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Comparison of the Effects of Parecoxib and Diclofenac in Preemptive Analgesia: A Prospective, Randomized, Assessor-Blind, Single-Dose, Parallel-Group Study in Patients Undergoing Elective General Surgery

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ABSTRACT

Background: Preoperative administration of analgesics may prevent or reduce hyperalgesia, inhibit inflammation, and reduce pain by reducing the synthesis of prostaglandins in response to tissue damage caused by surgery. Nonsteroidal anti-inflammatory drugs (NSAIDs) are a potent, widely used class of analgesic agents; however, they may not be as effective as selective cyclooxygenase (COX)-2 inhibitors.

Objective: The aim of this study was to compare the efficacy and tolerability of the COX-2 inhibitor parecoxib sodium and the NSAID diclofenac sodium as preemptive analgesics in patients undergoing elective general surgery.

Methods: This was a prospective, randomized, assessor-blind, single-dose, parallel-group, comparative trial. Patients aged 18 to 65 years undergoing elective general surgery were enrolled. A single IM injection of parecoxib 40 mg or diclofenac 75 mg was administered 30 to 45 minutes before the induction of anesthesia. Surgery was performed as per standard protocol. The primary measures of efficacy were pain intensity score (measured on a visual analog scale [VAS]), pain relief score, duration of analgesia, and platelet aggregation response to adenosine diphosphate. Tolerability assessment included monitoring of treatment-emergent adverse events (AEs), physical examination, laboratory analysis, electrocardiography, and chest radiography.

Results: Eighty patients (56 men, 24 women; mean [SD] age, 45.96 [12.83] years) were enrolled in the study (40 patients per treatment group). All patients completed the trial. No pain was reported by any patient in the parecoxib group up to 12 hours; in the diclofenac group, no pain was reported up to 6 hours. At

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12 hours, the mean (SD) VAS score was 2.33 (1.39) (moderate pain) in the diclofenac group and 0 (no pain) in the parecoxib group ($P < 0.05$). At 12 hours, total pain relief was reported by all 40 patients (100.0%) in the parecoxib group but by none (0.0%) in the diclofenac group, and 2 patients in the diclofenac group (5.0%) reported good pain relief (between-group difference for total + good pain relief, $P < 0.05$). Mean (SD) duration of analgesia was significantly longer in the parecoxib group than in the diclofenac group (19.48 [5.61] hours vs 8.32 [4.11] hours; $P < 0.05$). Platelet aggregation was significantly inhibited in the diclofenac group (change from baseline, 64.0%) but not in the parecoxib group (change from baseline, 12.0%) ($P < 0.05$). Both regimens were well tolerated, and no AEs were reported.

Conclusions: In this study of patients undergoing elective general surgery, patients treated with the COX-2 specific inhibitor parecoxib experienced no pain at 12 hours, and the treatment was well tolerated. The results of this study suggest that good postoperative analgesia and minimal interference with platelet function may make parecoxib an alternative to the nonselective NSAID diclofenac in providing preemptive analgesia in patients undergoing general surgery. (*Curr Ther Res Clin Exp.* 2004;65:383–397)

Key words: preemptive analgesia, parecoxib, valdecoxib, diclofenac, general surgery.

INTRODUCTION

Preoperative administration of analgesics may prevent or reduce hyperalgesia, inhibit inflammation, and reduce pain by reducing the synthesis of prostaglandins in response to tissue damage caused by surgery.[1] Nonsteroidal anti-inflammatory drugs (NSAIDs) are a potent, widely used class of analgesic agents. The mechanism of their anti-inflammatory and analgesic actions is the inhibition cyclooxygenase (COX) activity, the rate-limiting step in prostaglandin synthesis.[2] However, oral administration of postoperative analgesics has limitations. Some surgical patients are unable to tolerate oral medications, and oral administration is associated with a slower onset of action than parenteral administration.[3] Moreover, conventional NSAIDs are all nonselective for COX-1 and COX-2 in that they inhibit both enzymes to a considerable degree at therapeutic doses. Thus, the therapeutic effectiveness of conventional NSAIDs is a consequence of their COX-2 inhibition, and their toxicity is linked to their capacity to inhibit COX-1.[4–7] In addition, conventional NSAIDs are associated with undesirable adverse events (AEs; eg, upper gastrointestinal [GI] ulceration and bleeding) because they inhibit gastric mucosal COX-1. COX-1 inhibition also prevents the production of thromboxane A_2, which reduces platelet aggregation and thereby prolongs bleeding time.

