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Dangers of Non-Steroidal Anti-inflammatory Drugs in the Elderly

SUMMARY

NSAIDs are the most widely prescribed of all drugs when grouped by generic categories, and they are frequently given in the treatment of musculoskeletal disorders. These drugs are known to produce serious side-effects, particularly in the elderly. The author of this article lists various categories of typical side-effects and cautions against the routine use of NSAIDs, particularly in patients at risk for certain conditions and in combination with certain other types of medication. (*Can Fam Physician* 1989; 35:653-654.)

Key words: elderly, side-effects, contraindications

RÉSUMÉ

Les anti-inflammatoires non stéroïdiens (AINS) sont les médicaments le plus souvent prescrits lorsque regroupés par catégories génériques, et sont souvent prescrits pour le traitement de désordres musculo-squelettiques. Il est bien connu que ces médicaments produisent de sérieux effets secondaires, particulièrement chez les personnes âgées. L'auteur liste différentes catégories d'effets secondaires typiques et met en garde contre l'usage systématique des AINS, surtout chez les patients à risque de certaines conditions et lorsque combinés à d'autres catégories de médicaments.

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NON-STEROIDAL anti-inflammatory drugs (NSAIDs) are an integral part of treatment of rheumatoid arthritis, osteoarthritis, and pain and inflammation resulting from various musculoskeletal disorders.¹ Data from the Saskatchewan prescription drug plan indicate that 39% of women and 29% of men over the age of 74 were prescribed NSAIDs during a one-year period.

NSAIDs are now the most widely prescribed of all drugs when grouped by generic categories, and this does not include aspirin.² These drugs are known to produce serious side-

effects, particularly in the elderly: adverse drug reactions in the geriatric population are estimated to be at least twice that in the younger population, rising from 10% when a single drug is being taken to nearly 100% when 10 drugs are being taken.³

These reactions are discussed below.

Gastrointestinal Side-Effects

Gastrointestinal symptoms caused by NSAIDs include heartburn, constipation, abdominal pain, nausea, diarrhea, and vomiting. In a study by Summerville and colleagues,⁴ ulcer patients were found to be at least twice as likely as controls to be on NSAIDs. The risk of bleeding peptic ulcer was substantially increased in the NSAID users.

Cardiovascular Side-Effects

NSAIDs can raise blood pressure and cause retention of salt and water. Some antihypertensive drugs, such as

furosemide and captopril, work partly by stimulation of prostaglandin synthesis. Treatment with NSAIDs can decrease prostaglandin synthesis.⁵ Thus, careful consideration must be given to instituting treatment with NSAIDs in patients with hypertension or heart failure.

Side-Effects on the Central Nervous System

Headaches, dizziness and drowsiness are the most common symptoms caused by NSAIDs. Indomethacin is particularly likely to produce headaches and may also produce confusion and feelings of unreality.⁶

Tinnitus and hearing disturbances can occur with these drugs, as with aspirin.

Side-Effects on Skin

A wide variety of cutaneous reactions may occur to the use of NSAIDs. The incidence of reactions is reported to be between 3% and 9%.⁷ Urticarial and morbilliform eruptions are

most common, but reactions include bullous drug eruptions and Stevens-Johnson syndrome. Epidermal necrolysis, photosensitivity, exfoliative dermatitis, and erythema nodosum have all been reported. Patients with known allergy to aspirin are at high risk for cross sensitivity to NSAIDs. Patients with history of asthma, nasal polyps, and urticaria are at high risk for the development of allergic symptoms.

Renal Side-Effects

Non-steroidal anti-inflammatory drugs inhibit cyclo-oxygenase activity and thereby reduce prostaglandin synthesis.⁸

Prostaglandin E-2 and prostaglandin I-2 antagonize the intrarenal effect of vasoconstrictor peptides or catecholamines on the renal vasculature and glomeruli. Blockage of prostaglandin synthesis by the administration of an NSAID removes the prostaglandin-mediated vasodilatory effect and thereby intensifies vasoconstriction.⁹

Temporary vasoconstriction appears to be rapidly reversible, whereas prolonged reduction in renal blood flow leads to increased renal vasculature resistance and can lead to acute renal failure. Any pre-existing condition leading to reduced vasorenal blood flow, such as congestive heart failure or volume depletion, increases the likelihood of development of renal failure. This condition, which may progress to papillary necrosis, is usually reversible with discontinuation of the medication.

Another reversible renal syndrome, is interstitial nephritis. This syndrome is characterized by heavy proteinuria and a decline in renal function. Flank pain and hematuria can also occur.

