Vol 10| Issue 1| 2020 | 1-3.

e-ISSN 2248 – 9142
print-ISSN 2248 – 9134

International Journal of
Current Pharmaceutical & Clinical Research

www.ijcpcr.com

A BANNED DRUG –NIMESULIDE

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ABSTRACT

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) with pain medication and fever reducing properties. Its approved indications are the treatment of acute pain, the symptomatic treatment of Osteoarthritis and primary dysmenorhoea in adolescents and adults above 12 years old. Nimesulide was first launched in Italy as Aulin and Mesulid in 1985. Nimesulide is absorbed rapidly following oral administration. It undergoes extensive biotransformation, mainly to 4-hydroxynimesulide. Nimesulide as a relatively rapid onset of action, with meaningful reductions in pain and inflammation observed within 15 min from drug intake. It should be avoided by children under 12 and people with liver problems or flu-like symptoms because it can cause high risk of liver toxicity. It is a new, selective cyclooxygenase-2 inhibitor with few adverse effects on the gastrointestinal system. Nimesulide is the only NSAID related to the having a prevalent effect on COX-2, has a balanced action on both cyclooxygenase.

Key words: Nimesulide, Osteoarthritis and primary dysmenorrhoea.

INTRODUCTION

The antipyretic action and mechanism of action of 4-nitro-2-phenoxymethane sulfonamide (nimesulide), a new non-steroidal anti-inflammatory drug, was investigated in yeast-induced febrine rats. Nimesulide was aggressively promoted the status of nimesulide became questionable reports of fatal adverse drug reactions [1]. The continuing use of nimesulide for Indian children is shocking. Although some studies have indicated that nimesulide may be chosen for Osteoarthritis in selected patients with associated gastric problems. Numerous For this toxic effects, nimesulide is not used in the United states and many European countries also banned the drug for its unacceptable rate of serious adverse reactions. Published Indian studies indicate rampant abuse of nimesulide. At least 12 pediatric preparations of nimesulide are available in Indian, which affirms the widespread of the drug in children.

Literature review

Nimesulide is a potent non-steroidal anti-inflammatory and a selective cyclooxygenase-2 inhibitor [2-7]. The use of Nimesulide is increasing and recently concerns have been raised regarding its hepatotoxicity, especially in children. At least two deaths due to fulminant hepatic failure have been attributed to nimesulide. In India, nimesulide has been approved and about twelve pediatric preparations are available. Nimesulide has serious side effects and which has been banned in parts of Europe is still available in India, despite reports in the press of several deaths in the subcontinent among children who had been taking it. India approved this drug in 1994 for painful inflammatory musculoskeletal disorders, it is often used for pain relief and fever [8-10].

Dr Chandra Mohan Gulhati, editor of India's drug information bulletin, the monthly index of medical specialities, said that the drug had not been approved in the United States, parts of Europe, Canada or Australia and that year it was banned in Finland, Spain and Turkey. "But it continues to be marketed with impunity in India", he said [10-13].

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ADVERSE EFFECTS

Nimesulide is associated with rare and unpredictable but serious hepatic adverse reactions and the time of onset of liver reactions varied from several days to almost 1 year, suggest that the rare cases of liver injury may be caused by a metabolic idiosyncrasy. This implies that multiple individual host factors affect the toxicity to mitochondria in vitro, although it is unlikely that the high concentration required are therapeutically relevant [12-14].

Pharmacodynamic activity

The anti-inflammatory, analgesic and antipyretic activity of nimesulide, a non-steroidal anti-inflammatory drug (NSAID) of the sulfonamide class, have been demonstrated in a number of experimental models and in numerous clinical trials. Nimesulide has exhibited potency similar to or greater than that of indomethacin, diclofenac, piroxicam and ibuprofen in standard animal models of inflammation such as carrageenan-induced rat paw Oedema and inflammation, ultraviolet light-induced erythema in guinea-pigs and adjuvant arthritis in rats. Nimesulide has shown superior antipyretic potency to indomethacin, ibuprofen, aspirin and paracetamol in rats with yeast-induced fever.

Nimesulide is a relatively weak inhibitor of prostaglandin synthesis in vitro and appears to exert its effects through a variety of mechanisms including free-radical scavenging, effects on histamine release, the neutrophil myeloperoxidase pathway, bradykinin activity, tumor necrosis factor-alpha release, cartilage degradation, metalloprotease synthesis, phosphodiesterase type IV inhibition, platelet aggregation and synthesis of platelet activating factor. Animal studies have suggested that nimesulide is less ulcerogenic than aspirin, indomethacin, naproxen, piroxicam and ibuprofen. Nimesulide appears to have effect on renal prostaglandin synthesis in rats.

On the basis of clinical trials, administration of nimesulide orally or rectally twice a day (up to 4 week), was effective in reducing pain associated with Osteoarthritis, cancer, thrombophiebitis, oral surgery and dysmenorrhea in adults and reducing pain associated with general surgery in adults and children and pain, fever and inflammation accompanying respiratory tract infections, otorhinolaryngological diseases and traumatic injury in adults and children [15-17].

RESULTS

Various studies and reports shown that nimesulide is an effective COX-2 inhibitor and continued administration lead to serious liver damage in patients. The risk of acute and serious liver injury associated with the use of nimesulide and other NSAIDs, with a prevalence of use greater than or equal to 5% were estimated.

In 2002, Finland and Spain withdraw nimesulide from the market following reports of serious liver damage. Cases including 2 deaths had been reported in France at the time. The European Medicines Agency has confirmed the hepatic risks associated with nimesulide in 2007, but merely limited the duration of treatment, leaving patients exposed to an unjustifiable fatal risk.

CONCLUSION

The committee of Human Medicinal products recommends nimesulide for the treatment of acute pain and primary dysmenorrhea with a maximum daily dose of 100mg twice daily and for less than 15 consecutive days. Of the 1,387 GPs contacted, 1,277 were nimesulide prescribers and were included in the analysis. Prescribers of nimesulide represented 92% of the contacted physicians in all the countries in the survey, with the exception of Hungary (85%), Portugal (81%), Greece to 200 for Poland and 201 for Italy. 31,719 patients in total were estimated to be prescribed nimesulide per month, ranging from 1,242 patients in Greece to 7,457 Patient in Italy. On the average, 72% nimesulide prescriptions were for symptomatic treatment of Osteoarticular diseases.

Following the recent communication from the Drug Controller General of India (DCGI) to various industry, consumer and professional bodies to be part of the review committee for nimesulide, it has been reported in the news that Dr.Reddy's laboratories whose branded nimesulide reportedly accounts for about 40-45% share of Rs 190 crore domestic market, is believed to have withdraw its pediatric preparation of nimesulide from the market. If this is really true, we should appreciate the concern of this company.

It is also a great sorrow that matters relating to serious and fatal ADRs of drugs are discussed in the media first and not in scientific bodies. Many private companies producing nimesulide and cost less for higher profit, so that the continuous usage of this drug (above 3-4 weeks) lead to severe hepatotoxicity in patients.

AKNOWLEDGEMENT

Nil

CONFLICT OF INTEREST

Nil

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