TITLE: Celecoxib for Post-Operative Pain Management: A Review of the Clinical Benefit and Harm

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CONTEXT AND POLICY ISSUES:

Among the emerging treatments for post-operative pain, selective COX-2 inhibitors such as celecoxib, rofecoxib, valdecoxib, and parecoxib were developed with the aim of decreasing gastrointestinal toxicity and bleeding associated with non-selective non-steroidal anti-inflammatory drugs (NSAIDs).

Concerns over cardiovascular safety, however, have evolved based on the mechanism underlying the cardiovascular side effects of COX-2 inhibitors. It is necessary to review the clinical-effectiveness and safety of celecoxib to determine if there is evidence for its use in pain management following surgery.

RESEARCH QUESTION:

What is the evidence for the clinical benefit and harm of celecoxib for post-operative pain management following arthroplasty, spinal surgery, or orthopedic surgery?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 3, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and July 2009. No filters were applied to limit the retrieval by study type. Articles by Dr. Scott S. Reuben were not included due to journal retractions.
SUMMARY OF FINDINGS:

The literature search identified three systematic reviews on coxibs for post-operative pain\(^3\)\(^-\)\(^5\) and two randomized controlled trials on celecoxib for pain management after arthroplasty.\(^6\)\(^,\)\(^7\)

The 2008 Cochrane review on single dose celecoxib for acute post-operative pain in adults\(^3\) included eight randomized controlled trials, of which seven were on patients with dental pain. Only one study (2001) enrolled patients with pain following orthopedic surgery, and therefore the overall conclusion of this systematic review is not relevant to this report.

The 2006 systematic review examined the efficacy and safety of COX-2 inhibitors in the management of peri-operative pain.\(^4\) This review included 30 prospective studies, among them only one trial was on celecoxib (the remaining trials are on other coxibs) which was authored by Reuben S (2000). The overall conclusion of this review was also considered not relevant for this report since 29 of the 30 included studies were not on celecoxib.

A 2005 systematic review of randomized studies on the effect of coxibs on post-operative outcomes\(^5\) included 22 trials, among them only one trial (2003) was on celecoxib for spinal surgery (the remaining trials are on other types of procedures). The overall conclusion of this review was again not relevant as the majority of the included studies were not pertinent to this report.

A randomized, double-blind, placebo-controlled trial in 2006, supported by Pfizer Pharmaceuticals,\(^6\) examined the efficacy of peri-operative celecoxib in patients undergoing ambulatory arthroscopic knee surgery. The study enrolled 200 patients, with 99 receiving celecoxib and 101 given placebo. Patients were randomized to a single dose of celecoxib 400 mg or placebo administered one hour pre-operatively followed by celecoxib 200 mg or placebo post-operatively for pain relief when required. In the 24 hours following surgery, total analgesic opioid consumption was lower in the celecoxib group (3.6 tablets) compared with the placebo group (4.6 tablets; \(p = 0.009\)). The percentage of celecoxib-treated patients (22%) who required opioid analgesia following surgery was lower than that of placebo-treated patients (41%; \(p = 0.008\)). The incidence of opioid-related adverse effects was higher in the placebo group (12%) than in the celecoxib group (3%). The authors concluded that peri-operative celecoxib is effective for arthroscopic knee surgery.

Another randomized, single-blind (observer-blind) controlled study in 2008, not supported by industry,\(^7\) included 80 patients undergoing total knee arthroplasty. The study group (40 patients) received a single dose of celecoxib 400 mg one hour before surgery and celecoxib 200 mg every 12 hours for five days, along with analgesic morphine. The control group (40 patients) received only analgesic morphine for post-operative pain management. Compared to the control group, the celecoxib group used 40% less morphine; the decrease in morphine use was statistically significant (\(p = 0.03\)). Pain as measured by resting visual analog scale (VAS) pain scores (0 indicating no pain and 10 indicating worst pain) significantly improved in the celecoxib group as compared to the control group (2.13 ± 1.68 versus 3.43 ± 1.50; \(p = 0.03\)). Post-operative nausea/vomiting occurred in 43% of patients in control group, and in 28% of patients in celecoxib group, but the difference was not statistically significant (\(p = 0.57\)). There were no significant differences in peri-operative blood loss and post-operative blood transfusions between the two groups. The authors concluded that celecoxib administered peri-operatively for patients undergoing total knee arthroplasty is safe and effective.
CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Although results from two randomized controlled trials demonstrated clinical efficacy of celecoxib in reducing post-operative pain following arthroplasty, no studies were identified comparing celecoxib to other NSAIDs. There were also no studies identified on the effect of celecoxib on pain following spinal surgery and orthopedic surgery. Because of the lack of systematic reviews on the topic, no overall conclusion can be drawn on the clinical efficacy and harm of celecoxib for post-operative pain management following arthroplasty, spinal surgery, or orthopedic surgery.

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