

Time to ban nimesulide from the Libyan medicines market

Amal Y Benkorah^{1*}, Manal Hadood, Aisha Rafaei and Ghazi Benkura²

^{1*}Faculty of Pharmacy, University of Tripoli, Tripoli, Libya

²Faculty of Dentistry, University of Zawia, Zawia, Libya

*Correspondence: a.benkorah@uot.edu.ly or amalbenkorah@yahoo.com

Abstract: Nimesulide is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties which was launched in Italy as Aulin® in 1985. Huge concerns were raised regarding this drug as its users are at a high risk for developing a serious ADR called Drug-Induced liver Injury which may lead to liver failure. The goal of this study was to shed light on nimesulide which is present illegally in private pharmacies and to the harm that it may pose on public health; in order to draw the attention of the responsible authorities to the danger of its availability in our market. A survey of 65 pharmacies in Tripoli was conducted to identify the availability of nimesulide in these pharmacies. The knowledge of its different dosage forms, strength, brands available, pattern of prescribing, and ADRs among pharmacists and coworkers were all collected. 100 % response was obtained as 65 pharmacy personnel answered the questionnaire. We found out that this medicine is available in all of them. The response to the questionnaire is illustrated in figures from 1 to 4. Nimesulide dispensing pattern was shown to be almost always through patients' request. In conclusion, the uncontrolled presence of this medicine may pose a public health risk, therefore a request for its ban from Libyan market should be seriously considered.

Keywords: Nimesulide, adverse drug reaction, drug-induced liver injury, ban, Libya

Introduction

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. It works by inhibiting the cyclooxygenase-mediated conversion of arachidonic acid to pro-inflammatory prostaglandins. It is effective

in the treatment of a wide range of inflammatory and painful conditions including osteoarthritis, tendonitis, bursitis, post-operative pain and primary dysmenorrhea (1). The drug was launched in 1985 in Italy as Aulin® and Mesulide®. It is

available in more than 50 countries worldwide with different brand names including the generic product nimesulide (2). Huge concerns were raised regarding this drug. Patients who use nimesulide are at a high risk for developing a serious adverse drug reaction (ADR) called Drug-Induced liver Injury (DILI). It is a condition that mimics most kinds of acute and chronic liver pathologies symptomatically. DILI is the most common cause of acute liver failure in USA (3, 4) and in Europe (5, 6). It is considered the most serious ADRs and it is the main cause of discontinuing the development of new drugs, and most frequent reason for refusal to approve, or restriction of uses or withdrawal by regulatory agencies (7 - 9). Hepatotoxicity is a rare ADR and it is dose unrelated but serious, and could lead to death (10 - 11). In addition to the above mentioned serious ADR of nimesulide, it also has the known familiar side effects that all NSAIDs have in common, which are stomach and GIT problems.

The European Medicines Agency (EMA) conducted a review of the safety and effectiveness of systemic medicines containing nimesulide (capsules, tablets, suppositories and powder or granules for oral suspension). The committee for Medicinal

Products for Human Use (CHMP) assessed the benefit-risk ratio of systemically used nimesulide in total secrecy. It confirmed the hepatic risks of nimesulide in 2007, but they concluded that its benefit outweighs its risks and decided to restrict its indication for acute pain and primary dysmenorrhea and recommended that it should no longer be used for treatment of painful osteoarthritis since it is chronic condition. The agency also recommended that treatment duration should not exceed 15 days (packs were also limited to 2-week supply) with the lowest effective dose and that nimesulide should be restricted to second line treatment. CHMP committee noted in its assessment that nimesulide has the same risk of causing stomach and GIT problems while its effectiveness does not outweigh the effect of other NSAIDs (13). EMA has confirmed the hepatic risks associated with nimesulide, but merely limited the duration of treatment, leaving patients exposed to an unjustifiable fatal risk. It is quite unacceptable for the EU health authorities to decide to limit only the duration of use without presenting the rationale behind this decision. These half-hearted measures are all the more unacceptable, since this medicine offers no advantages over other NSAIDs. In addition, The International Society of Drug Bulletins (ISDB) issued a

statement, in Dec. of 2007 saying that nimesulide must be withdrawn worldwide. The claim was based on the fact that this drug exposes patients to fatal liver damage. ISDB considers it unacceptable that nimesulide has been allowed to remain in Europe and other countries across the world since it exposes patients to an unjustifiable fatal risk especially without a rational reason and an explanation coming out from the EMA (14). The question was and still is how did a majority of EU member states' rapporteurs who re-assessed nimesulide conclude that the product should remain on the market. Why is there such inconsistency among EU member states? No agreement among countries on whether or not to withdraw or restrict the use of nimesulide. Some countries have never approved its use, as in the USA, UK, Canada, Australia, New Zealand, Japan and other countries, over its safety profile concerns. Finland and Spain withdrew nimesulide from markets after serious liver damage reports in 2002. At that time cases including 2 deaths had also been reported in France. In 2007 Singapore and Ireland decided to withdraw nimesulide from the markets (12).

