Clinical Efficacy and Side Effects of Nabumeton Compared to Meloxicam in Osteoarthritis Pain

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ABSTRACT

Background: *Most patients who use non steroid anti-inflammatory drug (NSAID) in long-term or high-dose will experience NSAID gastropathy that appears as dyspepsia complaints. The aim of this study is to assess the efficacy of nabumeton and incidence of dyspepsia as side effect of treatment using nabumeton compared to meloxicam in patients with pain due to osteoarthritis.*

Methods: *Sixty patients with pain due to osteoarthritis at internal medicine clinic in Koja Hospital were included in this study and were given meloxicam or nabumeton within February 29th to March 25th 2013 period in double-blind manner. Primary disease pain degree and heartburn pain degree were evaluated three days after administration of the drug and a week was added if necessary. The statistical analysis used were student t-test to compare changes in pain scores between the 2 groups, and Chi-square test to assess differences in the number of dyspepsia in both groups.*

Results: *Pain scale reduction in meloxicam group was 0.57 ± 0.67 points, which is less than 1.27 ± 0.74 points in nabumeton group. In addition, the average recurrence of heartburn in the meloxicam was 18 out of 30 (60%) patients in total, while the average recurrence of heartburn in nabumeton was 2 out of 30 (60%) patients.*

Conclusion: *The use of nabumeton pain medication is better in terms of efficacy and side effects of heartburn compared to meloxicam.*

Keywords: *osteoarthritis, joint pain, meloxicam, nabumeton*

ABSTRAK

Latar belakang: *Sebagian besar pasien yang menggunakan obat anti inflamasi non-steroid (OAINS) jangka panjang atau dosis tinggi akan mengalami gastropati OAINS yang muncul sebagai keluhan dispepsia. Tujuan penelitian ini adalah untuk menilai efikasi terapi nabumeton dan timbulnya efek samping dispepsia pada pemberian nabumeton dibandingkan dengan meloksikam pada pasien dengan nyeri akibat osteoartritis.*

Metode: *Enam puluh pasien dengan nyeri akibat osteoarthritis pada klinik penyakit dalam Rumah Sakit Koja didata dan masing–masing diberikan meloksikam atau nabumeton pada Febuari 2013 hingga Maret 2013 secara acak, tersamar ganda. Skor nyeri sendi dan nyeri ulu hati dinilai pada hari ketiga dan kesepuluh. Analisa statistik yang digunakan ialah student t-test dan Chi-square test*

Hasil: *Penurunan skala nyeri pada kelompok meloksikam sebesar 0.57 ± 0.67 yang lebih sedikit dibandingkan dengan kelompok nabumeton 1.27 ± 0.74. Selain itu, rata-rata timbulnya nyeri ulu hati pada kelompok meloksikam sebanyak 18 (60%) dari 20 pasien, sedangkan pada kelompok nabumeton hanya 2 (6%) dari 30 pasien.*

Simpulan: *Nabumeton lebih efektif menghilangkan nyeri dibandingkan meloksikam, dan efek samping nyeri ulu hati nabumeton lebih sedikit dibandingkan dengan meloksikam.*

Kata kunci: *osteoartritis, nyeri sendi, meloksikam, nabumeton*

INTRODUCTION

Non steroid anti-inflammatory drug (NSAID) is a commonly used clinical drug.[1,2] Literature data indicate that as many as 85% of people aged over 65 years showed osteoarthritis (OA) on radiological examination. Autopsy studies show almost every person over the age of 45 years showed signs of osteoarthritis in joints that bear the body weight function.[3] Prevalence of radiological OA of the knee in Indonesia reached 15.5% in male and 12.7% in female. The main treatment of osteoarthritis is to provide anti-pain medication from the class of NSAIDs. Most patients who use NSAIDs in long-term or high-dose will experience side effects of NSAID gastropathy which emerge as dyspepsia complaints. Although osteoarthritis is not a fatal disease, but the side effects of NSAIDs can cause gastrointestinal bleeding resulting fatal conditions.[4,5] NSAIDs cause gastropathy through 2 ways: topically and systemically. Prostaglandin (PG) produced by COX-2 pathways causes inflammation, pain and fever, so it is expected that selectively COX-2 inhibitor NSAID is relatively safer than conventional NSAIDs.[6]

