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

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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*

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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 16^{th} , 20^{th},24^{th}. 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 600^{th} min (10 hours) is still constant until the $1,440^{th}$ 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.*

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วรรณี อันวีระวัฒนา. การศึกษาเปรียบเทียบผลการใช้ยาระงับปวดระหว่าง rofecoxib และ ibuprofen รับประทาน 1 ครั้งก่อนผ่าตัดฟันกรามคุดซี่ที่ 3. จุฬาลงกรณ์เวชสาร 2547 ก.ย; 48(9): 599 – 612

ปัญหา : *Rofecoxib ซึ่งเป็นยาสเตียรอยด์ชนิด specific COX –2 inhibitor มีประสิทธิภาพการออกฤทธิ์คล้ายคลึงกับยาสเตียรอยด์ชนิด non-specific COX inhibitor โดยทั่วไปผู้ป่วยส่วนใหญ่จะกลัวและวิตกกังวลต่อความเจ็บปวดหลังผ่าตัดฟันคุด*

วัตถุประสงค์ : *เพื่อศึกษาเปรียบเทียบประสิทธิภาพการใช้ยาระงับปวดระหว่าง rofecoxib 50 มิลลิกรัมและ ibuprofen 400 มิลลิกรัม โดยให้รับประทาน 1 ครั้งก่อนผ่าตัดฟันคุด เพื่อลดความเจ็บปวดของผู้ป่วยหลังผ่าตัดฟันคุด*

รูปแบบการวิจัย : *การวิจัยทางคลินิกแบบสุ่มตัวอย่าง*

ผู้ป่วยและวิธีการศึกษา : *ผู้ป่วยจำนวน 90 รายเข้าร่วมในโครงการวิจัยตั้งแต่ 1 ต.ค. 46 – 31 พ.ค. 47 ต้องมีสุขภาพแข็งแรง ไม่จำกัดเพศ และอายุ ≥ 18 ปี ไม่มีโรคทางระบบ ผู้ป่วยถูกจัดแบ่งเป็น 3 กลุ่มกลุ่มละ 30 คน ผู้ป่วยทุกคนได้รับความเจ็บปวดตั้งแต่ระดับปานกลางจนถึงรุนแรงหลังถอนฟัน ≥ 1 ซี่ แต่ต้องมีอย่างน้อย 1 ซี่ที่เป็นฟันคุด ผู้ป่วยจะได้รับการสุ่มตัวอย่างโดยวิธีจับสลาก แบ่งกลุ่ม และจะได้รับยา rofecoxib (Vioxx®) 50 มิลลิกรัม หรือ ibuprofen (Nurofen®) 400 มิลลิกรัม หรือยาหลอก ตามลำดับ 1 ครั้ง 1 ชั่วโมงก่อนผ่าตัดฟันคุด จากนั้นหลังผ่าตัดฟันคุดผู้ป่วยจะได้รับยาเสริมเพื่อแก้ปวดคือ acetaminophen 500 มิลลิกรัม (Tylenol® 500 มิลลิกรัม) หลังกลับบ้าน การผ่าตัดฟันคุดทำโดยการฉีดยาชาเฉพาะที่ ผู้ป่วยจะกรอกแบบสอบถามด้วยตนเอง โดยมีรายละเอียดเกี่ยวกับเวลาเริ่มต้นของการรับประทานยาระงับปวดก่อนผ่าตัดฟันคุด ระดับการลดความเจ็บปวด โดยใช้มาตราวัดแบบ 5 จุด (0 = ปวดไม่ลด, 1 = ปวดลดน้อย, 2 = ปวดลดปานกลาง, 3 = ปวดลดมาก, 4 =ปวดลดจนหมดไป) โดยบันทึกทุกช.ม.ใน 12 ช.ม.แรกหลังผ่าตัดฟันคุด จากนั้นบันทึกช.ม. ที่ 16, 20 และ 24 นอกจากนี้ผู้ป่วยจะบันทึกผลข้างเคียงของการใช้ยา เวลาที่เริ่มปวดครั้งแรก ความพึงพอใจต่อยาที่รับประทาน และรวมถึงจำนวนเม็ดของยา acetaminophen ที่ใช้ใน 24 ช.ม.*

ผล : *- จากการบันทึกและวิเคราะห์ข้อมูลทางสถิติ SPSS โปรแกรม วิธีทดสอบ Kruskal Wallis และ Chi-square พบว่าข้อมูลอายุ เพศ จำนวนซี่ฟันคุด*

