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Use of Adverse Drug Events Resulting in Healthcare

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Abstract

Women in comparison to men have lower bodyweight and organ size, more body fat, different gastric motility and lower glomerular filtration rate. These differences can affect the way the body deals with drugs by altering the pharmacokinetics and pharmacodynamics of the drugs including drug absorption, distribution, metabolism and elimination. Gender plays a role in the effect on ADRs.

Keywords: Drugs; Hospitalization; Women; Acute and Chronic Health; Populations; Isoenzymes

Introduction

A study of sex differences in ADRs to antiretroviral drugs indicates potential sex differences in the frequency and severity of ADRs to antiretroviral drugs. Hepatic enzyme CYP is more active in females than males which lead to different effects on drug metabolism. They also suggested that women are more prone than men to develop torsade de pointes ventricular tachycardia during the administration of drugs that prolong cardiac repolarization. Women restrict their activity because of acute and chronic health problems approximately more days per year than do men, spending approximately more days in bed each year than men. Women have twice as many physician visits and hospital stays as men. When reproductive and other sex-specific conditions are excluded, the difference in hospital stay virtually disappears, but the difference in ambulatory care is still approximate. After the age of 40s, when all sex-specific conditions are excluded, women continue to have approximately more physician visits, with men having a greater frequency of hospitalization. In a north Indian study on angiotensin converting enzyme inhibitors and cough, females had a higher incidence of cough compared to males [1]. In Chinese populations, the metabolism of midazolam in women is more than in men due to the activity of CYP3A4. Moreover, the pharmacodynamics differences between men and women are particularly seen with cardiac and psychotropic drugs. Chlorpromazine and fluspirilene seem to be more effective in women than in men for the same dosage and plasma concentration. Some drugs affect one sex without the other, e.g. colchicine which is used for the treatment of many diseases including Familiar Mediterranean fever might affect fertility in males but not in females. On the other hand, hepatic drug reactions are more common in females. It was estimated that the female gender is a risk factor for hepatotoxicity more than men. Gender differences refer not only to biologic differences but to physiologic, social, behavioural, and cultural differences as well. Results of various animal studies illustrated the fact that a significant difference in drug metabolism and elimination due to gender difference provide an impetus for sex based research in humans. Recent advances in the characterization of specific isoenzymes of drug metabolism paved the way for preliminary identification of the enzyme system affected by sex. Limited current studies showed apparent CYT activity higher in females than in males while other enzymes are increased in males. Men and woman show different pharmacodynamics responses to various drugs which may lead to different therapeutic responses [2]. Female specific issues such as pregnancy, menopause and menstruation may have profound drug effects in humans. A few clinically significant ones like increased elimination of anti-epileptics decreasing their efficacy in pregnancy, oral contraceptives interfering with metabolism of many drugs and conversely certain drugs can impair contraceptive efficacy. Moreover, the most pronounced differences between women and men were seen in a study about the incidence of ADRs caused by cardiovascular medications; low-ceiling diuretics caused a relative risk, cardio tonic glycosides caused a relative risk, high-ceiling diuretics caused a relative risk and coronary vasodilators caused a relative risk. One of the most consistent observations in health research is that women report symptoms of physical illness at higher rates than men [3]. Still unresolved is whether this is due to clinical differences in morbidity or disease severity, or to differences in the following: illness behavioural women are more likely than men to interpret discomfort as symptoms; symptom perception women's attentiveness to body discomfort increases their perception of symptoms and evaluation of those symptoms as illness, or symptom reporting women may be more likely to recall and report symptoms. Pregnancy has an impact on drug treatment. Not only are women affected by the drug, but the foetus will also be exposed to ADRs of the drug [4]. There are certain physiologic changes that occur during pregnancy which might affect drug pharmacokinetics and pharmacodynamics, these changes are, total blood volume increases, extravascular volume increase during trimester which leads to decreased plasma concentration of iron and some drugs, renal function improves with a renal plasma flow increment and GFR increases, serum protein lower, thus really excreted drugs would have an increased rate of excretion, cardiovascular changes are noted by an increase in cardiac output due to an increased heart rate and increased stroke volume, blood pressure is relatively constant. Motility, acidity and tone of GIT are decreased during pregnancy and this might interfere with drug absorption or excretion and finally drug metabolism may be affected at certain stages of pregnancy. Drugs during pregnancy might affect either the mother or the embryo or both. The impact of drugs on foetal organogenesis is crucial because it might lead to teratogenicity and Dysmorphogenesis [5]. Many drugs for example, antihypertensive drugs such as angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers pose a risk to the health and normal

