REVIEW ARTICLE

Pharmacovigilance: The Least Understood and Least Practiced Science in Dentistry

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Abstract

Aim: The purpose of this review was to explore the overall scenario of pharmacovigilance, its aims, challenges, and recommendations pertaining to dentistry for further improvements.

Materials and methods: Literature search was done with the help of the Endnote software, followed by vigilantly arranging the material in a coordinated way.

Results: Adverse drug reactions (ADRs) are among the top 10 leading causes of all-cause mortality. In order to reduce the harm to the patients and serve the public health mission, there is a definite need for developing mechanisms for evaluating and monitoring the safety of medicines in India. Therefore, the requirement for developing a well-organized pharmacovigilance system is imperative. Different countries have developed their own reporting guidelines for pharmacovigilance. The reporting guidelines are conceived to adapt to the specific requirements of any country and the prime focus of these adverse event reporting systems is improving the patient's health and safety. The Central Drugs Standard Control Organization (CDSCO) has initiated a nation-wide pharmacovigilance program in India. It aims to protect the health of the patients by assuring drug safety under the aegis of Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. In dentistry, the science of pharmacovigilance is rarely applied and its practice among dental health professionals, including reporting of ADRs, is minimal. However, studies have shown that the dental professionals comprehend the importance of pharmacovigilance and its application in dentistry.

Conclusion: It is essential to foster a sense of trust among patients regarding the medicines they use, to ensure that risks in drug use are anticipated and managed. This will eventually enhance the confidence of patients on the healthcare delivery system in general.

Clinical significance: The practice of dentistry involves prescribing various medications for patient use. It is therefore the duty of the dentist to comprehend and identify the adverse effects of the drugs. Dentists should also know about the right channel for reporting any instances of ADRs. They should also strive toward increasing the awareness among patients regarding possible side effects so that any untoward consequences can be avoided. This will be an invaluable aid in furthering the public health mission of improving the health of the populations.

Keywords: Dental professionals, Indian scenario, Pharmacovigilance.

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Introduction

The major cause of death and socioeconomic disruption globally is various diseases afflicting mankind. In recent times, many diseases have emerged that may not have effective control or preventive measures. Hence need of the hour is the availability of newer, better, and safe drugs to tackle these newer morbidities. The manner in which the diseases are managed and controlled has drastically changed with the advent of modern drug systems.

However, the incidence of adverse drug reactions (ADRs) cannot be entirely ruled out.[1] Adverse drug reaction has now emerged as one of the leading causes of all mortalities. The harm done by the drugs can be reduced by developing proper evaluation and monitoring methods for safety of the patients. This will be an invaluable aid in furthering the public health mission of improving the health of the populations. This can be carried effectively by developing a well-organized pharmacovigilance system.[2] According to the World Health Organization (WHO) collaborating center for International Drug Monitoring, "Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems."[3]

Pharmacovigilance begins at clinical trials and continues all long the product life. It can be broadly divided into before-marketing (premarketing) and after-marketing phases (postmarketing).

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The phase 1 of the clinical trial begins by collecting the information pertaining to the safety of the drug before the drug is approved. Studies will continue even after the release of the drug into the market. Postmarketing surveillance is now rendered mandatory by various drug regularity agencies around the world.[4] Pharmacovigilance also deals with the following:

- Issues related to substandard medicines
- Errors in medication
- Lack of efficient reports
- Inappropriate prescription of medications when it is not indicated
- Reports of cases for poisoning, both acute and chronic
- Cases of mortality due to drug use
- Misuse and abuse of medicines
- Adverse interactions with chemicals, food, and other medicines.

Aims of Pharmacovigilance[4]

- It aims to improvise the care given for the patients and their safety in relation to medicines and paramedical intervention
- It aims for improvement in safety of public health in relation to the drugs used by the public
- It aims in assessing the harm, risks, effectiveness, and benefits of the drugs and evaluating their safety, rational, and more effective use
- It aims to improve the knowledge, promote education, understanding, clinical training, and its communication to the public in pharmacovigilance.

Global Perspectives of Pharmacovigilance and ADR Reporting[4]

Pharmacovigilance guidelines are not uniform across the world and show considerable variation from country to country. Reporting guidelines are based on requirements that are specific for a nation and have evolved to form a system addressing the needs of that nation. The main aim of the reporting system is to monitor the harmful effects of the drugs, which helps in improving the health of the patients.

