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LETTER TO THE EDITOR

Drug safety issues of nimesulide in China—nimesulide-induced liver injury

Nimesulide is a non-steroidal anti-inflammatory drug. It is considered to be well-tolerated and has a relatively low occurrence of adverse drug reactions (ADRs) especially in the gastrointestinal tracts. Because its antipyretic effect is quick, nimesulide has become the saleable first-line medicine for fever in children, particularly in poor and backward areas, in China since 2002. Shelves are filled with various brands of pharmaceutical formulations of nimesulide in pharmacy throughout the country. Because drug supervision and management is lax in China, an anxious parent can purchase nimesulide easily for his or her child in fever in most urban and rural pharmacies, even though he or she has not obtained regular prescription from pediatrician.

The paradox is that almost at the same time, nimesulide has been withdrawn from the market in some countries because of nimesulide-induced severe liver injury and death. As early as 2002, nimesulide was withdrawn from market because of many case reports of liver failure in Finland, Spain, and Turkey. In Ireland, nimesulide-containing products were suspended to market in 2007. In India, nimesulide was forbidden to use for fever in children under 12 years old in 2011. In USA, nimesulide has never been available. All these suggested that nimesulide has potential safety risk.

Under this circumstance we can not help to ask: Is nimesulide safe for Chinese people?

In the beginning of this year, nimesulide ADRs event occurred in China. The event was ignited by a news report at CCTV, China Central Television, on 26 November 2010. Top pediatric medical experts from all over the world gathered in a symposium in Beijing to discuss the drug safety for children. They put forward that nimesulide should be used carefully because of its potential safety risk and should be prohibited to use for fever in children under 12 years old.

Because nimesulide is the most used and a blockbuster drug for fever in children in China, this news aroused huge social concerns. Nimesulide safety became the focus of public attention overnight. On 14 February 2011, an in-depth report in 21st Century Business Herald claimed that many ADRs are induced by nimesulide, especially severe liver damage in children, based on the ADR database in China. The in-depth report put the cat among the canaries.

Hainan Honz Pharmaceutical is the biggest listed company. Nimesulide is its competitive product whose output was estimated at 740 million bags last year. This meant that each child was taken an average of 3 bags for 250 million children in China in 2010. The spokesman of Honz responded to media claiming that the in-depth report was "purely fabricated".

According to our clinical practice and experience, we think the response from Honz is irresponsible. As a matter of fact, we happened to observe an ADR case in our hospital at the end of last year. A young girl toddler, 18 months old, was given nimesulide orally by her parents at home for her fever, 1/3 bag (50 mg per bag) a day. On next day, her face skin showed xanthochromia, and she vomited several times, with body temperature 37–38 °C. The girl was sent to see a doctor and treated with antibacterial agent ceftriaxone and gastrointestinal drug domperidone. However, the abdominal distension and xanthochromia were gradually increased. Hepatic function test showed ALT 711 IU/L and AST Undetectable High. The case was diagnosed drug-induced liver damage. The drug here is nimesulide.

We further reviewed medical literature in China Journal Full-text Database from 1991–2011. Fifty first-hand ADRs case reports induced by nimesulide were collected. Among them, 20 (40%) cases were drug-induced liver damage, including 4 cases of drug-induced hepatitis, and 2 cases died of liver failure (one was a child).[1–3] The others were edema (11 cases), kidney damage (oliguria, hematuria) (9 cases), erythema fixed/multiforme eruption (5 cases), upper gastrointestinal hemorrhage (2 cases), phlebitis of superficial veins of lower extremity (1 case), hiccup (1 case), and decreased

vision (1 case). These evidences showed that nimesulide is not safe for Chinese people, although it has low occurrence of ADRs in the gastrointestinal tracts. It could induce severe liver damage and even death.

In China, ADRs might be concealed by a pharmaceutical company because of conflict of interests. However, ADRs could not be ignored by health professionals. As professionals, we have responsibility and obligation to require that nimesulide should no longer be used for fever in children in China. Children in China can not become the victim of a listed company interest. If State Food and Drug Administration (SFDA) in China insisted that nimesulide is a safe drug and continue its clinical use for children, we prefer not to recommend nimesulide as first-line medicine. We will educate every parent of a sick child that nimesulide may induce liver damage.[4] We will also require SFDA modify the nimesulide dispensatory and emphasize its potential severe toxicity—liver damage. We hope SFDA can conduct a large sample survey for ADRs occurrence of nimesulide in China to answer the public uncertainty about nimesulide safety.

Although China has made some achievements in GDP, we still have a long way to go. ADR monitoring workers in China shoulder heavy responsibilities. We need work together to build a safe environment for children growth.

CONFLICT OF INTEREST

The authors have no conflicts of interest that are directly relevant to the content of this article. The views presented in this paper are entirely personal and have no connection to current and former employers of the authors or to any professional or scientific society the authors are associated with.

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