Drugs 2004; 64 (20): 2344-2345
0012-6667/04/0020-2344/$34.00/0

Nabumetone

Therapeutic Use and Safety Profile in the Management of Osteoarthritis and Rheumatoid Arthritis

The nabumetone review by Hedner et al.[1] in this issue of *Drugs* dramatises the tremendous leap in critical assessment of the role of selective cyclooxygenase (COX)-2 NSAIDs and their limitations, especially, and most recently, through controlled and epidemiological studies.

When I first presented the pharmacology of nabumetone at its introduction in the US, selective COX-2 isoenzymes were not officially recognised in our literature.[2] However, the controlled comparison study of nabumetone versus ibuprofen and ibuprofen with misoprostol highlighted the unique gastro-sparing advantages of this agent.[3] I believe that explains its leap to the top of the NSAID prescription list for almost a decade until the aggressive marketing of the newer selective COX-2 drugs. Although nabumetone does not qualify in this category, its safety record has been documented and compares favourably with the continuing experience of both first- and second-generation COX-2 drugs.

However, I believe the Hedner et al.[1] nabumetone review article should also consider host risk as a persuasive argument to, at times, not use any of these agents.

When I first described NSAID gastropathy in the medical literature as separate from classic acid peptic disease,[4] I emphasised the tremendous danger of this drug-induced complication. However, I also pointed out that gastroprotective co-therapy left much to be desired (and that continues to be the case), but there were other choices.[5]

Those choices include non-acetylated salicylates that are totally prostaglandin sparing.[6] These much older, very inexpensive, generic agents are neither toxic to the gastric mucosa nor directly interfere with renal functions as all other NSAIDs do. Although the mechanism of action is still not well understood, it is recognised that they are all anti-inflammatory at therapeutic doses, if not always very analgesic.

Therefore, although non-acetylated salicylates spare prostaglandins and are, therefore, absent usual NSAID toxicities, the trade-off often had to be with lesser pain control. However, now that analgesics, and especially opioids, are more commonly used in place of NSAIDs that trade-off is no longer the same issue.

In fact, this therefore brings us to our major choice in dealing with arthritis. In osteoarthritis where inflammatory activity may not be an issue, and in rheumatoid and related systemic arthritis where antiproliferative and disease-modifying therapies are implicitly used, the issue of an anti-inflammatory effect may be redundant. In these patients we are left with pain relief as the major factor for co-therapy, and there is no better pain relief than with the many pure analgesic choices.

Twenty-four hour opioid therapy is now recognised as a legitimate choice in the face of the more significant levels of pain seen with arthritis.[7] Within the opioid spectrum there are a range of alternatives that can fit both the pain and co-morbidity and co-therapy problems of the individual patient. Opioids are *not end-organ toxic*; therefore, in the face of host risk they may be not only the most effective but also the safest alternatives. This is especially true for the elderly, those with peptic ulcer and renal dysfunction, and with multisystemic health problems.

So ‘back to the future’, with nabumetone as an older nonselective COX-2 NSAID that offers significant safety benefits which compare favourably to the COX-2 NSAIDs.[8] But also let us not forget the non-acetylated salicylates and the non-NSAIDs analgesic choices. Finally, topical NSAIDs should soon be available in the US, as they are in the rest of the world in most cases, and the data supports that they are equipotent for local and shorter term use in place of systemic therapies and absent end-organ toxicities.[9]

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