Comparative study of refecoxib and ibuprofen on post-surgical pain control: effects of single dose administration before removal of impacted third molar tooth

Wannee Unwerawattana*


Background: Rofecoxib, a specific cyclooxygenase-2 inhibitor, has analgesic efficiency similar to that of nonspecific nonsteroidal anti-inflammatory drugs (NSAIDs). Usually, most patients are worried and afraid of post-surgical dental pain.

Objective: The purpose of this study was to determine the analgesic efficacy of a single oral dose of rofecoxib 50 mg compared with ibuprofen 400 mg on post-surgical dental pain. And another purpose was to reduce post-surgical dental pain.

Research design: Randomized clinical trial

Patients and method: 90 healthy patients were recruited from October 1st, 2003 to May 31st, 2004. They had no systemic disease, no predilection of sex, ages ≥ 18 years. They were categorized into 3 groups (30 patients/each group). Every subject was informed that they would experience moderate or severe pain after the extraction of ≥ 1 molars, at least one of which was an impacted tooth. Subjects were randomized to receive rofecoxib (Vioxx®) 50 mg or ibuprofen (Nurofen®) 400 mg or placebo, for one dose 1 hour before their dental surgery. Also, every subject would receive

*Department of Dentistry, King Chulalongkorn Memorial Hospital
rescue medicine for analgesic effect which was acetaminophen 500 mg (Tylenol® 500 mg) at home. The procedure was performed under local anesthesia and subjects were requested to respond to self-administered questionnaires about the starting time their received study medicine, the level of pain relief based on 5-point scale (0 = none, 1 = a little, 2 = some, 3 = a lot, 4 = overwhelming) every hour within the first 12 hours, and then at hour 16th, 20th, 24th. Together with this, the subjects were asked to record all adverse reactions of the study medicine they experience, their time of pain perception, their degree of satisfaction to the study medicine with the amount of rescue medicine (acetaminophen 500 mg) used in the first 24 hours after the procedure.

Result: SPSS program, Kruskal Wallis test and Chi-square test were used for data analysis. They showed age, sex, the number of impacted tooth, the location of impacted tooth, type of impacted tooth and method employed for tooth extraction. The differences of their means were not of statistical significance. Also, the means of the adverse reactions of the study medicines were not statistically different. However, the amounts of rescue medicine were of statistically significant difference such as mean (95 % CI) of rofecoxib, ibuprofen and placebo were 2.87(1.5-4.24), 5.9(4.86-6.94), 6.8(5.43-8.17), respectively; p < 0.001. The difference of the means of patients’ satisfaction to the study medicines was statistically significant among the 3 groups.

- Kruskal Wallis test and histogram showed a tendency of relieving pain among the 3 groups at $H_0, H_2, H_6, H_{10}, H_{16}, H_{20}$. It is concluded that rofecoxib 50 mg had higher efficiency in relieving pain than ibuprofen 400 mg and placebo on post-surgical dental pain. (p < 0.001).
- Kaplan-Meier test showed the median time of pain perception, 95% CI of rofecoxib; ibuprofen and placebo were 485, (163-807) / 255, (234-276) / 180, (162-198), respectively; \( p < 0.001 \) was taken as significant statistical difference. Linear graphic illustration indicated that rofecoxib 50 mg produces higher efficiency and has longer duration of analgesic effect than ibuprofen 400 mg and placebo. Also, the level of pain-free rate was constant at 600th min (10 hours) is still constant until the 1,440th min (24 hours) and maintains a constant pain-free rate at 0.4

**Conclusion**: The study concluded that rofecoxib 50 mg given as a prophylactic drug for pain taken 1 hour before surgical removal of impacted third molar tooth is more efficient and has longer duration of pain relief than ibuprofen 400 mg. And the difference of the efficiency on pain relief of both drugs is not of statistical significance within the first 6 hours. Ibuprofen 400 mg given every 6 hours is another alternative way for reducing pain but we should concern of GI bleeding and platelet aggregation and bleeding time disorder.

