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Relationship Between Cognitive Impairment Severity and Levels of Receptors for Advanced Glycation End Products: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: Alzheimer's disease (AD) is a neurodegenerative condition that primarily affects the elderly and is a global health concern. The concept of mild cognitive impairment (MCI) has received increasing attention in recent years, particularly as a possible prodromal stage of AD. There is increasing evidence to support the hypothesis that the receptor for advanced glycation end products (RAGEs) may act as a risk marker for AD and other conditions. Nevertheless, limited investigation has been conducted to compare the two groups' circulating RAGE levels. Hence, due to the inconsistencies between studies, we aimed to summarize current evidence by conducting a systematic review and meta-analysis.

Search Strategy: This systematic review and meta-analysis complied with PRISMA guidelines and Cochrane systematic review principles. PubMed, Scopus and Web of Science were systematically searched using keywords "Advanced Glycation End Products" and "Cognitive Impairment" and their related synonyms. Observational studies that investigated the difference in RAGE levels in serum between AD and MCI groups were inspected. Exclusion criteria included duplicate publications, review articles, interventional and animal/cell studies, letters to the editor, and conference papers. Screening was performed using EndNote v. 20.1. Data was extracted according to a predefined list of variables. Newcastle-Ottawa Scale was used for the quality assessment. The heterogeneity of the studies was checked using the I2 statistics. A random effect model of standardized mean difference (SMDs) was applied for statistical analysis (Cohen's d). All statistical analyses were performed using STATA v. 14.

Results: A total of 634 studies were initially identified, with 207 duplicates and 423 irrelevant articles removed. In the final analysis, we included four studies with 147 MCI patients and 277 AD patients (mostly older than 60). Through meta-analysis, we established a correlation indicating lower serum levels of RAGEs in AD patients compared to those with MCI (SMD: -0.43; 95% CI: -0.77 and -0.09]; I2: 58.3%; p = 0.03).

Conclusion and Discussion: Our findings suggest that there might be a significant difference in RAGE serum levels in patients with AD compared to those with MCI. These data suggest that a decrease in circulating RAGEs can be identified as a prognostic indicator of AD in MCI patients.

Keywords: Cognitive dysfunction, Alzheimer disease, Glycation end products

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