Comparison of Endoscopic Gastric Mucosa Features After Administration of Piroxicam to Meloxicam and Their Correlation with Dyspepsia Symptoms in Elderly Patient with Knee Osteoarthritis


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ABSTRACT

Aim: to know the effect of piroxicam (COX-1 and COX-2 inhibitor NSAID) and meloxicam (selective COX-2 inhibitor NSAID) against the gastric mucosa.

Methods: a random, double-blind-parallel study and repeat measurement against 20 elderly-patients with knee-OA was conducted. Patients were divided into 2 equal groups, every group got piroxicam 20 mg/day or meloxicam 15 mg/day for 3 weeks. On the second group, sukralfat 2 x 1 g/day were given. To examine the difference before and after treatment, we used Wilcoxon signed rank test, to examine the difference within those groups we used Mann-whitney U test, to examine the correlation between endoscopic score and dyspepsia, we used the Spearman correlation test with significant correlation interpretation by Guilford rules.

Results: one of piroxicam group was resigned, so that there was 19 person left to complete this study. Piroxicam has caused elevation of endoscopic score in 78% subject compared to the beginning of study, and 22% of the subject has developed ulcers. Alteration of endoscopic feature after administration of this piroxicam was statistically significant (p < 0.05). Mild dyspepsia symptoms after piroxicam administration were positive on 67% subjects (p < 0.05).

After administration of meloxicam, 40% subjects have elevated endoscopic score compared to beginning of the study (p < 0.05). Mild dyspepsia symptoms after meloxicam administration were positive on 40% subjects (p > 0.05). Meloxicam has less elevation of endoscopic score compared to the piroxicam (p < 0.05). By statistics, both of groups showed no difference in dyspepsia symptoms (p > 0.05). There was no significant correlation between elevation of endoscopic score and dyspepsia on both of groups. Nevertheless, it tends to have weak positive correlation (piroxicam group r = 0.306; p > 0.05, meloxicam group r = 0.330; p > 0.05).

Conclusion: on this study, we conclude that the administration of either piroxicam or meloxicam in elderly-patient with knee-OA has caused the gastric mucosa impairment. The impairment after meloxicam administration is milder than piroxicam. There is no significant difference of dyspepsia symptoms in both of groups. There is no correlation between endoscopic gastric mucosa features with the dyspepsia symptoms.

Key words: piroxicam, meloxicam, endoscopic score, dyspepsia

INTRODUCTION

The growing life expectancy has caused larger amount of elderly citizen. Osteoarthritis is chronic disease that often predominantly found in elderly. In general, Osteoarthritis patients usually have tried to overcome their disease themselves and have tried various manner to reduce or to eliminate their pain symptoms such as by o.t.c. drugs that have been promoted to reduce the pain. Since 1970, non-steroid anti inflammatory drugs has been widely used over the world. In outpatient rheumatology clinic of Hasan Sadikin Hospital, Bandung, in the period of July 1999 to June 2000, Osteoarthritis had the first rank (68.61%) and most of them were about knee (86.75%). The drug that most widely used to overcome pain in Osteoarthritis is NSAID. Besides of its analgesic and anti-inflammatory effect, NSAID also has side effect on gastrointestinal system. The therapeutic and side effects are caused by inhibition on cyclooxygenase (COX) enzyme, which play role to convert the arachidonate acid into prostaglandin.
There are 2 COX iso-enzyme, i.e. the constitutive COX-1, which has role in physiological function and the inducible COX-2, which has role in inflammation reaction. In pharmacology, NSAID has developed from unselective drugs to selective drugs against COX-2. The old generation of NSAID (indomethacin, piroxicam, ibuprofen, aspirin, etc) inhibit both COX-2 and COX-1, so that in therapeutic dose it may cause side effect, predominantly on gastrointestinal tract.

The new NSAID selectively inhibit COX-2, thus theoretically it has less side effect on gastrointestinal tract. Considering the low gastrointestinal side effect on the patient who had COX-2 selective inhibitor NSAID, then this study was conducted, by comparing how much the alteration of gastric mucosa with the usage of COX-2 selective inhibitor NSAID compared to the NSAID that inhibits COX-1 and COX-2.

In this study, by ethical consideration in order to reduce the side effect of NSAID on the stomach, we used sucralfat 2 x 1 g/day.