Although many orally administered NSAIDs are available, the choice of injectable NSAIDs is limited for patients who need rapid-onset analgesia or who are unable to consume or tolerate orally administered drugs for 1 or more reasons, including surgical procedures (during which patients are not to ingest anything until ≥6 hours after surgery).[8] In India, only 2 parenterally administered NSAIDs are available: ketorolac and diclofenac sodium. Ketorolac, like other conventional NSAIDs, is associated with a high incidence of AEs, including impairment of platelet function and operative-site and GI bleeding.[6,9,10] Case reports of deaths due to operative-site and GI bleeding have led to the discontinuation of ketorolac use in some countries and to limitation of its use to ≤5 days in the United States.[11] Thus, ketorolac is no longer a drug of choice for preemptive analgesia.

Diclofenac, the most commonly prescribed NSAID worldwide, is effective for the treatment of acute pain, as well as the signs and symptoms associated with the chronic, painful conditions osteoarthritis and rheumatoid arthritis.[12] For postoperative analgesia, diclofenac is administered at a dosage of 50 to 75 mg, IM or IV, BID or TID.[12] However, the limitation of IV diclofenac is that the solution needs to be buffered before administration. The bioavailability of diclofenac 75 mg administered IM has been shown to be 100%.[13] Preoperative IM administration of diclofenac has been shown to be effective in reducing postoperative pain and the need for supplemental analgesics after laparoscopic cholecystectomy.[14,15] Some studies have reported massive hemolysis[16] and fatal necrotizing fasciitis[17,18] with IM diclofenac, although it was found to be well tolerated in other studies.[14,15] Diclofenac has also been shown to be associated with GI bleeding, ulceration, and perforation, and it can inhibit platelet aggregation, thereby prolonging bleeding time[18–22] after multiple doses (although GI bleeding, ulceration, and perforation rarely occur with single doses[23]). Increased incidences of postsurgical wound drainage, hematoma, and bruising have been reported with diclofenac.[22] Spontaneous bleeding and hematomas after short- and long-term diclofenac therapy have also been reported.[24,25] Many patients are at risk for these AEs in the perioperative period due to enforced starvation (ie, no food or beverages allowed before or during surgery), dehydration, and tissue damage. Hence, diclofenac does not appear to be an ideal agent for use in preemptive analgesia in surgical patients.

Thus, there is a need for a preemptive analgesic agent that is not only efficacious but also devoid of the AEs generally associated with nonselective NSAIDs (eg, ketorolac, diclofenac). Parecoxib sodium is an amide prodrug of valdecoxib, a novel oral COX-2 specific inhibitor. It is the first injectable, highly specific COX-2 inhibitor for the management of pain.[26] In single IV doses, parecoxib has been shown to exhibit linear pharmacokinetic properties up to 100 mg, to be well tolerated, and to have a rapid onset of analgesia.[26] The clinical efficacy of postoperative doses of parecoxib 20 and 40 mg IM and IV in providing analgesia after gynecologic and orthopedic surgery has been well documented in randomized, controlled clinical studies.[27,28] In a previous study,[23] we found that a single 40-mg dose of parecoxib provided greater overall analgesic

efficacy over 12 hours, a more rapid onset of analgesia, and a longer duration of effect than a single 75-mg dose of diclofenac in patients with moderate to severe pain associated with general or orthopedic surgery. We also found that compared with diclofenac 75 mg BID, a single dose of parecoxib provided greater overall analgesic efficacy over 24 hours. Moreover, the route of administration of parecoxib had no significant effect on the mean pain intensity difference, pain relief score, time to onset of action, or duration of analgesia.[23]

The role of parecoxib in preemptive analgesia has been examined by various investigators. The administration of parecoxib before oral surgery has been found to be effective and well tolerated.[29] Joshi et al[30] observed that preoperative parecoxib was a valuable opioid-sparing adjunct to the standard of care for treating pain after laparoscopic cholecystectomy and that subsequent treatment with oral valdecoxib extended the clinical benefit. In addition, we[31] found that a single preoperative dose of parecoxib was more efficacious in providing postoperative pain relief as measured using the visual analog scale (VAS) and onset of analgesia than a postoperative dose in providing analgesia in the postoperative period in patients undergoing general surgery.

