Is nimesulide safe in a cardiovascular-compromised patient?

Nimesulide, a non steroidal antiinflammatory drug (NSAID), has been available in India since 1997. There is no report proving its superiority as an antipyretic over paracetamol and as an antiinflammatory compared with diclofenac and piroxicam. Nimesulide should not be used as the primary mode of treatment as an antipyretic or analgesic, when better and safer choices are available. Nimesulide is not used in the United States, Finland, Spain, Portugal and Israel. These countries and other European countries have withdrawn the pediatric formulation of nimesulide. The drug was never licensed for use in Canada, Britain and Australia. The continuing use of nimesulide in India is disturbing. No dependable post-marketing surveillance for adverse drug reactions (ADRs) is undertaken. Unlike in a developed economy, Indian doctors are not under any supervision and therefore do not necessarily keep themselves updated with information about ADRs.

Numerous studies have shown life-threatening ADRs with nimesulide such as hepatotoxicity, renal toxicity, severe skin reactions, gastrointestinal toxicity, potentiation of seizures and potentiation of colitis in passive cigarette smoking. Nimesulide should be used with great caution in patients with compromised renal function, cirrhosis of liver, congestive heart failure, renovascular disease, volume or salt depletion. We hereby report nimesulide-induced coronary artery insufficiency (CAI).

A 78-year-old man weighing 53 kg, without any history of smoking, alcohol intake, diabetes mellitus or hypertension, had myocardial infarction 10 years back. He was maintained on Tab Isosorbidemononitrimate 20 mg twice daily, and Tab Acetylsalicylic acid 350 mg + Calcium carbonate 105 mg half tablet once a day. He was also taking Isapghol, Milk of Magnesia and Liquid paraffin. He sustained injury in the left wrist for which he was prescribed Tab Nimesulide 100 mg twice daily. After 36 h of nimesulide intake with ongoing treatment for CAI, the patient developed breathlessness on exertion which gradually increased in intensity leading to disturbed sleep with cough. Next morning (48 h), the patient developed severe dyspnoea, cyanosis and restlessness. BP was 110/70 mmHg; pulse rate was 80 min, regular and low volume. Respiratory rate was 24/min. No lymphadenopathy and pallor were seen. Jugular venous pressure was not raised. No hepatosplenomegaly and pedal edema was seen. On auscultation, a few fine crepitations at base were heard. Heart sounds were normal. The patient gradually lost consciousness followed by cardio-respiratory failure. ECGs did not reveal any findings of ischemia, arrhythmias or MI except slow ventricular beats (4-8 min). Cardio-respiratory resuscitation did not help and the patient died. Also, considering the severity of the ADR leading to death, this warrants reporting. Naranjo ADR Probability Scale Evaluation, was done to assess the likelihood of CAI occurring due to nimesulide. It gave a score of 2 indicating a 'possible' relationship between the ADR (CAI) and (Nimesulide) therapy in this patient. The WHO causality categories confirmed its 'possible' link. It seems that breathlessness, cough, central cyanosis and fine crepitations may be because of left ventricular failure because of coronary artery spasm precipitated in an old compromised patient. Some reports have suggested a causal relation between the use of NSAIDs and the onset of congestive cardiac failure (CHF).

Cardiovascular ADRs associated with COX-2 inhibitors like celecoxib and rofecoxib include heart rate and rhythm disorders, increased BP, congestive heart failure, myocardial infarction, and cerebrovascular and thromboembolic events. A study evaluated the relative expression and immunoreactive levels of COX-1 and COX-2 in the renal cortex and medulla of rats with congestive heart failure, and revealed upregulation of medullary COX-2, but not of COX-1, in rats with advanced heart failure.

Authors believe that the inhibition of prostaglandin synthesis may adversely affect cardiovascular homeostasis in patients with a propensity to develop CHF. More pharmacological data is needed to quantify the risk of CHF attributable to the use of NSAIDs, particularly nimesulide. In such patients, it is advisable to avoid the use of NSAIDs, particularly nimesulide. When safer drugs are available, it is irrational to prescribe drugs of doubtful efficacy.

Even if the Indian authorities are reluctant to impose a total ban on nimesulide, they should immediately discourage its use. It is unfortunate that we continue to wait for another "committee" report before stopping the use of nimesulide when the previous one formed by the Drugs Controller General of India in 2002 to review the hepatotoxicity reported distrustful findings.

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References


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