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REVIEW

Factors affecting the development of adverse drug reactions (Review article)

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Abstract *Objectives:* To discuss the effect of certain factors on the occurrence of Adverse Drug Reactions (ADRs).

Data Sources: A systematic review of the literature in the period between 1991 and 2012 was made based on PubMed, the Cochrane database of systematic reviews, EMBASE and IDIS. Key words used were: medication error, adverse drug reaction, iatrogenic disease factors, ambulatory care, primary health care, side effects and treatment hazards.

Summary: Many factors play a crucial role in the occurrence of ADRs, some of these are patient related, drug related or socially related factors. Age for instance has a very critical impact on the occurrence of ADRs, both very young and very old patients are more vulnerable to these reactions than other age groups. Alcohol intake also has a crucial impact on ADRs. Other factors are gender, race, pregnancy, breast feeding, kidney problems, liver function, drug dose and frequency and many other factors. The effect of these factors on ADRs is well documented in the medical literature. Taking these factors into consideration during medical evaluation enables medical practitioners to choose the best drug regimen.

Conclusion: Many factors affect the occurrence of ADRs. Some of these factors can be changed like smoking or alcohol intake others cannot be changed like age, presence of other diseases or genetic factors. Understanding the different effects of these factors on ADRs enables healthcare professionals to choose the most appropriate medication for that particular patient. It also helps the healthcare professionals to give the best advice to patients. Pharmacogenomics is the most recent science which emphasizes the genetic predisposition of ADRs. This innovative science provides a new perspective in dealing with the decision making process of drug selection.

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1. Introduction

Safety issues arise whenever medical choices have to be made (Bauer, 2008). ADRs can occur in all settings where healthcare is provided. Most of the current evidence comes from hospitals because the risks associated with hospital treatment are higher (Yurdaguel et al., 2008). Many such events occur in other healthcare settings such as consulting rooms, nursing homes, pharmacies, community clinics and patients' homes (Steven et al., 2008). While the drug manufacturing process has been revolutionized by modern techniques, drug safety assessment stays behind and is still reliant on technologies that have been used for several decades (Powley et al., 2009). Current conceptual thinking on the safety of patients places the prime responsibility for ADRs on deficiencies in system design, organization and operation – rather than on individual practitioners or products. Berwick and Leape (1999) recommended that checks and quality assurance should be built into the use system, rather than assuming that all will be well. By the time a drug is marketed, only about 1500 patients may have been exposed to the drug. Thus, only those ADRs occurring at a frequency of greater than 1 in 500 will have been identified at the time of licensing (Andrade et al., 2007). Pirmohamed et al., 1998 suggested that the assessment of ADRs therefore is likely to represent an important aspect of drug therapy. Bates et al., 2003 showed that the overall rate of ADRs is estimated to be 6.5 per 100 admissions; 28% of these reactions are preventable. Once marketed, a drug loses the scientific environment of clinical trials and is legally set free for consumption by the public (Russell et al., 1992). At this point, most drugs will only have been tested for short-term safety on a limited number of previously defined and selected individuals.

ADR is defined 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 modification of physiological function (WHO, 1973). It is also defined as an undesirable effect, reasonably associated with the use of the drug that may occur as a part of the pharmacological action of a drug or may be unpredictable in its occurrence (Edwards and Aronson, 2000).

1.1. Magnitude of ADRs

ADRs are one of the leading causes of morbidity and mortality in healthcare. The Institute of Medicine, in the United States (US) (2000) reported that between 44,000 and 98,000 deaths occur annually from medical errors. Of this total, an estimated 7000 deaths occur due to ADRs. Analyzing 39 studies of the American pharmaceutical system over four decades found that in 1994, 106,000 people died as a result of ADRs. More than 2 million suffered serious side effects (Pomeranz and Bruce, 1998). These figures showed that there was a trend of increasing death and injury from ADRs. That would make ADRs the fourth leading cause of death in the US behind heart disease, cancer and strokes (Jemal et al., 2005). In another survey conducted by the American Society of Health-System Pharmacists, Byrne et al. (2006) found that 85% of patients who responded to the survey expressed concerns about at least one drug-related issue, such as receiving interacting drugs, having harmful adverse effects from a drug, or receiving the wrong drug. ADRs are a significant public health problem in the world. Not only do ADRs cause death and injury but they also affect the length of stay in hospitals which in turn leads to increased healthcare costs and decreased patient productivity. Moura et al. (2009) determined the frequency of ADRs in intensive care units and evaluated their effect on the length of stay and found out that each ADR presented by the patient was related to an increase of 2.38 days in the ICU. In research