Efficacy and Safety of Escitalopram in the Treatment of Major Depressive Disorder in Chinese Patients: A Meta-Analysis Study

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Abstract: To evaluate the efficacy and safety of escitalopram in the treatment of major depressive disorder in Chinese patients using meta-analysis. *Methods:* Randomized controlled trials of escitalopram in the treatment of depression were searched through Chinese databases, including VIP Database for Chinese Technical Periodicals (VIP), China National Knowledge Infrastructure (CNKI), and Wanfang Data. Then, the efficacy of escitalopram and other antidepressants was compared using meta-analysis, including their cure rate and adverse reactions. Furthermore, the fixed-effect model was used for the data. *Results:* No heterogeneity (I^2 = 0%) was noted in the treatment effect, and no significant difference was observed in the efficacy of escitalopram in the treatment of depression in China compared with the control group [relative risk (RR), 1.17; 95% confidence interval (CI): 0.89–1.56]. In each treatment group, eight major adverse reactions were found. Furthermore, the research revealed no significant difference in the incidence of adverse reactions (e.g., nausea, xerostomia, dizziness, insomnia, liver dysfunction, other gastrointestinal reactions, palpitations, and fatigue) between escitalopram and other antidepressants. *Conclusions:* The efficacy and safety of escitalopram were similar to those of other antidepressants (e.g., paroxetine, citalopram, flumipramine, fluoxetine, sertraline, and venlafaxine); however, escitalopram was the most cost-effective drug overall.

1. Introduction

Depression, a chronic mental disorder with a high recurrence rate, adversely affects personal health and social function, making it a common public health problem [1]. Drug therapy remains the primary treatment for senile depression. Escitalopram and fluoxetine are new antidepressants for depression-related diseases. Among them, selective serotonin reuptake inhibitors (SSRIs) are the first-line antidepressants in the clinic setting. Escitalopram is an S-isomer of citalopram and a highly selective 5-HT reabsorption inhibitor, with a stronger inhibitory effect on human serotonin transporter [2].

2. Materials and Methods

2.1 Literature review

In this study, the following databases were retrieved by computer: VIP Database for Chinese Technical Periodicals (VIP), China National Knowledge Infrastructure (CNKI), and Wanfang Data. A randomized controlled study of escitalopram and other antidepressants in the treatment of depression in China was screened from 2006 to 2019 (up to June 1). Keywords were as follows: "Escitalopram, Depressive disorder, Depressive episode, Depression, Antidepressive, Antidepressant, Chinese." Besides, search results were screened manually to screen the research literature included in the analysis.

2.2 Eligibility criteria

The inclusion criteria were as follows: (1) randomized controlled trials (RCTs) of escitalopram and other antidepressants; (2) participants in the study must fulfill the following requirements:

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compliance with “Diagnostic and Statistical Manual of Mental Disorders” (DSM), “International Classification of Diseases” (ICD), or “Chinese Classification and Diagnostic Criteria of Mental Disorders” (CCMD), patients’ age >18 years, Chinese patients, gender not limited, selected patients excluded from serious physical diseases, drug abuse history, pregnant women, and breast-feeding women; and (3) Hamilton Depression Scale (HAMD) score (>18 points).

The exclusion criteria were as follows: (1) repeated publication or lack of crucial data; (2) exclusion of bipolar disorder or dysthymia research literature; and (3) neither Chinese nor English literature.

2.3 Quality evaluation

In this study, effectiveness and cure rate were evaluation indexes of the drug treatment effect. The criteria were HAMD score and reduction rate, which were defined as follows: reduction rate = (pretreatment score – posttreatment score)/pretreatment score × 100%, HAMD reduction rate (>75%) suggesting recovery, HAMD reduction rate (>25%) suggesting validity, HAMD reduction rate <25% suggesting invalidity, and total effective rate = (healing + effective number)/total number of patients × 100%. Next, cure rate = number of patients cured/total number of patients × 100%. Adverse reactions included nausea, xerostomia, dizziness, insomnia, liver dysfunction, other gastrointestinal reactions, palpitations, and fatigue.

2.4 Literature screening and data extraction

In the preliminary literature screening, the studies were screened by first reading the article title; after excluding the unrelated literature, reading the abstract and full text to determine its eligibility for the analysis. The data extraction process included the following: (1) title, source of literature, author(s), and publication date; (2) extraction of various drug efficacy indicators and adverse drug reactions indicators; and (3) classification and extraction of the total number of each group and the number of incidents.

2.5 Statistical analysis

Using RevMan 5.3 software, the efficiency and incidence of adverse reactions were analyzed. While counting data were expressed by relative risk (RR), measurement data were expressed by the standardized mean difference (SMD); both of these were expressed by 95% confidence interval (CI). In addition, Q-test was used to analyze the heterogeneity, and I^2 was used to assess the heterogeneity. When $P > 0.1$ and $I^2 < 50\%$, the fixed-effect model was used, while the random effect model was used in case no match occurred.