However, according to a MEDLINE search (key terms: *parecoxib, valdecoxib, preemptive analgesia,* and *general surgery*; years: 1970–2004), no studies have compared the effects of preemptive doses of parecoxib with those of diclofenac in providing pain relief in the postoperative period. Therefore, the present study was undertaken to compare the efficacy and tolerability of a single preoperative dose of parecoxib or diclofenac in patients undergoing elective general surgery.

PATIENTS AND METHODS

Study Design

This prospective, single-center, randomized, assessor-blind, single-dose, parallel-group comparative study was conducted at the Department of Surgery, Sir JJ Group of Hospitals, Mumbai, India. Study protocols were reviewed and approved by the institutional review board at the Sir JJ Group of Hospitals. The study was conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki and its amendments.

Inclusion/Exclusion Criteria

Male and female patients aged 18 to 65 years requiring elective ambulatory surgery (eg, hernioplasty, appendectomy, cholecystectomy) were initially screened for enrollment in the study. Patients were assessed for eligibility within 14 days before undergoing surgery; provided a full medical history; and underwent a complete physical examination, including vital sign measurements and laboratory analysis (including hematology, serum biochemistry, and urinalysis).

Patients were excluded from the study if their surgical procedure was to last <30 minutes or >4 hours. Patients were also excluded if they had a history of

hypersensitivity to NSAIDs or COX-2 inhibitors; conditions predisposing them to GI dysfunction (eg, a history of peptic ulceration, upper GI disease, ulcerative colitis, smoking, concurrent administration of corticosteroids, alcohol abuse); or a history of bleeding tendencies, cirrhosis, or esophageal varices. Patients with a history of severe cardiac, hepatic, renal, or cerebrovascular disease; malignancy; chronic, uncontrolled systemic disease (eg, diabetes, hypertension, asthma, collagen disorders); or any other serious medical illness were excluded. Patients with a history of hematologic abnormalities, keloid formation, or abnormal scarring were ineligible. Pregnant (as determined by a positive serum pregnancy test) or breastfeeding female patients were excluded.

Written informed consent was obtained from each participant before study admission.

Treatment

On the day of surgery, eligible patients were randomized, in a 1:1 ratio using a computer-generated list of random numbers, to receive a single preoperative dose of either parecoxib 40 mg or diclofenac 75 mg. Both drugs were administered IM 30 to 45 minutes before the induction of anesthesia. All patients in the diclofenac group were administered a second dose of study drug 12 hours after the efficacy assessments were completed as per protocol, which was expected because the recommended dosing regimen for diclofenac is 75 mg BID or TID. Because the formulations were dissimilar in appearance, it was not possible to use a double-blind design. Instead, 1 physician administered the study medication, and another assessed efficacy and tolerability. Thus, the study was assessor blind.

Surgical Procedures

Patients received either local or general anesthesia, depending on the nature of the surgery. Patients who underwent similar surgical procedures received the same type of anesthesia. Anesthesia and surgery were performed according to standard protocols. The duration of surgery was limited to between 30 minutes and 4 hours to avoid confounding the primary end point, the median time to first use of rescue medication. Patients were required to remain in the study center during the entire 24-hour postsurgical assessment period.

Medications routinely used in surgical settings (eg, hypoglycemics, antihypertensives, drugs for the treatment of ischemic heart disease) were permitted to be administered perioperatively at the discretion of the investigator; however, the following medications were specifically prohibited: intrathecal opioids, systemic corticosteroids, analgesics, nerve or plexus blocks, succinylcholine chloride, NSAIDs, paracetamol, aspirin, warfarin and other drugs affecting platelet function within 12 hours of dosing with the study medication, sedating antiemetics, topical peritoneal anesthetics, antipsychotics, and antiepileptics. If pain was unbearable, the permitted rescue analgesic (ketorolac 60 mg IM) was administered after the assessment at 12 hours. Although having patients wait 12 hours for rescue medication may seem unduly harsh, it was done to avoid

variation in the assessment of efficacy. The details of rescue-medication use were recorded on case-report forms.

Efficacy Assessments

As mentioned previously, the primary end point was the time to use of rescue medication; the primary efficacy outcome measures were pain intensity and pain relief scores, duration of analgesia, and platelet aggregation responses to adenosine diphosphate (ADP).