In addition to the use of NSAIDs that selectively inhibit COX-2, there was another attempt to avoid NSAID gastropathy, which is by using a non-acid NSAIDS like nabumeton.[7,8] Both of these drugs, nabumeton and meloxicam are widely used to overcome joint pain, as well as in Internal Medicine Department, Koja Hospital. However, the study to assess the efficacy of both in dealing with pain has not been done, and dyspepsia adverse effects arising from the use of nabumeton or meloxicam. Therefore, this research aims to compare the clinical efficacy and side effects of nabumeton and meloxicam in management of pain in osteoarthritis patient population, both in outpatients and hospitalization setting in Internal Medicine Department, Koja Hospital.

METHOD

This study used double-blind design, with study population of all patients with osteoarthritis or joint disorders at Internal Medicine Clinic in Koja Hospital. Samples were taken using a consecutive sampling method. Inclusion criteria were patients with symptoms of OA and joint pain. Exclusion criteria were other diseases presented with pain, not due to OA or have no complaints of stomach pain before. Patients who do not comply or are taking other drugs than those prescribed or not taking medications as suggested will be dropped out.

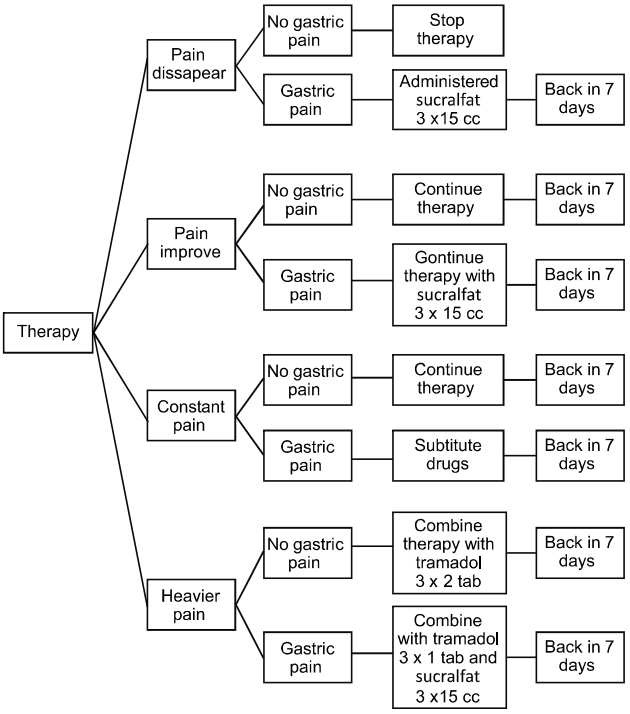

Figure 1. Workflow study describing patients treatment

Randomly 30 patients will be clustered in group A, while 30 other patients will be grouped in group B. One group was given meloxicam 15 mg once daily for 3 days and the other group was given nabumeton 500 mg twice daily for 3 days. Both meloxicam and nabumeton were given in their original factory preparation. Subjects and investigators were masked to medication received from each group; drugs code were revealed at the end of the study. Both groups would be assessed (post-test) on day 3. If pain was not reduced, then second post-test on day 10 was performed. Quality of the joint pain presence and dyspepsia complaints were assessed. If there were no more complaints of dyspepsia and joint pain, therapy was stopped. When complaint of joint pain was reduced and no complaint of heartburn was present, therapy was continued and data collecting (post-test) was performed at day 10. If joint pain was reduced and no dyspeptic complaints was present, therapy was followed by administration of additional sucralfate 15 cc thrice times, and data collection (post-test) was performed at day 10. If there were no pain changes and no heartburn was present, therapy was continued. If there was no change in pain, but gastric pain was present, drugs were replaced by other drug from other groups. If the pain worsened or persisted after the drug was prolonged and no gastric pain was present, tramadol was given with 1 tablet thrice a day. When therapy was extended for a week, the pain scale was reviewed in the next week. The workflow can be seen in Figure 1.