This study therefore, sheds some light on the contraband medicine nimesulide which is present illegally in Libyan private

pharmacies. A survey was conducted to investigate its presence in the city of Tripoli, to draw the attention of the responsible authorities to the danger of its availability in our market in order to ultimately request its ban. The rationale behind our request to ban nimesulide from the Libyan market is owed firstly to the fact that this drug is not on the Libyan National Medicines List therefore, the Libyan health authority will not be able to protect the consumer except by preventing and fighting its presence in private pharmacies through the municipal guards, and by penalizing its illegal sale. Secondly, medicines available in the community pharmacies are not necessarily under the control and authorization of a registered pharmacist. In other words, this medicine and many other prescription medications may be sold without a prescription in Libya, so consumers may request to buy this product without questions asked, not to mention that even when it is dispensed with a prescription, patients will come back asking for the product due to its fast pain relieving ability and ease of presentation in a sachet form, which render it safer than any other dosage form in the eyes of the consumer. The danger of such practice is that consumers may be unjustifiably exposed to preventable harm and higher risk of fatal hepatic disorders

when taking this medicine. At the same time, this medicine doesn't offer any therapeutic

Materials and methods

Sixty five pharmacies were included in the survey. A questionnaire was constructed to assess the knowledge and awareness of the serious ADRs of nimesulide among pharmacists. Information regarding different doses strength, dosage forms, and brands

Results

100 % response was obtained, as 65 pharmacy personnel answered our questionnaire and the drug was available in all of them. Nimesulide was available in both tablets and sachets form in 28 out of the 65 pharmacies, while 37 pharmacies carry only the sachet dosage form. 71% (46 pharmacy personnel) of those interviewed knew that nimesulide has been abandoned in several

When asked about how often they receive a prescription of nimesulide per year, all 65 pharmacy personnel responded that they rarely receive written prescriptions for nimesulide (not more than 2 to 3 prescriptions per year). The vast majority of nimesulide dispensing pattern was through patients' request for the medicine. 61 % of

advantage, or better gastrointestinal safety when compared with other NSAIDs.

available in these pharmacies were also collected, in addition to the pattern of prescribing of this drug by physicians and dentists, including; strength and duration of treatment

countries worldwide as shown in figure 1; 21 of which were physician and 25 were pharmacists. Only 20 of the 46 knew exactly why; 12 of which were pharmacists. Of those who admitted that they knew about nimesulide's risks, 57 % were pharmacists and 43% were physicians. Responses to the questionnaire are shown in figures 1 to 4.

those who answered that they dispense it upon patient's request were pharmacists and 39% were physicians. Only 5 prefer not to dispense the medicine at all, 3 of which were pharmacists (60%) and 2 were physicians (40%).

Figure 1: Number of pharmacists and physicians working in 65 private pharmacies & their knowledge about Nimesulide's ban worldwide

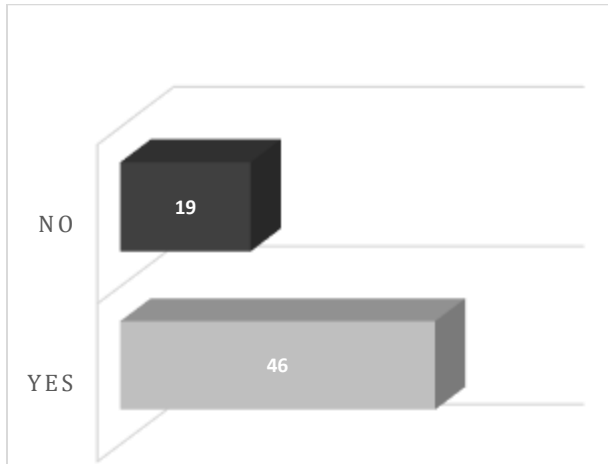


Figure 2: Answers about the reason behind Nimesulide withdrawal in most countries

