Prophylaxis of heterotopic ossification of the hip: systematic review and meta-analysis

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CRD summary
This generally well-conducted review concluded that there was no evidence for a statistically significant or clinically important difference between non-steroidal anti-inflammatory drugs (NSAIDs) and radiation in preventing heterotopic ossification of the hip after surgery. The authors’ conclusions were based on the results of the review and appear appropriate.

Authors' objectives
To assess the effectiveness and safety of non-steroidal anti-inflammatory drugs compared with radiation in the prevention of heterotopic ossification of the hip after surgery.

Searching
MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched without date or language restrictions. Search terms were reported, but search dates were not. Reference lists of retrieved articles were also searched.

Study selection
Prospective randomised controlled trials (RCTs) and quasi-randomised trials that compared non-steroidal anti-inflammatory drugs (NSAIDs) with radiation in patients following total hip replacement or open reduction and internal fixation surgery were eligible for inclusion. Trials had to have a minimum of six months follow-up.

The included trials compared NSAIDs (diclofenac, indomethacin or aspirin) with radiation (in varying regimens ranging from 1x7cGY preoperative to 4x3cGY at up to five days postoperatively) in patients following total hip arthroplasty or open reduction and internal fixation surgery. The mean age of participants ranged from 43 to 67 years; the proportion of female ranged from 30 to 64%.

Two authors independently performed study selection; disagreements were resolved by discussion or consultation with a third reviewer.

Assessment of study quality
Two authors independently assessed quality using the Jadad 5-point scale, which assessed randomisation, blinding and attrition bias.

Data extraction
Two authors independently extracted data on the end-point incidence of heterotopic ossification and complications. These were used it to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

Methods of synthesis
The pooled risk ratios, together with 95% confidence intervals, were calculated using a random-effects DerSimonian-Laird model. Statistical heterogeneity was assessed using the Cochrane Q statistic and $I^2$. Meta-regressions were used to explore the impact of several variables on treatment effects.

Publication bias was assessed using funnel plots and Egger's weighted regression.

Results of the review
Nine trials were included in the review (n=1,345 participants), including six trials of total hip arthroplasty and three trials of open reduction and internal fixation surgery. The sample size of included trials ranged from 50 to 585 participants. The mean Jadad score was 1.8 (95% CI 0.9 to 2.8). There was no evidence of publication bias.
Preventing heterotopic ossification (eight trials; n=1,295 participants): There was no statistical difference in the rate of heterotopic ossification with NSAIDs compared with radiation (RR 1.17, 95% CI 0.76 to 1.79). There was a high degree of statistical heterogeneity (p<0.001). There was an association between age and the risk ratio of heterotopic ossification for total hip arthroplasty only patients (p=0.028).

Complications (five trials; n=992 participants): There was no statistical difference in the rate of complications with NSAIDs compared with radiation (RR 0.79, 95% CI 0.44, 1.41). There was a high degree of statistical heterogeneity (p<0.001).

**Authors’ conclusions**
There was no evidence for a statistically significant or clinically important difference between NSAIDs and radiation in preventing heterotopic ossification after hip surgery.

**CRD commentary**
Inclusion criteria for the review were broadly defined and several relevant databases were searched for articles in any language. Publication bias was assessed, and was not found to be a problem. Two authors independently undertook study selection, data extraction and quality assessment, which should have minimised the possibility of error and bias.

The results of the quality assessment indicated the poor quality of the included trials, which the authors acknowledged. A random-effects meta-analysis was undertaken and statistical heterogeneity was explored, which was appropriate.

The review was generally well conducted. The authors’ conclusions were based on the results of the review and appear appropriate.

**Implications of the review for practice and research**
**Practice:** The authors stated that NSAIDs are an effective and safe option to prevent a potentially severe complication after hip surgery.

**Research:** The authors stated that future studies should aim to collect information on quality of life, possibly in association with a cost-utility study.

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Record Status
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