Pain assessment was performed by the subjects, by answering questions given about the pain scale. Pain scale assesment used five-point verbal rating scale (VRS) as described in Table 1.[9]

Table 1. Pain assessment score

Pain Scale	Score
No pain	1
Mild pain	2
Moderate pain	3
Severe pain	4
Worst possible pain	5

RESULT

Research has been conducted to 60 patients with joint pain caused by osteoarthritis, in the period of February 2013 to March 2013. Of 9 (15%) subject were female. After a block randomization, 30 subjects were assigned to group A (nabumeton) and the other 30 subjects to group B (meloxicam). Mean age of these subjects was 55 years, with 5 (8.3%) subjects aged less than 40 years, 36 (60%) subjects aged between 40-60 years and 19 (31%) subjects aged over 60 years. A total of 24 (40%) subjects had a body mass index (BMI) classified as normal, 24 (40%) subjects overweight (25-30 kg/m^2), 3 (5%) subjects underweight (< 18.5 kg/m^2), and 9 (15%) subjects obese (> 30 kg/m^2). Average pain scale pre-test group meloxicam 3.33 (SD = 0.84) and in group nabumeton 3.23 (SD = 0.82), while from the first post-test (day 3) average scale pain obtained in meloxicam group was 2.76 (SD = 0.97) and in group nabumeton was 1.96 (SD = 1.03). Thus a decrease in the pain scale meloxicam group was 0.57 (SD = 0.69), which were less than the nabumeton 1.27 (SD = 0.69). Heartburn side effects in meloxicam group were present in 18 out of 30 (60%) patients. Gastric pain side effects on nabumeton group were amounted in 2 out of 30 (6.67%) patients. The data of subject characteristics is presented in Table 2.

A total of 16 (26.6%) subjects stated that joint pain disappeared as observation was completed. Twenty three (38.3%) subjects stated joint pain was reduced on day 3. While the remaining 21 (35%) subjects stated constant or increased joint pain; thus, therapy was continued and was observed in the second post-test. In the second post test, it was stated that two subjects experiened disappeared joint pain and 19 of them improved. Monitoring results of pain relief and side effects dyspepsia appearance shown in Figure 2.

On day 3 monitoring, from 60 subjects studied, 66.7% had no dyspeptic complaints. The remaining 33.3% complained of heartburn, 2 subjects (3.3% of the sample population) belong to nabumeton group and 18 subjects (30% of the sample population) belong to meloxicam group.

In the first phase of post test decrease pain scores was obtained from both groups. In group A pain

Table 2. Subject characteristic

Variable	Total	Group	
	Subject (% or SD)	A (% or SD)	B (% or SD)
Subject (n)	60 (100%)	30 (50%)	30 (50%)
Sex			
Male	9 (15%)	5 (16%)	4 (13%)
Female	51 (85%)	25 (83.3%)	26 (86%)
Mean of age	55 ± 11.62	55.5 ± 10.95	55.2 ± 12.43
Age group (years old)			
< 40	5 (8.3%)	1(3.3%)	3 (10%)
40-60	36 (60%)	19 (63.3%)	18 (60%)
> 60	19 (31%)	10 (33.3%)	9 (30%)
BMI (kg/m^2)			
Underweight (<18.5)	3 (5%)	2 (6%)	1 (3)
Normal (18.5-24.9)	24 (40%)	13 (43)	11 (36.7)
Overweight (25-29.9)	24 (40%)	13 (43)	11 (36.7)
Obese (>30)	9 (15%)	2 (6)	7 (23.3)
Pain scale mean			
Pre-test	3.28 ± 0.82	3.23 ± 0.82	3.33 ± 0.84
Post-test	2.36 ± 1.07	1.96 ± 1.03	2.76 ± 0.97
Reduction	0.92 ± 0.79	1.27 ± 0.74	0.57 ± 0.67
Gastric pain incident rate	20 (33.3%)	2 (6.7%)	18 (60%)

