

Reaching a Consensus on Managing the Patient at Risk for NSAID Toxicity

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Summary and Goals

The ultimate goal of this consensus conference is to develop specific strategy guidelines for understanding the management issues associated with non-steroidal anti-inflammatory (NSAID) drug use among patients who may be at risk for NSAID-induced toxicity and side effects. Ideally, since it has been determined that the majority of patients requiring NSAID therapy will initially consult and most likely be treated by a primary care physician, these guidelines should address how the nonspecialist can best detect and deal with potential NSAID-related problems.

NSAID use in the United States is extremely common and every physician is likely to encounter situations where the analgesic, anti-inflammatory properties of these drugs will be of immense benefit to their patients. While NSAIDs are considered generally safe, there are patients for whom long-term NSAID use, such as that needed for chronic osteoarthritis or rheumatoid arthritis, may produce adverse effects. There are also some patients who will have unexpected, idiosyncratic adverse effects after relatively short courses of NSAID treatment.

Any consensus on managing patients at risk for NSAID toxicity should focus on the three organ systems most often affected by the mechanisms of action of

NSAIDs. These are the gastrointestinal tract, the kidneys, and blood clotting. It must be kept in mind that while general suggestions can be developed, many patients with certain, more severe risk factors may require additional consideration, and in some cases, referral to a specialist in the area of concern.

Also, a myriad of drug interactions should be considered when using these consensus guidelines. Some patients, particularly the elderly who are often taking more than one medication, will usually require special attention before an NSAID should be prescribed.

As indicated during the conference presentations, different NSAIDs have different profiles and some may be better suited for a certain group of patients. Therefore, it would be helpful for the physician using these guidelines to become familiar with the specific properties of these drugs, including those formulated for over-the-counter sale.

The guidelines must also be based on the currently available clinical research and statistical data. However, many studies involving newly developed as well as older NSAIDs and their adverse effects are underway and are likely to be initiated in the near future. The results of these investigations may help to further clarify some of the NSAID toxicity issues discussed during this conference.

Consensus Guidelines for Managing Patients at Risk for NSAID Toxicity:

- A medical history should be obtained for each individual requiring nonsteroidal anti-inflammatory (NSAID) treatment to determine if there has been a prior history of peptic ulcer disease or other acid-dependent problems such as gastritis, esophagitis, etc. If a history of an ulcer is present, the patient should undergo testing for *H pylori* and should be treated if positive.
- Additional protective measures may be considered for patients with a history of complications due to ulcer disease who require long-term NSAID therapy. If NSAID treatment is necessary, prophylactic misoprostol, omeprazole, or an H₂-blocker may be prescribed in order to try to alleviate potential NSAID-related gastropathy.
- A baseline serum creatinine level should be obtained for all patients before starting NSAIDs. This should be followed closely in the patients who are on antihypertensive medication, diabetics, or those with impaired renal function. If serum creatinine is greater than 2.2 mg/dL at baseline, an NSAID with fewer renal effects, such as nabumetone, is preferred. NSAID use by patients with more than one risk factor for renal toxicity should be used with extreme caution.
- Both serum creatinine and potassium levels should be monitored regularly in patients taking an NSAID who are concomitantly taking any antihypertensive medications or who have a history of renal disease. Monitoring should be more frequent when a patient has more

than one risk factor for renal toxicity or when renal disease is more severe. This is especially necessary for patients taking potassium-sparing diuretics or angiotensin converting enzyme (ACE) inhibitors for their hypertension. Consideration should be given to discontinuing potassium-sparing diuretics during NSAID use and patients should be asked about and advised against the use of potassium-laden salt substitutes during NSAID therapy. Discontinuation of an ACE inhibitor may be considered when NSAID treatment is imperative; however, the benefits of the ACE inhibitor will usually be more important and should be maintained. Referral to a rheumatologist or nephrologist may be considered.

- Patients who are borderline hypertensive but are not taking blood pressure medication should undergo blood pressure monitoring more often—preferably once a month—when they are taking an NSAID.
- Caution should be exercised when faced with prescribing NSAID therapy for patients on anticoagulation therapy, regardless of whether there is a history of ulcer disease. The effects of the NSAID on platelets and any previous lesions should be considered.
- NSAID use should be discontinued 5 days prior to elective surgery and aspirin should be stopped 10 days before surgery.

There is significant evidence that an NSAID such as nabumetone, which is relatively cyclooxygenase-1 (COX-1) sparing can be expected to produce a lower incidence of adverse gastrointestinal, renal, and hematological effects.