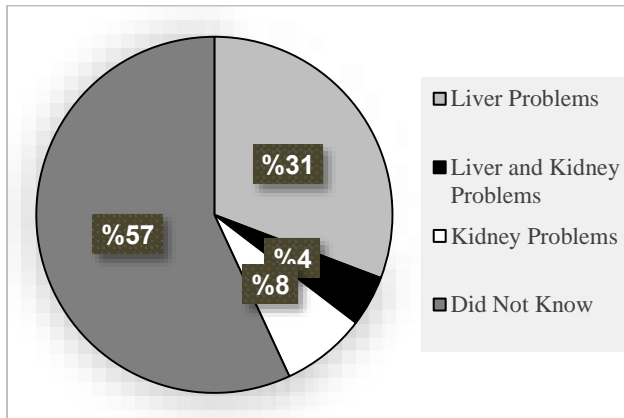


Figure 3: Source of knowledge on Nimesulide among personnel working in 65 private pharmacies in greater Tripoli

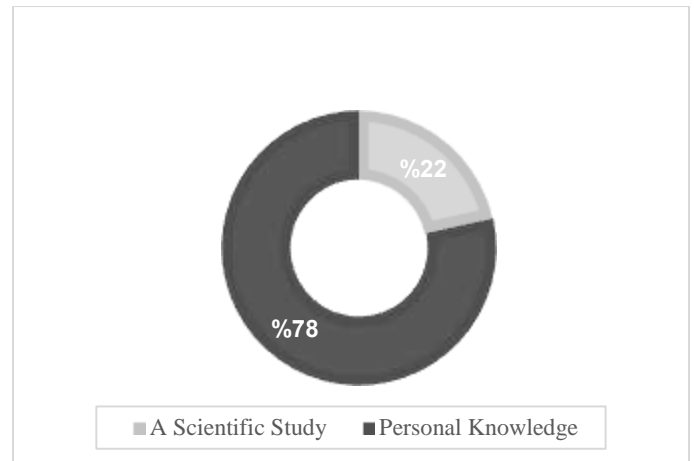
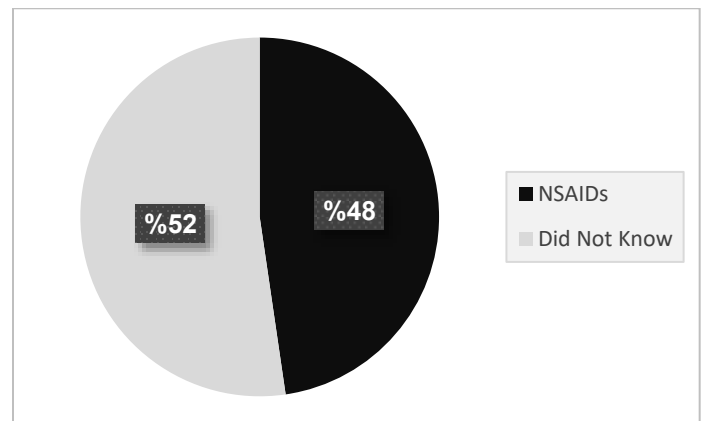


Figure 4: Pharmacists and physicians' scientific background of Nimesulide's therapeutic class



Discussion

Through answering the questionnaire directed to personnel working in 65 pharmacies at different regions in Tripoli city it was clear how conflicting the information is, among pharmacists and physicians regarding this issue. Dispensing medications without prescriptions is a common practice by private pharmacies in Libya. Just as these practices are punishable by law, they are also considered an infringement on physicians' rights to proper diagnosis and prescribing of the appropriate medications for different medical conditions. It also violates the patient's right to appropriate treatment of his/her condition as the physician sees it appropriate. Physicians' dispensing in the pharmacy premises on the other hand, is a malpractice that may result in the wrong diagnosis if they are acting as physicians, as this action requires clinical settings. It also violates the right of the pharmacist who should be the only health practitioner who is responsible for dispensing medicines while providing patient counseling and advice-giving when it comes to medicines. Private pharmacies should therefore be continuously monitored for selling unlicensed products due to the risks and harm that they may impose on the public.

For all the shortcomings that face the procurement of medicines in Libya, this study emphasizes the importance of strict censorship and vigilance on medicines available in the Libyan market. It also points out the wrong practices that the pharmacy profession is facing. We firmly believe that the disadvantages of nimesulide to treat pain outweigh any advantage, and that there are many NSAID alternatives which may be safely used without exposing consumers to any of its risks. This leads us to conclude that there is no rational justification behind its presence in the private pharmacies. Accordingly, the Libyan Food and Drug Center together with the Customs and Municipal Guard must bear the responsibility by taking this issue seriously, and preventing this drug and other contraband medicines from entering the Libyan market by deciding the fate of the presence of nimesulide in Libya. In addition, the pharmacovigilance unit at the Ministry of Health should play active role in educating healthcare professionals, as there is conflicting information between pharmacists, dentists, and patients regarding knowledge of their unsafe use.

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