Research Article

Awareness survey for reporting of herbal drug adverse reaction among community pharmacist in Amravati

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ABSTRACT

Introduction: Adverse drug reactions (ADRs) are one of the major problems associated with medication. Efficiency and success of any the pharmacovigilance program rely heavily on the participation of all health professionals. The World Health Organization defined ADR as any response to a drug that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy, excluding failure to accomplish the intended purpose. **Aim:** The aim of this project is to describe pharmacist reporting of adverse drug reaction in herbal drugs. **Objectives:** The study was conducted to examine awareness about ADRs in drug-treated hypertensive patients. The objectives of the present study were to create awareness among select community pharmacists about ADRs reporting of herbal drugs. **Conclusion:** The pharmacists need to upgrade knowledge and should be aware about all the aspects of ADR of herbal drugs.

Keywords: Adverse drug reactions, Pharmacovigilance, Community pharmacist

Introduction

According to one definition of pharmacovigilance, it is "the study of the safety of marketed medications under the realistic circumstances of clinical use in broad populations."[1] The goal is to increase safety monitoring and identify pharmacological adverse events that had gone unrecognized in the past while being assessed in clinical trials. These techniques were designed to monitor pharmaceutical drugs, but they are also used to assess the safety of other medications, such as herbal remedies, blood products, vaccinations, and even medical gadgets.[2]The reports of probable toxicity and adverse events have grown along with the usage of herbal medications.[3] Such unfavorable effects may result from I side effects, which are typically detectable by pharmacodynamics and frequently predictable; (ii) reactions brought on by overdose, overduration, tolerance, dependence, and addiction (detectable either by pharmacodynamics or pharmacovigilance); (iii) hypersensitivity, allergic, and idiosyncratic reactions; and (iv) short- and long-term toxic effects, such as liver, renal, cardiac, and pharmacovigilance is crucial for spotting adverse responses since many herbal medications on the market have not been adequately evaluated for their pharmacology and toxicity.[4]

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Challenges in monitoring the safety of herbal medicines

1. Regulation: The national licensing and regulation of herbal medicines varies from nation to nation. Herbal medications may be classified as either prescription or over-the-counter drugs in jurisdictions where they are controlled. Other classifications besides medications are also possible for herbal items.[5]
2. Quality assurance and control: Every country that regulates herbal medicines should have quality assurance and control measures in place, including national quality specifications and standards for herbal materials, good manufacturing practices for herbal medicines, labeling, and licensing schemes for manufacturing, imports, and marketing.[6]
3. Safety monitoring of herbal medicines: Clinical trials and unprompted reports are the most prevalent sources of data on adverse occurrences and responses to medications (voluntary and unsolicited communications on marketed medicinal products). Over the course of a product's existence, the latter often out

number the former in both numbers and kind, particularly severe reports. Physicians are required to record adverse reactions in certain nations, and these reports are considered spontaneous.[7]

4. Recording and coding the identity of herbal medicines: It is preferable to use an uniform categorization and identification when sending reports to the UMC. It is recommended that the coding of adverse events and adverse responses to herbal medicines be consistent with that for other medications.[8] The World Health Organization (WHO) Drug Dictionary (WHO-DD), which was created to contain organized and categorized information on the names of herbal products and their constituents in the same manner as equivalent information on other medications, is what the UMC recommends using as a result. The UMC suggests the herbal anatomic-therapeutic-chemical (HATC) classification for the therapeutic categorization of herbal products, which is structurally identical to the ATC classification used for chemical compounds in other treatments. To integrate with the worldwide WHO database, HATC is being deployed under the WHO-DD framework. A system checklist for cross-referencing botanical and common names used as ingredient names is proposed using the HATC classification and the extended worldwide WHO. The UMC advises that the national pharmacovigilance centers should find the WHO-DD, the HATC classification, and the checklist to be helpful tools when posing questions to the reporter to improve the clarity and accuracy of reports.[9]