ตำแหน่งฟันคุด ลักษณะของฟันคุด ลักษณะฟันที่ถอนของผู้ป่วยทั้ง 3 กลุ่ม จะมีค่าเฉลี่ยที่ไม่แตกต่างกันอย่างมีนัยสำคัญ และอาการข้างเคียงของยาจะมีค่าเฉลี่ยที่ไม่แตกต่างกันอย่างมีนัยสำคัญด้วย ส่วนจำนวนยาเม็ดแก้ปวดที่ใช้จะมีค่าเฉลี่ยที่แตกต่างกันอย่างมีนัยสำคัญ Mean (95 %CI) ของกลุ่ม rofecoxib 50 มิลลิกรัม และ ibuprofen 400 มิลลิกรัม และ Placebo โดยลำดับดังนี้ 2.87 (1.5 - 4.24), 5.9 (4.86 - 6.94), 6.8 (5.43 - 8.17) ตามลำดับที่ $p < 0.001$ และพบว่าค่าเฉลี่ยความพึงพอใจที่มีต่อยาที่รับประทานทั้ง 3 กลุ่มจะมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ

- จากบันทึกข้อมูลการลดระดับความเจ็บปวดที่เวลา H_0 (ระหว่างผ่าตัด), H_2, H_6, H_{10}, H_{16}, H_{20} และแสดงผลในรูปกราฟแท่ง สรุปได้ว่ายา rofecoxib 50 มิลลิกรัม ให้ประสิทธิภาพการลดความเจ็บปวดดีกว่า ibuprofen 400 มิลลิกรัม และ ยาหลอก หลังผ่าตัดฟันคุด

- จาก Kaplan-Meier test แสดงค่าเฉลี่ยระยะเวลาที่เริ่มรู้สึกปวดครั้งแรก ช่วงความเชื่อมั่นที่ 95 % ของกลุ่ม rofecoxib, ibuprofen และ กลุ่มยาหลอก โดยลำดับดังนี้ 485, (163 – 807)/255, (234 – 276)/180, (162-198) โดยทั้ง 3 กลุ่มจะมีความแตกต่างอย่างมีนัยสำคัญที่ $p < 0.001$ จากกราฟเส้นแสดงว่า rofecoxib 50 มิลลิกรัมให้ประสิทธิภาพการออกฤทธิ์ในการลดความเจ็บปวดดีกว่าและยาวนานกว่า ibuprofen 400 มิลลิกรัมและกลุ่มยาหลอก และระดับการลดความเจ็บปวดจะคงที่ที่นาทีที่ 600 (10 ช.ม.) และยังคงที่จนถึงนาทีที่ 1,440 (= 24 ช.ม.) โดยคงที่ที่ระดับ 0.4

สรุป : *จากผลการวิจัยพบว่าการรับประทาน rofecoxib 50 มิลลิกรัมก่อนผ่าตัดฟันคุด 1 ช.ม. จะให้ประสิทธิภาพในการออกฤทธิ์ลดความเจ็บปวดได้ดีกว่าและยาวนานกว่ายา ibuprofen 400 มิลลิกรัม ขณะที่ประสิทธิภาพในการออกฤทธิ์ เพื่อลดความเจ็บปวดของยาทั้ง 2 ชนิดใน 6 ช.ม. แรกไม่มีความแตกต่างกันอย่างมีนัยสำคัญ การรับประทานยา ibuprofen 400 มิลลิกรัม ทุก 6 ชั่วโมง อย่างต่อเนื่องจะมีประสิทธิภาพลดความเจ็บปวด ซึ่งต้องคำนึงถึงระบบกระเพาะลำไส้เป็นแผลมีเลือดออกและมีผลต่อแข็งตัวของเกร็ดเลือด ตลอดจนความผิดปกติของระยะเวลาเลือดออก*

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 oro-pharyngeal 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 1st,2003 to May 31st, 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 (Vioxx®) 50 mg, or non-specific COX inhibitor, ibuprofen (Nurofen®) 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 (Tylenol® 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 16th hour, 20th hour, 24thhour 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 ($p <.001$).

Table 3 and histogram show a tendency of pain relieving among the 3 groups at H_0(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 H_{20} the level of

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

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

a = Kruskal Wallis test ($p < 0.05$)

b = X^2 (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

$$\alpha_{new} = \frac{\alpha}{3 \text{ groups}} = \frac{0.05}{3} = 0.0167$$

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.

Result	Rofecoxib (n = 30)	Ibuprofen (n = 30)	Placebo (n = 30)	p-value p<0.05
Adverse reaction				
have adverse reaction	1 (3.3 %)	3 (10 %)	0 (0 %)	0.160 b
No adverse reaction	29 (96.7 %)	27 (90 %)	30 (100 %)	
The amount of rescue medicine	2.87(1.50-4.24)	5.9(4.86-6.94)	6.8(5.43-8.17)	<0.001 a
Patient's satisfaction to the study medicine	2.97 (2.65-3.28)	2.83 (2.48-3.19)	2.03 (1.65-2.42)	<0.001 a

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.