3. Results

3.1 Literature screening process and results

In this study, 720 studies from CNKI, 839 from Wanfang Data, and 886 from VIP were retrieved. After reading the title and abstract of those studies, some studies not related to the purpose of the study were excluded. After further reading the full text, excluding nonconforming studies, 12 studies were finally included in the analysis (Table 1).

3.2 Basic characteristics of research literature

A total of 12 studies fulfilled the inclusion criteria in this study. Of these, five were comparative studies of escitalopram and citalopram, while the remaining seven were comparative studies of escitalopram and paroxetine (n = 3), escitalopram and fluoxetine (n = 1), escitalopram and flumipramine (n = 1), escitalopram and sertraline (n = 1), and escitalopram and venlafaxine (n = 1).

Table 1: Studies included in the meta-analysis

Reference	Duration (week)	*N*	Research subjects	Dose of Escitalopram (mg/d)	Control	Dose of Control (mg/d)	Assessment
Guo [3]	6	46	Adults, CCMD-3	15–20	Paroxetine	40–60	HAMD17
Sun et al. [4]	6	58	Adults, CCMD-3	20–40	Flumipramine	150–250	HAMD17
Cui [5]	6	60	Adults, CCMD-3	10–20	Citalopram	20–30	HAMD17
Wang et al. [6]	8	119	Adults, DSM-IV	10–20	Paroxetine	20–40	HAMD17
Yan et al. [7]	6	126	Adults, CCMD-3	10–20	Citalopram	20–40	HAMD17
Ou et al. [8]	6	240	Adults, DSM-IV-TR	10–20	Citalopram	20–40	HAMD17
Chen et al. [9]	6	240	Adults, CCMD-3	10–20	Citalopram	20–40	HAMD17
Liu et al. [10]	6	80	Adults, CCMD-3	10–20	Paroxetine	10–40	HAMD17
Mao et al. [11]	8	240	Adults, DSM-IV	10	Fluoxetine	20	HAMD17
Zhao [12]	6	52	Adults, CCMD-3	10–20	Venlafaxine	100–225	HAMD17
Qian et al. [13]	6	68	Adults, CCMD-3	10–20	Sertraline	50–200	HAMD17
Li et al. [14]	6	56	Adults, CCMD-3	10–20	Citalopram	20–40	HAMD17

3.3 Meta-analysis of efficacy

No heterogeneity (I^2= 0%) was noted in the treatment effect, and no significant difference was observed in the efficacy of escitalopram in the treatment of depression in China compared with the control group (RR, 1.17; 95% CI: 0.89–1.56; Figs. 1 and 2).

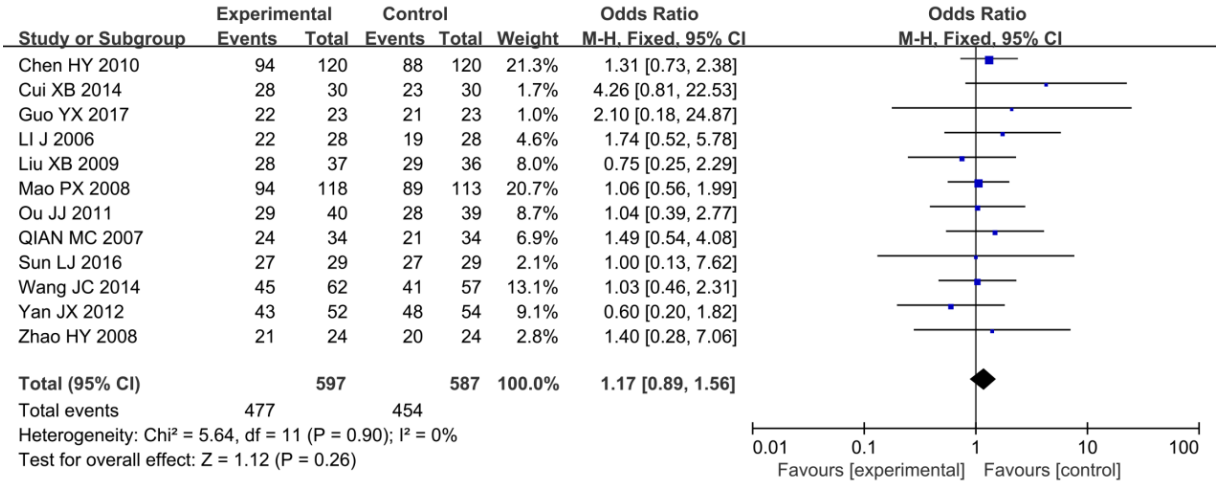

Figure 1: Forest plot of efficacy.

