 Comparison of analgesic effectiveness on the duration of primary headache

Duration of Effect	Mefenamic Acid	Paracetamol	Ibuprofen	Total
< 4 hours	2 (50,0%)	37 (60,7%)	2 (25,0%)	41 (56,2%)
4–8 hours	1 (25,0%)	23 (37,7%)	4 (50,0%)	28 (38,3%)
> 8 hours	1 (25,0%)	1 (1,6%)	2 (25,0%)	4 (5,5%)
p-value				0,060

No statistically significant differences were observed in the duration of analgesic effect among the three medications ($p = 0.060$).

The analysis of onset of action showed that 46.6% of respondents experienced analgesic effects within less than 30 minutes, 46.6% within 30–60 minutes, and only 6.8% after more than 60 minutes. Users of mefenamic acid had the highest proportion of rapid onset (<30 minutes; 75%), followed by ibuprofen (50%) and paracetamol (44.3%). Although the number

of mefenamic acid users was relatively small ($n = 4$), three of them reported a rapid onset, suggesting a descriptive trend that mefenamic acid may provide a faster initial analgesic response than other medications.^{11,17,22} Most paracetamol users reported an onset of 30–60 minutes, which corresponds with its pharmacokinetic characteristics, indicating rapid

gastrointestinal absorption and peak plasma concentrations occurring within 30–60 minutes.^{12,23} In contrast, ibuprofen users showed greater variability in analgesic response, which may be influenced by genetic differences affecting drug metabolism and cyclooxygenase (COX) enzyme activity, contributing to interindividual variability in NSAID responsiveness.^{24–26} The duration of analgesic effect also showed distinct patterns. More than half of respondents (56.2%) reported durations of less than 4 hours, followed by 38.3% with durations of 4–8 hours, and 5.5% with durations exceeding 8 hours. Ibuprofen users had the highest proportion of durations longer than 8 hours (25%), compared with mefenamic acid (25%) and paracetamol (1.6%). This finding is consistent with ibuprofen's pharmacokinetic profile, including its relatively long elimination half-life (1.8–2 hours), as well as its mechanism as a non-selective NSAID that inhibits both COX-1 and COX-2, thereby providing supplementary anti-inflammatory effects that may prolong analgesic duration..^{15,16,24,27} Paracetamol, on the other hand, primarily acts through central COX inhibition and undergoes rapid hepatic metabolism, resulting in a shorter duration of action. This aligns with the finding that 60.7% of paracetamol users reported analgesic duration of less than 4 hours.^{12,18}

Mefenamic acid exhibited a shorter duration than ibuprofen, consistent with its relatively short half-life (2 hours) and more limited anti-inflammatory activity.^{11,17,22}

The Kruskal–Wallis test indicated no statistically significant differences in onset ($p = 0.472$) or duration of action ($p = 0.060$) among the three analgesics. Statistically, this suggests that the overall analgesic effectiveness, based on both onset and duration, was comparable among mefenamic acid, paracetamol, and ibuprofen. The lack of a significant difference may be explained by the small sample sizes in the mefenamic acid and ibuprofen groups, which reduced statistical power. Nevertheless, descriptive trends suggest that ibuprofen provides the longest duration of action, whereas mefenamic acid has the fastest onset. These patterns are consistent with pharmacological theory and the existing literature, which describes NSAIDs as having longer analgesic durations than paracetamol, with onset of action influenced by absorption rates and COX inhibition profiles.^{15,16,27} Reported side effects were relatively low (<10%) and mostly mild, consistent with established evidence showing that paracetamol has a favorable gastrointestinal safety profile. In contrast, NSAIDs such as ibuprofen and mefenamic acid carry a higher risk of gastrointestinal irritation.^{9,10,16} Overall, these findings support rational self-

medication practices among medical students, who generally choose analgesics based on availability, rapid onset, and short-term safety.^{6,8} However, the cross-sectional design and reliance on self-reported perceptions limit the ability to capture true pharmacodynamic effects fully. Therefore, future experimental studies with controlled dosing and objective measures such as the Visual Analogue Scale (VAS) are recommended to strengthen the evidence regarding the comparative effectiveness of these analgesics.²⁸

CONCLUSION

This study demonstrates that mefenamic acid, paracetamol, and ibuprofen show comparable effectiveness in managing primary headaches among medical students. Statistical analysis revealed no significant differences in either the onset of action ($p = 0.472$) or the duration of analgesic effect ($p = 0.060$) among the three analgesics. Descriptive trends indicated that ibuprofen tended to provide a longer duration of action, whereas mefenamic acid exhibited the fastest onset. Paracetamol remained the most frequently used analgesic, likely due to its wide availability and favorable safety profile. Although adverse effects were reported infrequently and were generally mild, responsible use of over-the-counter analgesics remains important. Given the

limitations of the cross-sectional design and reliance on self-reported perceptions, future controlled experimental studies employing standardized pain assessment tools are recommended to compare the pharmacodynamic profiles of these non-opioid analgesics more accurately. Additionally, strengthening education on the rational use of non-prescription analgesics among medical students is essential to promote safe and effective self-medication practices.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the conduct of this study.

ACKNOWLEDGMENT

The authors would like to express their deepest gratitude to all medical students of the Faculty of Medicine, Universitas Jenderal Achmad Yani, Class of 2024, who participated as respondents, as well as to the Faculty of Medicine, Universitas Jenderal Achmad Yani, for providing the necessary facilities and support during the implementation of this study. Finally, the authors wish to acknowledge the assistance of all parties who contributed, directly or indirectly, to the successful completion of this research.

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