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Efficacy and Safety of Repeated Transcranial Magnetic Stimulation Combined with Escitalopram in the Treatment of Major Depressive Disorder: A 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 28 November 2023 and was last updated on 28 November 2023.

INTRODUCTION

Review question / Objective Thus far, the efficacy and safety of repeated transcranial magnetic stimulation (rTMS) combined with escitalopram in MDD treatment remain unclear. Hence, a meta-analysis was conducted to objectively evaluate the efficacy and safety of rTMS combined with escitalopram in treating patients with MDD, thereby providing further evidence for clinical treatment. This meta-analysis was conducted to objectively evaluate the efficacy and safety of rTMS combined with escitalopram in treating patients with MDD, thereby providing further evidence for clinical treatment.

Condition being studied Major depression disorder (MDD) is a mental disease that presents with persistent depression and anhedonia as the core symptoms; moreover, MDD poses a heavy disease burden. With an accelerated pace of life and increased social pressure, the incidence of MDD has been on the rise in recent years. Furthermore, there is data to indicate that MDD affects approximately 280 million people, or 3.8% of the global population, and has become one of the leading causes of disability worldwide. With a complex pathogenesis, MDD appears to be caused by a combination of genetic, environmental (such as recent negative life events), psychological (such as cognitive patterns), and biological (such as inflammation and the monoamine pathway) factors.

Major depression disorder (MDD) is a mental disease that presents with persistent depression and anhedonia as the core symptoms; moreover, MDD poses a heavy disease burden. With an accelerated pace of life and increased social pressure, the incidence of MDD has been on the rise in recent years. Furthermore, there is data to indicate that MDD affects approximately 280 million people, or 3.8% of the global population, and has become one of the leading causes of

disability worldwide. In clinical practice, the most commonly used treatment scheme for MDD is drug therapy. International guidelines currently recommend SSRIs as the first-line treatment for most patients with MDD. Among these SSRIs, escitalopram is the most selective antidepressant for 5-HT transporters. Yan found that escitalopram, which is the S-isomer of citalopram, exerts a faster effect in the treatment process, exhibits a better therapeutic effect, and leads to fewer symptoms of nausea and gastrointestinal reactions. However, due to the long-term use of antidepressants and their side effects, patients develop tolerance to existing antidepressants, thus reducing patient compliance. The limitations of existing treatment options for MDD have prompted the development of novel treatment options to improve patient compliance and reduce the recurrence rate of MDD. A previous study showed that for patients with drug-resistant depression, adding rTMS therapy after drug therapy failure can significantly improve the efficacy of antidepressants. The results of a RCT by Lv et al. showed that in MDD treatment, the combination of rTMS and escitalopram can effectively improve the clinical efficacy of MDD and reduce the occurrence of adverse reactions. However, the study by Zhu et al. showed no significant difference in the clinical efficacy and incidence of adverse reactions of rTMS combined with escitalopram for MDD compared with the control group treated with escitalopram alone. Thus far, the efficacy and safety of rTMS combined with escitalopram in MDD treatment remain unclear.

Thus far, the efficacy and safety of rTMS combined with escitalopram in MDD treatment remain unclear. Hence, a meta-analysis was conducted to objectively evaluate the efficacy and safety of rTMS combined with escitalopram in treating patients with MDD, thereby providing further evidence for clinical treatment.

METHODS

Participant or population Major Depressive Disorder.

Intervention Repeated Transcranial Magnetic Stimulation combined with Escitalopram.

Comparator Escitalopram or Escitalopram combined with pseudo-stimulation.

Study designs to be included RCT.

Eligibility criteria The exclusion criteria were as follows: (1) studies with inconsistent subject and object; (2) studies with data duplication; (3) studies with full text not available and those with incomplete data; and (4) studies on subtypes of MDD (such as severe postpartum depression, severe post-stroke depression, etc.).

Information sources In this study, several Chinese and English databases were searched electronically. The relevant literature was retrieved primarily from PubMed, Embase, Cochrane, Web of Science, CNKI, Wanfang, VIP, and China Biomedical Literature databases. The search time was from the inception of these databases to May 27, 2023.

Main outcome(s) Primary Outcomes included clinical effectiveness, HAMD scores, and adverse events, while the secondary outcome indicators included Pittsburgh Sleep Quality Index (PSQI), 5-HT, norepinephrine (NE), and BDNF.

Quality assessment / Risk of bias analysis The Cochrane Handbook of Systematic Reviews was followed to conduct quality reviews, including generation of random sequences, assignment concealment, blinding of participants and implementers, blinding of outcome reviews, exit and loss of follow-up, selective publication, and other risks of bias. The evaluation criteria were classified as "low risk", "high risk," and "unclear risk."

The funnel plot and Egger's test were used to check the publication bias. $P < 0.05$ was considered to be statistically significant.

Strategy of data synthesis Data were analyzed using R 4.2.2, and the $\chi 2$ test was used to assess heterogeneity. When all the studies demonstrated statistical homogeneity ($p \geq 0.05$, $I2 \leq 50\%$), a fixed-effect model was used. If P 50%, a large heterogeneity was considered present between the studies, and a random-effect model was used in this case. For the comprehensive effects analysis, weighted mean difference (WMD), odds ratio (OR), and 95% confidence interval (95% CI) were used as the effect indicators. In addition, subgroup analysis was performed according to different rTMS frequencies, intensities, stimulation sites, and ages for investigating the potential heterogeneity between the studies and the efficacy of rTMS combined with escitalopram in treating MDD.

Subgroup analysis Subgroup analysis was performed according to different rTMS frequencies, intensities, stimulation sites, and ages for investigating the potential heterogeneity between the studies and the efficacy of rTMS combined with escitalopram in treating MDD.

Sensitivity analysis Sensitivity analysis was performed on the HAMD scores and clinical effectiveness results of rTMS combined with escitalopram intervention for MDD. Consequently, one article was excluded, and a meta-analysis was performed on the remaining articles.

Country(ies) involved China.

Keywords major depressive disorder, MDD, repeated transcranial magnetic stimulation, rTMS, escitalopram, meta-analysis.

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