

However, some clinicians have found that maximal benefits are not obtained until indomethacin has been given for a month or more. With prolonged administration, 10% to 15% of the patients who responded initially must stop taking indomethacin because of its untoward effects.

It has been reported that indomethacin reduces joint swelling and edema in some patients with rheumatoid arthritis. However, results have been equivocal in the few studies in which objective measurements of joint size were made. The erythrocyte sedimentation rate was not affected.

When given alone, indomethacin is less effective than the corticosteroids in the treatment of rheumatoid arthritis. When given concomitantly, however, the dose of the steroids often can be halved and in some patients completely withdrawn. Thus, indomethacin may be especially useful in patients who have been receiving long-term therapy with corticosteroids. However, the hazards of combined therapy with steroids and indomethacin have yet to be fully evaluated.

Indomethacin has been particularly useful in the treatment of mild to moderate osteoarthritis of the hip joint, a condition that is resistant to all other anti-inflammatory agents. It also appears to relieve the pain of ankylosing spondylitis as effectively as does phenylbutazone.

Indomethacin produces anti-inflammatory effects in patients with gout and may be as effective as phenylbutazone in its promptness of action and the degree of relief it provides. Because it has produced relief in acute attacks within 48 hours, and because it lacks the untoward effects of colchicine, some clinicians consider it to be the drug of choice for these attacks; however, controlled trials are needed to determine how its effectiveness compares with that of colchicine. Indomethacin may be useful as a supplement to colchicine in the management of severe cases of gout. Whether it is useful as a prophylactic agent in gouty arthritis remains to be established.

ADVERSE REACTIONS

Central nervous system effects (headaches, usually severe in the morning; vertigo; light-headedness; mental confusion) occur during the early weeks of therapy in about 20% to 30% of patients taking indomethacin. These symptoms may occur within the first few hours after administration or may be delayed for two or three days; they frequently disappear with continued use and are reversible when the drug is discontinued. Generally, these effects are dose-related and are less likely to appear if the daily dosage is 100 mg. or less given in divided amounts.

Gastrointestinal reactions (nausea, indigestion, epigastric burning, stomatitis, diarrhea), which have been observed in about 25% of the patients, often are transient and can be minimized by giving the drug after meals and with milk at bedtime. These symptoms are severe enough to require discontinuing the drug in less than 10% of the patients but, even in these, the adverse effects may not recur when administration of the drug is resumed.

Indomethacin should be regarded as potentially ulcerogenic, although the available evidence on this point is contradictory. Some patients with a history of peptic ulcer have tolerated the drug without experiencing gastrointestinal symptoms or having evidence of an active ulcer; other patients have developed ulcers after having taken the drug for 1½ to 3 years. Since most patients who developed ulcers had received doses of 150 to 300 mg. a day, dosage may well be a contributing factor. Occult bleeding and resulting anemia may occur in the absence of an ulcer; persistent indigestion may be a symptom of this. Although measurements indicate that the occult blood loss associated with indomethacin is less than that produced by clinically equivalent doses of aspirin, hemoglobin determinations should be made regularly and the drug should be discontinued if any evidence of gastrointestinal bleeding develops.

No significant hematologic reactions or alterations in the glucose tolerance test, electrolyte balance, or liver and kidney function have occurred after administration of indomethacin for periods as long as three years. However, more long-term studies are needed to completely assess the effects of its prolonged use.

Other adverse effects reported infrequently are edema; psychic reactions such as depression; angioneurotic edema; drowsiness; tinnitus; blurred vision; and dermatologic reactions such as pruritus, urticaria, and rash. Indomethacin should be discontinued if these reactions occur. Leukopenia has been reported in a few patients.