It is sometimes impossible to identify every constituent in herbal medications since they frequently include many. In these situations, it is advisable to write down the product name and refer it to the UMC, which will aid in identification. The product will be added, along with any pertinent data, if it is not already in the worldwide WHO database.[10] A single herbal product could have many indications and so show up in several categories under the HATC categorization.[7] When feasible, the specific Latin binomial botanical name of the medicinal plant (genus, species, and author, as well as name of family) should be given, together with details on the plant components utilized and the extraction and preparation techniques used. With the use of this data, precise comparisons to other reports are possible.[11] To prevent the filing of a report from being postponed or cancelled, a popular vernacular term may be employed. Regarding taxonomy (botanical and chemical) identification and botanical and vernacular nomenclature, national pharmacovigilance centers should cooperate with pharmacognosydepartments of universities as well as with botanists, zoologists, and botanical garden employees.[12]

Toxicity and adverse health effects of some common herbal medicines

The widespread belief that herbal medications or treatments are very safe and free of side effects is not only false but also deceptive. It has been shown that a variety of unfavorable or unpleasant responses may be produced by herbs, some of which can result in fatal or life-threatening diseases, severe injuries, or even death. Poisoning cases have been documented in large numbers and with absolute certainty in the literature.[13] An unpublished case report of a young adult male who used the herbal product Yoyo "Cleanser" Bitters® for self-medication and was later admitted to the hospital due to liver failure served as the impetus for the recent toxicity evaluation of this polyherbal formula that was carried out in our laboratory.[14] Yoyo "Cleanser" Bitters® is one of the herbal treatments that is heavily promoted in the different Nigerian media. As a result, it has been widely accepted by the general public over time and continues to experience rising consumer demand, particularly in the South-west of the nation. Our research showed that after 30 days of treatment to rats, this herbal remedy was capable of increasing plasma levels of liver enzymes and causing hypokalemia. We saw that the risk linked with this herb during this sub-acute exposure or toxicity trial was increased potassium loss, which has the potential to predispose to harmful arrhythmias. We previously conducted an experimental model safety assessment of the "super B blood purifier" and "super B seven keys to power" mixes over 10 years ago.[15] A recognized Nigerian business that produced therapeutic herbal concoctions and grew medicinal plants sold these herbal combinations. The manufacturer's assertion that "they are safe, offer strength, and cleanse the blood and body of illness" supports the widespread use of the herbal blood tonics by regular people. Entandrophragma utile and Anacardiumoccidentalis were collected, and we looked at both the individual plant extracts and the herbal tonics manufactured from them. Although all of the extracts and tonics were shown to be safe during an acute toxicity assessment, a lung tumor case and 10% of mice given E. utile or either of the two tonics developed splenic enlargement during chronic toxicity testing.[16] There has recently been information of a link between the usage of traditional herbal remedies and the occurrence of liver fibrosis in research participants in Uganda. Numerous herbal remedies from China and other countries across the globe have also been linked to poisoning incidents. Numerous them have been shown to contain hazardous chemicals that may interact with DNA and other cellular macromolecules, producing genotoxicity and/or cellular toxicity.[17]

The majority of nations do not require any safety or toxicological testing before the introduction of herbal medications and associated goods to the market. Many of these nations also lack efficient equipment to control production standards and procedures. Most of the time, these herbal products are regularly made accessible to customers without a prescription, and the risks of using a subpar product are seldom acknowledged.[18]

Only a few regularly used herbal medications' adverse responses are discussed here for the sake of brevity and other obvious limits.

Aristolochic acids and *Aristolochia* species

Numerous investigations that followed the identification of the nephrotoxic and carcinogenic potentials of aristolochic acids verified their genotoxic activity and showed the existence of DNA adducts linked to aristolochic acids in patient kidney tissues. When generated, these mutagenic adducts often undergo poor repair and have a long persistence time in DNA.[18] Different Asian medicinal herbs have been shown to contain aristolochic acids I and II, and slimming items have also reportedly included these substances. Because of this, medications

containing these acids are now prohibited in Belgium, the UK, Canada, Australia, and Germany.[19]

Ephedra sinica

Ephedra is a widely used plant that has a long history of usage in treating respiratory issues. This herb is now listed in the Chinese Pharmacopoeia for medicinal use and is categorized as non-toxic since its effectiveness has been shown in several randomized, double-blind, and clinical studies.[20] The usage of ephedra has been linked to a variety of major deleterious effects on the cardiovascular and central nervous systems (CNSs), and it has been sold as a weight-loss dietary supplement in the US. *E. sinica* and dietary supplements containing ephedra have also been associated in some case reports to negative side effects such hepatotoxicity and temporary blindness.[21]