A program under the WHO termed International Drug Monitoring was initiated in 1978, with only 10 countries participating in it. It has now grown by leaps and bounds at the global level, with the active participation of 120 countries.

Functions of National Pharmacovigilance System[5–7]

Following WHO's suggestions in January 2010 and also considering review of the Advisory Committee regarding Safety of Medical Product (ACSoMP) in April 2010, the National Pharmacovigilance System has adopted specific functions. These functions are as follows:

- Promotion of pharmacovigilance in a country has to be implemented by collecting the ADR reports along with substandard drugs and reports of medical errors
- The information should be collected from existing ADRs of the country and also cohorts that monitor internationally in defined patients or populations. This information has to be collaborated and harmonized for further considerations
- Drug safety indications pertaining to unknown and poorly characterized adverse events and other events that occur due to combination of drugs have to be identified
- The assessment of risk of ADR and outlining its management is to be undertaken
- The recognition of the quality of the medicine and endorsing it, also to identify the resulting ADRs that may occur due to the drug
- The team should also take responsibility for the effective communication on drug safety and also dispel the rumors of the toxicity of medicines and vaccines
- The information from pharmacovigilance has to be applied appropriately as it benefits individual patients, national medicine policies, public health programs, and treatment guidelines
- The development and maintenance of information related to drug utilization has to be undertaken
- The issues regarding unregulated prescribing of medicines and their dispensing are to be identified.

Pharmacovigilance Structure in India[8]

A nationwide pharmacovigilance program to protect the health of the patients was initiated by the Central Drugs Standard Control Organization (CDSCO). As a part of this program, the safety of drugs is assured under Directorate General of Health Services, Government of India, and Ministry of Health and Family Welfare, Government of India. Suggestions put forth by the WHO in the document titled "Safety Monitoring of Medicinal Products: Guidelines for Setting up and Running a Pharmacovigilance Center" were implemented. The Indian Pharmacopoeia Commission based in Ghaziabad functions as the National Coordinating Center (NCC) and it synchronizes the program under supervision of a steering committee. The National Pharmacovigilance Program was officially inaugurated on 23 November 2003 in New Delhi. Offices were established at regional and peripheral, zonal, and national levels to synchronize various activities pertaining to pharmacovigilance in India (Fig. 1).

Broad Objectives of the Program

- To develop the culture of reporting and notification of unfavorable events
- To establish a robust and broader ADR monitoring system in India.

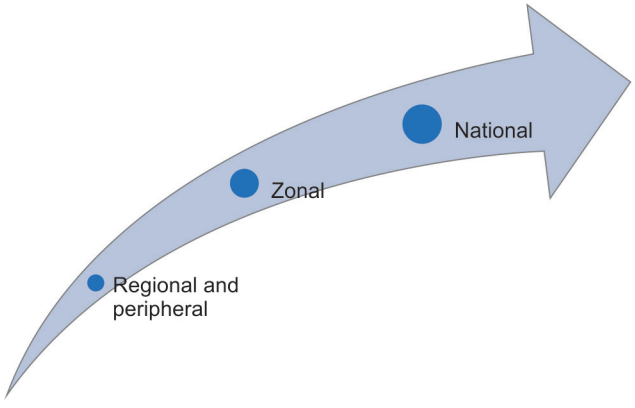

Fig. 1: Hierarchical structure of the pharmacovigilance centers in India

Discrete Objectives of the Program

- To make an ADR database for the population of India
- To create awareness regarding observation of ADRs among general people
- To guard the safety of drugs in India
- Development of infrastructure for the regulatory reviews of periodic safety update reports (PSURs).

National Pharmacovigilance Center[9]

The National Pharmacovigilance Center is at CDSCO and performs the following activities:

- To ascertain the harmful drug reactions of the medicines that should be identified beforehand or to indicate certain commonly occurring reactions
- To always maintain a record of the periodic safety update reports (PSURs) provided by the pharmaceutical companies
- To exchange information on the drug safety and to establish contacts with the international organizations and agencies of pharmacovigilance
- To promulgate safety regulations outlining the actions to be taken, if necessary, to improve the safe use of the drug
- To disseminate the information on the adverse effects of drugs through bulletins, alerts, news, and seminars.

