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ORIGINAL ARTICLE

A prospective study on Adverse Drug Reactions of antibiotics in a tertiary care hospital

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Abstract Adverse reactions are the recognized hazards of drug therapy and they can occur with any class of drugs and many studies revealed that the incidence is more in case of antibiotics. The main aim of this study was to detect and analyze Adverse Drug Reactions of antibiotics in inpatients of a tertiary care hospital. A prospective spontaneous reporting study by active and passive methods was carried out for a period of six months. A total of 49 ADRs were reported during the study period with male predominance (53.06%) and geriatric age group. More number of ADRs was from General Medicine and Pediatric departments in which the most affected organ systems were the GIT (38.77%) and the skin (30.61%). The antibiotic classes mostly accounted were cephalosporins (34.69%) followed by fluoroquinolones and others in which type A reactions were more compared to type B and 59.18% of them were predictable. The severity assessment revealed that most of them were moderate (63.26%) followed by mild and severe reactions. Of the reported reactions, 55.10% were definitely preventable and causality assessment was done which showed that 71.42% of the reactions were probable, possible (18.36%), definite (10.20%) and no reactions were unlikely. The study concluded that Adverse Drug Reactions to antibiotics are common and some of them resulted in increased healthcare cost due to the need of some interventions and increased length of hospital stay. The health system should promote the spontaneous reporting of Adverse Drug Reactions to antibiotics, proper documentation and periodic reporting to regional pharmacovigilance centers to ensure drug safety.

1. Introduction

Drugs are the most common medical interventions, primarily used to relieve sufferings. But it has been recognized long ago that drug themselves can prove fatal; as the saying rightly goes "Drugs are Double Edged Weapons". Adverse reaction monitoring and reporting are very important in identifying

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the adverse reaction trends in local population (Phatak and Nagari, 2003).

In its simple definition an ADR is any undesirable effect of a drug beyond its anticipated therapeutics occurring during clinical use. The WHO defines an ADR as ''any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function.'' Thus this definition excludes overdose (either accidental or intentional), drug abuse, and treatment failure and drug administration errors (Ramesh et al., 2003).

Drug toxicity is a major limitation in providing health care to patients at a global level. It affects patient's recovery as well as the economy of health care. With the increase in production of various pharmaceutical products, newer drugs are being introduced every year. Hence, the need for an active surveillance system to remove the harmful drugs that have entered the market was well realized by the WHO. This has been the basis for starting the international drug monitoring program by the WHO (Surendiran et al., 2010).

Adverse reactions are recognized hazards of drug therapy. Adverse Drug Reactions (ADRS) are important causes of mortality and morbidity in both hospitalized and ambulatory patients. In many countries ADRs rank among the top 10 leading causes of mortality. So there is a need to study ADRs seriously to create awareness about ADRs among patients to motivate health care professionals in the hospital to report ADRs to minimize the risk. Early detection, evaluation and monitoring of ADR are essential to reduce harm to patients and thus improve public health (Pirmohamed and Brecken, 1998).

The safety of drug prescribing has become a highly visible topic in medicine, due in part to research suggesting that there are important ADRs caused by commonly used medications. Patients constitute a vulnerable group with regard to rational drug prescribing since many new drugs are released into the market without the benefit of even limited experience. This deficiency causes a practitioner to often prescribe drugs in an 'off label' manner, thereby increasing the risk of drug toxicity. As more drugs are marketed and as more individuals take multiple drugs, the occurrence of Adverse Drug Reaction will probably continue to increase. Therefore, better approaches must be devised for reporting and assessment and management of individuals who present with drug induced diseases (Mohammed Misbah et al., 2010).

ADRs have a considerable negative impact on both health and healthcare costs. ADR monitoring and reporting activity is in its infancy in India. India is a developing country with a large drug consuming population. It is the fourth largest producer of pharmaceuticals in the world with more than 6000 licensed drug manufacturers and over 60,000 branded formulations. Thus it is essential that the drug treatment should be safe, efficacious and cost effective. It is also emerging as a clinical trial hub exposing larger population to newer drug treatments. It is the need of the hour to identify Adverse Drug Reactions as early as possible and to prevent them if possible, to ensure the well-being of the patient at a reasonable cost. The Ministry of Health and Family Welfare had initiated the National Pharmacovigilance Program (NPP) on 1st January 2005 which was further revived in July 2010. This program is overseen by the Central Drugs Standard Control Organization (CDSCO), New Delhi (Vikas et al., 2004; Amrita and Singh, 2011).

Adverse reaction can occur with any class of drugs. According to a study conducted by Novotny et al., the most troublesome classes of drugs contributing to Adverse Drug Reactions were antibiotics followed antitumor agents, they are responsible for the recorded adverse effects in approximately 16% and 15% of cases, respectively (Novotny and Novotny, 1999).

Antibiotics belong to different classes such as penicillins, cephalosporins, sulfonamides, and aminoglycosides, and they vary in respect of their mechanism of actions and adverse effects. Antibiotics are used commonly in routine practice for treatment and prophylaxis of various disease conditions (Tripathi, 2007).

Over half of all hospitalized patients are treated with antimicrobial agents and their use account for 20–50% of drug expenditures in hospitals. More than 70% of ICU patients receive antibiotics for therapy or prophylaxis, with much of this use being empiric and over half of the recipients receiving multiple agents. The total costs associated with antibiotics are not only related to antibiotic use itself, but also to co-medication and adverse drug events. In Darchy's report, antibiotics accounted for 11% of iatrogenic disease. Classen states that, although adverse events seem to occur in a small proportion of antibiotic courses, the frequency of antibiotic use makes them account for 23% of all adverse events recorded (Stavreva et al., 2008; Granowitz and Brown, 2008).

The main aim of this study was to detect and analyze Adverse Drug Reactions (ADR) to antimicrobial drugs in hospitalized patients of a tertiary care hospital.

2. Methodology

A prospective spontaneous reporting study involving, active methods (pharmacist actively looking for suspected ADRs) and passive methods (stimulating prescribers to report suspected ADRs) was carried out in all departments of a tertiary care referral hospital, Kerala for a period of one year. Patients of all age groups who developed Adverse Drug Reactions of antibiotics were included for the study. The data for the study were taken from case sheets, investigation reports of patients who had experienced an ADR, personal interviews with reporting persons or clinicians, personal interviews with patient or patient's attendant, past history of medication use, which were generally obtained from, prescriptions from the past, reports of Medical and surgical interventions, referral letters, etc.

The causality assessment of the reported ADRs was carried out using the ''Naranjo causality assessment scale''. In the Naranjo Algorithm, the drug reaction can be classified as definite, probable, or possible. The modified Schumock and Thornton scale classifies ADRs as definitely preventable, probably preventable and not preventable based on a set of questions for each level. The modified Hartwig and Siegel scale classifies severity of ADR as mild, moderate or severe with various levels according to factors like requirements for change in treatment, duration of hospital stay, and the disability produced by the Adverse Drug Reaction.

3. Results

During the study period, a total of 49 antibiotic Adverse Drug Reactions were reported among 15,037 patients admitted for antibiotic use. The incidence rate of antibiotic Adverse Drug