Pain intensity was rated by patients 30 minutes after surgical closure (baseline), and 15 and 30 minutes and 1, 2, 4, 6, 8, 10, 12, and 24 hours after study drug administration on a 10-cm VAS (0 = no pain to 10 = worst pain imaginable or excruciating pain). The same person administered the VAS to all patients.

Pain relief was assessed by patients at baseline and 12 and 24 hours after study drug administration on a 4-point scale (0 = no relief; 1 = mild or some relief; 2 = good relief; and 3 = excellent or total relief). Patients' pretreatment values were used for all posttreatment comparisons. Patients were to remain seated for 10 minutes before all pain assessments.

The duration of analgesia was measured by recording the time to return of pain after the patient reported being pain-free after receiving study medication.

To measure platelet aggregation, 9-mL blood samples were drawn 30 minutes before and 1 hour after study drug administration, using a 19-G sterile needle and siliconized glass syringes into vacuum tubes containing 3.8% sodium citrate, with a final citrate:blood volume ratio of 1:9. A layer of platelet-rich plasma (PRP) was prepared by centrifuging the blood sample at 900 rpm at room temperature for 10 minutes and then removing the PRP layer. The remaining blood sample was centrifuged for an additional 10 minutes at 3000 rpm at room temperature, and the liquid layer (platelet-poor plasma [PPP]) was removed. Platelet aggregation response to ADP was assessed according to the light transmission method of Born,[32] using a single-channel optical aggregometer (Payton Associates, Scarborough, Ontario, Canada). The aggregometer was calibrated for maximum light transmission using 1.0-mL samples of the PPP from each participant at each time point. The PRP (0.9 mL) was then placed in the aggregometer at 37°C for 3 minutes; 0.1 mL of the aggregating agonist (ADP) was then added to the PRP. The degree of platelet aggregation was measured as a change in optical density recorded as a percentage of the difference in optical density between PRP and PPP achieved within 5 minutes of the addition of ADP.

Tolerability Assessments

Tolerability was assessed using monitoring of treatment-emergent AEs, physical examination (including vital sign measurements), laboratory analysis (including hematology, serum biochemistry, and urinalysis), electrocardiography, and chest radiography at baseline and 24 hours after surgery. The risk for postoperative bleeding with the study drugs was determined by assessing the degree of inhibition of platelet aggregation. Comparisons of safety results between the

treatment groups included all patients who took ≥1 dose of the study medication and consisted primarily of incidences of AEs, withdrawals attributable to AEs, and serious AEs.

Statistical Analysis

The sample size calculation was based on the time to second dosing of study medication or use of rescue medication. It was determined that 40 patients per group would be sufficient to detect (with 80% power and a type I error at $\alpha = 0.05$ for 2 comparisons) a difference of ≥3 hours in the median time to second dosing of study medication or use of rescue medication. All efficacy analyses were performed in the randomized patients who took the dose of the study medications 30 to 45 minutes before surgery and whose surgery was completed within the required time limit. Baseline demographic data, vital sign measurements, biochemistry, and duration of analgesia were analyzed using the Student *t* test; surgical data, pain relief scores, and AEs were analyzed using the chi-square test. Pain intensity scores were analyzed using the Mann-Whitney *U* test. SPSS version 10.2 (SPSS Inc., Chicago, Illinois) was used in the statistical analysis.

RESULTS

Of the 90 patients who were screened for the study, 80 patients (56 men, 24 women; mean [SD] age, 45.96 [12.83] years) met the inclusion criteria and were enrolled in the study. There were 40 patients in each treatment group. Because all of the patients completed the study, the data for all 80 patients were included in both the efficacy and tolerability analyses.

Baseline Data

The treatment groups were statistically comparable with respect to demographic characteristics (**Table I**), vital sign measurements (**Table II**), and surgical data (**Table III**).

In the parecoxib group, 24 patients (60.0%) received spinal anesthesia and the remaining 16 (40.0%) received general anesthesia. In the diclofenac group, 26 patients (65.0%) received spinal anesthesia and 14 (35.0%) received general anesthesia. Thus, the 2 treatment groups were statistically comparable with respect to the type of anesthesia received.

Medications other than study medications consumed included oral hypoglycemic agents in 6 diabetic patients (3 [7.5%] in each group), antihypertensive agents in 11 hypertensive patients (5 [12.5%] in the parecoxib group and 6 [15.0%] in the diclofenac group), and treatment for ischemic heart disease in 3 patients (2 [5.0%] in the parecoxib group and 1 [2.5%] in the diclofenac group).