**Keywords**: Pain relief, Specific cyclooxygenase (COX)-2 inhibitor, Non-specific cyclooxygenase (COX) inhibitor.
วารสาร อันวิรัตนาน. การศึกษาป้องกันผลภัณฑ์การใช้ยารักษาปวดประสาทระหว่าง rofecoxib และ ibuprofen รับประทาน 1 ครั้งท่อน้ำดักเพิ่มขึ้นกระจายคุณที่ 3. จุฬาลงกรณ์เวชสาร 2547 ก.ย.; 48(9): 599 – 612

ปัญหา : Rofecoxib ซึ่งเป็นยาต้านอักเสบชนิด specific COX –2 inhibitor มีประสิทธิภาพทางยาต้านอักเสบหลักที่มากกว่ายาต้านอักเสบชนิด non-specific COX inhibitor โดยทั่วไปผู้ป่วยส่วนใหญ่จะกล่าวถึงและวิเคราะห์กิจวัตรสุขภาพ ซึ่งเป็นภาวะที่ปวดด้านพื้นคุณ

วัตถุประสงค์ : เพื่อศึกษาเปรียบเทียบประสิทธิภาพการใช้ยาสูตรประกอบระหว่าง rofecoxib 50 มิลลิกรัมและ ibuprofen 400 มิลลิกรัม โดยให้รับประทาน 1 ครั้งต่อวันในกลุ่มที่มีอาการปวดด้านพื้นคุณ เพื่อแสดงความเข้าใจในศักยภาพของผู้ป่วยที่จะน้ำดักพื้นคุณ

วิธีการจัดการ : การวิจัยทางคลินิกแบบสุ่มตัวอย่าง

ผู้ป่วยและวิธีการศึกษา : ผู้ป่วยจัดจำนวน 90 คนเข้าร่วมในโครงการวิจัยต่อเนื่อง 1 ปีตั้งแต่ 1 ส.ค. 46 – 31 พ.ค. 47 ต้องมีอายุไม่เกิน 60 ปี ไม่พบโรคทางระบบ ผู้ป่วยจัดแบ่งเป็น 3 กลุ่ม กลุ่ม A มี 30 คน ผู้ป่วยทุกคนได้รับยาที่ระบุตามแผนที่ค่อนข้างมากก่อนเริ่มในกลุ่มที่ 1 ซึ่งแตกต่างมีอย่างน้อย 1 ซึ่งเป็นพื้นคุณ ผู้ป่วยจะได้รับยาสูตรประกอบโดยวิธีระดับสูง แบ่งกลุ่ม และจะได้รับยา rofecoxib (Vioxx®) 50 มิลลิกรัม หรือ ibuprofen (Nurofen®) 400 มิลลิกรัม หรือยาหลอก ตามลำดับ 1 ครั้งต่อวัน การน้ำดักพื้นคุณ ผู้ป่วยจะได้รับยาสูตรประกอบ โดยมีระดับเข้มข้นต่ำกว่าร้อยละ 50 มิลลิกรัม ที่ 16, 20 และ 24 นั้นจากผู้ป่วยจะน้ำดักพื้นคุณ ระดับการลดความเจ็บปวดโดยใช้เครื่องวัดแบบ 5 จุด (0 = ปวดไม่ได้, 1 = ปวดน้อย, 2 = ปวดน้อย, 3 = ปวดกลาง, 4 = ปวด

ผล : - จากการวิเคราะห์และวิเคราะห์ข้อมูลทางสถิติ SPSS โปรแกรมวิเคราะห์สถิติ Kruskal Wallis และ Chi-square พบว่าข้อมูลต่างๆ ที่มีข้อมูลทางสถิติที่มีใน 24 รูปแบบ
ต้านฝังพันคุด ลักษณะของพันคุด ลักษณะพันคุดที่เกิดขึ้นของผู้ป่วยทั้ง 3 กลุ่ม จะมีค่าเฉลี่ยที่แตกต่างกันอย่างมีนัยสำคัญ และจากการเข้าดิบของมะเร็งมีนัยสำคัญด้วย สำนักงานยาเสพติดคลีนิค 1997 ได้แก่ ค่าเฉลี่ยมีนัยสำคัญ Mean (95%CI) ของกลุ่ม rofecoxib 50 มิลลิกรัม และ ibuprofen 400 มิลลิกรัม และ Placebo โดยล่าดับดังนี้ 2.87 (1.5 - 4.24), 5.9 (4.86 - 6.94), 6.8 (5.43 - 8.17) ตามลำดับที่ p < 0.001 และพบว่าค่าเฉลี่ยความพึงพอใจที่มีคัดว่าที่รับรู้จากผู้ที่รับ 3 กลุ่มจะมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ

- จากบันทึกข้อมูลการคลังคิดความเจ็บปวดที่เวลา H(5) (ระหว่างวันดังกล่าว) H(2), H, H(1), H(0), H(0) และแสดงผลในตารางพื้นที่ สรุปได้ว่า rofecoxib 50 มิลลิกรัม ให้ประสิทธิภาพการลดความเจ็บปวดดีกว่า ibuprofen 400 มิลลิกรัม และยาเหลือง หลังจากพันคุด

