Effects of selenium supplementation in patients with mild cognitive impairment or Alzheimer's disease: a systematic review

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ABSTRACT

Introduction: Selenium (Se) is an essential trace element for human health and has an important role in the development and maintenance of the central nervous system functions; Se deficiency has been associated with cognitive decline. Stress oxidative is one of the hypotheses for the appearance and aggravation of neurodegenerative diseases such as Alzheimer's disease (DA). Due to Se antioxidant and anti-inflammatory capacity, it is important to study its effects in these pathologies. **Aim:** To assess the effects of Se supplementation in patients with DA or mild cognitive impairment (MCI) on Se levels, oxidative stress, and cognitive performance through a systematic review. **Methods:** The systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO; #CRD42021240649).The search strategy followed the *Preferred Reporting Items for Systematic Reviews and Meta-Analysis* (PRISMA) guideline, the data were systematically searched and collected on electronic databases (PubMed, Scielo, Scopus, and Cochrane Library), using the keywords “selenium supplementation”,“selenium”, “neuroinflammation”, “Alzheimer’s disease” and “mild cognitive impairment” and boolean operators OR and AND. The eligibility criteria included cohort and clinical trial studies, published until December 2020, that analyzed Se supplementation in individuals with DA or MCI. For

the study appraisal and synthesis methods, the papers selection process was performed out by six reviewers, divided in pairs, that in the first stage independently read the titles and abstracts of the papers in relation to the eligibility criteria, and the potentially eligible records was read in the full text at a second stage. Included studies pass through by extraction of data. Cases of non-consensus in all stages were evaluated and defined by a seventh reviewer. The quality assessment was carried using the Version 2 of the Cochrane Risk of Bias Tool for Randomized Trials (RoB 2).**Results:** 1350 scientific papers were collected from 4 electronic databases. Of those, 226 were duplicates, 65 the abstract was unavailable and, 1049 were excluded because did not meet the eligibility criteria; 1 paper was added manually, resulting in a total of 11 papers (4 papers only Se supplementation and 7 papers Se plus other nutrients) for the systematic review. Regarding studies that evaluated only selenium supplementation found that there was an improvement in selenium levels in serum, plasma or cerebrospinal fluid, and in some cognitive tests. When Se was administered with other nutrients, it was possible to observe improvement in cognitive tests, but it does not improve malondialdehyde (MDA), Se levels in most articles did not measure this parameter and those that measured it did not change. In the analysis of risk of bias, the analyzed studies obtained a medium to high risk of bias, this was due to domain 2 (intervention analysis) because some protocols did not have placebo intake in the control group. **Conclusion:** In conclusion, Se supplementation is a good alternative to DA and MCI patients, improving the body Se levels. More detailed studies must be carried out to evaluate the Se effects in the DA and MCI cognitive deficit and oxidative stress.

Keywords: Selenium supplementation, Neurodegenerative disease, Brazil nut, oxidative stress