Allium sativum: Garlic

In addition to its usage as a meal or food additive, garlic has been proven to be relevant for the control of hypertension and hypercholesterolemia.[22] It is known to contain alliin, which when crushed or chopped without the use of heat or acid transforms into allicin when activated by alliinase. There have been reports of adverse reactions to garlic extract, including gastrointestinal discomfort, nausea, diaphoresis, and lightheadedness. In addition, this extract may result in contact dermatitis and excessive garlic consumption has been linked alone to a severe spontaneous spinal epidural hematoma.[23]

Piper methysticum: Kava

Kava is a well-known CNS depressant with a history of usage as an anxiolytic. After oral administration, this medicinal plant often causes headaches, dizziness, gastrointestinal pain, and regional numbness.[24] Large doses have been proven to be capable of causing dry, scaly skin, nail discoloration, photosensitivity, and redness of the eye, as well as yellowish discoloration of the skin and nails. Photophobia and diplopia may also result from excessive kava use.[25]

Methodology

A validated self-administered questionnaire was given to 100 pharmacists in the Amravati as part of a cross-sectional research. There were 21 items in this cross-sectional questionnaire-based observational study. Within the next 24 h, the responders completed the surveys and sent them back to us. Thus, data from completed surveys were analyzed. All clinical trials and adverse drug reactions (ADR) reports were searched. We gathered pertinent data, such as gender and age. The questionnaire is included in Tables 1 and 2, along with the pharmacist's answer.

Results and Discussion

This is the first study conducted by us to evaluate and compare information and vision regarding awareness of pharmacovigilance and ADR reporting of herbal drugs among community pharmacists in Amravati District. In the present study, a total response rate of 100% was recorded. From the results, it was noted that overall in our research, knowledge and opinion were better among the young pharmacists compared to the elderly ones. As they were students of pharmacy once, this is not surprising as pharmacy students are exposed to all the basics features of pharmacovigilance in their syllabus during the academic years. It was also evident in the knowledge-based research question of pharmacy students; they were found to know more about pharmacovigilance and basic common ADR's reporting a reaction. This is because they are taught about identification, testing, understanding, and preventing drug reactions to some degree in their syllabus. It has been reported that pharmacy students should be given greater emphasis on pharmacovigilance and reporting ADRs that would encourage them to participate promoting ADR reporting to other health students.

The results are summarized in Figure 1 and 2.

After asking questions to pharmacist, we got response as, 96% of community pharmacist well known about pharmacovigilance and 4% did not aware about it. All the pharmacists were found known about ADR but when asked about adverse event, 4% were known about it and remaining 96% were unknown to this term. Only 42% pharmacist found aware about reporting ADR to authorized person. About 48% pharmacist found aware about identification of ADR.

It was found in survey that ADR related to herbal drugs was observed by only 10% community pharmacist and 90% were unknown about it. Same found in case of reporting of ADR of herbal drugs, only 10% pharmacist have found to known about ADR reporting of herbal drugs. According to 90% pharmacist, patients prefer herbal drug as

Table 1: Questions asked to pharmacist and their response (Question set 1)

S. No	Common questions	Yes	No
Q1	Do you know about Pharmacovigilance?	96%	04%
Q2	Do you know about ADRs?	100%	0%
Q3	Do you know about Adverse Events?	96%	4%
Q4	Do you know how to report ADRs to authorize person of office?	42%	58%
Q5	Do you know how to identify ADRs?	48%	52%

ADRs: Adverse drug reactions

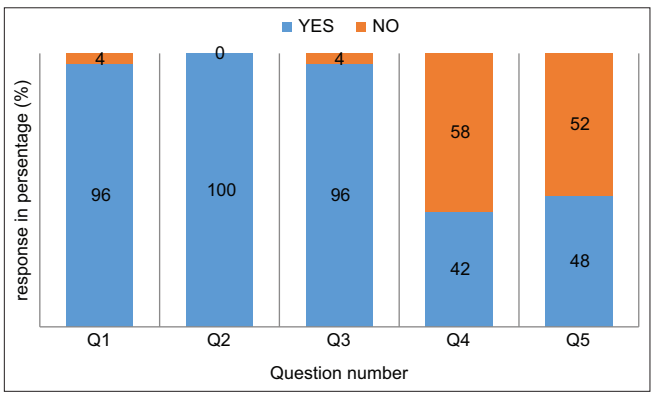

Figure 1: Response of pharmacist to question set 1

Table 2: Questions related to herbal drugs (Question set 2)