BMI: body mass index

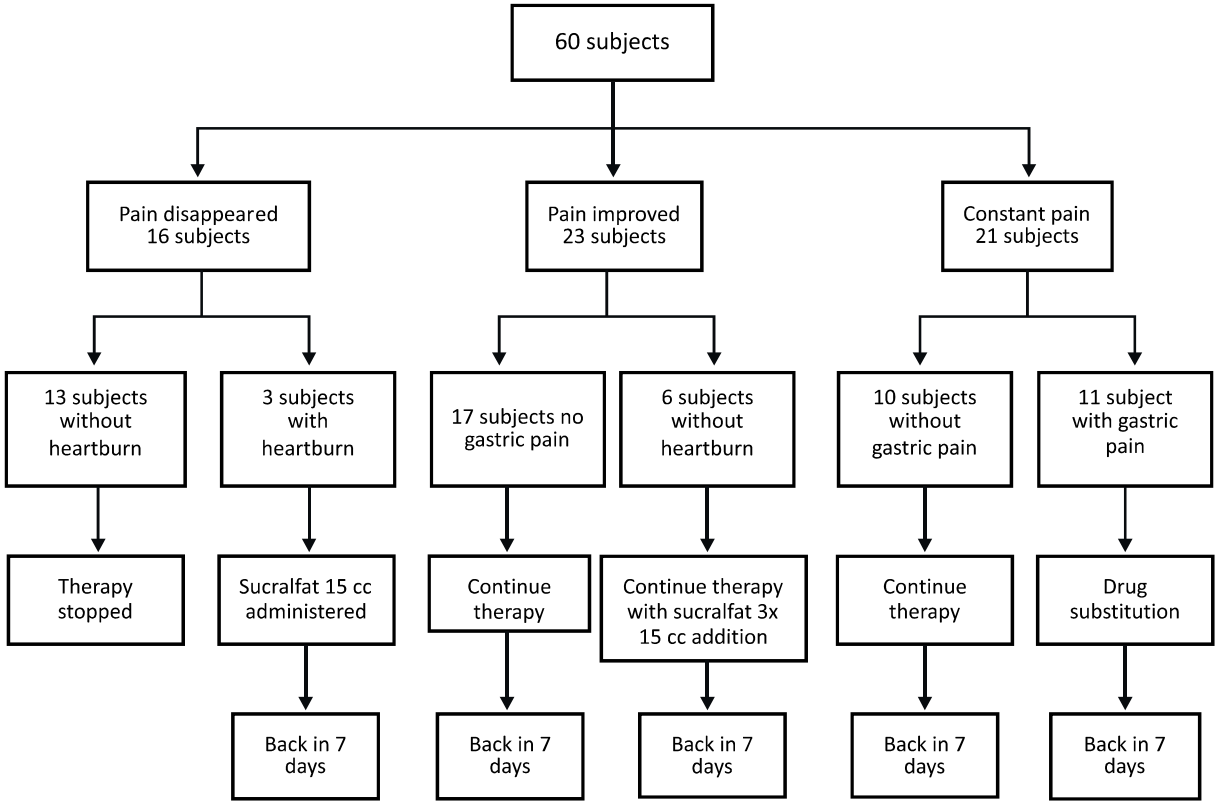

Figure 2. Monitoring results of pain relief and the emergence of dyspepsia side effects

score decreased from 3.23 ± 0.82 to 1.96 ± 1.03, with difference of 1.27 ± 0.74, whereas in group B pain score decreased from 3.33 ± 0.84 to 2.76 ± 0.97, with difference of 0.67 ± 0.57. Decrease in pain score was greater than meloxicam group. Student t-test confirmed that the pain score reduction was significantly different, with $p < 0.000$ (Figure 3).