Pain Intensity

No pain was reported by any patient in the parecoxib group up to 12 hours (ie, pain intensity scores = 0), whereas in the diclofenac group no pain was

Table I. Baseline characteristics of study patients undergoing preemptive analgesia (N = 80).*

Variable	Parecoxib 40 mg (n = 40)	Diclofenac 75 mg (n = 40)
Age,† mean (SD), y	46.39 (11.26)	45.52 (13.26)
Height,† mean (SD), cm	164.53 (4.91)	165.44 (4.39)
Body weight,† mean (SD), kg	57.32 (9.08)	58.32 (10.01)
Sex,‡ no. (%)		
Male	27 (67.5)	29 (72.5)
Female	13 (32.5)	11 (27.5)
Anesthesia type,† no. (%)		
Spinal	24 (60.0)	26 (65.0)
General	16 (40.0)	14 (35.0)

*No significant between-group differences were found.
†Analysis by Student *t* test.
‡Analysis by chi-square test.

reported by any patient up to 6 hours. At 10 and 12 hours, the mean (SD) pain intensity scores were significantly higher in the diclofenac group than in the parecoxib group (1.32 [1.06] at 10 hours and 2.33 [1.39] at 12 hours vs 0 at baseline; both, $P < 0.05$) (**Figure 1**). At the end of 24 hours, mean (SD) pain intensity scores remained significantly lower in the parecoxib group (1.05 [1.36]) compared with the diclofenac group (3.98 [2.12]) ($P < 0.05$).

Pain Relief

Twelve hours after treatment, all 40 patients in the parecoxib group (100.0%) reported total pain relief; in the diclofenac group, none of the patients (0.0%) reported total pain relief, and 2 patients (5.0%) reported good relief of pain (between-group difference for total + good pain relief, $P < 0.05$). At the end of 24 hours, 30 patients in the parecoxib group (75.0%) reported good or total

Table II. Profile of vital parameters at baseline.* (Values are expressed as mean [SD].)

Variable	Parecoxib 40 mg (n = 40)	Diclofenac 75 mg (n = 40)
Body temperature, °F	97.88 (0.36)	98.06 (0.23)
Respiratory rate, breaths/min	16.32 (2.99)	17.14 (3.20)
Blood pressure, mm Hg		
Systolic	127.53 (7.23)	128.42 (7.36)
Diastolic	80.40 (7.01)	79.80 (6.99)

*No significant between-group differences were found (Student *t* test).

Table III. Number (%) of patients undergoing different types of surgery.*

Surgery	Parecoxib 40 mg (n = 40)	Diclofenac 75 mg (n = 40)
Hernioplasty	8 (20.0)	7 (17.5)
Appendectomy	6 (15.0)	8 (20.0)
Diagnostic laparoscopy	3 (7.5)	3 (7.5)
Hydrocele	3 (7.5)	2 (5.0)
Leg skin grafting	3 (7.5)	2 (5.0)
Gastrectomy	3 (7.5)	2 (5.0)
Retrovaginal fistula repair	2 (5.0)	3 (7.5)
Hemithyroidectomy	2 (5.0)	1 (2.5)
Orchidectomy	2 (5.0)	1 (2.5)
Splenectomy	2 (5.0)	1 (2.5)
Other†	6 (15.0)	10 (25.0)

*No significant between-group differences were found (chi-square test).
†Includes nephrectomy, amputation, hepatic cyst excision, and cholecystectomy.

