EDITORIAL

Women & Risk For Developing ADR's

Sudhaa Mahajan*, Vishal R. Tandon, Sachin Kumar

Sex is an important determinant of drug use and drug Response. Women tend to have a higher risk of adverse drug reactions with a 1.5 to 1.7-fold greater risk than men (1). Older age and female gender are significantly associated with ADR related hospital admissions (2). If analyzed separately by age groups, this gender difference becomes significant at an age of > 81 years (2).

Women are more at risk for developing adverse drug reactions (ADRs) due to differences at pharmacokinetics & pharmacodynamics level (3-7). In women, absorption, protein binding, volume of distribution, clearance and metabolism of drugs may differ due to hormonal influences on physiological functions. Sex-related differences exist for phase I (cytochrome P450) as well as phase II (especially glucuronidation) reactions. Since many women world-wide take oral contraceptives, and drugs are likely influenced by estrogens and progestogens as they interact at various enzymes and receptors levels.

A sex difference in pharmacodynamics, the effect of the body on the drug, is, for example, the occurrence of drug-induced torsade de pointes, which is much more frequent in women. Two-thirds of the cases of drug-induced torsade de pointes occur in women.Estrogens facilitate bradycardia-induced prolongation of the QT interval and the emergence of arrhythmia whereas androgens shorten the QT interval and blunt the QT response to drugs.

Women are perceived to be more prone to ADRs than men. Such a propensity may result from gender-associated differences in drug exposure, in the number of drugs prescribed (polypharmacy), in drug pharmacology, as well as from possible differences in the way the adverse event is perceived. Moreover, in the elderly the comorbidities and correlated multiple regime therapy cause an increased incidence of ADRs (4).

The differences between the sexes in risk for ADR-related hospitalization are found for antineoplastic, immunosuppressive drugs, antirheumatics, anticoagulants ,salicylates, cardiovascular, neurological drugs, steroids and antibiotics (1). The most common ADRs in comparison to men are electrolyte imbalances and over-anticoagulation. Diuretics and vitamin K antagonists are significantly correlated with ADRs (2). Other classes of agents exhibiting gender-based variation in pharmaceutical efficacy and toxicity include anaesthetics, HIV-1 therapies and antiarrhythmic drugs (3). In the older group, antibiotics are more frequently involved, whereas in the <65 years, nonsteroidal antinflammatory drugs account for most cutaneous reactions. (4).

Thus, clearly women are at more risk to develop ADRs in comparison to men and however to obtain more insight into the difference in ADRs between men and women more research is needed. However, this factor must be given due consideration before prescribing medicines to elderly women.

References

1. Rodenburg EM, Stricker BH, Visser LE. Sex-related differences in hospital admissions attributed to adverse drug reactions in the Netherlands. *Br J Clin Pharmacol* 2011 ; 71(1):95-104
2. Hofer-Dueckelmann C, Prinz E, Beindl W, Szymanski J, Fellhofer G, Pichler M, Schuler J. Adverse drug reactions (ADRs) associated with hospital admissions - elderly female patients are at highest risk. *Int J Clin Pharmacol Ther*. 2011; 49(10):577-86.
3. Nicolson TJ, Mellor HR, Roberts RR. Gender differences in drug toxicity.*Trends Pharmacol Sci* 2010 ;31(3):108-14
4. Ventura MT, Laddaga R, Cavallera P, *et al*. Adverse drug reactions as the cause of emergency department admission: focus on the elderly. *Immunopharmacol Immunotoxicol* 2010 ; 32(3):426-29
5. Thürmann PA, Hompesch BC. Influence of gender on the pharmacokinetics and pharmacodynamics of drugs. *Int J Clin Pharmacol Ther*. 1998; 36(11):586-90.
6. Anderson GD. Sex and racial differences in pharmacological response: where is the evidence? Pharmacogenetics, pharmacokinetics, and pharmacodynamics. *J Womens Health (Larchmt)* 2005; 14: 19-29.
7. Drici MD, Clément N. Is gender a risk factor for adverse drug reactions? The example of drug-induced long QT syndrome. *Drug Saf* 2001;24(8):575-85.

From the ADRM Centre, PG Deptt. of Pharmacology & Therapeutics &*Obst & Gyane, GMC, Jammu J&K- India
Correspondence to : Dr Vishal R. Tandon, Incharge ADRM Centre, Deptt. of Pharmacology & Therapeutics, Govt Medical College, Jammu J&K-India