Pain Medicine
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A Multiple-Day Regimen of Parecoxib Sodium 20 mg Twice Daily Provides Pain Relief After Total Hip Arthroplasty.

Eugene R. Viscusi, MD*
Joseph S. Gimbel, MD†
Andreas M. Halder, MD, PhD‡
Michael Snabes, MD, PhD§
Mark T. Brown, MD_
Kenneth M. Verburg, PhD

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Parecoxib sodium (parecoxib), an injectable cyclooxygenase-2 (COX-2) selective inhibitor, is the prodrug of valdecoxib. Parecoxib has been shown to provide rapid and prolonged analgesia after surgery. 1–3 Following hip or knee arthroplasty, a single dose of parecoxib 40 mg produced onset of analgesia within 11 min.[3,4] In addition, the median duration pf analgesia (based on the need for rescue medication) was approximately 6 to 8 h. The elimination half-life pf valdecoxib, the active moiety of parecoxib, is approximately 5 to 10 h. The majority of patients undergoing major orthopedic surgery have pain requiring treatment with analgesics for several days after surgery. To further characterize the optimal dosing regimen of parecoxib, the primary objective of our study was to assess the analgesic efficacy of two dosing regimens pf parecoxib compared with placebo when administered to patients for 3 to 5 days after total hip arthroplasty (THA).

To further characterize the optimal dosing regimen of parecoxib, the primary objective of our study was to assess the analgesic efficacy of two dosing regimens pf parecoxib compared with placebo when administered to patients for 3 to 5 days after total hip arthroplasty (THA). Previous studies showed that an initial 40-mg
parecoxib dose was consistently the most effective single or initial dose, and that parecoxib 20 mg bid was the optimum daily dose. [3,4,7] The secondary objectives of the trial were to evaluate general safety, effect on health outcome measures and effect on opioidrelated symptoms.

This was multicenter, multiple-dose, randomized, double-blind, parallelgroup study compared the analgesic efficacy and safety of two dosing regimens pf parecoxib sodium (parecoxib) versus placebo after total hip arthroplasty. METHODS: On study Day 1, 490 patients received a postoperative initial loading dose of IV parecoxib 40 mg, followed by a re-dose of parecoxib 20 mg in 484 of 490 patients. There were no statistically significant differences among the treatment groups with respect to patient demographic and baseline characteristics. Subsequently, 479 randomized patients received double-blind treatment with parecoxib 20 mg bid (*n* _ 159), parecoxib 20 mg qd (*n* _ 159) followed by placebo, or placebo (*n* _ 161) on Day 2.

RESULTS: Patients treated with parecoxib 20 mg bid reported significantly lower summed pain intensity over 24 h (SPI-24) scores and improved patients' global evaluation of study medication (PGESM) ratings compared with placebo-treated patients on Days 2 to 5 (*P* _ 0.05). For patients treated with parecoxib 20 mg qd, SPI-24 scores were significantly lower on Days 3 and 4 (*P* _ 0.05), and PGESM
ratings significantly improved on Day 5 compared with placebo. The incidence pf adverse events was similar in all treatment groups with the exception of fever, vomiting and impaired concentration, which were significantly more common in the placebo group compared with one or other of the parecoxib treatment groups
(*P* _ 0.05).

CONCLUSION: The primary measures of efficacy, the SPI-24 categorical scale and PGESM on Days 2 and 3, showed that parecoxib was effective and well tolerated in the postsurgical treatment of THA. Patients receiving parecoxib 20 mg bid reported significantly less pain. The results of this study also indicate that multiple-day treatment with the parenteral COX-2 selective inhibitor parecoxib can reduce postoperative acute pain to a clinically meaningful extent in patients undergoing THA. Treatment with parecoxib 20 mg bid, and to a somewhat lesser extent parecoxib 20 mg qd, significantly reduced pain over 4 days of treatment compared with placebo, as well as modestly reducing the need for rescue medication. The improved management of pain in these patients was achieved without increasing the occurrence or postoperative burden of adverse events. Thus, on balance, the bid parecoxib 20-mg regimen provided a more consistent level of efficacy than 20 mg once daily. Neither parecoxib regimen provided consistently measurable effects on health outcome measures or on opioid-related symptoms in our study; however, modest benefits that were evident occurred largely in patients treated with parecoxib 20 mg bid. Taken together, the results of our study support the use of parecoxib as part of a multimodal analgesic plan in managing acute postsurgical pain over several days.[12,13] Based on our experience across a number of postsurgical settings, the total amount of supplemental and rescue opioid medication taken by PCA, injection, or oral administration and converted to morphine equivalents was low across all treatment groups. This may have contributed to the inability to detect reductions in opioid requirements and accompanying improvement in tolerability. As a result of low opioid use, there were no significant differences between the parecoxib and placebo groups, which contrasts with other trials designed to examine the opioid-sparing effect of parecoxib in the THA and total knee arthroplasty surgical setting. [5,6] Parecoxib was well tolerated with no evidence pf increasing patient burden for adverse effects above standard of care alone. In conclusion, Multiple-day administration of parecoxib 20 mg once or twice daily is effective and generally well tolerated after total hip arthroplasty.

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Адреса редакції: 01054, м. Київ, вул. Воровського, 27. Тел.: (044) 331-95-06,
тел./факс (044) 200-01-17, e-maik: journal.uato@gmail.com
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