Review Article

Efficacy and Safety of Citalopram for the Treatment of Poststroke Depression: A Meta-Analysis

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Objective: To objectively evaluate the efficacy and safety of citalopram versus other antidepressant drugs in poststroke depression (PSD) treatment. *Methods:* We searched randomized controlled trials (RCTs) that compared citalopram with other Selective serotonin reuptake inhibitors (SSRIs) and Serotonin norepinephrine reuptake inhibitor (SNRIs) on PSD treatment. The methodological quality of RCTs was assessed according to the Cochrane risk of bias tool. Meta-analysis was conducted using RevMan 5.3 software with standard mean difference (SMD) or Relative risk (RR) and their 95% confidence interval (CI). *Results:* A total of 20 studies involving 1485 patients were included .The RR of efficacy index compared to other SSRIs was 1.04 [95% CI: .98-1.09, $P = .17$], and to SNRIs was 1.01 [95% CI: .93-1.09, $P = .83$]. The RR of cure index compared to other SSRIs was .99 [95% CI: .82-1.19, $P = .88$], and to SNRIs was .95 [95% CI: .71-1.27, $P = .74$]. Significant decreases on Hamilton Depression Scale scores were observed in favor of citalopram when compared to other SSRIs after 4-, 6-week treatment [SMD = −.44, 95% CI: −.85 to −.03, $P = .03$; SMD = −.50, 95% CI: −.98 to −.02, $P = .04$], and no significant difference was found with SNRIs in any week [$P > .05$]. The rate of adverse effects also showed no significant difference between citalopram and other antidepressants [$P > .05$]. *Conclusions:* This meta-analysis indicates that the efficacy of citalopram is similar to that of other SSRIs and SNRIs, but citalopram takes action faster than other SSRIs. The adverse effects of citalopram have no significant difference compared to other antidepressants and those adverse effects are less and mild.

Keywords: Citalopram—poststroke depression—randomized controlled trial—meta-analysis.

Introduction

Poststroke depression (PSD) is characterized by depression, decreased interest, pessimism, restlessness, lack of initiative and general fatigue, and so on[1] and is one of the common complications of cerebrovascular disease. About a third of patients after stroke are associated with depression, a study indicated that the prevalence of depression was 29% and remains stable up to 10 years after stroke, with a cumulative incidence of 39%-52% within 5 years of stroke.[2] What is more, there is a scenario complicated by the bidirectional relationship between depression and stroke: stroke increases the risk of PSD, depression negatively affects patients' ability to rehabilitation.[3] Currently, the first line of drugs to treat PSD are selective serotonin reuptake inhibitors (SSRIs), selective serotonin norepinephrine reuptake inhibitors (SNRIs), and noradrenergic and specific serotonergic antidepressants (NaSSAs).[4-] There are 5 commonly used SSRIs: fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, commonly SNRIs with venlafaxine and duloxetine, and mianzapine as the drug for NaSSAs. Traditional tricyclic antidepressants and monoamine oxidase inhibitors have been phased out

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Received April 9, 2018; revision received July 12, 2018; accepted July 16, 2018.

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1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.07.027

due to their large side effects or poor safety.[4] But at present, there is still controversy about the best selection of existing first-line drugs in the treatment of PSD. For further understanding the difference of efficacy and safety between citalopram and other first-line drugs in treating PSD, we conduct this meta-analysis. Now the results are as follows.

Materials and Methods

Search Strategies

Such databases as PubMed, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), the Wanfang Digital Journal Database, the Chinese National Knowledge Infrastructure (CNKI), and the China Science and Technology Journal Database (VIP) were searched from their establishment to November 2017 for collecting the randomized controlled trials (RCTs) related to citalopram and PSD. Combinations of the following search terms were used: ("Citalopram" or "Lu-10-171" or "Lu10171" or "Escitalopram" or "Lexapro") AND ("post-stroke depression" or "vascular depression" or "PSD"); ("Stroke" or "Cerebrovascular Accident" or "Cerebrovascular Apoplexy" or "Brain Vascular Accident") AND ("Depressive Symptom" or "Depressions" or "Emotional Depressions" or "mood disorders" or "Depressive disorder") AND ("Citalopram" or "Lu-10-171" or "Lu10171" or "Escitalopram" or "Lexapro").The languages we only select English and Chinese, and the retrieval condition is based on the subject terms, key words, or title.

Study Selection

(1) All were RCTs. (2) No significant difference between the experimental group and the control group in age, gender, and course of disease. (3) Stroke, ischemic, or hemorrhagic diagnosed depending on the 4th National conference on the diagnosis of Cerebrovascular Disease academic standards in 1995, and was confirmed by computed tomography (CT) or magnetic resonance imaging (MRI). The depressive disorders diagnosed by the criteria of the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition), or the CCMD-3 (Chinese Classification of Mental Disorders). (4) The severity of depression was assessed by the Hamilton Depression Scale (HAMD). The adverse reactions in the treatment were evaluated by the Treatment Emergent Symptom Scale (TESS). (5) Only used one antidepressant drug, and the method, dosage, and course of treatment were clearly described.

Exclusion Criteria

(1) Not RCTs. (2) The patients were not diagnosed as PSD. (3) The patients included were complicated with severe organ dysfunction, conscious impairment, severe aphasia or recently had a history of mental illness or accepted other antidepressants at recent time. (3) The data of studies were incomplete, incorrect, or unusable.

Data Extraction and Quality Assessment

Two authors (CM and WF) independently selected studies according to the inclusion and exclusion criteria. Controversy was discussed with the third author (HCY) by referencing the standard protocol. The methodological quality of RCTs was assessed in accordance with the risk of bias tool described in the Cochrane handbook for systematic reviews of interventions (Review Manager 5.3). Seven elements were assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias. The effect of the methodological quality of included studies was discussed and considered during interpretation of the results.

Data Synthesis and Analysis

HAMD scores were extracted before treatment and after treatment for 1, 2, 4, 6, and 8 weeks. HAMD reducing rate ≥25% was regarded as an effective event, and HAMD reducing rate ≥75% as a cured event.[5] The adverse events of each study were assessed according to adverse reaction scale of TESS. All statistical analyses were performed using RevMan 5.3 software. Standard mean difference (SMD) for continuous variables and relative risk (RR) for dichotomous data were calculated, the standard normal distribution was expressed as 95% confidence interval (CI), statistical significance level was set at $P < .05$. The calculation of pooled RR and 95% CI was performed using the fixed effects model or the random effects model. The heterogeneity was detected by a χ^2-based Q statistic test and the I^2 index. The random effects model would be used when there was indicative of significant heterogeneity ($P_{Q\text{-test}} \leq .05$ or $I^2 \geq 50\%$). Publication bias of the literature was determined using the inverted funnel plots.

Results

After the primary searching, we got 1067 studies from the defined 6 databases, full text report of 26 studies were downloaded after reading the title and abstract, and finally 20 studies met all inclusion criteria and were included in the final analysis. Six articles were excluded for not conforming to the inclusion criteria: 1 article had no control group, and 1 article did not conform to the diagnosis of PSD, and 1 article was not RCT, 3 articles did not have a complete data so that the articles could not be analyzed. Totally 20 RCTs containing 1485 (734 in the citalopram groups and 751 in the control groups) patients were included for the analysis. There were 15[6-12,19-25] RCTs comparing citalopram with other SSRIs, 5[14-18] RCTs comparing citalopram with SNRIs, and 1[13] RCT involved