Epilepsy

PHARMACOEPIGENETICS OF ANTIEPILEPTIC DRUGS

NEETHU MOHAN[1], M. BANERJEE[1]

Department of Neurobiology, Rajiv Gandhi Centre for Biotechnology, India

Background: Antiepileptic drugs are the mainstay for the treatment of epilepsy. Studies in human have been shown that these AEDs tend to have teratogenic potential. And it is becoming evident that these pharmaceutical drugs can cause changes in gene expression that persist long after the exposure has ceased. Pharmacoepigenetic studies explain the role of epigenomics in intrapersonal and interpersonal variations in response of individuals to drugs, in the effects of drugs on gene-expression profiles, in the mechanism of action of drugs and adverse drug reactions.

Method: The present study involves assessing the epigenetic modifications induced by antiepileptic drugs in cell culture model. The effect of AEDs on global DNA methylation and underlying gene expression was studied. The experimental cell line was treated with varying concentration of AEDs at different time intervals, following global DNA methylation assay and the gene expression of epigenetic modulators including DNA methyltransferases (DNMTs) and Ten-eleven translocases (TETs) was assessed.

Results: Data suggests decreased global DNA methylation for AED treated cells and the global DNA methylation changes show similar pattern with respect to DNMTs gene expression .As treatment duration increased from 12 to 48 hours, we observed a decrease in DNMTs (methylation) and increase in TETs (demethylation) expression.

Conclusion: The antiepileptic drug induced changes in global DNA methylation were observed in HEK293 and the modulation of global DNA methylation status in cell line can be attributed to variability in underlying DNMT and TET gene expression.

Keywords: Antiepileptic drugs, Pharmaco-epigenetics, DNA methylation, DNMTs, TETs.