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Commentary

Drug induced diseases (DID): Need for more awareness & research

Iatrogenic disease or drug induced disease (DID) is an ever enduring concern for patients, healthcare professionals and health administrators. In spite of being a major concern in clinical practice, DID has not been given the due attention it deserves. One of the reasons for this may be that DID causes apprehension among health care professionals making them uncomfortable as well as unwilling to be part of studies undertaken to reduce DID. In India, several individual case reports have been published related to specific iatrogenic disease but a comprehensive study on this problem is not yet published. The true incidence or prevalence of DID in our country is not known. The results of the study by Tandon *et al*[1] in this issue provide information on DID in Indian setting. Although the study has a few limitations and overlap between adverse drug reactions (ADR) and DID, yet it flags an important issue which needs attention.

The magnitude of adverse drug reactions which includes DID is huge. Considering its importance, the Central Drugs Standard Control Organisation (CDSCO), New Delhi, Government of India, had initiated a nation-wide Pharmacovigilance Programme of India (PvPI) in July 2010. The total number of Individual Case Safety Reports (ICSR) in PvPI database is 84,470[2]. In the US, it was reported that ADRs accounts for more than one lakh death each year and it is between the fourth and sixth leading cause of death[3]. In our country, we do not have statistics on DID but the total ADRs in PvPI database for the last few years are less than one lakh. This indicates the scenario of under reporting of ADRs in our country compared to United States of America[3].

A classic paper published in 1981 found that 36 per cent of 815 consecutive patients in general medical service of a tertiary care hospital had iatrogenic illness[4]. Likewise a prospective study from Portugal reported that 22.9 per cent of patients admitted in the department of internal medicine developed iatrogenic disease[5]. In the present study by Tandon and colleagues[1], the reported incidence of DID is 38.8 per cent. However, contrary to previous studies, the present study was retrospective and the data were obtained from the ADRs reported to Adverse Drug Reaction Monitoring Center, functioning under PvPI. As this study methodology may not be considered as ideal, there is a need for prospective and well-designed epidemiological studies to be undertaken in this area. Further, future studies should also focus on elderly who are prone to have chronic illness, consulting multiple physicians and receive polypharmacy. Most of the published reports on DID are from tertiary care hospitals including the present one[1]. However, the epidemiology of ADR (including DID) occurring in primary care and in general practice remains uncertain.

The various factors contributing to DID can be related to pharmacokinetic and pharmacodynamics of drugs, non-adherence to prescribed drug therapy as well as medication errors[6]. Concurrent diseases (*e.g.* liver and renal impairments), genetic polymorphisms in drug metabolizing enzymes and transporters, nutritional factors (hypo-albuminaemia may result in more free drug of highly protein bound drugs) and concomitantly administered drugs may also contribute to alteration in drug metabolism as well as target receptor activities of drugs. Hence in this era of personalized medicine, prescribers need to understand and update their knowledge on the rapidly transforming drug information.

In the present study[1], 99.3 per cent of the total DIDs were reported as Type A (predictable) reactions. As these reactions are anticipated extension of drug's known pharmacological action, the acquaintance of pharmacokinetic and pharmacodynamic knowledge of

a drug can help to prevent the DID. Moreover, a good understanding of pharmaceutical formulations and their applications can help in reducing DID. Peyriere *et al*[7] have reported that 57.9 per cent of drug related admissions in internal medicine or during hospitalization are preventable. These ADRs were associated with therapeutic errors namely inappropriate administration, drug-drug interactions, dosage error and continuation of drug despite the onset of ADRs[7]. Correspondingly, a report has suggested that nearly 73.8 per cent of iatrogenic events as a cause of intensive care unit admission are probably preventable[8].

Being on the front lines of patient care as well as pharmacotherapy, healthcare professionals need to be knowledgeable regarding the risk of drug-induced diseases, including methods of detection, prevention, and management. The published studies reveal that, to be more efficient, health care practitioners need to be skillful in patient consultation and education in addition to possessing knowledge on complex biomedical science. However, effectiveness in these roles requires lifelong learning to keep pace with rapidly changing information about drugs and their effects. In fact, the issue of drug safety in general is an excellent focus for interdisciplinary education in health care.

The WHO-UMC (Uppsala Monitoring Centre) Global drug safety database[9] for the year 2013 has 8.5 million ADR reports. In this, India's contribution accounts for nearly 0.7 per cent of the global data base[9]. In the last 30 years, India has witnessed banning or withdrawal of nearly 90 drugs for manufacture and sale by CDSCO (Central Drugs Standard Control Organization)[10]. This forecasts the urgent need to expand the countrywide PvPI activities so as to implement safety decisions and policy at the regulatory levels in the interest of patient safety.

Policy decisions regarding patient safety and medication errors can be achieved through promotion of population based surveillance of DIDs by PvPI in association with CDSCO. In addition, continuing medical educational programmes and training need to be imparted on the healthcare professionals to keep them updated about DIDs as well as on the measures taken to prevent them. The importance of spontaneous reporting of adverse drug reaction needs to be included in the curriculum of all healthcare professionals and the habit needs to be cultivated right from the undergraduate level. While doing so care should be taken to maintain confidentiality of the patients as well as reporting personals so as to encourage further reporting. Likewise during diagnosis as well as while teaching medical graduates, emphasis needs to be given on deliberation of DID as one of the causes of the disease.

Basic and epidemiological researchers interested in evidence based medicine and personalized medicine can be motivated to contribute towards the detection, quantification and reduction of DIDs of the marketed drugs. In addition, carrying out systematic reviews as well as meta analysis to generate evidence towards the occurrence of DID can add required information to the armamentarium of pharmacovigilance[11]. Tools of personalized medicine such as pharmacogenomics, transcriptomics, proteomics, metabolomics, epigenomics, bioinformatics, systems biology, *etc*. can be used to identify individual patients suffering from DID due to genetic polymorphisms[12]. These details related to drugs as well as patients need to be compiled, correlated and to be made easily accessible to physicians using technology available in the hospitals.

A few developed countries have integrated Electronic Medical Records into an electronic prescription module for their patients[13]. Similar systems can be introduced in our country after imparting training to the healthcare professionals on their use. Integrating Electronic Health Record (EHR) system with evidence driven decision support can be presented to the physicians, along with crucial evidence-based literature to promote timely and informed medical decision making. Further integration with a single platform solution that includes an electronic prescribing module provides the physician with objective, medication therapy decision support at the point of prescribing[14]. In addition, EHR may offer the benefit of analyzing related information across various patients thus providing a better source for detecting DIDs. Hence, including EHR system in the hospitals all over the country through PvPI could be a better option to pool all the data and get more information on DIDs at one place.

DID could be a consequence of either anticipated effects as seen in the present study[1] or else could also be due to unanticipated effects as seen in idiosyncratic adverse effects. In addition to pharmacokinetic changes contributing to DID in elderly and children, it could also result from drug-drug and food-drug interactions. Thus

pharmacovigilance needs to be continuously under the vigil of regulatory authorities, drug manufacturers, healthcare professionals and the administrators of health care. Last but not the least, measures should be taken to inculcate the practice of physicians considering themselves as an integral part of PvPI, as reporting of ADR is not just an option but an obligation.

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