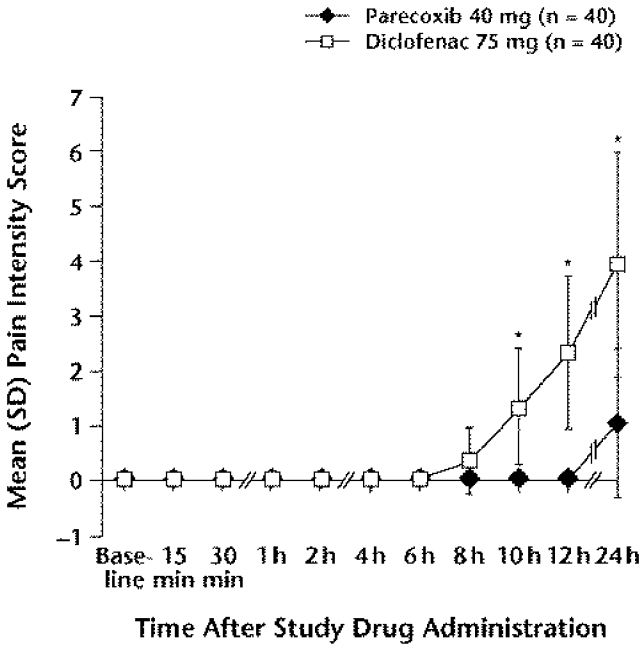

Figure 1. Mean pain intensity scores after administration of parecoxib or diclofenac. Scale: 0 = no pain to 10 = worst pain imaginable or excruciating pain. *$P < 0.05$ vs parecoxib group.

relief, compared with 15 patients in the diclofenac group (37.5%) ($P < 0.05$) (**Figure 2**).

Duration of Analgesia

Patients in the parecoxib group had a significantly longer mean (SD) duration of analgesia (19.48 [5.61] hours) compared with diclofenac-treated patients (8.32 [4.11] hours) ($P < 0.05$). None of the patients in either group received any rescue analgesics during the study period. However, all of the patients in the diclofenac group were administered the second dose of the drug 12 hours after the efficacy assessments were completed.

Platelet Aggregation

At baseline, the mean platelet aggregation responses to ADP were comparable in the 2 treatment groups. **Figure 3** shows the mean percentages of platelet aggregation induced by ADP in the 2 groups at baseline and at 1 hour postdose. Platelet aggregation was significantly inhibited in the diclofenac group (change from baseline, 64.0%; $P < 0.05$) but not in the parecoxib group (change from baseline, 12.0%). The reduction from baseline in platelet aggregation was significantly larger in the diclofenac group compared with the parecoxib group ($P < 0.05$) (**Figure 3**).

Safety Profile

Both drugs were well tolerated, and none of the patients in either study group reported any treatment-emergent AEs. Hematology, serum biochemistry, urinalysis, electrocardiography, chest radiography, and vital sign measurements were unremarkable in both groups at baseline and at 24 hours. No drug interactions were reported between the study drugs and the anesthetic agents used.

DISCUSSION

Preemptive analgesia works to prevent the process of central neuroplasticity due to surgical nociception and the resultant hyperalgesic state, thereby ensuring a more positive overall surgical experience.[33] In the present study, preoperative parecoxib 40 mg IM was effective in reducing or eliminating postoperative pain after general surgery. A single dose of parecoxib was associated with decreased pain intensity, significantly more patients with pain relief, and a longer duration of analgesia. Thus, the overall interpretation of the results indicates the effectiveness of preemptive analgesia with parecoxib for the management of postoperative pain. Other studies[29,31] have demonstrated the efficacy of preoperative doses of parecoxib in the management of postoperative pain after oral and general surgical procedures. In 1 study,[30] a group receiving a preoperative dose of parecoxib followed by oral valdecoxib had higher scores on a postoperative pain-relief VAS than a group receiving placebo ($P < 0.05$), and parecoxib was shown to have opioid-sparing effects in patients undergoing

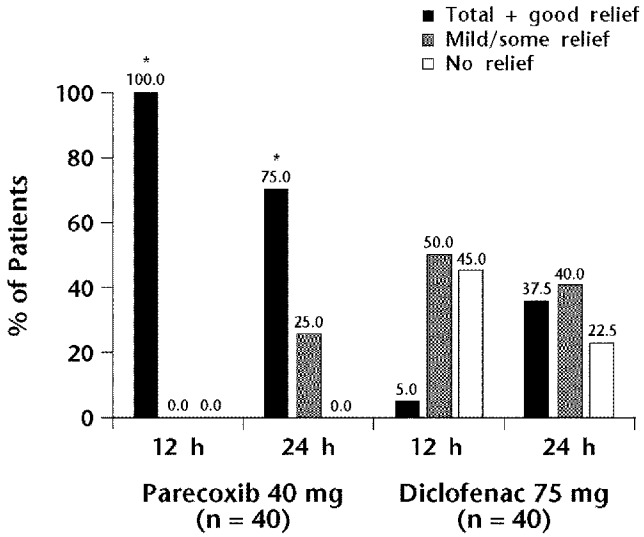

Figure 2. Pain relief in the parecoxib and diclofenac groups 12 and 24 hours after therapy. *$P < 0.05$ versus diclofenac (chi-square test).