METHODS

This study is a double blind clinical trial, with parallel design enclosed by repeated measurement. The study was conducted at Dr. Hasan Sadikin Hospital, Bandung, since March 2002 – August 2002.

The subject was part of the study of “The Effect of Meloxicam and Piroxicam Against Renal Hemodynamic on elderly patient with knee osteoarthritis”. Through the random permuted blocks, patients were allocated to have meloxicam 1 x 15 mg/day or piroxicam 1 x 20 mg/day for 3 weeks period.

The inclusion criteria for this study were all outpatient subject with symptomatic knee osteoarthritis and had not had any NSAID minimal in the period of three weeks before the study began, signing the informed consent, first endoscopic examination was normal, or if the mucosa was abnormal, then they had maximal defect as followed: hyperemia or erosion with endoscopic score ≤ 3 (in keeping with endoscopic score table by Lanza). The exclusion criteria were: if the patient had any allergy of NSAID, suffered for liver disease, liver cirrhosis, or the value of transaminase enzyme was 2 times of highest normal value, the thrombocyte was <150,000 /mm³), positive history of congestive heart failure. The sample size was determined by non-statistical measures, because of cost consideration, then it was conducted for 20 elderly patient with knee osteoarthritis. The endoscopic diagnosis was established based on the table 1.

<table>
<thead>
<tr>
<th>Endoscopic Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal Mucosa</td>
</tr>
<tr>
<td>1</td>
<td>1-10 Petechiae</td>
</tr>
<tr>
<td>2</td>
<td>&gt; 10 Petechiae</td>
</tr>
<tr>
<td>3</td>
<td>1-5 Erosion</td>
</tr>
<tr>
<td>4</td>
<td>6-10 Erosion</td>
</tr>
<tr>
<td>5</td>
<td>11-25 Erosion</td>
</tr>
<tr>
<td>6</td>
<td>&gt; 25 Erosion</td>
</tr>
<tr>
<td>7</td>
<td>Ulcer</td>
</tr>
</tbody>
</table>

Classification criteria for knee osteoarthritis knee pain plus minimal one of 3 conditions as follow:
- Age > 50 years
- Stiffness < 30 minute
- Crepitation (+)
- Positive osteophyte by radiology

The dyspepsia symptoms categorized by Talley into mild, normal and severe dyspepsia.

To examine the difference before and after treatment by ordinal rate measurement, we used Wilcoxon Signed-rank test, to examine the difference between the group that had piroxicam and had meloxicam, we used Mann-whitney U test. To know relationship between endoscopic score and dyspepsia, we used Spearman correlation test, with significant correlation interpretation by Guilford rules.

RESULTS

By randomized and double blind methods, the subjects were divided into 2 groups i.e. 10 person in A group and 10 person in B group. One of male in A group was resigned.

The Patient’s General Characteristic

The comparison of general characteristic of subjects, i.e. the A and B group could be seen on table 2. Male patients were lesser than the females i.e. 6 males (30%) and 14 females (70%).

We could see that the patient’s general characteristic on both of group has no significant difference.
The Result of Endoscopic Examination and Dyspepsia Before Having Treatment

On table 3 we could see the result of endoscopic examination before having treatment. The difference of endoscopic score within those group before having treatment were not significant ($p > 0.05$).

The dyspepsia score on group A and B were 0 (normal) because if there was any dyspepsia symptom then they could not participate in this study.

Table 3. The Result of Endoscopic Examination Before Having Treatment

<table>
<thead>
<tr>
<th>Score</th>
<th>Group A (n=9)</th>
<th>Group B (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>0</td>
<td>1 (11)</td>
<td>0 (10)</td>
</tr>
<tr>
<td>1</td>
<td>2 (22)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>2</td>
<td>2 (22)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>3</td>
<td>4 (45)</td>
<td>3 (70%)</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>4 (0)</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>5 (0)</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>6 (0)</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>7 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (100)</td>
<td>10 (100)</td>
</tr>
</tbody>
</table>

The Effect of Piroxicam Against Gastric Mucous

Based on this study, piroxicam administration had increased the endoscopic score. In this study, 78% of them had worse gastric mucosa impairment compared to before having treatment. About 22% had developed ulcer on antrum pyloric (Table 4). This alteration was statistically significant ($p < 0.05$). All of the patient on piroxicam group had more severe impairment of gastric mucosa compared to before treatment (Figure 1).