- จาก Kaplan-Meier test แสดงค่าเฉลี่ยระยะเวลาที่เริ่มรู้สึกปวดครั้งแรกของความเจ็บปวดมีนัยสำคัญที่ 95% ของกลุ่ม rofecoxib, ibuprofen และกลุ่มยาหลอก โดยลำดับดังนี้: 485, (163 – 807)/255, (234 – 276)/180, (162-198) โดยกลุ่ม 3 กลุ่มจะมีความแตกต่างอย่างมีนัยสำคัญที่ p < 0.001 จากการทดสอบ_ulong 400 มิลลิกรัมให้ประสิทธิภาพการ ออกไปในความเจ็บปวดดีกว่าและยาวนานกว่า ibuprofen 400 มิลลิกรัมและกลุ่มยาหลอก และระดับการเจ็บปวดจะมีนัยสำคัญที่ 600 (10 ช.ม.) และยังคงที่เป็นนัยสำคัญที่ 1,440 (= 24 ช.ม.) โดยค่าที่ต้อง ระดับ 0.4

สรุป:

จากผลการวิจัยพบว่าการรับประทาน rofecoxib 50 มิลลิกรัมและยาหลอกพันคุด 1 ช.ม. จะมีประสิทธิภาพในการลดปวดหลังจากการเจ็บปวดได้ดีกว่าและยืนนานกว่ายา ibuprofen 400 มิลลิกรัม ขณะที่ประสิทธิภาพในการออกไปในความเจ็บปวดยาวนาน 2 ชั่วโมงใน 6 ช.ม. แต่ไม่มีความแตกต่างอย่างมีนัยสำคัญ การรับประทานยา ibuprofen 400 มิลลิกรัมทุกๆ 6 ชั่วโมง อย่างต่อเนื่องจะมีประสิทธิภาพลดความเจ็บปวด ซึ่งต้องคำนึงถึงระดับภูมิคุ้มกันค่าในแต่ละคนและมีผลกระทบต่อคุณภาพชีวิตที่ดี ตลอดจนความมิดภูมิคุ้มกันระยะยาวที่ดี

คำสำคัญ: การลดความเจ็บปวด, Specific cyclooxygenase (COX)-2 inhibitor, Non-specific cyclooxygenase (COX) inhibitor
Surgical removal of impacted third molar tooth is an oral surgery procedure that often raises the patient's concern. In Thailand, dental surgery is normally performed under local anesthesia. Because the area is difficult to clean, it often causes oropharyngeal infection. The difficulty of the surgical procedure often demands careful planning.

Unlike in other countries where the patients of the same disease are operated under general anesthesia \(^{1,4}\) or local anesthesia with iv sedation.\(^5\) Up-dated NSAIDs are very efficient and are mostly used for reducing pain. Specific COX-2 inhibitor has an analgesic effect similar to that of nonspecific NSAIDs.\(^6,13\) In this study, the patients received a single dose of NSAID (prophylactic dose) 1 hour before dental surgery to reduce post-surgical dental pain as a simple and convenient alternative way. However, it has less adverse reaction than under GA or LA with iv sedation, simply because it is suitable a method for the economy of our country. The advantages of this study are to improve the quality of our dental services with more up-dated and effective analgesic medicine that raises higher success rate for the surgical procedure.

**Patient and method**

This study was performed at the Department of Dentistry, King Chulalongkorn Memorial Hospital, after the approval of the Ethics Committee for Research, Faculty of Medicine, Chulalongkorn University. The research was performed from October 1\(^{st}\), 2003 to May 31\(^{st}\), 2004. We recruited 90 patients. Exclusion criteria included systemic diseases such as diabetes, hypertension, heart diseases, bleeding disorders, mental disorders, and severe GI disturbances. The subject had to be \( \geq 18 \) years, healthy and they were recruited without any predilection of gender. The subjects were further categorized in 3 groups. Each group consisted of 30 patients. Every patient had to experience moderate or severe pain after extraction of \( \geq 1 \) molars, one among which was at least an impacted tooth. The subjects were randomized to 2 experimental groups and 1 control group, each of which was randomized to receive either specific COX-2 inhibitor, rofecoxib (\(^9\) Vioxx\(^\circledR\) 50 mg, or non-specific COX inhibitor, ibuprofen (\(^9\) Nurofen\(^\circledR\) 400 mg or placebo. Every subject received the study medicine 1 hour before their dental surgery.