NSAIDs are particularly likely to cause sodium and water retention in patients with congestive heart failure, cirrhosis, nephrotic syndrome, and other causes of decreased renal function. The sodium-retaining effects of NSAIDs are further increased in situations where these agents are used in combination with diuretics.⁹ If resistant edema develops, it is desirable to discontinue the NSAID if possible.¹⁰

NSAIDs can cause positive potassium balance and increase the serum potassium concentration. Therefore,

careful monitoring of potassium levels is important, especially if some degree of renal insufficiency is present, or if the patient is on a potassium-sparing drug, such as triamterene or captopril.

Hepatic Side-Effects

Abnormal liver-function tests, jaundice, cholestasis, and hepatitis may all occur.⁶ Hematologic side-effects such as eosinophilia, granulocytopenia, leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia, and hemolytic anemia have all been reported. In addition, all NSAIDs are inhibitors of prothrombin synthesis and platelet aggregation.

Other Reactions

Newman and Ling¹¹ have reported harmful effects of NSAIDs on osteoarthritic hips. They found a significant relationship between acetabular destruction and NSAID intake. This damage can lead to less satisfactory potential for arthroplasty.¹¹ It is suggested that these effects may be caused by altered metabolism of cartilage and bone, as well as by increased stress after the relief of pain.

Anaphylactoid reactions characterized by angioedema, urticaria, hypotension, and shortness of breath have been described with virtually all NSAIDs.¹²

Before elderly patients are put on an NSAID, a careful risk-factor analysis should be done. Dehydration, diuretic therapy, cirrhosis, and underlying renal disease should all be screened for. Renal function should be assessed before and one month after beginning therapy. Serum potassium levels should be monitored, particularly in the patient on other potassium-sparing drugs. Other drugs that the patient is taking must be considered so that adverse interactions can be avoided. The most significant adverse reactions are the interactions of NSAIDs with the anticoagulant drugs, which result in prolongation of prothrombin time and inhibition of platelet function.

NSAIDs decrease the hypotensive effects of many antihypertensives and diuretics.¹³ NSAIDs can also produce a mild elevation of blood pressure in normotensive individuals.

It is not unusual for patients to take over-the-counter (OTC) medications

without consulting their physician. Many of these OTCs contain aspirin or other analgesics which may have a cumulative effect with NSAIDs. Therefore any unusual sign or symptom in a patient on NSAIDs should prompt a thorough review of medications and systems to ensure that the NSAID is not directly or indirectly responsible.

These drugs are often prescribed for chronic incurable conditions, particularly in the elderly. We need to remind ourselves that they are potent drugs that require careful and frequent monitoring in long-term use. ■

References

1. Dick WC, DeCeulaer K. Nonsteroidal antirheumatic drugs. In: Kelly WN, Harris Jr ED, Ruddy S, Sledge CB, eds. *Textbook of Rheumatology*. New York: WB Saunders, 1981: 768-84.
2. Feter VJ. Boom in arthritic drugs. New York: New York Times, 1982; Apr 23: D1,D4.
3. Katzung BG. *Basic and clinical pharmacology*. 1987; 64:761.
4. Sommerville K, Faulkner G, Langman W. Non-steroidal anti-inflammatory drugs and bleeding peptic ulcer. *Lancet* 1986; i:462-4.
5. Davis A, O'Day R, Begg EG. *Aust NZ J Med* 1986; 16: 537-46.
6. Boardman PL, Hart FD. Side-effects of indomethacin. *Ann Rheum Dis* 1967; 26:127-32.
7. Krogh CM, ed. *Compendium of Pharmaceuticals and Specialties*. Ottawa: Canadian Pharmaceutical Association, 1988: 587.
8. Sedor JR, Davidson EW, Dunn MJ. Effects of non-steroidal anti-inflammatory drugs in healthy subjects. *Am J Med* 1986; 81(2b):58-70.
9. Dunn MJ. Non-steroidal anti-inflammatory drugs and renal function. *Ann Rev Med* 1984; 35:411-28.
10. Attallah AA. Interaction of prostaglandins with diuretics. *Prostaglandin* 1979; 18:369.
11. Garella S, Matarese RA. Renal effects of prostaglandins and clinical adverse effects on non-steroidal anti-inflammatory agents. *Med* 1984; 63:165-78.
12. Newman NN, Ling RSM. Acetabular bone destruction related to non-steroidal anti-inflammatory drugs. *Lancet* 1985; ii:11-4.
13. O'Brien WH, Bagby GF. *Anaphylactoid reactions to non-steroidal anti-inflammatory drugs. Advances in inflammation research. VI*. New York: Raven Press, 1984: 203-7.
14. Brown J, Dollery C, Valdez G. *Am J Med* 1986; 81:43-53.