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Valdecoxib

A Viewpoint by Frank A. Wollheim

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Selective cyclo-oxygenase-2 (COX-2) inhibitors (coxibs) have gained a large market share since their launch in 1998. In most studies, coxibs provide pain relief comparable to that of conventional, and cheaper, nonsteroidal anti-inflammatory drugs (NSAIDs), but with improved gastrointestinal safety. These compounds carry similar renal risks to non COX-2 selective NSAIDs, and there is some concern that coxibs may increase the risk for cardiovascular events in at-risk patients. Valdecoxib has convincingly shown selectivity for COX-2 in oral doses up to 80mg twice daily. This is based on lack of inhibition of platelet aggregation and lack of effects on thromboxane levels in *ex vivo* studies in volunteers and patients. Valdecoxib is structurally closely related to celecoxib and rofecoxib, and shares the lipophilic features of these drugs. Like celecoxib, valdecoxib has a sulfonamide group and binds to the side pocket in the COX-2 catalytic channel.

The published clinical studies show analgesic effects of valdecoxib after oral administration in patients undergoing oral or orthopaedic surgery, as well as in patients with osteoarthritis of the knee and hip. In rheumatoid arthritis, only one controlled trial has been published to date. Whilst the preparation seems to be well tolerated in short-term trials, and equipotent to NSAIDs such as naproxen, it is not clear in what way it differs from already available coxibs. A prodrug compound of valdecoxib, parecoxib, can be used parenterally and has been approved by the European Agency for the Evaluation of Medicinal Products. Evidence supporting parenteral analgesic potency of parecoxib in connection with tooth extraction has been published.[1] Interestingly, in several studies valdecoxib 40mg twice daily was no more effective than 20mg twice daily, and in the osteoarthritis trials, dosages as low as 10mg twice daily seemed efficacious. As with some NSAIDs, the recommended valdecoxib dosage may change as clinical experience is accrued. Gastrointestinal effects have been documented by endoscopic examination only, and valdecoxib seems to be superior to non-selective NSAIDs in this respect.

Valdecoxib was licenced by the US Food and Drug Administration in November 2001 with a label for rheumatoid arthritis, osteoarthritis and primary dysmenorrhoea. The emergence of comparative studies with the oral coxibs celecoxib and rofecoxib, as well as further studies employing parenteral administration of parecoxib, would be of interest. ▲

Reference

1. Desjardins PJ, Grossman EH, Kuss ME, et al. The injectable cyclooxygenase-2-specific inhibitor parecoxib sodium has analgesic efficacy when administered preoperatively. Anesth Analg 2001 Sep; 93 (3): 721-7