Apart from this they were allowed to receive rescue medicine for analgesic effect, acetaminophen 500 mg (\(^\circledR\) Tylenol\(^\circledR\) 500 mg) at home. The data were collected from self-administered questionnaires which were recorded the starting time of study medicine, the pain relief level in 24 hours after dental surgery, the measurement of pain relief was weighted according to a 5-point scale: 0 = none, 1 = a little, 2 = some (moderate), 3 = a lot, 4 = overwhelming. The subjects would record every hour from the beginning of treatment to the first 12 hours, then at 16\(^{th}\) hour, 20\(^{th}\) hour, 24\(^{th}\) hour and further at the time when pain was perceived after dental surgery in order to evaluate the analgesic effects of the medicines. The amount of rescue medicine (acetaminophen 500 mg) used in 24 hours was also recorded, including its adverse reaction and the patients' satisfaction to the study medicine were also recorded by weighting degree of satisfaction: 0 = none, 1 = a little, 2 = some, 3 = a lot, 4 = very much.
Results

We collected data from self-administered questionnaires and presented as following tables and figures.

Table 1 shows Kruskal Wallis test and Chi-Square test; at p < 0.05 no difference of the means shows statistical significance in age, sex, the amount and location and type of impacted tooth with the method of extraction employed. Table 2 shows Kruskal Wallis test and Chi-square test; at p < 0.05 no difference of the means shows statistical significance in adverse reaction to medicine. As well as, table 2 also shows the differences of the means of the amount of rescue medicine which show statistical significance: Mean (95 % CI) of rofecoxib, ibuprofen and placebo were 2.87 (1.5-4.24), 5.9 (4.86-6.94), 6.8 (5.43-8.17), respectively (p < 0.001). Statistically, the patients in rofecoxib group took less rescue medicine than the other two groups. The mean score of patient's satisfaction to the study medicine were statistically significant different among the 3 groups (p < 0.001).

Table 3 and histogram show a tendency of pain relieving among the 3 groups at H₀ (during surgery). There was no statistically significant difference of pain relief among the 3 groups, because every subject had adequate local anesthesia during their surgery (p = 0.610). Higher efficiency of pain relief is seen in rofecoxib group. The efficiency of pain relief in ibuprofen group is good in the first 6 hours, after then it decreased, but in H₁₀ the level of

Table 1. Table of baseline characteristic according to treatment assignment.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rofecoxib (n = 30)</th>
<th>Ibuprofen (n = 30)</th>
<th>Placebo (n = 30)</th>
<th>p-value p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean (SD)</td>
<td>27.57 (9.13)</td>
<td>25 (7.51)</td>
<td>26 (8.23)</td>
<td>0.603 a</td>
</tr>
<tr>
<td>Sex: male</td>
<td>18 (60 %)</td>
<td>14 (47 %)</td>
<td>16 (53 %)</td>
<td>0.585 b</td>
</tr>
<tr>
<td>female</td>
<td>12 (40 %)</td>
<td>16 (53 %)</td>
<td>14 (47 %)</td>
<td></td>
</tr>
<tr>
<td>The amount of impacted tooth</td>
<td>1.23 (0.50)</td>
<td>1.10 (0.31)</td>
<td>1.13 (0.35)</td>
<td>0.510 a</td>
</tr>
<tr>
<td>Location of impacted tooth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>upper impacted tooth</td>
<td>7 (23.3 %)</td>
<td>6 (20 %)</td>
<td>3 (10 %)</td>
<td>0.365 b</td>
</tr>
<tr>
<td>lower impacted tooth</td>
<td>17 (56.7 %)</td>
<td>21 (70 %)</td>
<td>24 (80 %)</td>
<td></td>
</tr>
<tr>
<td>upper and lower impacted tooth</td>
<td>6 (20 %)</td>
<td>3 (10 %)</td>
<td>3 (10 %)</td>
<td></td>
</tr>
<tr>
<td>Type of impacted tooth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>soft tissue</td>
<td>3 (10 %)</td>
<td>1 (3.3 %)</td>
<td>1 (3.4 %)</td>
<td>0.561 b</td>
</tr>
<tr>
<td>partially bony</td>
<td>22 (73.3 %)</td>
<td>20 (66.7 %)</td>
<td>22 (75.9 %)</td>
<td></td>
</tr>
<tr>
<td>completely bony</td>
<td>5 (16.7 %)</td>
<td>9 (30 %)</td>
<td>6 (20.7 %)</td>
<td></td>
</tr>
<tr>
<td>Type of extracted tooth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opposing to impacted tooth</td>
<td>8 (100 %)</td>
<td>7 (100 %)</td>
<td>15 (93.8 %)</td>
<td>0.616 b</td>
</tr>
<tr>
<td>Not opposing to impacted tooth</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td>1 (6.3 %)</td>
<td></td>
</tr>
</tbody>
</table>

a = Kruskal Wallis test (p < 0.05)
b = X² (chi – square) test (p < 0.05)
pain relief in ibuprofen groups was lower than that of the placebo (level 1.97,2.17, respectively; p = 0.004) because in this study we did not limit the ceiling of the rescue medicine. Frequently, the patients in the placebo group (control group) felt pain and they took rescue medicine when needed. (Figure 1.)

