Selective COX-2 inhibitor versus nonselective COX-1 and COX-2 inhibitor in the prevention of heterotopic ossification after total hip arthroplasty: a meta-analysis of randomised trials

Xue D, Zheng Q, Li H, Qian S, Zhang B, Pan Z

CRD summary
This review found no difference between selective COX-2 inhibitors and nonselective COX-1 and COX-2 inhibitors for prevention of abnormal bone formation following total hip replacement. These conclusions reflect the evidence presented. The possibility of new trials appearing in the years between publication of the review and preparation of this commentary should be taken into account.

Authors' objectives
To compare the effectiveness of selective COX-2 inhibitors versus nonselective COX-1 and COX-2 inhibitors for prevention of heterotopic ossification (abnormal formation of new bone) after total hip replacement.

Searching
Five databases including MEDLINE, EMBASE and Cochrane CENTRAL were searched to June 2009. Search terms were reported. Searches were not restricted by language. Clinical trial registers were searched for unpublished and ongoing trials. Reference lists of included studies were screened.

Study selection
Randomised controlled trials (RCTs) that compared selective COX-2 inhibitors versus nonselective COX-1 and COX-2 inhibitors for prevention of heterotopic ossification after total hip replacement were eligible for inclusion. The primary outcome was heterotopic ossification based on the Brooker classification system. Secondary outcomes were gastrointestinal adverse effects and hip joint function.

Included RCTs compared meloxicam, rofecoxib or celecoxib with indomethacin (three out of four trials) or ibuprofen. Duration of treatment ranged from seven to 14 days.

Two reviewers independently screened studies for inclusion.

Assessment of study quality
Study quality was assessed based on the recommendations of the Cochrane Handbook. It appeared that two reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted data to derive the relative risk of heterotopic ossification and associated 95% confidence interval. Disagreements were resolved by consensus.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated by meta-analysis. Fixed-effect models were used for meta-analysis; when statistical heterogeneity ($I^2$) was considered significant, random-effects results were also reported.

Results of the review
Four RCTs (808 participants) were included. Randomisation was considered adequate in all trials, allocation concealment in three and blinding in two. Length of follow-up ranged from three to 15 months.

There was no difference between groups in overall incidence of heterotopic ossification (RR 1.08, 95% CI 0.71 to 1.64; $I^2$=64%) or of any particular Brooker class of ossification (results reported fully in the paper). Discontinuation due to gastrointestinal adverse effects was 2.7% in the selective group and 4.4% in the nonselective group. Hip joint function was reported in only one trial (details in the paper).

Authors' conclusions
Selective COX-2 inhibitors were as effective as nonselective COX-1 and COX-2 inhibitors for prevention of heterotopic ossification after total hip replacement.

**CRD commentary**
The review question and inclusion criteria were clear. The search covered a range of relevant databases, was performed without language restrictions and included efforts to locate unpublished and ongoing trials. Review methods were generally satisfactory and reported adequately.

The authors' conclusions reflect the evidence presented. However, the small number of included trials and high levels of heterogeneity suggest that the findings might be more cautiously interpreted as no evidence of a difference rather than evidence of no difference.

Searching for the review was completed in 2009 and this commentary was written in May 2014. We are not aware of any more recent systematic reviews on this topic but it is possible that additional relevant trials have been published subsequently.

**Implications of the review for practice and research**

**Practice:** The authors stated that, given the two groups were equally effective, selective COX-2 inhibitors should be preferred to nonselective drugs because of their lower risk of gastrointestinal adverse effects.

**Research:** The authors stated that further well-designed RCTs were required to confirm the review findings.

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