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

From Kruskal Wallis test at $p<0.05$

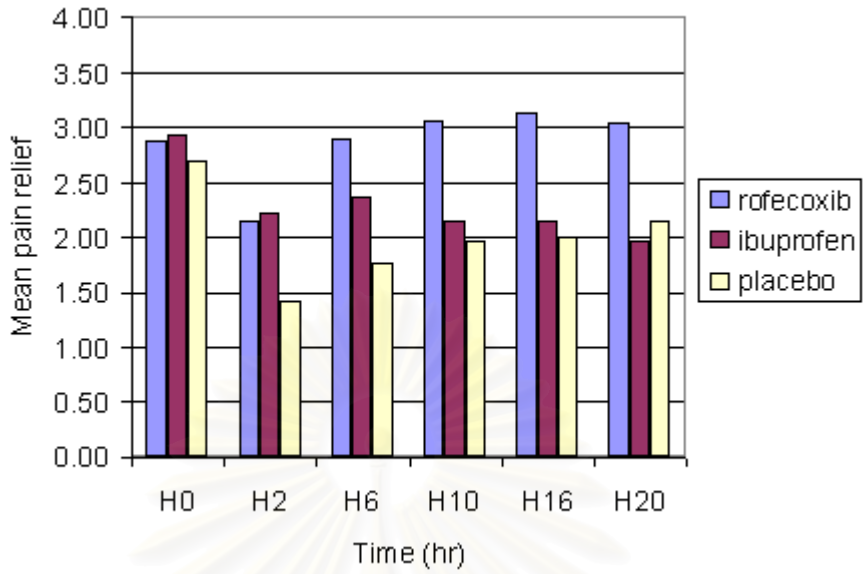

Figure 1. Histogram showed mean pain relief of three groups at different times.

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},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).

Result	Rofecoxib-Placebo p-value	Ibuprofen-Placebo p-value	Rofecoxib-Ibuprofen p-value
Patient's satisfaction to the study medicine	<.001	.002	.572
The amount of rescue medicine	<.001	.229	<.001
H_2 (post-operative 2 hrs)	.016	.013	.848
H_6 (post-operative 6 hrs)	<.001	.043	.056
H_{10} (post-operative 10 hrs)	<.001	.490	.011
H_{16} (post-operative 16 hrs)	.001	.721	.003
H_{20} (post-operative 20 hrs)	.008	.583	.003

Table 5. Kaplan-Meier test compared median time of pain perception and 95% CI among 3 groups ($p<0.001$).

	Rofecoxib	Ibuprofen	Placebo
Median time, (95% CI)	485, (163 - 807)	255, (234 - 276)	180, (162 - 198)

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_{16},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^{th} min (10 hours) and constant until 1440^{th} 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^{th} min – 280^{th} min, 140^{th} min - 210^{th} 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.[14] Conventional nonspecific NSAIDs inhibit both COX-1 and COX-2 , and in so

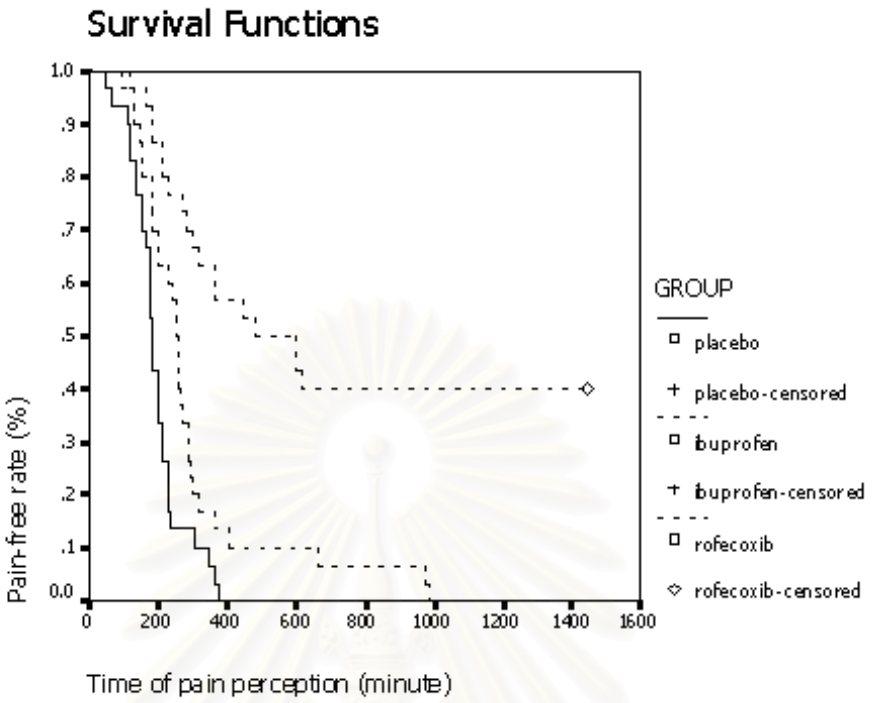

Figure 2. Linear graph showed median time of pain perception and pain-free rate among three groups.

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® 50 mg) or nonspecific COX inhibitor (ibuprofen or Nurofen® 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.[8] 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.

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