We used Mann-Whitney test for statistical analysis of the data in Table 4 and took p-value from Bonferroni method. Because Mann-Whitney test was used to compare between 2 groups and accepted p-value was founded from

\[ \alpha_{new} = \alpha = 0.05 = 0.0167 \]

3 groups
3

Table 4 illustrates an analysis of Mann-Whitney test comparing rofecoxib group to placebo group regarding patient’s satisfaction to the study medicine, the amount of rescue medicine and the pain relief level at \( H_2, H_6, H_{10}, H_{16}, H_{20} \) were statistically significant different (p < 0.0167). We concluded that rofecoxib has higher efficiency for pain relief than placebo.

---

### Table 2. Table of comparable adverse reaction, the amount of rescue medicine and patient’s satisfaction to the study medicine among 3 groups.

<table>
<thead>
<tr>
<th>Result</th>
<th>Rofecoxib (n = 30)</th>
<th>Ibuprofen (n = 30)</th>
<th>Placebo (n = 30)</th>
<th>p-value p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>have adverse reaction</td>
<td>1 (3.3 %)</td>
<td>3 (10 %)</td>
<td>0 (0 %)</td>
<td>0.160 ( ^{a} )</td>
</tr>
<tr>
<td>No adverse reaction</td>
<td>29 (96.7 %)</td>
<td>27 (90 %)</td>
<td>30 (100 %)</td>
<td></td>
</tr>
<tr>
<td>The amount of rescue medicine</td>
<td>2.87(1.50-4.24)</td>
<td>5.9(4.86-6.94)</td>
<td>6.8(5.43-8.17)</td>
<td>&lt;0.001 ( ^{a} )</td>
</tr>
<tr>
<td>Patient’s satisfaction to the study medicine</td>
<td>2.97(2.65-3.28)</td>
<td>2.83(2.48-3.19)</td>
<td>2.03(1.65-2.42)</td>
<td>&lt;0.001 ( ^{a} )</td>
</tr>
</tbody>
</table>

\( ^{a} \) = Kruskal Wallis test (p< 0.05)

\( ^{b} \) = \( X^2 \) (chi-square) test (p < 0.05)

### Table 3. Mean pain relief among 3 groups at different time.

<table>
<thead>
<tr>
<th>Time</th>
<th>Rofecoxib Mean (95%CI)</th>
<th>Ibuprofen Mean (95%CI)</th>
<th>Placebo Mean (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( H_0 ) (during surgery)</td>
<td>2.87(2.41-3.32)</td>
<td>2.93(2.93-3.41)</td>
<td>2.7(2.25-3.15)</td>
<td>.610</td>
</tr>
<tr>
<td>( H_2 ) (post-operative 2 hrs)</td>
<td>2.17(1.72-2.62)</td>
<td>2.23(1.79-2.68)</td>
<td>1.43(1.00-1.87)</td>
<td>.018</td>
</tr>
<tr>
<td>( H_6 ) (post-operative 6 hrs)</td>
<td>2.90(2.56-3.24)</td>
<td>2.37(1.96-2.78)</td>
<td>1.77(1.32-2.21)</td>
<td>.001</td>
</tr>
<tr>
<td>( H_{10} ) (post-operative 10 hrs)</td>
<td>3.07(2.71-3.42)</td>
<td>2.17(1.65-2.69)</td>
<td>1.97(1.55-2.39)</td>
<td>.002</td>
</tr>
<tr>
<td>( H_{16} ) (post-operative 16 hrs)</td>
<td>3.13(2.80-3.47)</td>
<td>2.13(1.64-2.63)</td>
<td>2.00(1.51-2.49)</td>
<td>.001</td>
</tr>
<tr>
<td>( H_{20} ) (post-operative 20 hrs)</td>
<td>3.03(2.67-3.39)</td>
<td>1.97(1.45-2.48)</td>
<td>2.17(1.71-2.63)</td>
<td>.004</td>
</tr>
</tbody>
</table>

From Kruskal Wallis test at p<0.05
Figure 1. Histogram showed mean pain relief of three groups at different times.

