Parecoxib versus Tramadol for Post-Appendectomy Pain

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Open uncomplicated appendectomy is known for low to medium degree of postoperative pain and a short hospital stay. Based on multimodal pain therapy, non-opioid analgesics have widely been a part in pain control. Parecoxib and tramadol have advantages over traditional opioids that are causing less nausea or vomiting, respiratory depression and sedation. As a result, the authors aimed to compare parecoxib and tramadol regarding quality of pain control after open appendectomy. Fifty patients, underwent open appendectomy with spinal anesthesia, were randomized to receive either parecoxib or tramadol (n = 25 each). Parecoxib 40 mg and tramadol 50 mg IV were administered twice, when closing the peritoneum and at 12 h later. Doses of rescued meperidine for 24 h were recorded. Pain score, sedation, nausea or vomiting and satisfaction scores were assessed at 6, 12 and 24 h after operation. The mean rescued doses of meperidine were 4.6 ± 10.9 and 18.6 ± 21.0 mg in parecoxib and tramadol groups respectively (p = 0.005). There was a significantly higher pain score at 24 h (p = 0.01) and sedation score at 6 h (p = 0.003) in the tramadol group. Parecoxib provided a lower pain and sedation scores and lesser meperidine consumption than tramadol for post-appendectomy pain. Implication: Parecoxib, as a primary analgesic, is better in analgesia and has less sedation than tramadol for post-appendectomy pain.

Keywords: *Analgesics, Parecoxib, Tramadol, Surgery, Appendectomy*

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Current therapeutic strategies for the management of acute pain are predominantly dependent on opioid analgesics. Though opioid analgesics provide excellent analgesia, they have a range of side effects such as respiratory depression, sedation, nausea or vomiting[1]. In recent years, there are the advents of new NSAIDs, COX-2-selective inhibitors, which have rationales supporting their usefulness for acute pain control. First, both COX-1 inhibited and COX-2-selective inhibited NSAIDs are known to suppress peripheral sensitization due to their anti-inflammation effect then leading to less central sensitization, which finally lead to cause less perception of pain[2]. Interestingly, COX-2-selective inhibitors, especially the 2nd generation, are more responsible to counteract inflammation and pain than COX-1 inhibitor[3]. Second, COX-2-inhibitors have been proved to produce fewer undesirable side effects such as platelet dysfunction[4] and GI bleeding[5] than conventional NSAIDs. Finally, COX-2-inhibitors are analgesics with opioid-sparing side effects. Predominantly, nausea or vomiting is common and dissatisfied events for those anesthetized patients. A COX-2-inhibitor has been reported for its opioid-sparing effect, which are less nausea or vomiting and greater patient satisfaction[6,7]. Consequently, parecoxib-the 2nd generation of COX-2-inhibitor and the only parenteral form, is considered as the pain inhibited competitor of opioid analgesics for treatment of mild to moderate postoperative pain. Tramadol despite being a weak opioid agonist is broadly used as an adjuvant analgesic due to its fewer side effects than traditional opioids[8]. For uncomplicated open appendectomy, it is likely to treat postoperative pain with weak -to- moderate potent analgesics since there was evidence of low visual analog pain scores in a prospective study[9]. Also the length of hospital stay in the mentioned study was shorter around 29.2 ± 16.5 hours[9]. These evidences imply that they should pro-

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vide the potency of analgesia as appropriate as the severity of pain. Otherwise, it might cause those, avoidable, mentioned side effects and prolong hospital stays. Consequently, this randomized prospective double-blinded trial comparing parecoxib and tramadol was performed to evaluate quality of pain control after appendectomy.

Material and Method

The study design and randomization process were reviewed and approved by the institution's review board for human research. The present study was carried out in a tertiary-care, residency-training hospital. Patients who were diagnosed with suspected acute appendicitis, 15-60 years old, ASA status I-II, over 45 kilograms of weight met the inclusion criterion. Exclusion criteria included a known allergy or sensitivity to sulfa, tramadol, bupivacaine, meperidine or any NSAID, a contraindication to spinal anesthesia, renal insufficiency, a history of peptic ulcer, a history of bleeding diathesis, a history of asthma, pregnancy and receiving general anesthesia. After obtaining written informed consent, the patients were randomly divided into 2 groups that were parecoxib and tramadol groups. Randomization was allocated according to computer-generated randomization lists. The sample sizes were calculated from a mean difference and standard deviations of postoperative meperidine consumption between parecoxib and tramadol in a pilot study. With the power of 0.8 and the significance of 0.05, the sample sizes were 25 each (The means and SD were 5.00 $\pm$ 10.80 and 23.21$\pm$ 22.41 mg consecutively).