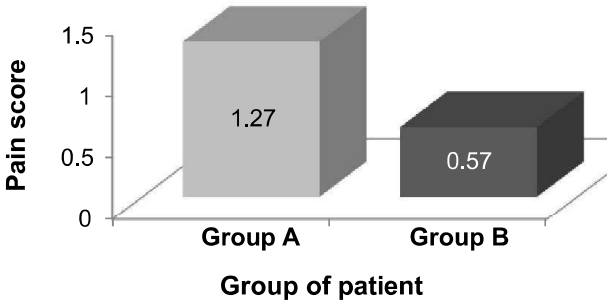

Figure 3. The average pain score reduction was greater in group A compared to group B, with p < 0.00

Dyspepsia occurred in both groups, with a number of different events. At nabumeton group, it was obtained that 2 (6.7%) subjects complained of dyspepsia, while on meloxicam group 18 (60%) subjects had the same complaint. By using the Chi-square test, statistically significant differences was found, with $p < 0.000$ (Figure 4).

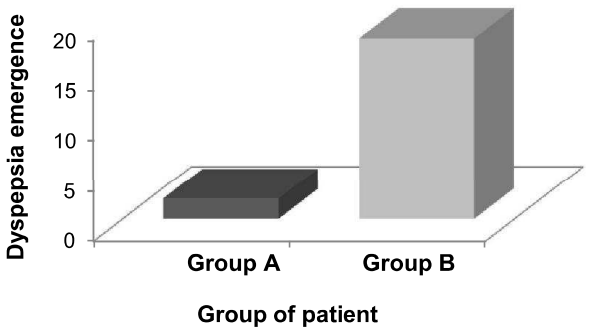

Figure 4. Average dyspepsia emergence rate in group A than in group B, with p < 0.00

DISCUSSION

Although the literature stated that the prevalence of radiological knee OA in Indonesia reached 15.5% in male and 12.7% in female,[2] our study showed more female patients came for treatment with symptoms of OA and joint disorders. This might be caused by the fact that female have the time to come to the Internal Medicine Clinic in Koja Hospital which operates at work hour, while the male still have to work on work hour.

Dominant age group was between 40 - 60 years by 36 (60%) subjects, followed by the age group > 60 years by 19 (31%) subjects, and age groups < 40 years by 5 (8.3%) subjects. This shows that the incidence

of OA and other joint disorders is more in old age (> 40 years) than in younger age (< 40 years). As stated by Loeser, age is a major risk factor of OA, possibly due to aging in cells and tissues that make the joints more susceptible to damage and less able to sustain homeostasis.[9]

Subjects with a BMI of overweight and obese have a large portion of our total subjects. This pointed that excess of weight has greater tendency to experience joint disorders. These findings affirm Tukker et al report, that overweight is associated with osteoarthritis, especially in the hip and knee.[10]

Average pain score reduction was more superior in nabumeton group, with the score of 1.27 compared with 0.57 in meloxicam group. Meloxicam result on statistical tests for group differences in pain scores reduction 1.27 ± 0.74 in nabumeton group and 0.57 ± 0.9 in meloxicam group with p less than 0.000. This difference was statistically significant.

Waranugraha et al reported that types of NSAIDs do not provide the gastropathy differences in clinical symptoms, as well as the usage manner, either periodic or continous.[11]

However, from the results of our study on the prevalence of heartburn nabumeton by 2 subjects, i.e. 6.67% in the whole group nabumeton and 3.3% compared to the entire population, while the meloxicam total of 18 subjects, i.e. 60% in the whole group or 30% of all population. Statistical test result for differences in incidence rates of dyspepsia: nabumeton group 2 subjects, meloxicam groups 18 subjects, with p less than 0.000. This difference was statistically significant.

CONCLUSION

The use of Nabumeton is more advisable than the use of conventional NSAIDs meloxicam in terms of efficacy and prevention of side effects such as gastric pain. Further study is required to assess the efficacy and side effects of this drug with a better study design, larger sample size, and longer treatment duration.

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