Fransen M, Anderson C, et al. Safety and efficacy of routine postoperative ibuprofen for pain and disability related to ectopic bone formation after hip replacement surgery (HIPAID): randomised controlled trial. BMJ,doi:10.1136/bmj.38925.471146.4F (published 2 August 2006)

Design: Randomized clinical trial

Population/sample size/setting:

- 898 patients (54% men, mean age 66) undergoing elective total hip replacement in 20 hospitals in Australia and New Zealand
- Eligible if identified within 24 housr os completed surgery
- Ineligible if treating physician identified a definite indication for treatment with an NSAID (such as unsuitability of any other analgesic), definite contraindication for NSAID (previous adverse reaction, GI bleed, renal impairment, known bleeding disorder), administration of any NSAID within 48 hours prior to surgery

Main outcome measures:

- Randomized to 14 days of ibuprofen 400 mg tid (n=449) or placebo (n=449) using minimization algorithm stratified by study center and type of surgery (primary vs. revision)
- 875 patients started the randomized treatment; 24% stopped prematurely in the ibuprofen group and 19% stopped prematurely in the placebo group (difference not significant) on medical advice
- Hip pain and physical function measured by WOMAC did not differ between groups, who experienced similar improvement between baseline and follow-up 6 to 12 months after surgery
- Physical and mental components of the SF-36 also improved equally in both groups between baseline and follow-up; exercise tolerance and walking speed also were equal
- Ectopic bone on x-ray was seen more often in the placebo group than in the ibuprofen group: no ectopic bone was reported in 230 placebo and 274 ibuprofen patients; grade 1 (mild) in 108 placebo and 78 ibuprofen patients; grade 2 (moderate) in 43 placebo and 28 ibuprofen pts, grade 3 (severe) in 22 placebo and 9 ibuprofen pts, and grade 4 (bony ankylosis) in 4 placebo and 2 ibuprofen pts
- Higher grades of ectopic bone had a trend toward higher pain and worse function, but this was not significant
- Bleeding events during hospital admission (wound, hematoma, melena, etc) were reported in 21 ibuprofen and 10 placebo patients (borderline statistical significance)

Authors' conclusions:

- Ibuprofen shows no evidence of clinical benefit 6 to 12 months after hip arthroplasty

- Some concern about safety of ibuprofen is raised by the increased incidence of bleeding in that group
- Ectopic bone formation most patients is not associated with worse clinical outcomes
- NSAIDS can be considered for patients at high risk of heterotopic bone formation (if the patient has a past history)
- Routine use of NSAID for prophylaxis of heterotopic bone may result in net harm than net benefit

Comments:

- Study was carried out in many hospitals in two countries; there might have been enough data for subgroup analyses but these were not commented on
- Although the pain and function differences for the higher grades (3 and 4) of ectopic bone were reported as a nonsignificant trend, Table 6 does not give enough information to allow for an estimation of the upper and lower bounds of a confidence interval; this might have given valuable insight into the possible clinical importance of more severe ectopic bone formation
- Patients undergoing hip arthroplasty may have risk factors (age) that are associated with risk of coronary artery disease; recent precautions from the FDA about NSAID use may provide an additional precaution about their routine use in this setting

Assessment: High quality