



THERAPEUTICS INITIATIVE

Evidence Based
Drug Therapy

Should we be using NSAIDS for the treatment of Osteoarthritis and "Rheumatism"

It is essential that we prescribe non-steroidal anti-inflammatory drugs (NSAIDs) with knowledge and care; inappropriate prescribing puts our patients unnecessarily at risk of morbidity and mortality. There are many different NSAIDs available for prescription in British Columbia. The large number of drugs and formulations makes it difficult for the primary care physician to choose the best drug for his/her patient. The choice can be markedly simplified by a review of the published evidence on effectiveness and safety and by taking into consideration the cost of the drug. Using these principles most patients can probably be treated with the use of four drugs.

- **Is there evidence of differences in effectiveness of the different NSAIDs?**

There are relatively few clinical trials comparing the effectiveness of different NSAIDs. These trials have not demonstrated any consistent superiority of one NSAID over another. Differences that have been published can often be explained by the failure to use equivalent doses.¹

- **What is the treatment of choice for osteoarthritis?**

The long term use of NSAIDs for osteoarthritis in the elderly is common, however, the drug of first choice in these patients is acetaminophen 500 mg TID titrated to a maximum dose of 1 gram QID. Acetaminophen is safer, less expensive, and as effective as NSAIDs in approximately 50% of patients, particularly in those where arthralgia is the primary manifestation.^{2,3} If acetaminophen is ineffective in relieving symptoms enteric coated acetylsalicylic acid (ECASA), ibuprofen or naproxen can be tried.

- **Is ketorolac (Toradol) a more effective analgesic than other NSAIDs?**

All of the NSAIDs have analgesic properties, usually at doses lower than the effective antiinflammatory doses. This is also true of keforolac which is chemically similar to tolmetin. There is no convincing evidence that ketorolac is a better analgesic than the other NSAIDs.



- **Is there evidence that NSAIDs have a disease-modifying effect?**

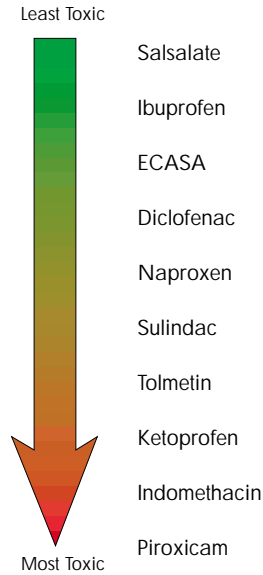
There is no evidence that NSAIDs alter the natural course of osteoarthritis. The patient should be made aware that NSAIDs represent symptomatic therapy, and that the therapy is associated with some risks.

- **What are the major risks of NSAIDs in my patients?**

The major risk is gastrointestinal ulceration associated with bleeding or perforation, both of which can be fatal.^{4,5} This risk is increased with higher dose and longer duration of therapy and is increased in the elderly. The relative risk of this complication has been studied in a practice setting^{4,5} and differs between the different NSAIDs (Table 1). Another common adverse consequence is the capacity of NSAIDs to elevate blood pressure; in a recent meta-analysis the magnitude of this effect was estimated to be 5 mm Hg.⁶ In patients on long term therapy this would lead to a significantly increased risk of hypertension-related morbidity. NSAIDs can also cause salt and water retention and may precipitate congestive heart failure in susceptible patients.



table 1: Rank According to Risk of Gastrointestinal Toxicity * 4,5



• How can I minimize the risk of NSAIDs in my patients?

The best way to minimize the risks is to use the simple analgesic, acetaminophen, whenever possible. When an NSAID is essential for control of symptoms prescribe the safest NSAID in the lowest effective dose for the shortest period of time (e.g. ibuprofen 200 mg TID for 1 to 2 weeks). Patients in whom chronic therapy is found to be necessary should be reassessed by decreasing the NSAID dose and/or stopping it at 3 to 6 month intervals. Administration of misoprostol (Cytotec) during NSAID therapy has been shown to reduce the incidence of significant GI events by 0.38% from 0.95% to 0.57% (unpublished MUCOSA Study). Unfortunately misoprostol also causes side effects, e.g. diarrhea, average incidence 11.9%.

• What are the least expensive NSAIDs?

The doses and daily ingredient costs of the various NSAIDs available in B.C. are shown in Table 2. The three least expensive NSAIDs are ECASA, ibuprofen, and naproxen. Fortunately these are also amongst the safest.

Table 2: Dosing and Cost Table for Selected NSAIDs

| Drug Name | Trade Name | Dosage Range | Daily Cost* |
|------------------------|---------------------------|-----------------------|----------------------|
| ASA | Enteric Coated ASA | 325-975 mg QID | \$0.07-\$0.44 |
| Diclofenac | generic, Voltaren | 25-50 mg TID | \$0.62-\$1.25 |
| Diclofenac/Misoprostol | Arthrotec | 50/200 mg TID | \$1.86 |
| Diflunisol | generic, Dolobid | 250-500 mg BID | \$0.93-\$1.41 |
| Fenoprofen | Nalfon | 300-600 mg TID | \$0.97-\$1.76 |
| Floctafenine | Idarac | 200-400 mg TID | \$1.20-\$1.99 |
| Flurbiprofen | generic, Ansaid, Froben | 50-100 mg TID | \$0.88-\$1.18 |
| Ibuprofen | generic | 200-600 mg TID | \$0.09-\$0.15 |
| Indomethacin | generic, Indocid | 25-50 mg TID | \$0.34-\$0.58 |
| Ketoprofen | generic, Rhodis, Orudis | 50-100 mg TID | \$0.53-\$1.14 |
| Ketorolac | Toradol | 10 mg QID | \$2.55 |
| Mefenamic | Ponstan | 250 mg QID | \$2.46 |
| Nabumetone | Relafen | 1-2 g daily | \$1.64-\$2.68 |
| Naproxen | generic, Naprosyn | 125-500 mg BID | \$0.12-\$0.46 |
| Naproxen sodium | generic, Anaprox | 275-550 mg BID | \$0.70-\$1.39 |
| Piroxicam | generic, Feldene | 10-20 mg daily | \$0.45-\$0.74 |
| Salsalate | Disalcid | 0.75-1.75 g BID | \$0.73-\$1.46 |
| Sulindac | generic, Clinoril | 150-200 mg BID | \$0.83-\$1.04 |
| Tenoxicam | Mobiflex | 20 mg daily | \$1.36 |
| Tiaprofenic acid | Surgam | 300 mg BID | \$1.29 |
| Tolmetin | Tolectin | 200-600 mg TID | \$1.33-\$2.69 |

* least expensive available formulation in BC, 1993

References

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The Therapeutics Initiative was established to disseminate up to date evidence based drug therapy information to physicians and pharmacists. We are also committed to evaluating the effectiveness of all our educational activities using the Pharmicare data base. The data will be in a form such that individual physicians, pharmacies or patients will not be identified. If you do not wish to be part of this evaluation process, please notify us and you will be excluded from the evaluation.