Australasian Medical Journal 2009, 1, 9, 78-81

Unregulated Sale of Nimesulide in India

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RESEARCH

Please cite this paper as: Oberoi DV, Goraya H, Mungee A, Sharma S, Dang A, Agarwal K, Kulkarni T, Khatri D, Rajeev A. Unregulated Sale of Nimesulide in India. AMJ 2009, 1, 9, 78-81. Doi 10.4066/AMJ.2009.144

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Abstract

Introduction
Nimesulide has been withdrawn from a number of countries. However it continues to be available over the counter in India.

Methods
A survey of 1460 drug stores and 1531 families in India on their perceptions of the potential side effects of Nimesulide.

Results
A high proportion (78.96%) of the drug stores sold the drug without prescription from a licensed physician. More than one in four families (26.95%) preferred Nimesulide to other drugs. A relatively small proportion drug store owners and families (12.14% and 9.6% respectively) were aware of the potential adverse effects of this drug.

Discussion
There is an urgent need to tighten regulation of dangerous drugs freely available to Indian consumers. Further research to increase public awareness about drug side effects is required in order to reduce the potential for harm from under regulation.

Introduction
The appropriate use of prescribed drugs is a burning issue in healthcare. One closely scrutinized class of drugs is the NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). Among the NSAIDs Nimesulide has received particular attention over the past few years. Ever since its launch in 1985 in Italy, Nimesulide, a cyclooxygenase-2 inhibitor (COX-2) NSAID has been the subject of considerable controversy because of its reputed side effects. [1, 2, 3] Concern about its adverse effects has led to the drug being withdrawn from a number of countries.

On one hand clinical data has led to the conclusion that Nimesulide is a safe and effective NSAID, with the particular advantage of fewer gastrointestinal side effects due to its COX-2 selectivity. [4-8] At the same time many studies have documented serious adverse drug reactions (ADRs) associated with Nimesulide. [9] Some researchers claim it can cause extensive liver damage and rarely, death due to fulminant hepatic failure. [10, 11, 12] Several studies urge caution in the use of this drug for febrile illness highlighting safer alternatives such as Paracetamol. [13, 14] Recent studies have questioned the safety of Nimesulide in patients suffering from cardiovascular ailments, and also in chikungunya disease, where the cause of death may be linked to Nimesulide taken for the joint pain [15]. Impaired immunity and renal failure have also been linked to Nimesulide. [16, 17] The use of Nimesulide in children younger than 12 years is prohibited in most European and Asian countries; however there are about 12 paediatric formulations still available in India. [18-21] So far orders to withdraw the paediatric preparations from India, as recommended by the Drugs Controller General of India (DCGI), have been disregarded in the absence of any legally binding directives. [20]

The drug is still available in over 50 countries across the world including India and has a significant market share among analgesics and antipyretics. [22, 23] However adverse drug reaction (ADR) surveillance is not reliable in some parts of the world although it is encouraging that there are international trends to improve surveillance systems. [24, 25] For instance, in China the drug safety and post marketing surveillance system is considered an important public health issue priority whereas in India, the surveillance system is less well established and may account for easy availability of a variety of drugs of questionable safety without the need for a prescription in other words 'Over The Counter' (OTC). [26, 27, 28] It is possible that Nimesulide is still available in India for commercial reasons. [29] In 2003, the turnover for

Nimesulide in India was estimated at around US$ 39.5 million. [30] It was notable that the DCGI commissioned a report rather than recommend any action despite the substantial number of patients reporting to hospital with ADRs due to NSAIDs [31].

While the scientific community debates the safety of many drugs the general population remains largely oblivious about this issue in relation to OTC drugs. There is a need to raise awareness about OTC drugs in countries like India, where nearly 70% of the population resides in rural areas and the majority self medicate or consult local pharmacies for minor health ailments.

In this study we aimed to evaluate the extent of OTC sale and usage of Nimesulide in India and also to explore participants' awareness of the potential adverse effects of the drug compared to paracetamol, another very commonly used drug for minor ailments and symptom relief.

Methodology

We conducted a researcher administered survey on OTC sale and use of Nimesulide and paracetamol across 1460 medical stores and 1531 consenting families in India. Ethical clearance was obtained from Sai Padmavati College of Pharmacy, Tirupati, Andhra Pradesh, India and informed consent was obtained from all study participants.

The sample was recruited at the nine major states distributed across the North zone (Delhi, Punjab, Haryana, Uttar Pradesh and Uttaranchal), South zone (Karnataka, Tamil Nadu) West zone (Maharashtra) and Central zone (Madhya Pradesh) India. The participants were selected at random and included the drug store owners and one adult from each selected families for the purpose of survey. No incentives were offered and the survey was administered in an appropriate local language. Those willing to participate were interviewed on the spot. The survey questionnaire was piloted among a small group from both categories of participants and tested for face validity and user friendliness prior to the main study.

