The Turkish Journal of Occupational / Environmental Medicine and Safety

Vol:1, Issue Supplement 1 Web: http://www.turjoem.com ISSN : 2149-4711 Oral Presentation

S2. PHARMACOGENETICS APPLICATIONS IN FORENSIC TOXICOLOGY

H. Sinan SÜZEN
Ankara University, Faculty of Pharmacy, Department of Toxicology, Tandogan-Ankara, TÜRKİYE

Pharmacogenetics is genetic basis of medication response and adverse drug reactions (ADRs) in pharmacotherapy. Over the last three decades, the role of genetic variation in drug response and toxicity has been increasingly recognised (Scott, 2011). Factors affecting an individual's pathophysiological phenotype related to drug efficacy and ADRs are genetic variations, (gene deletions, gene duplications, sequence variation), developmental stage (age, gender), physiological factors (mental and physical stress, hormonal changes, seasonal and circadian factors), environmental factors (personal environmental history, lifestyle, diet, exposure to environmental toxins, concomitant use of alcohol(s) and drugs), potential, specific associations (diabetes, obesity, gut microbiology). Among these factors, genetic variations has an important role in pharmacotherapy since inter-individual variations in DNA sequence related to drug pharmacokinetics or pharmacodynamics, including polymorphisms in genes encoding transporters, drug-metabolizing enzymes, receptors and other proteins.

Pharmaceutical agents are one of the most commonly determined matters of adverse events, causing in important morbidity and mortality worldwide. Among deaths attributed to medications, the most common drug categories are opioid analgesics, psychotherapeutics, and antiepileptic and antiparkinsonism drugs (Jones, 2013). Despite well-defined reference drug toxicity levels are established, interpretive hindrances are usually encountered the field of forensic toxicology in some cases. Pharmacogenetics has the potential to become a supplemental tool for the forensic toxicology in the interpretation of drug-related deaths, especially accidental drug poisoning or cases of sudden death with normal autopsy (Sajantila et al., 2010).

Several different types of changes exist in the DNA sequence which range from single nucleotide polymorphisms (SNPs), indel/s to larger structural alterations such as copy number variations (CNVs) and big deletions (Shen et al., 2013). These genetic variations in the genes which encode the drug-metabolizing enzymes may lead to normal (extensive metabolisers, EMs), deficient/low (poor metabolisers-PMs/intermediate metabolisers-IMs), or higher enzyme activities (ultrarapid metabolisers, UMs). Individuals having variant alleles are at increased risk of encountering from adverse drug reactions as a result of drug overdose or of experiencing therapeutic failure by reason of poor metabolism of a prodrug to the active metabolite. In contrast, UMs have significantly elevated enzyme activity, which can result in subtherapeutic serum concentrations of the medicine.

Interpretation of toxicology results from the perspective of pharmacogenetics has a great potential in decisions concerning the cause and manner of death, as well as in legal proceedings. In the forensic context, pharmacogenetics may serve as an adjunct for certifying drug-related fatalities.