Fifty patients were applied spinal anesthesia with 3.6-4.0 mL. of 0.5% hyperbaric bupivacaine. The anesthetic level was controlled to reach the 4th thoracic dermatome for at least. Sedation with 0.05 mg kg-1 of intravenous midazolam was given for some discomforts if needed. Moderate to severe degree of shivering was treated by IV meperidine 0.25 mg. kg-1. Either parecoxib 40 mg or tramadol 50 mg was administered intravenously after peritoneum closure and at 12 hours later. For pain rescue, intravenous meperidine (0.5 mg. kg-1) was administered on request every 4 hours. Data collectors who were blinded for the administered drug assessed pain, sedation, nausea or vomiting and satisfaction scores at 6, 12, and 24 h after surgery. The pain and satisfaction scores were self-administered assessment using visual analog scale (VAS; 0 =" no pain or absolutely not satisfied" and 10 = " worst pain imaginable or very satisfied"). Degree of sedation was determined ranging from 0 to 2 (0 = alert, 1 = drowsy but rousable to voice, and 2 = very drowsy, but rousable to shaking). Degree of nausea or vomiting was determined ranging from 0 to 2 (0 = no nausea, 1 = feel nausea, 2 = vomit). Total meperidine consumption for 24 hours was recorded.

Descriptive statistics are expressed as mean $\pm$ SD unless otherwise stated. All variables were tested for normal distribution by Kolmogorov-Smirnov test. Student's t-test was used for comparison the means of

Table 1. Patient characteristics

	Parecoxib (n = 25)	Tramadol (n = 25)
Age (yr)	29.7 $\pm$ 9.7	34.0 $\pm$ 12.1
Body weight (kg)	57.5 $\pm$ 9.5	56.0 $\pm$ 7.8
Gender (number)		
Male	14	11
Female	11	14
Midazolam		
Number	11	6
Dose (mg)	0.8 $\pm$ 1.1	0.4 $\pm$ 0.7
Shivering		
Number	9	14
Treat with meperidine (mg)	7.8 $\pm$ 10.8	12.0 $\pm$ 13.4
Duration of anesthesia (min)	79.5 $\pm$ 24.3	73.2 $\pm$ 22.1
Final diagnosis (number)		
Acute appendicitis	22	23
Ruptured appendicitis	3	2

Values are number or mean $\pm$ SD. No significant differences were found between two groups

Table 2. Sedation scores

Time after Surgery (h)	Parecoxib (n = 25)			Tramadol (n = 25)		
	Score			Score		
	0	1	2	0	1	2
6*	19	6	0	9	15	1
12	19	6	0	14	11	0
24	25	0	0	22	3	0

Values are number. * significant level < 0.05

Table 3. Nausea or vomiting and satisfaction scores

Score of	Parecoxib (n = 25)			Tramadol (n = 25)		
	time after surgery			time after surgery		
	6	12	24	6	12	24
Nausea or vomiting						
0	23	23	23	18	20	24
1	2	2	1	7	5	1
2	0	0	1	0	0	0
Satisfaction						
Median	9	9	9	8	9	9
Mode	10	10	10	8	9	10

Values regarding to nausea or vomiting are number. Values regarding to satisfaction are the satisfaction score. No significant difference was found

weight. Mann-Whitney U-test was used for age, duration of operation, degree of pain, sedation, nausea or vomiting, satisfaction and meperidine consumption. Wilcoxon Sign Rank Test was used to compare the result at 6,12 and 24 hours with in the same group. Numerical data were analyzed using chi-square or Fisher's exact test, as appropriate. A value of $P < 0.05$ was considered statistically significant.

Results

No patient was excluded due to receiving general anesthesia. There were no significant differences between the groups with respect to demographics and intraoperative data (Table 1). There was a statistical difference of pain score at 24 h ($p = 0.01$) with a higher pain score in the tramadol group (Figure 1). There were 4 and 13 patients who received postoperative meperidine in parecoxib and tramadol groups respectively ($p = 0.016$). The mean rescued doses of meperidine were 4.6 ± 10.9 mg in the parecoxib group and 18.6 ± 21.0 mg in the tramadol group ($p = 0.005$). There was a significantly higher sedation score at 6 h of the tramadol group, but no difference in the other times (Table 2). No statistical significance of nausea or vomiting and satisfaction scores was found at any time (Table 3).

