Pharmacogenetics: A hope for difficult to treat chronic pain patients

Pharmacogenetics has been referred to as "the study of variability in drug response due to heredity."[1] Another term, often used interchangeably is pharmacogenomics, referred to as "all genes in the genome that may determine drug response."[2] It is also referred to as "the field of new drug development based on our rapidly increasing knowledge of all genes in the human genome."[1]

The history of pharmacogenetics can be easily extrapolated way back to 510 BC when it was noted by Pythagoras that ingestion of fava beans resulted in a potentially fatal reaction in some persons, but not in all;[3] though the term pharmacogenetics was first published by the German Physician Friedrich Vogel in 1959.[4] Initial breakthrough research in the field included the identification of succinylcholine-induced prolonged apnea during anesthesia due to autosomal recessive butyrylcholinesterase deficiency,[5] severe adverse effects after antituberculosis treatment with isoniazid subsequently shown to be due to N-acetyltransferase (NAT) variant alleles,[6] and primaquine-induced hemolytic anemia subsequently shown to be due to glucose-6-phosphate dehydrogenase variant alleles.[7]

DNA-based testing began in 1978 when the diagnosis of sickle-cell disease was made by identifying the causative mutation in the β-globin gene using polymorphism of a restriction endonuclease site for antenatal diagnosis of sickle-cell disease.[8] With the advancement in techniques and mapping of human genome, the possibilities in this field are tremendous. Very recently, it has been shown that polymorphisms of NAT2, CYP2E1, and glutathione S transferase-1 could increase patients' susceptibility to isoniazid-induced hepatotoxicity.[9] Pharmacogenetics has not only been implicated in diseases and adverse effects of drugs in some individuals only but also has opened the avenues for personalized medicine for every patient too.[4]

Very recently, the concept of pharmacogenetics has been extended to patients who show little signs of pain relief even after the use of the analgesics. In a poster presentation during the proceedings of the American Academy of Pain Medicine 2016, the researchers showed that the therapeutic failure in a patient taking 100 mg morphine 3 times a day for 4 years was due the fact that the patient was an ultrarapid metabolizer of the CYP-allele 2D6, which metabolizes oxycodone.[10] The pain score on visual analog scale of the patient dropped from 10 with morphine only to 4 after only three visits, with the addition of gabapentin and low-dose methadone which is mainly metabolized by CYP 3A4. Further, for a period of 2 years, researchers looked at 70 pain patients, with an average initial pain score of 8.6, and when pain medications were adjusted according to the patient's genetic profile, pain scores went down. There was an average decrease of 55% in pain scores.[10]

Researchers concluded that genetic testing is a very important adjunct in treating chronic pain patients and can certainly reduce their pain scores and suggested that it should be used in every patient to improve outcomes and decrease side effects. So hopefully with these new recommendations, patients with difficult to treat chronic pain will have a ray of hope.

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