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Editorial

An Overview on Adverse Drug Reactions

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An enormous number of drugs are introduced to the market every year and practically it is not feasible to avoid potential drug interactions. These drug interactions can lead to altered systemic exposure, resulting in disparities in drug response of the other co-administered drugs. Additionally, associated ingestion of dietary supplements, citrus fruit/juice could also change systemic exposure of drugs, thus leading to Adverse Drug Reactions (ADRs). In 1972, World Health Organization (WHO) defined ADR as 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function'. Multiple drug courses for therapy carry the risk of adverse interactions, which may result to loss of efficacy. Therefore, it is crucial to assess potential drug interactions and risk-benefit analysis prior to market approval as well as during the post-marketing period.

ADRs are one of the chief reasons of morbidity and mortality in health care, costing around $136 billion annually [1] which is more than the cost of cardiovascular or diabetic care in United States. In 2000, The Institute of Medicine reported that from 44,000 to 98,000 deaths occur annually from medical errors [2] out of which, ~ 7,000 deaths occur due to ADRs. However, other studies carried on hospitalized patient populations have shown much higher estimates on the incidence of serious ADRs. These studies shows that ~ 6.7% of hospitalized patients have a serious adverse drug reaction with a casualty rate of 0.32% [3]. If these assessments are right, then there are more than 2,216,000 serious ADRs in hospitalized patients, causing over 106,000 deaths annually and ADRs are the 4th leading cause of death, before pulmonary disease, diabetes, AIDS, pneumonia, accidents, and automobile deaths. Also, it is assessed that over ~ 350,000 ADRs occur in United States nursing homes every year [4]. The precise number of ADRs is not certain but it epitomizes a note worthy public health problem that can beavertible.

In the recent past, an exceptional number of drugs have been withdrawn from the United States market due to safety issues as revealed through post marketing surveillance. These drugs include fenfluramine (Pondimin), dexfenfluramine (Redux), terfenadine (Seldane), bromfenac (Duract), astemizole (Hismanal), mibefradil (Posicor), grepafloxacin (Raxar) and, very recently, the rotavirus vaccine (Rotashield). Serious drug interactions were a cause in the withdrawal of three of these drugs (terfenadine, astemizole and mibefradil). In 1999, United States Food and Drug Administration (USFDA) alarmed new safety warnings regarding following drug interactions [5], which include interactions between celecoxib (Celebrex) and warfarin (Coumadin), methotrexate (Rheumatrex) and radiotherapy, pimozide (Orap) and cytochrome P450-3A (CYP3A) inhibitors, cisapride (Propulsid) and grapefruit juice, and nevirapine (Viramune) and methadone.

ADRs result in one out of 5 injuries or deaths per year to hospitalized patients [6]. Occurrence and severity of ADRs differ by patient features (Eg, age, sex, ethnicity, existing disorders, genetic or geographic factors) and by drug (Eg, type of drug, administration route, treatment duration, dosage, and bioavailability). Most ADRs are dose-related; others are allergic or idiosyncratic (unexpected ADRs that are not dose-related or allergic). For dose-related ADRs, altering the dose or removing or decreasing precipitating factors may be enough. Enhancing the rate of drug elimination is seldom required. For allergic and idiosyncratic ADRs, the drug usually is withdrawn and swapping to a different drug class is often vital for allergic ADRs and sometimes required for dose-related ADRs.

USFDA has established Med Watch, the FDA Medical Products Reporting Program [7], in 1993 due to vital significance of post marketing surveillance on new drugs. This program has 4 objectives:

a. Increase attentiveness for drug, device and other medical product that may induce ADRs and the importance of reporting ADRs to FDA by physicians, nurses, pharmacists, and other health care practitioners.
b. Clarify what should (and should not) be reported. Health professionals should report serious adverse reactions so as to improve the quality of individual reports and facilitating the FDA and the manufacturer to emphasis on the most important ADRs.
c. Facilitate easy reporting to the FDA.
d. Offer feedback to health care professionals about new safety problems with pharmaceuticals and medical devices. Med Watch also monitors changes in the nature and frequency of ADRs.

Prevention of ADRs is very crucial and therefore ADR monitoring and reporting must be taken into consideration [8]. Reviewing of ADR reports must be done regularly and information should be provided to professional staff regarding the incidence and impact of ADRs. A good medication history of the patients must be taken before prescribing medicines to them. Identification of high-risk patients such as, pregnant women, breast-feeding women, the elderly, children, and patients with renal or liver dysfunction, must be done carefully and they must be closely monitored by physicians and pharmacists that will help prevent serious adverse reactions. Discussion should be done regarding changes in the formulation or standard treatment guidelines for recurring problems with ADRs. The staff must be educated, especially providers, concerning ADRs. Computer-based analysis should be used to cross check the potential drug interactions and re-analysis should be done whenever drugs are altered or added. Drugs and initial dosage must be cautiously selected for the elder patients. If patients develop nonspecific symptoms, ADRs should always be considered before starting symptomatic treatment.

The incidence of severe or fatal ADRs is very low (typically < 1 in 1000) and may not be obvious during clinical trials. Thus, these ADRs may not be detected till after a drug is released to the market for patients' usage. Clinicians should not assume that all ADRs are known after the drug is introduced to the market and hence post-marketing surveillance is extremely important for tracing low-incidence ADRs. Reviewing of medication errors and product quality complaints is essential to ensure that they are not contributing to the incidence of ADR at the hospital. In conclusion, ADRs must be under strict vigilance in order to reduce the morbidity and mortality from drug interactions and thus building a safer healthcare system for the society.

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