Guest editorial

Avoid cox inhibitors after skeletal surgery!

Nonspecific cox inhibitors (NSAIDs), such as indomethacin or diclofenac, inhibit posttraumatic bone formation. They have been successfully prescribed to prevent postoperative heterotopic ossification (Neal et al. 2000). Animal studies indicate that fracture healing, spinal fusion and porous ingrowth are also inhibited (Keller et al. 1989, Trancik et al. 1989, Hogevold et al. 1992, Cook et al. 1995, Dimar et al. 1996). Hardly any studies have been done about the effects on fracture healing in humans, but one study has found a 10-fold increase in the risk of nonunion in patients taking cox inhibitors in the early postoperative period (Giannoudis et al. 2000). This study was retrospective, and the relation between cause and effect uncertain.

Of course, not all studies trying to show this inhibitory effect have been successful. There may be type 2 errors. Since marked inhibition has been found in several animal models, it would not have been considered acceptable to start postoperative treatment with cox inhibitors if it had not already been done. The current argument for giving cox inhibitors after surgery is that the pain relief is excellent and that no adverse effect on fracture repair or implant fixation is seen in everyday practice. The latter may be true only because one has not looked for it. Postoperative cox inhibitor treatment has not been recorded in prosthesis registers.

This treatment may be harmful not only for porous ingrowth, but also after insertion of cemented prostheses. Bone apposition to the cement surface results from biological processes that can be affected by giving drugs systemically. Postoperative osteoclast inhibition by a bisphosphonate improves fixation in patients (Hilding et al. 2000). Therefore osteoblast inhibition may have the opposite, harmful effect.

The inhibitory effects on bone formation seem to be due to cox-2. At the Orthopedic Research Society meeting in 2002, selective cox-2 inhibitors were reported to have inhibitory effects on fracture repair and porous ingrowth (Goodman et al. 2002, Leonelli et al. 2002). Mice lacking a functional cox-2 gene showed a dramatic impairment in fracture repair and a reduced ability to stimulate membranous bone formation (Simon et al. 2002, Zhang et al. 2002).

With the reduced gastrointestinal side effects of selective cox-2 inhibitors and the introduction of injectable preparations, it can be feared that the use of postoperative cox inhibition will increase in the near future. Anesthesiologists prescribing postoperative pain relief may not always be aware of the effects of cox inhibitors on bone biology. Both animal and clinical data indicate that the first postoperative week may be of crucial importance (Hogevold et al. 1992, Persson et al. 1998). This means that we are currently using prescriptions for postoperative pain relief at considerable risk, in most cases without even planning to measure the outcome.

Cox inhibitors should be prescribed only after surgery within the framework of randomized studies designed to evaluate whether the benefits are worth the risk.

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