The Effect of Meloxicam Against Gastric Mucosa

On table 4, we could see that after having meloxicam, 40% of them had more severe impairment of gastric mucosa. The alteration of this endoscopic score was statistically significant ($p < 0.05$). The endoscopic score of four patients (40%) were unaltered. (Figure 2)

Comparison of The Altered Endoscopic Score Within The Groups

The alteration of endoscopic score after meloxicam administration was lesser than piroxicam. The comparison of endoscopic score on both groups were significantly different ($p < 0.05$).

The Effect Piroxicam And Meloxicam Effect Against Dyspepsia Symptom

On table 5 we could see that piroxicam had increased the dyspepsia symptoms. About 67% had mild dyspepsia ($p < 0.05$). On the meloxicam group, about 40% had mild dyspepsia, but this alteration was not significant ($p > 0.05$).

The alteration of dyspepsia score on both of groups had no significant difference ($p > 0.05$).
Correlation Between Endoscopic Score and Dyspepsia on Piroxicam Treatment

From figure 3, we could see that there was no significant difference about endoscopic score and dyspepsia ($p > 0.05$). Nevertheless, it tend to have weak positive correlation.

Table 4. The Result of Endoscopic Examination Before and After Having Treatment

<table>
<thead>
<tr>
<th>Score</th>
<th>Piroxicam Before</th>
<th>Piroxicam After</th>
<th>Meloxicam Before</th>
<th>Meloxicam After</th>
</tr>
</thead>
<tbody>
<tr>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
</tr>
<tr>
<td>0</td>
<td>1 (11)</td>
<td>0</td>
<td>1 (10)</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>2 (22)</td>
<td>0</td>
<td>1 (10)</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2 (22)</td>
<td>0</td>
<td>2 (10)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>3</td>
<td>4 (45)</td>
<td>2 (22)</td>
<td>7 (70)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1 (11)</td>
<td>0</td>
<td>4 (40)</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1 (11)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>3 (34)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>2 (22)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>9 (100)</td>
<td>9 (100)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
</tbody>
</table>

Correlation Between The Endoscopic Score and Dyspepsia on Meloxicam Treatment

On figure 4, we could see that the correlation between endoscopic score and dyspepsia after meloxicam administration was not significant ($p > 0.05$). After having meloxicam, eventhough it was not significant, it appeared to have weak positive correlation between the endoscopic score and dyspepsia ($r = 0.330$).

DISCUSSION

The mean age of subjects was over 60 years old. It was the high-risk group of gastric mucosa impairment resulted from NSAID. Before treatment, most of the patient had already had gastric mucosa impairment.

In this study, we could see that either piroxicam or meloxicam had caused the gastric mucosa impairment. The piroxicam administration had cause more severe impairment compared to the meloxicam.

The study of Patoia et al $^{18}$ demonstrated that meloxicam had not caused significant increase of endoscopic score. On this study, the meloxicam administration had increased the endoscopic score significantly compare to endoscopic score before
having treatment. The different result of this study and the Patoia et al study may caused by smaller n amount and difference of subject selection.

By ethical consideration, we gave sucralfate in this study in order to protect the gastric mucosa. But, in reality, the gastric mucosa impairment after piroxicam or meloxicam administration had happened. This indicated that sucralfate as one of cytoprotector drugs was not fully prevent the gastric mucosa impairment by NSAID.

There was mild dyspepsia symptom on most of patient after piroxicam administration. On the meloxicam group, after drug treatment, there was no significant alteration about the dyspepsia symptoms. Comparison of dyspepsia symptoms after drug administration on both of groups had no significant difference.

In this study, even there was no correlation between endoscopic features and dyspepsia but it appeared to have tendencies of weak positive correlation either on piroxicam or meloxicam group. This result was different in Larkai et al 19 and Wallace 20 study, which explained that there was no correlation between endoscopic defect and the dyspepsia symptoms, so we need more clarification through studies with more optimal and larger sample.

CONCLUSION

The administration of 20 mg/day piroxicam or meloxicam 15 mg/day for 3 weeks on the elderly patient with knee osteoarthritis may cause gastric mucosa impairment.

Meloxicam has milder effect of gastric mucosa impairment compared to the piroxicam

There was no difference of dyspepsia symptoms after administration of piroxicam or meloxicam.

There was no correlation between the gastric mucosa impairment by endoscopic with the dyspepsia symptoms after administration of piroxicam or meloxicam.

REFERENCES