Results

The response rate of participants was 76.69%, (1112/1460) for the drug store owners and 73.68%, (1128/1531) for household families. We observed that a very high fraction 78.96%, (878/1112 95% C.I: 76.46-81.25) of the drug stores in the survey sold the drug Nimesulide without a prescription from a licensed physician as a single or combination drug. Around 8.9% of the stores (99/1112; 95% C.I:7.37-10.32) required a prescription from the customer before sale and a slightly higher proportion of the stores 12.14%; (135/1112. 95% CI: 10.35-14.19) were aware of its adverse effects and did not stock the drug. On the other hand 100% of the drug stores stocked Paracetamol and sold it without prescription as an over the counter drug. Among families, we found that nearly a quarter of the population, 26.95%, (304/1128, 95%C.I: 24.44-29.61) preferred Nimesulide over other drugs during episodes of fever and joint or menstrual pain. In this group, around one in three families (33.84%, 103/304 95% C.I: 28.79-39.38) reported having been prescribed Nimesulide when they first used it and subsequently OTC. Nearly one in four families (23%, 70/304 95% C.I: 18.3–27.8) have subsequently recommended the drug to friends or relatives. A small proportion of families (9.6%, 29/304 95% C.I: 6.2 – 12.8) admitted to awareness of potential adverse effects of the drug but would continue to take the drug as long as it provided symptomatic relief. In the latter group a significant proportion (52%, 15/29) of families were not reluctant to administer the drug to their children and were happy with symptomatic relief offered. Those who were reluctant to administer the drug to children opted for drugs like Crocin (Paracetamol formulation), Ibuprofen or Aspirin. Almost one in three families (34%, 384/1128 95% C.I: 31.34-36.85) preferred Paracetamol during episodes of fever or pain while the remaining 39 % (440/1128; 95% CI: 36.20-41.88) preferred to take their doctor's or local pharmacist's advice before administering anything.

Discussion

The availability of medicines in India is an important issue where the sale of many potentially dangerous medicines is unregulated. [28] The issue is also considered important elsewhere in the world . [32, 33] The ready availability of drugs promotes self-medication, with the potential for poisoning, drug interactions and unrecognized adverse reactions [34]. Self-management of common symptoms coupled with poor access to qualified medical advice may lead to avoidable morbidity and mortality. [35] NSAIDs have been reported to lead to significant interactions with anti-coagulants, corticosteroids and anti-hypertensives and, their inadvertent inappropriate use could lead to analgesic nephropathy or even fatalities. [36,37] The lack of accessible information, public debate and misconceptions about the incidence of adverse effects of OTC drugs is a challenge that may be addressed by doctors and underlines the need for counselling when prescribing preparations that may also be available without a prescription.

Recently the Indian government noted that drug formulations not approved by India's drug regulatory agency were being prescribed or sold across the country. [30] Despite the recognized multiple adverse effects, the continuing sale of the Nimesulide is of concern. Our study reveals that a small proportion of the drug stores only supply Nimesulide on a doctor's prescription while the majority continue to sell a product that is not available in many countries. Even neighbouring south Asian countries like Sri-lanka and Bangladesh have withdrawn the drug. [29] An alternative in the form of paracetamol is readily available and has an established safety profile. [38, 39]

In India the restrictions on the sale of pharmaceutical drugs is very limited and drugs like Nimesulide are easily available over the counter. [27, 28] Recent reports suggest that the

generous marketing budgets of the pharmaceutical sector may influence the prescribing and retail decisions. [40, 41] A study from neighbouring Pakistan reported that pharmaceutical companies are the primary source of information about medicines for general practitioners [42]. The condition may not be very different in India where not many non-teaching government hospitals or private clinics are equipped with the drug updates via medical journals. However, some journals have failed to offer impartial advice. [43] Finally we acknowledge that this study has a number of limitations. We were unable to validate the results of the survey with actual sales data for Nimesulide. There may be social desirability bias in the response to researcher administered questions.

Conclusions

There is an urgent need to increase the regulation of potent and dangerous drugs freely available to Indian consumers. Potential adverse reactions need to be published on packaging with recommendations to immediately cease taking the drug in case of the clearly described side effects. Further research on public awareness about drug side effects is urgently required in order to reduce the potential for harm from under regulation.

ACKNOWLEDGEMENT

We wish to thank all the colleagues, friends and medical students who volunteered to collect the data for the study.

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AUTHORS' CONTRIBUTIONS

DVO, HG, SS, TK, AR, AD, AM contributed to study design, literature search, data analysis and manuscript writing. DVO, HG, KA, AM, DK contributed to data collection.

COMPETING INTERESTS

None

PEER REVIEW

Not commissioned; externally peer reviewed