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development of a foetus. The foetus, which is exposed to any drugs circulating in maternal blood, is very sensitive to drug effects because it is small, has few plasma proteins that can bind drug molecules and has a weak capacity for metabolizing and excreting drugs. Once drug molecules reach the foetus, they may cause teratogenicity or other ADRs. Gestational age is subdivided into three trimesters; first, second and third trimester. The effect of drugs on each trimester is different depending on the degree of foetal development [6]. Drug teratogenicity is most likely to occur when drugs are taken during the first trimester of pregnancy, when foetal organs are formed. For drugs taken during the second and third trimesters, ADRs are usually manifested in the neonate or infant as growth retardation, respiratory problems, infection, or bleeding. Overall, effects are determined mainly by the type and amount of drugs, the duration of exposure, and the level of foetal growth and development when exposed to the drugs. Both therapeutic and nontherapeutic drugs may affect the foetus. Creatinine clearance reflects the function of the kidneys which are responsible for the excretion of many drugs. Any change in the renal profile might increase drug toxicity or decrease therapeutic effect. Kidney disease affects drug clearance and metabolism. Venitz concluded that chronic renal failure affects both renally excreted drugs and also drugs metabolized by the liver through the effect of uremia caused by renal failure. This in turn may affect the disposition of a highly metabolized drug by changes in plasma protein binding and hepatic metabolism [7]. Sun stated that alterations of drug transporters, as well as metabolic enzymes, in patients with renal failure can be responsible for reduced drug clearance. This reduced metabolic enzyme activity can affect the clearance of the drug. The effect of renal diseases on non-renal drug excretion leads to any disease accompanied with renal insufficiency being affected by this insufficiency and increases the possibility of the appearance of ADRs in that patient. Drug independent cross-reactive antigens can induce sensitizations, which can manifest as a drug allergy [8]. The existence of such cross-reactivity is supported by medical literature. After primary sensitization to a causative drug, a second exposure causes affected T cells and antibodies to enter the elicitation phase, corresponding to the type of immune reactions. Most of the drug allergies observed are type of reactions, type II and III reactions are only encountered infrequently. The formation of immune complexes, a common event in a normal immune response, usually occurs without symptoms. Rarely, immune complexes bind to endothelial cells and lead to immune complex deposition with complement activation in small blood vessels. The clinical symptoms of a type III reaction include serum sickness, mediation-induced lupus erythematous, and vascularise. T-cell-mediated drug hypersensitivity may have a variety of clinical manifestations, ranging from involvement of the skin alone to fulminant systemic diseases. Frequently, the drugs involved are sulpha antibiotics and b-lactams. In the body, drugs are distributed to and from the blood and various tissues of the body. After a drug is absorbed into the bloodstream, it rapidly circulates through the body. As the blood recirculates, the drug moves from the bloodstream into the body's tissues. Once absorbed, most drugs do not spread evenly throughout the body. Some drugs dissolve in water, such as the antihypertensive drug atenolol. Some drugs tend to stay within the blood and the fluid that surrounds cells [9]. Drugs that dissolve in fat, such as the anaesthetic drug halothane, tend to concentrate in fatty tissues. Other drugs concentrate mainly in only one small part of the body, because tissues have a special attraction for and ability to retain the drug. Drugs penetrate different tissues at different speeds, depending on the drug's ability to cross membranes [10]. For example, the anaesthetic thiopental, a highly fat-soluble drug, rapidly enters the brain, but the antibiotic penicillin, a water-soluble drug, does not. In general, fat-soluble drugs can cross cell membranes more quickly than water-soluble drugs.

Conclusion

For some drugs, transport mechanisms aid movement into or out of the tissues. Some drugs leave the bloodstream very slowly, because they bind tightly to proteins circulating in the blood. Others quickly leave the bloodstream and enter other tissues, because they are less tightly bound to blood proteins. Some or virtually all molecules of a drug in the blood may be bound to blood proteins. The protein-bound part is generally inactive. As the unbound drug is distributed to tissues and its level in the bloodstream decreases, blood proteins gradually release the drug bound to them.

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Conflict of Interest

None

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