Table 4 illustrates an analysis of Mann-Whitney test comparing ibuprofen group to placebo group regarding patient’s satisfaction to the study medicine, the pain relief level at \( H_2 \) were statistically significant different, but at \( H_6 \) it was not clear because \( p \)-value = 0.043 which was \(< 0.05 \) but \( > 0.0167 \). We conclude that the pain relief at \( H_6 \) was not statistically significant different. The amount of rescue medicine and the pain relieving level at \( H_{10} \), \( H_{16} \), and \( H_{20} \) were not statistically significant different. The effect decreased when the time was prolonged. So the patient took more rescue medicine that raised the amount of rescue medicine (\( p=0.229 \)).

Table 4. Table of comparing rofecoxib group with placebo group, ibuprofen group with placebo group and rofecoxib group with ibuprofen group, respectively from Mann-Whitney test and accepted \( p \)-value from Bonferroni method (\( p<0.0167 \)).

<table>
<thead>
<tr>
<th>Result</th>
<th>Rofecoxib-Placebo p-value</th>
<th>Ibuprofen-Placebo p-value</th>
<th>Rofecoxib-Ibuprofen p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s satisfaction to the study medicine</td>
<td>(&lt;.001)</td>
<td>0.002</td>
<td>0.572</td>
</tr>
<tr>
<td>The amount of rescue medicine</td>
<td>(&lt;.001)</td>
<td>(&lt;.001)</td>
<td>(&lt;.001)</td>
</tr>
<tr>
<td>( H_2 ) (post-operative 2 hrs)</td>
<td>0.016</td>
<td>0.013</td>
<td>0.848</td>
</tr>
<tr>
<td>( H_6 ) (post-operative 6 hrs)</td>
<td>(&lt;.001)</td>
<td>0.043</td>
<td>0.056</td>
</tr>
<tr>
<td>( H_{10} ) (post-operative 10 hrs)</td>
<td>(&lt;.001)</td>
<td>0.490</td>
<td>0.011</td>
</tr>
<tr>
<td>( H_{16} ) (post-operative 16 hrs)</td>
<td>0.001</td>
<td>0.721</td>
<td>0.003</td>
</tr>
<tr>
<td>( H_{20} ) (post-operative 20 hrs)</td>
<td>0.008</td>
<td>0.583</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Table 5. Kaplan-Meier test compared median time of pain perception and 95% CI among
3 groups (p<0.001).

<table>
<thead>
<tr>
<th></th>
<th>Rofecoxib</th>
<th>Ibuprofen</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time, (95% CI)</td>
<td>485, (163 - 807)</td>
<td>255, (234 - 276)</td>
<td>180, (162 - 198)</td>
</tr>
</tbody>
</table>

Table 4 also illustrates an analysis of Mann-Whitney comparing rofecoxib group to ibuprofen group regarding the amount of rescue medicine and the level of pain relief at $H_{10}, H_{15}, H_{20}$, the differences of which were of statistical significance. But the differences of patient's satisfaction and the level of pain relief at $H_{2}, H_{6}$ were not of statistical significance. We conclude that ibuprofen 400 mg was efficiency in relieving pain in the first 6 hours. Pain relief decreased when time of observation was prolonged. On the contrary, rofecoxib still maintained its efficiency in relieving pain although the time of observation was prolonged until $H_{20}$.

Table 5 illustrates an analysis of Kaplan-Meier test which was survival analysis of time regarding the median time of pain perception: 95%CI of rofecoxib, ibuprofen and placebo were 485, (163-807)/255, (234-276)/180, (162-198), respectively; level of statistical significance of the difference when p < 0.001. The linear graph indicates that rofecoxib 50 mg produced higher efficiency and longer duration of analgesic effect than ibuprofen 400 mg and placebo. The duration of pain-free state in rofecoxib group was constant at 600 min (10 hours) and constant until 1440 min (24 hours) and was constant at the pain-free rate of 0.4. Whereas pain-free duration of ibuprofen group and placebo group dropped in 180 min - 280 min, 140 min - 210 min, respectively. Both groups had similarly pain-free duration curves, but ibuprofen group showed longer duration of analgesic effect than placebo group. (Figure 2.)