National Pharmacovigilance Program in a Nutshell

This program provides the information regarding the ADRs of all the drugs that are available in the country and reports to the Central Drug Regulatory Authority (CDSCO). National Pharmacovigilance Advisory Committee (NPAC) coordinates the program constituted by the Ministry of Health and Family Welfare, Government of India. The program comprises the following steps:

Step 1: to recognize various centers that would provide the ADR-related data

Step 2: health professionals as participants of the national pharmacovigilance program have to be trained and calibrated.

Pharmacovigilance in Dentistry

The adverse effects of the drugs can be manifested as oral signs and symptoms such as dry mouth, oral ulcerations, taste disturbances, or swellings. Among adverse reactions that occur in 200 most frequently prescribed drugs, dry mouth is very common, constituting 80.5%. This is followed by dysgeusia (47.5%) and stomatitis (33.9%). Evidence was collated from case reports, randomized double-blind controlled studies, nonpeer-reviewed reports, and case series of the oral manifestation of the adverse effect of the drugs.[10]

Efficacy and safety of the drug are main issues to be considered when the drug is administered. It is relatively easier to measure the efficacy of the drug but it may prove to be tedious to measure the safety of the drug. Patients can show different intensities of the adverse effects that occur due to the drug.[11] Adverse reactions of the drugs are being reported more frequently among hospitalizations. In a systematic review of prospective observational studies, it was estimated that the prevalence of ADR cases reported was 0.16–15.7%.[12] The hazards of developing ADRs are growing on one hand, while on the other hand, the identification and reporting standards of ADRs are not adequate.[13] Geriatric population and medically indigent groups faced the brunt of severe ADRs.[14]

Adverse drug reaction-related international data are found to be meager due to professional attitudes and behavior of the healthcare workers. Hence, for the safer usage of the medicines for the public, there should be appropriate detection, recording, and reporting measures for ADR. A suitably developed pharmacovigilance system might play a critical role in the same. Feely et al.[15] have reported that reporting of ADRs can be enhanced by offering financial incentives to healthcare workers for every case of ADR that they report. Further studies on methods for strengthening reporting of ADRs among healthcare professionals will shed more light on this aspect of pharmacovigilance.

The pharmacovigilance programs in India are implemented by the government agencies to reduce the frequency of ADRs being reported. There are many ADR monitoring centers in major cities across India established by the Indian Council of Medical Research (ICMR) and Drug Controller General of India. Although there are numerous tertiary care facilities available, the pharmacovigilance system is in its early stages. The major reason may be the minimal understanding and awareness of the pharmacovigilance among healthcare workers in India. In our country, there is underreporting of the cases of ADR, which may be due to the improper training of the staff members or lack of the awareness. Case detection, communication, and the monitoring should be spontaneous among the health workers, which include nurses, dentists, physicians, and pharmacists. The training and methods of enactment should be constantly regulated among different healthcare workers.

Previously reported studies on pharmacovigilance have shown shortcomings in the attitude as well as the knowledge of the healthcare workers pertaining to reporting of ADRs.[16–22] Every healthcare worker should know where and importantly how to report an ADR. The principles of the pharmacovigilance can be achieved only when there is an active involvement and participation of all the healthcare professionals.

Various studies have explored knowledge, attitudes, and practices of the dental practitioners regarding the ADRs. Iffat et al.[23] conducted a study in Pakistan, which revealed that many of the dental as well as the medical students felt that reporting the ADR cases to the concerned ministry was important. The respondents also reported that the potential role of the pharmaceutical company was important. In a similar study conducted by Talattof and Azad among dental professionals, authors reported that the dentists had little information regarding the importance, goal, and process of reporting established ADRs.[24]

Praveen et al.[25] had reported attitude, knowledge, and practice relating to the ADRs among dental and medical practitioners. Authors have observed that there was a significant gap of knowledge in reporting ADRs but favorable attitudes toward reporting ADRs among the participants. Shalini et al.[26] conducted a similar study on the attitude and knowledge of dental students in a university at Malaysia regarding ADR and pharmacovigilance. Results show that the respondents had low knowledge but reported positive attitude regarding the ADR reporting system and the pharmacovigilance. A study by Bansode et al.[27] pertaining to the awareness of pharmacovigilance among tertiary care hospitals or resident doctors also revealed low awareness among respondents. To improve the awareness and practices regarding pharmacovigilance, there is an immediate need to train the healthcare professionals.