Discussion

The multimodal-analgesia concept is a combination of opioid and non-opioid analgesia drugs in order to provide better analgesia and fewer side effect of opioids. Recently, COX-2 inhibitors-parecoxib has been proved for its good postoperative pain control in various operations such as laparoscopic cholecystectomy, total hip arthroplasty, total knee arthroplasty and total abdominal hysterectomy[7,10-12]. Thus, parecoxib could possibly be used as the first line drug in such a low-to-medium degree of post-appendectomy pain. Tramadol has been proved as an efficient adjuvant for postoperative pain control in adenotonsillectomy and arthroscopic knee surgery[13-15]. Consequently, it is possible that its analgesic property could be sufficient for control post-appendectomy pain. Since tramadol has the action duration as long as, and has some opioid-sparing effect as parecoxib. Besides, there has not ever been a comparison between these two drugs. Thus, it is reasonable to reveal and compare their analgesic effects.

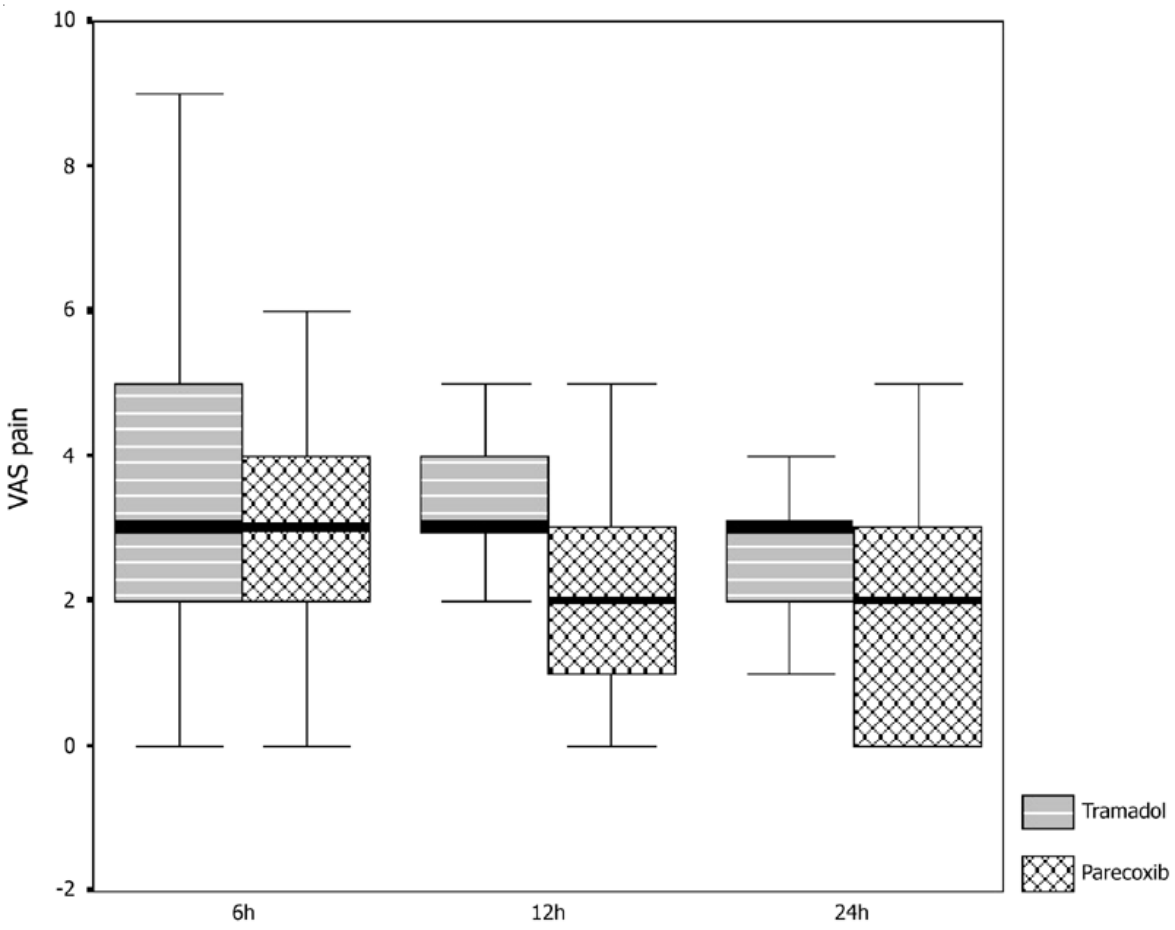

Fig. 1 Pain scores at 6, 12, 24 h in parecoxib and tramado groups. Tramadol group had a significant higher pain score only at 24 h than parecoxib group ($p < 0.05$)*

