Coxibs were not cost-effective for arthritis pain in patients with average risk for ulcer complications

Spiegel BM, Targownik L, Dulai GS, Gralnek IM. **The cost-effectiveness of cyclooxygenase-2 selective inhibitors in the management of chronic arthritis.** Ann Intern Med. 2003;138:795-806.

QUESTION

In patients with osteoarthritis or rheumatoid arthritis, does the reduction in gastrointestinal (GI) complications seen with coxibs offset their increased cost compared with nonsteroidal anti-inflammatory drugs (NSAIDs)?

DESIGN

Cost–utility analysis using a decision analytic model from the perspective of a third-party payer considering direct medical costs.

SETTING

United States.

PATIENTS

A hypothetical cohort of patients 60 years of age with osteoarthritis or rheumatoid arthritis who were not taking aspirin and required NSAID therapy for moderate-to-severe arthritis pain.

INTERVENTION

Patients who entered the model were treated with a coxib (celecoxib, 200 mg once daily, or rofecoxib, 25 mg once daily) or a nonselective NSAID at the maximum dose approved by the U.S. Food and Drug Administration (naproxen, 500 mg twice daily). The model was designed to test the hypothesis that coxibs are cost-effective alternatives to NSAIDs.

MAIN COST AND OUTCOME MEASURES

A decision tree was constructed to represent the coxib and naproxen strategies. Clinical probability estimates were derived from a systematic review of the literature using MEDLINE and hand-searching 2 subspecialty journals (January 1985 to December 2002). Validated utilities were assigned for GI outcomes: 0.87 for severe dyspepsia, 0.91 for moderate dyspepsia, 0.49 for ulcer hemorrhage, and 0.46 for complicated ulcer requiring surgery. The main outcome was the incremental cost per quality-adjusted life-year (QALY) gained, expressed in 2002 U.S. dollars. All costs and outcomes were discounted at an annual rate of 3%. Explicit assumptions were made to bias the analysis in favor of the coxib strategy. Both deterministic and probabilistic sensitivity analyses were done.

MAIN RESULTS

In the base-case analysis, the coxib strategy had an incremental cost of $275 809 per additional QALY compared with the NSAID strategy. When a cohort of high-risk patients (previous ulcer hemorrhage) was evaluated, the incremental cost-effectiveness ratio decreased to $55 803 per QALY. Sensitivity analysis showed the model was sensitive to the cost per coxib pill, number of coxib pills consumed daily, cost per naproxen pill, and the probability of upper-GI complications with naproxen.

CONCLUSIONS

In average-risk patients with osteoarthritis or rheumatoid arthritis, the reduction in gastrointestinal complications seen with coxibs did not offset their increased costs compared with nonsteroidal antiinflammatory drugs. Coxibs were more cost-effective in patients at increased risk for gastrointestinal complications.

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COMMENTARY

Cyclooxygenase-2 specific inhibitors (coxibs) cause fewer symptomatic ulcers, GI complications, and upper GI symptoms, than nonselective NSAIDs. Although clinical and quality-of-life (QOL) outcomes are the primary focus of physicians and patients, limited resources mandate consideration of cost in management decisions.

Cost-effectiveness analyses assess expected costs per clinical outcome (or QOL-adjusted outcome). When a new drug is safer or more effective but more expensive than standard therapy, 3 possible situations may occur: 1) the drug is cost-saving because higher drug costs are outweighed by decreased medical costs because of better outcomes (e.g., fewer hospitalizations); 2) overall costs are increased but the extra cost is considered worth the benefit; or 3) the additional cost for an improved outcome is considered too expensive.

The meticulous analysis by Spiegel and colleagues indicates that the cost per QALY gained with coxibs is unacceptably high in average-risk patients. Use of QALYs is recommended in cost-effectiveness studies to allow comparisons across disparate interventions (e.g., is it better to invest in childhood vaccination or liver transplantation?). However, since QALYs relate to duration and decrement in QOL, they may undervalue serious nonfatal acute illnesses (e.g., hospitalization for ulcer bleeding was assigned only a 7-d QOL decrement in this analysis). The analysis also did not consider lower GI events, which may account for about 15% to 40% of all GI complications and seem to be decreased with coxibs (1, 2). Furthermore, the estimated 10.9% lifetime probability of dyspepsia with NSAID use is lower than many would accept.

Nevertheless, Spiegel and colleagues' conclusions are certainly qualitatively correct. Use of coxibs in average-risk patients is unlikely to achieve traditional levels of "cost-effectiveness" at current U.S. prices. As the risk for GI events increases, the number of patients needed to treat (NNT) to avert an additional upper GI event decreases (e.g., age < 65 y, NNT = 66; age > 75, NNT = 10) (3), and coxibs become more cost-effective. In the highest-risk patient, coxibs may actually be cost-saving: Spiegel and colleagues report that a 5.6-fold increase in risk for ulcer complications is the threshold for cost-savings.

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References

1. **Singh G, Rosen Ramey D.** NSAID induced gastrointestinal complications: the ARAMIS perspective—1997. Arthritis, Rheumatism, and Aging Medical Information System. J Rheumatol Suppl. 1998;51:8-16.
2. **Laine L, Connors LG, Reicin A, et al.** Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use. Gastroenterology. 2003; 124:288-92.
3. **Laine L, Bombardier C, Hawkey CJ, et al.** Stratifying the risk of NSAID-related upper gastrointestinal clinical events: results of a double-blind outcomes study in patients with rheumatoid arthritis. Gastroenterology. 2002; 123:1006-12.