S. No	Questions related to herbal drug	Yes	No
Q6	Did you ever come across patients experiencing ADRs related to herbal drugs?	10%	90%
Q7	Did you report an ADR related to herbal?	10%	90%
Q8	Do patients prefer herbal drug as OTC product?	90%	10%
Q9	Do you record patient history before dispensing herbal drug?	50%	50%
Q10	Do you observe any severe ADR of herbal drug?	10%	90%
Q11	Have you listed out herbal drugs that patient report complaint about?	30%	70%
Q12	Do you council about reported ADR of herbal drugs with patient or prescriber?	15%	85%
Q13	Do you maintain record of patient and herbal drug dispensed to them?	89%	11%
Q14	Do you participate in ADR management of herbal drug?	7%	93%
Q15	Have you noticed age group preferring herbal drug and for which disorders these are preferred?	59%	41%
Q16	Does ADR of herbal drug differ from person to person? Can you identify ADR?	50%	50%
Q17	Should herbal drugs be dispensed by pharmacist without prescription?	10%	90%
Q18	Do you think herbal drugs need ADR recording too?	75%	25%

ADR: Adverse drug reaction

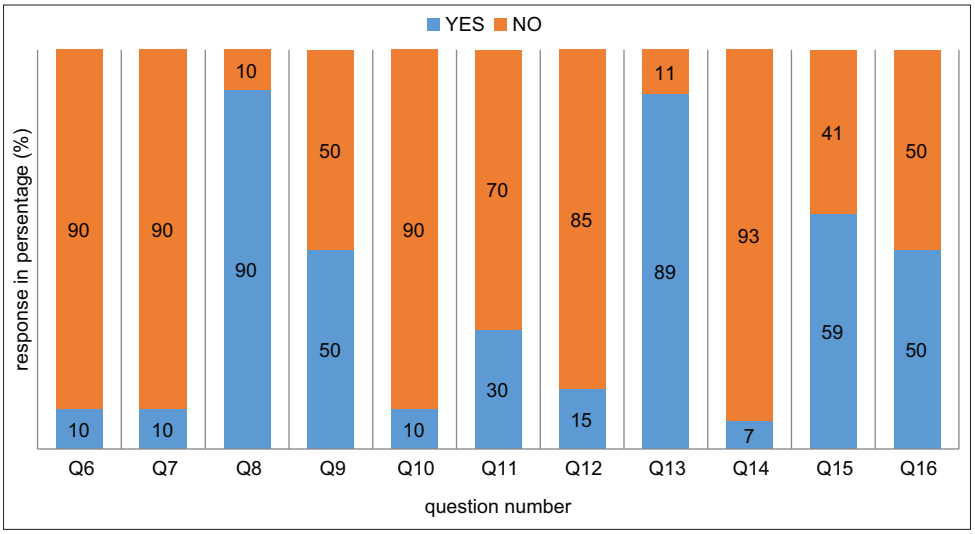

Figure 2: Response of pharmacist to question set 2

OTC product. About 50% pharmacist record patient history before dispensing herbal drug and 50% does not. About 10% pharmacist have observed some severe ADR of herbal drugs while remaining did not. About 30% pharmacist listed out herbal drugs that patient report complaint about and 70% did not. About 15% council about reported ADR of herbal drugs with patient or prescriber, 85% not interested in counseling. About 89% maintain record of patient and herbal drug dispensed to them. Only 7% pharmacist participate in ADR management of herbal drug. About 59% pharmacist noticed age group preferring herbal drug and for which disorders these are preferred. About 50% pharmacist say that ADR of herbal drug differ from person to person and they can identify ADR. About 10% pharmacist thinks herbal drugs be dispensed by pharmacist without prescription while majority says that it should be dispensed against prescription only. About 75% pharmacist think herbal drugs need ADR recording too while 25% says no need to record ADR for herbal drugs.

Conclusion

Pharmacist have very casual behavior for herbal drugs. The awareness about ADR of herbal drug and its reporting is not sufficient thus we should make pharmacist aware about all the aspects of herbal drug ADR.

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