Discussion
Non-steroidal anti-inflammatory drugs (NSAIDs) are available worldwide and widely used. They are first drugs of choice for the treatment of acute myalgias, orthopedic injuries, post-surgical dental pain, chronic rheumatoid arthritis and osteoarthritis. The mechanism that NSAIDs provide analgesia and suppress inflammation is through the inhibition of enzyme cyclooxygenase which results in the decrease of prostaglandin synthesis. The suppression of prostaglandin synthesis also produces gastric and renal toxicity, as well as impairment of their normal functions. Also, NSAIDs are associated with potentially harmful side effects. Cyclooxygenase exists in two isoenzymatic forms: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). COX-1 appears to be constitutively expressed in many tissues and produces prostaglandins which regulate normal cellular functions. However, COX-2 activity is induced by pro-inflammation cytokines and produces prostaglandins that mediate the inflammation response and pain signaling transmission. Conventional nonspecific NSAIDs inhibit both COX-1 and COX-2, and in so
Figure 2. Linear graph showed median time of pain perception and pain-free rate among three groups.

doing, not only that they decrease inflammation and pain but they also cause gastrointestinal damage and bleeding.\(^{4,12,14-18}\) The potential clinical benefit of COX-2 inhibitor is significant due to the colossal number of patients treated with NSAIDs, in spite of the higher risk of gastrointestinal bleeding and death associated with conventional NSAIDs.\(^{14,17}\) In this study patients received the study medicine which was either specific COX-2 inhibitor (rofecoxib or Vioxx\(^{6}\) 50 mg) or nonspecific COX inhibitor (ibuprofen or Nurofen\(^{6}\) 400 mg ). The results show that both rofecoxib 50 mg and ibuprofen 400 mg have similar analgesic efficiency; however, the rofecoxib group has longer duration of action.\(^{6-13,19-20}\) Ehrich E W et al. indicated that total pain relief (TOPAR) the 6 hours after dosing was similar between 50 mg and 500 mg rofecoxib and 400 mg ibuprofen (P >0.20).\(^{9}\) Gopikrishna V et al. also indicated that in 4-h and 8-h periods, both rofecoxib 50 mg and ibuprofen 600 mg significantly provided better pain relief than placebo.\(^{13}\) Fine PG concluded that the advantages of using specific NSAIDs include convenient once-daily dosing schedule and improved safety compared to conventional NSAIDs. Absence of any effect platelet aggregation and bleeding time further distinguishes these agents from conventional NSAIDs.\(^{19}\) Morrison BW et al. suggested that rofecoxib, at a dose of 50 mg is effective in the management of postoperative dental pain.\(^{21}\) Jeske AH suggested that the older NSAIDs, such as ibuprofen, naproxen, diflunisal and others, remain first drugs of choice for the treatment of mild-to-moderate pain in dentistry in patients who have no contraindication for the drugs. The same author also proposed several years ago that the major contraindications to NSAIDs can be remembered by “SAAB Rule”, an acronym which stands for “Stomach problem, Aspirin Allergy” and “Bleeding problems”, in addition to pregnancy, hepatic and renal disease.\(^{22}\)
Dionne R suggested that the analgesic effect of ibuprofen is well characterized by acute pain, and short-term treatment is well tolerated. In an experimental model of pain, ibuprofen promptly suppresses prostaglandin E2 concentrations and has a faster onset of action than celecoxib (specific COX-2 inhibitor).\(^{15,23}\) Zuurmond WW suggested that ibuprofen has been known as one of the safe NSAIDs in some countries including the Netherlands which it has been known as an over-the-counter medicine.\(^{24}\) Many studies\(^{6,8,10,19,25}\) suggested that rofecoxib 50 mg was more effective than placebo in all measures of analgesic efficacy. Rofecoxib 50 mg exhibited overall analgesic effects, onset of analgesia and analgesic effects that were not significantly different from ibuprofen 400 mg, with a significantly longer duration of action (p<0.05). Because of its higher favorable gastrointestinal toxicity profile compared with nonselective NSAID, rofecoxib is safer in older patients for whom anti-inflammatory or analgesic therapy is indicated. Jeske AH suggested that the disadvantages of COX-2 inhibitors NSAIDs were more expensive than conventional NSAIDS and not available over the counter.\(^{22}\)