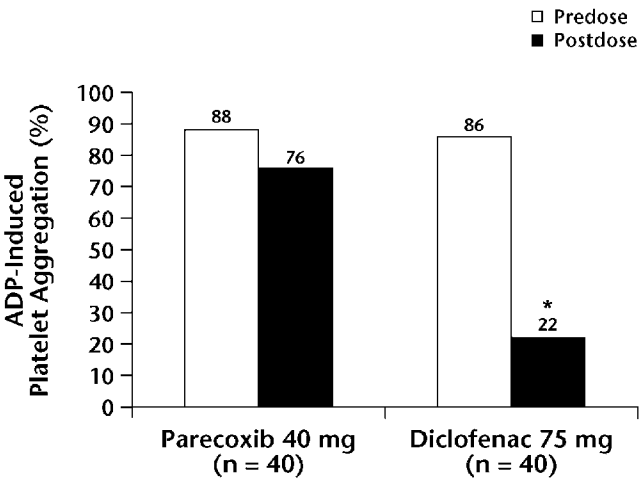

Figure 3. Effect of parecoxib and diclofenac on platelet aggregation in the perioperative period (1 hour after study drug administration). ADP = adenosine diphosphate. *$P < 0.05$ versus predose and parecoxib.

laparoscopic cholecystectomy. Furthermore, a group receiving parecoxib administered postoperatively had higher scores on a pain-relief VAS compared with a group receiving postoperative doses of diclofenac ($P < 0.05$).[23] However, according to our literature search, no studies have compared the preemptive analgesic efficacy of parecoxib and diclofenac. The results of the present study suggest that a single IM dose of parecoxib may be more suitable for preemptive analgesia than diclofenac.

Although rescue medication was permitted if the pain was unbearable 12 hours after study drug administration, none of the patients in either treatment group required rescue analgesia.

In the present study, we also compared the effects of parecoxib with those of the conventional NSAID diclofenac on platelet aggregation. The results were in accordance with the mechanism of COX-2 specific inhibition of the active moiety valdecoxib formed in vivo by the hydrolysis of the prodrug parecoxib. In contrast, the nonselective COX inhibitor diclofenac predictably and significantly decreased platelet aggregation ($P < 0.05$), even with a single dose. Noveck et al[3] reported that parecoxib BID had little or no effect on ADP-induced platelet aggregation or on aggregation induced by arachidonic acid and collagen compared with ketorolac. Those investigators concluded that the absence of effect on platelet aggregation and bleeding time observed in their study suggested that parecoxib was less likely to be associated with excessive bleeding during surgery and was therefore a potentially safer option than ketorolac for use in patients undergoing surgery, irrespective of age.

Like ketorolac, diclofenac is associated with decreased platelet function and increased bleeding time,[14–22] resulting in excessive blood loss. Increased bleeding may also exacerbate the severity of NSAID-induced gastric ulceration and hemorrhage.[18,34]

In addition, patients already at risk for postoperative bleeding due to use of antiplatelet or anticoagulant therapies for cardiovascular disease are at even higher risk for bleeding after therapy with conventional NSAIDs (eg, diclofenac).[3] The absence of an effect on platelet aggregation observed in the present study indicates that parecoxib is less likely to be associated with excessive bleeding during and after surgery and may therefore be a potentially safer option in preemptive analgesia compared with diclofenac. The association of diclofenac with the inhibition of platelet aggregation suggests that the drug might cause bleeding, potentially making it less suitable than parecoxib for preemptive analgesia in patients undergoing surgery in which impairment of platelet function is undesirable. In addition to providing more effective anti-inflammatory and analgesic action without compromising platelet function, parecoxib provided the significant clinical advantage of preoperative single-dose administration over the conventional NSAID diclofenac, which is commonly administered at the end of the surgical procedures rather than preoperatively to overcome its shorter duration of action and greater risk for bleeding complications.

CONCLUSIONS

In this study of patients undergoing elective general surgery, patients treated with the COX-2 specific inhibitor parecoxib experienced no pain at 12 hours, and the treatment was well tolerated. The results of this study suggest that good postoperative analgesia and minimal interference with platelet function may make parecoxib an alternative to the nonselective NSAID diclofenac in providing preemptive analgesia in patients undergoing general surgery.

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