Arjun et al.[28] have reported very poor knowledge and poor attitude regarding the pharmacovigilance among the healthcare

workers in a teaching hospital. Pimpalkhute et al.[29] have assessed awareness regarding pharmacovigilance and ADR monitoring in tertiary care hospitals with resident doctors with the help of a questionnaire. Authors observed that the lesser numbers of ADRs being reported may be due to poor knowledge regarding the reporting process followed by lack of time due the increased workload in their clinics. Deficient pharmacovigilance training and awareness programs regarding risks of medicines and ADRs at the undergraduate level might also be one of the major impediments.

Khan et al.[30] explored attitudes, knowledge, and practices of dentists regarding ADRs in a hospital. It was observed that deficiency in attitude and knowledge may be the main reason for low reporting of ADRs by a dentist. A study of attitude regarding pharmacovigilance and ADR reporting was undertaken among healthcare professionals including dentists by Sudhakar et al.[31] The authors observed that the respondents reported moderate attitude regarding the ADRs without any significant association with gender, experience, and qualification. Gupta et al.[19] explored the attitude, knowledge, and perceptions of the resident healthcare workers in reporting the ADRs and pharmacovigilance. It was concluded that the awareness regarding the type of event that occurred or the drug that caused the ADR and its reporting mechanisms was found to be deficient. Inadequacy of expertise, lack of sufficient time, poor knowledge regarding the reporting mechanism, and tedious procedures could be the main reasons for the underreporting of the ARDs.[32] Chhabra et al.[33] have reported that dental students in Jodhpur, India, had appropriate attitude scores but low knowledge and behavior scores related to pharmacovigilance. In a similar study conducted by Kumar et al.,[34] it was observed that medical and dental students in Wardha, India, had favorable attitude scores. In a systematic review on knowledge, attitude, and practices related to pharmacovigilance among health professionals in India, it was observed that there were many lacunae in knowledge, attitude, and practices among respondents. The authors have highlighted the need for increasing awareness about pharmacovigilance among various health professionals in India.[35]

Challenges that the Pharmacovigilance will Face in Future

- The information available on the Internet regarding the free availability of drugs may not be entirely reliable. Such information regarding the safety, quality, and efficacy of drugs that are unregistered, prescription drugs, traditional or herbal drugs, and highly controlled substances, may be questionable
- Complications from overdose, interactions, irrational drug use, traditional or herbal medications, polypharmacy, drug abuse, and illegal sale of medications due to the self-medication practice based on the knowledge attained from the Internet, medication error, and also lack of the efficiency of medications all come under the purview of pharmacovigilance
- Imperfections and conflicts in the pharmaceutical industry while dealing with the public's health and their safety in the drug use.
- The generic sector has not fully recognized that it is their responsibility to monitor the safety of the released drug throughout the world
- Understandings of the harm, benefits, and the extent of the acceptable risk regarding the medicines have become less meaningful in the current era of information. In developed and developing countries, the drug-induced diseases have recently been given importance due their increasing morbidity and mortality due to ADRs.

Conclusion

It can be concluded that pharmacovigilance continues to play a crucial role in meeting the challenges posed by the ever-increasing range and potency of medicines, all of which carry an inevitable and sometimes unpredictable potential for harm. Although health professionals report that paying attention to ADRs and timely reporting is very important, underreporting of ADRs is still a substantial problem. Undergraduate training in pharmacovigilance and awareness about risks associated with medicine use may be either deficient or unsatisfactory to prepare the prospective doctors for the job of ADR monitoring and reporting in their future career.

While prescribing medications in clinical practice, usually a trade-off between potential benefits and harms has to be taken into consideration. The harm that could be caused by medicines can be minimized by improving quality, safety, and efficacy of the medicines and of course rational use. Expectations and concerns of the patient should be taken into consideration when any therapeutic decisions are made. Risks in drug use need to be anticipated and managed effectively. There is a definite need to improve communication between health professionals and the public and educate health professionals to understand the effectiveness or risk of medicines that they prescribe. Pharmacovigilance has definite public health implications as the frequency of ADRs being reported is increasing.[36] It is essential to foster a sense of trust among patients in the medicines they use, which would eventually pave the way for enhanced confidence in the healthcare delivery system.

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