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MEETING ABSTRACT Open Access

Association of CYP2D6*4 genetic polymorphism on the metabolism of Donepezil with Alzheimer's disease in Indian population

Vivekanandhan Subbiah[1*], Sonali Nirmal[1], Manjari Tripathi[2], Rajesh Sagar[3]

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Background

Alzheimer's disease (AD) is the most common adult form of dementia.1 It is an age-associated neurodegenerative disorder pathologically characterized by the abnormal accumulation of intracellular neurofibrillary tangles and extra cellular amyloid plaques in selected brain regions. Donepezil is a cholinesterase inhibitor currently being used in the treatment of Alzheimer's disease is metabolized via CYP2D6 enzymes. The present study was undertaken to investigate CYP2D6*4 polymorphism on the serum concentration of Donepezil with responders and non-responders to Alzheimer's patients.

Materials and methods

40 Alzheimer's patients with responders to Donezepil drug and 40 Alzheimer's patients with non-responders to donezepil drug were investigated for CYP2D6*4 polymorphism using polymerase chain reaction - restriction fragment polymorphisms (PCR-RFLP). Allele frequencies were derived from genotypic data. Drug responders - non-responders' comparisions were made using Chi-Square tests. Deviations from the Hardy -Weinberg equilibrium were also tested. Drug levels of Donezepil were determined using HPLC method.

Results

The CYP2D6*4 Polymorphism was seen to be in Hardy - Weinberg equilibrium and showed significant allelic association and genotypic association between responders and non-responders of donezepil. Genotypic: P = 0.05; OR = 0.39 (0.13-1.15), Allelic: P = 0.008; OR = 2.79(1.20-6.58).

Conclusions

Our finding suggest that the CYP2D6 *4 genetic polymorphism may be associated with the individual differences in donezepil metabolism. An individualized dosage regimen design incorporating such genetic information would help to increase the clinical efficacy of donezepil in Alzheimer's patients.

Author details
[1]Department of Neurobiochemistry, All India Institute of Medical Sciences, New Delhi, Delhi, India. [2]Department of Neurology, All India Institute of Medical Sciences, New Delhi, Delhi, India. [3]Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, Delhi, India.

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[1]Department of Neurobiochemistry, All India Institute of Medical Sciences, New Delhi, Delhi, India