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The Changes of Blood and CSF Ion Levels in Depressed Patients: A Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 October 2023 and was last updated on 18 October 2023.

INTRODUCTION

Review question / Objective In order to determine whether there were changes in blood and cerebrospinal fluid (CSF) levels of these ions in depressed patients compared with healthy controls and depressed patients treated with TCAs, SSRIs, or lithium, we applied a systematic review andmeta-analysis.

Rationale Micronutrient deficiencies and excesses are closely related to developing and treating depression. Traditional and effective antidepressants include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and lithium. There is no consensus on the fluctuation of zinc (Zn2+), magnesium (Mg2+), calcium (Ca2+), copper (Cu2+), iron (Fe2+), and manganese (Mn2+) ion levels depressed individuals before and after therapy.

Condition being studied Depression is a devastating disease affecting at least 322 million people globally, some of whom have suffered from depression since childhood (13 years and younger) .Micronutrient deficiencies and excesses are closely related to developing and treating depression. All trial participants were separated into groups of depressed patients with no therapy and depressive patients using lithium, TCAs, or SSRIs, respectively. Additionally, we disqualified depressed individuals as well as healthy controls who took specialized diets and trace element-containing medications. All patients were in good health, except those suffering from depression, based on their medical histories and physical examinations.

METHODS

Search strategy The databases of PubMed, EMBASE, Google Scholar, Web of Science, China National Knowledge Infrastructure (CNKI), and W AN FANG were searched for studies reporting the relationship between various ion levels in blood and CSF and the use of TCAs, SSRIs, and lithium

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in depressed patients from their inception to July 2022. The terms "depression," "zinc," "magnesium," "calcium," "copper," "iron," "manganese," "SSRIs," "TCAs," "lithium," "blood," "serum," "plasma," and "CSF" in both English and Mandarin were searched. We also reviewed the relevant references of some articles as a way to expand the search.

Participant or population Healthy controls, depressed patients, depressed patients treated with TCAs, SSRIs, or lithium.

Intervention Depressed patients, depressed patients treated with TCAs, SSRIs, or lithiumAntidepressants: TCAs, SSRIs, and lithium.

Comparator Healthy controls.

Study designs to be included RCT.

Eligibility criteria Diagnostic criteria for depression.

Information sources PubMed, EMBASE, Google Scholar, Web of Science, China National Knowledge Infrastructure (CNKI), and W AN FANG databasesDiagnostic criteria for depression.

Main outcome(s) In the blood, the levels of Zn2+ and Mg2+ in depressed patients had decreased while the Ca2+ and Cu2+ levels had increased compared to healthy controls, Fe2+ and Mn2+ levels have not significantly changed. After treatment with SSRIs, the levels of Zn2+ and Ca2+ in depressed patients increased while Cu2+ levels decreased. Mg2+ and Ca2+ levels were increased in depressed patients after Lithium treatment.

Data management Endnote.

Quality assessment / Risk of bias analysis Cochrane.

Strategy of data synthesis STATA17.0 software was chosen to analyze the data, I-squared greater than fifty percent was considered to be heterogeneous, the presence of heterogeneity was chosen to combine the effect sizes in a random effects model, and the absence of heterogeneity was chosen to combine the effect sizes in a fixed effects model.

Subgroup analysis To evaluate the influence of study features as possible causes of high heterogeneity, such as the geography (Europe, Asia, North America, Africa and Oceania) and ages (early adulthood (18-30 years old), middle adulthood (31-49 years old) and late adulthood(50+ years old)) of studied participants [29], a subgroup analysis was conducted.

Sensitivity analysis Sensitivity analyses were performed by Stata 17.0 software to reflect the sensitivity of an article by the change in effect size after deleting one of the articles.

Language restriction No language restrictions.

Country(ies) involved China.

Keywords depression; ion levels; tricyclic antidepressants; selective serotonin reuptake inhibitors; lithium; meta-analysis.

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