The present study demonstrated that parecoxib 40 mg IV twice per day provided a better pain control than tramadol 50 mg IV twice per day. As a higher in numbers who requested meperidine and the total comsumption was found in the tramadol group. Remarkably, despite the higher consumption of meperidine, the pain score at 24 h remained significantly higher than that of the parecoxib group. These might be explained by the advantageous mechanism of COX-2 inhibitors over tramadol, which has suppression peripheral sensitization[2,7]. The higher sedation score at 6 h in the tramadol group was possibly caused by the higher rescue doses of meperidine. Surprisingly, nausea or vomiting showed no statistical difference despite the opioid agonist of tramadol. It could explain that the sample size was not enough for differentiation of these side effects. High scores of satisfaction were found in both groups probably due to sufficiency of pain control and avoidance of nausea or vomiting. For safety issue, the present study was not designed to monitor side effects of parecoxib. Because many studies have clearly indicated the safety of GI, platelet disturbance and kidney[4,16,17]. Spinal anesthesia is a technique of preemptive analgesia, thus, it might concern a different result if general anesthesia was applied.

Parecoxib provided a lower pain score, sedation and lesser meperidine consumption than tramadol in open appendectomy undergoing spinal anesthesia.

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การเปรียบเทียบผลระงับความปวดระหว่างยา parecoxib และ tramadol ภายหลังการผ่าตัดไส้ติ่งอักเสบ

วัชริน สินธวานนท์, ปกรณ์ อุรุโสภณ, ปิ่น ศรีประจิตติชัย, ตุลชัย อินทรัมพรรย์

***บทนำ**: การระงับปวดภายหลังผ่าตัด นิยมใช้ยากลุ่ม opioid ผลข้างเคียงที่พบได้บ่อยจากยากลุ่มนี้ ได้แก่ อาการคลื่นไส้อาเจียน เนื่องจากความรุนแรงของอาการปวดไม่มาก ภายหลังการผ่าตัดไส้ติ่งอักเสบที่ไม่ซับซ้อน การหลีกเลี่ยงยากลุ่ม opioid สำหรับระงับความปวดภายหลังผ่าตัดชนิดนี้ จึงมีความเป็นไปได้*

***วัตถุประสงค์**: เพื่อศึกษาเปรียบเทียบผลการระงับความปวดภายหลังการผ่าตัดไส้ติ่งอักเสบ ระหว่างยา parecoxib และยา tramadol*

***วัสดุและวิธีการ**: เป็นการศึกษาในผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นไส้ติ่งอักเสบแบบเฉียบพลัน มีการสุ่มตัวอย่างเป็นสองกลุ่ม ได้แก่ กลุ่มที่ได้รับ parecoxib ขนาด 40 มก. และ กลุ่มที่ได้รับ tramadol ขนาด 50 มก. โดยให้ยา parecoxib หรือยา tramadol สองครั้ง คือ ครั้งที่หนึ่งให้ขณะเริ่มปิด peritoneum และครั้งที่สอง ให้ภายหลังให้ยาครั้งแรก 12 ชั่วโมง ผู้ป่วยทุกรายได้รับการฉีดยาชาเข้าช่องไขสันหลัง บันทึกจำนวนยา meperidine, คะแนนความปวด, คะแนนความง่วงซึม, คะแนนการคลื่นไส้อาเจียน และคะแนนความพึงพอใจ ที่ 6, 12 และ 24 ชั่วโมงภายหลังผ่าตัดเสร็จ*

***ผลการศึกษา**: จำนวนยา meperidine เฉลี่ยที่กลุ่ม parecoxib และ กลุ่ม tramadol ได้รับใน 24 ชั่วโมง คือ 4.6 $\pm$ 10.9 และ 18.6 $\pm$ 21.0 มก.ตามลำดับ ($p = 0.005$) คะแนนความปวดที่ 24 ชั่วโมง ($p = 0.01$) และคะแนนความง่วงซึมที่ 6 ชั่วโมง ($p = 0.003$) ของกลุ่ม tramadol สูงกว่ากลุ่ม parecoxib อย่างมีนัยสำคัญทางสถิติ*

***สรุป**: ยา parecoxib ระงับความปวดได้ดีกว่ายา tramadol ภายหลังการผ่าตัดไส้ติ่งอักเสบ ภายใต้การระงับความรู้สึกโดยการฉีดยาชาทางช่องไขสันหลัง*