This study (table 2) showed that one patient in rofecoxib group got dizziness and three patients in ibuprofen group got nausea, diarrhea, skin rash on the face and extremities that corresponds to the adverse reaction from previous studies.\(^{4,6,11,18,20,25-26}\) All of them felt normal by self recovering because in this study they received single dose studying medicine so it caused mild adverse reaction. The patient's satisfaction to rofecoxib and to ibuprofen were not statistically significant different may be from emotional involvement or from similarly analgesic efficiency of both studying medicine. We suggested that conventional NSAIDs were still the first drugs of choice for mild to moderate dental pain. Selecting drugs for short-term relief of postoperative dental pain should be based on careful assessment of all relevant pharmacological characteristics given agent, especially those related to maximum dosage, duration of action and efficacy.\(^{26}\) But on the other hand, specific COX-2 inhibitor is more efficient, it has faster onset and longer duration of analgesic efficiency. It was effective for the treatment of moderate to severe dental pain. According to the low risk of adverse reaction and longer duration of analgesic efficiency, the author suggested that specific COX-2 inhibitors (rofecoxib 50 mg) is good for prophylactic dose, 1 hour before dental procedure to reduce postoperative dental pain. It was simple, convenient, low cost and low risk of adverse reaction when compared with the procedures which performed under GA or LA with sedation. Because of different half-life, rofecoxib has longer half-life than ibuprofen and the single dose ibuprofen is effective in reducing pain within the first 6 hours. We should suggest that continuing dose every 6 hours of ibuprofen cause more continuing effects.

**Conclusion**

This study is an alternative way to improve the planning and treatment of dental services. The objectives of the study are to compare the analgesic efficiency of rofecoxib 50 mg with that of ibuprofen 400 mg regarding their ability to reduce pain after dental surgery. We conclude that rofecoxib 50 mg serves as an effective prophylactic treatment of pain when taken 1 hour before surgical removal of third molar impacted tooth and it also has longer duration
of pain relief than ibuprofen 400 mg, whereas the
difference of the efficiency of pain relief in the first 6
hours of both drugs are not of statistical significance.
Because of adverse reaction, higher cost and no
difference of the efficiency of pain relief in the first 6
hours of both rofecoxib and ibuprofen we also
concluded that ibuprofen taken every 6 hours is
another alternative way for reducing pain but we should
concern of GI bleeding and platelet aggregation and
bleeding time disorder.

Acknowledgements
The author would like to thank Mrs. Chanpen
Tangtrakul for her kindness and her encouragement,
Miss Korakot Rochanabha for her good assistance,
Mr. Wasan Punyasang who helped with data analysis
to its final state, and lastly the Venerable Dr.
Mettanando Bhikkhu for editing the paper.

References
1. Holmgren WC, Baddour HM, Tilson HB. Unilateral
mydriasis during general anesthesia. J Oral
2. Bertrand M, Greffe B, Dageneux JC.Hoguet L,
Rollnat-Levasseur AL. General anesthesia
for multiple dental extractions. Ann Anesthesiol
Fr 1976;17(6): 615 - 20
3. Chapman PJ, Ganendran A. Prolonged analgesia
following preoperative bupivacaine neural
blockade for oral surgery performed under
general anesthesia. J Oral Maxillofac Surg
1987 Mar; 45(3): 233 - 5
randomised controlled clinical trial effect
of preoperative ibuprofen, diclofenac, para-
cetamol with codeine and placebo tablets
for relief of postoperative pain after removal
of impacted third molars. Br J Oral Maxillofac
5. Holland IS, Stassen LF. Bilateral block: is it safe
and more efficient during removal of third
34(3): 243 - 7
6. Chang DJ, Fricke JR, Bird SR, Bohidar NR, Dobbins
TW, Geba GP. Rofecoxib versus codeine/acetaminophen in postoperative dental pain:
A double-blind, randomized, placebo-and
active comparator-controlled clinical trial. Clin
Ther 2001 Sep; 23(9): 1446 - 55
7. Peretz A. COX-2 inhibitor non-steroidal anti-
inflammatory drugs myth or reality? Rev Med
Brux 2001 Sep; 22(4): A377 - 80
8. Jeske AH. Selecting new drugs for pain control:
evidence-base decisions or clinical impres-
1052 - 6
9. Ehrich EW, Dallob A, De Lepeleire I, Van Hecken A,
Riendeau D, Yuan W, Porras A, Wittreich J,
Seibold JR, De Schepper P, et al. Characteri-
zation of rofecoxib as a cyclooxygenase
isoform inhibitor and demonstration of
analgesia in dental pain model. Clin Pharmacol
Ther 1999 Mar; 65(3): 336 - 47
10. Morrison BW, Christensen S, Yuan W, Brown J,
Amlani S, Seidenberg B. Analgesic efficacy
of the cyclooxygenase-2-specific inhibitor
rofecoxib in post-dental surgery pain: a
randomized, controlled trial. Clin Ther 1999
Jun; 21(6): 943 - 53
11. Malmstrom K, Daniels S, Kotey P, Seidenberg


24. Zuurmond WW. Pain treatment with NSAIDs, primary focus on ibuprofen. Clin Rheumatol 2001 Nov; 20 Suppl 1: S6 - 8
