Antioxidant enzymatic activities in Alzheimer's disease: the relationship to acetylcholinesterase inhibitors


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Background

Acetylcholinesterase Inhibitors (AChEIs) potentiate neuronal transmission in Alzheimer's Disease (AD). Animal studies have also consistently described a role for AChEIs in enhancement of antioxidants and attenuation of oxidative stress. The influence of AChEIs on blood antioxidants in AD patients has not been established before. Further, AChEIs treatment, or lack of it, may have contributed to the inconsistent antioxidant data reported by other studies so far. Here we sought to investigate the potential modulation effect of AChEIs on blood antioxidants in AD patients.

Methodology

All participants in the study (n = 102) were recruited via memory clinics in East Sussex, England (mean age = 80.92 ± 7.68, 63.7% female). The AD patient group included 68 participants, 25 of whom were drug naïve for AChEIs and 43 were receiving therapeutic doses of an AChE inhibitor (donepezil, rivastigmine or galantamine) specifically for the treatment of their AD (group B). Participants in group C served as controls and had no memory complaints, no diagnosis of a dementia illness and scored 10/10 on the Abbreviated Mental Test. Blood samples were collected from all participants at the time of cognitive assessment. Samples were centrifuged at 10,000 x g and serum was collected and stored at -80 oC immediately after collection. The spectrophotometric enzyme essay kits were supplied by Cayman Chemical Company (Michigan, USA) which were used to analyse CAT. GR activity was assessed via monitoring the oxidation of NADPH to NADP+ at 340 nm.

Results

A statistically significant difference for Catalase Transferase (CAT) and Glutathione Reductase (GR) was observed between the two AD groups (A and B) when compared to the control Group C (KW-H = 36.530, p < 0.001; post hoc tests p < 0.001 and KW-H = 37.814, p < 0.001; post hoc tests p < 0.001, respectively). In contrast, CAT and GR activities did not differ significantly among the two AD groups and were not influenced by AChEIs treatment.

Conclusion

Our data show that treatment with AChEIs in AD patients did not significantly change the peripheral blood activities of CAT and GR - two important antioxidant enzymes. To our knowledge this is the first report assessing antioxidant measures in AD patients in specific relation to treatment with AChEIs. The importance of this research is that the results in this human cohort do not accord with theories generated by animal studies over the past decade. This report raises questions (especially if results are replicated by further studies) about whether AChEIs efficacy in humans is mediated by processes beyond neuron to neuron enhancement of transmission.