Migraine Treatment of the Month

Humble but Mighty Indomethacin

Indomethacin is hardly a newcomer to medical therapeutics. This nonsteroidal anti-inflammatory drug (NSAID) initially became available for general clinical use in 1963, and it continues to be used frequently for treating such common disorders as osteoarthritis, tendonitis and acute gouty arthritis. While the mechanism of action responsible for its anti-inflammatory activity is quite similar to that of many other NSAIDs, it possesses additional properties that indicate it is much more than "just another NSAID".

Administered intravenously, indomethacin can rapidly reduce increased intracranial pressure by reducing cerebral blood flow. The drug's action on brain blood vessels – and on the neurotransmitter, nitric oxide - may account for why the oral formulation is so uniquely effective for treating certain primary headache disorders (see "Migraine Myth of the Month" in this issue).

Those disorders include hemicrania continua, paroxysmal hemicrania and cluster headache, each of which is termed a "trigeminal autonomic cephalalgia" (TAC). Within some members of the TAC group, attacks of headache appear to result from activation of the superior salivatory nucleus, a cluster of cells located within the brainstem, and indomethacin's *invariable* effectiveness in treating hemicranias continua and paroxysmal hemicrania may result from its ability to inhibit that activation process.

In patients with hemicrania continua or paroxysmal hemicrania the response to indomethacin is typically nothing less than spectacular, but unfortunately that success in eliminating headache may come at a price (see below). Why indomethacin is inconsistently effective in treating cluster, the "King of the TACs", is unknown.

As for migraine, indomethacin can be helpful but is no "magic bullet". Migraine is a neuro-inflammatory disorder, and as with any NSAID, indomethacin's anti-inflammatory action may be helpful in treating acute migraine headache. Whether it is any more or less effective for this purpose than, say, naproxen sodium or ibuprofen, remains unknown.

What *is* known is that this potent NSAID may cause a number of gastrointestinal side effects that range in severity from occasional heartburn to life-threatening peptic ulcer disease. Chronic use of indomethacin on a scheduled (e.g., 3 times daily) basis should be accompanied by a careful discussion between provider and patient regarding potential side effects, prescription of a "stomach protectant" medication such as omeprazole, the option of administering the medication with meals and regular blood tests to ensure the drug is not asymptomatically impairing kidney or liver function.

That said, this long available and cheaply priced capsule can produce therapeutic magic when administered for treatment of the appropriate primary headache disorder.