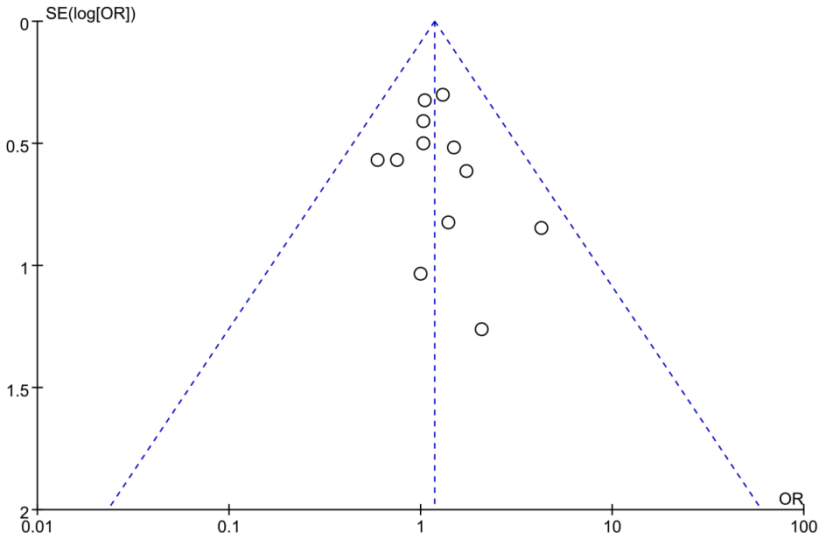

Figure 2: Funnel plot of efficacy.

3.4 Meta-analysis of safety

In each treatment group, eight major adverse reactions were found. In addition, no significant difference was noted in the incidence of adverse reactions (e.g., nausea, xerostomia, dizziness, insomnia, liver dysfunction, other gastrointestinal reactions, palpitations, and fatigue) between escitalopram and other antidepressants (Figs. 3 and 4).

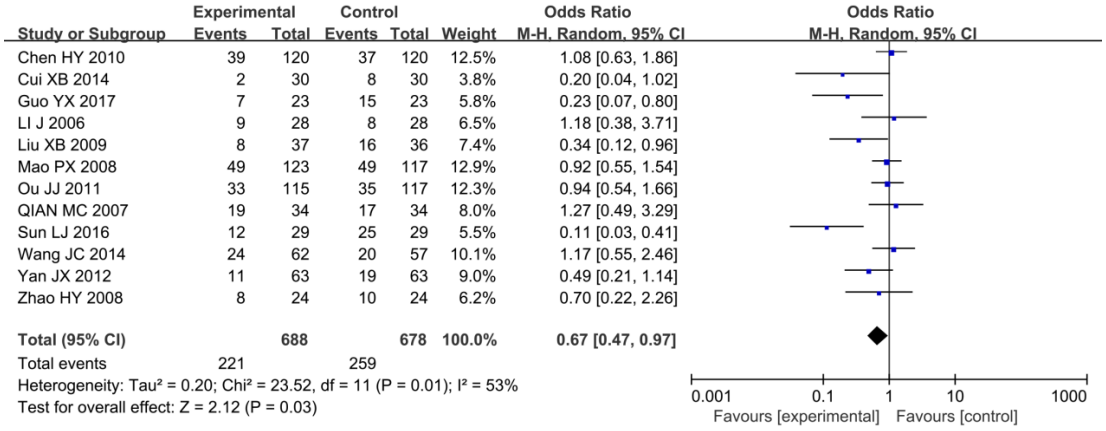

Figure 3: Forest plot of safety.

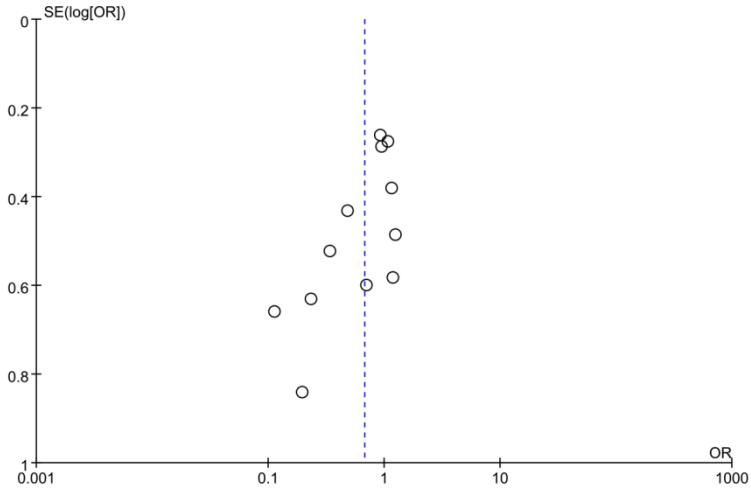

Figure 4: Funnel plot of safety.

3.5 HAMD score

HAMD, compiled by Hamilton in 1960, is the most extensively used scale in the clinical evaluation of depression. The scale has 17, 21, and 24 items. In this study, two trained evaluators performed HAMD joint examination on patients, usually using conversation and observation. After examination, two evaluators scored independently. Before and after treatment, the severity of the disease and the therapeutic effect could be assessed. Figures 5 and 6 present the meta-analysis results obtained using the stochastic effect model.

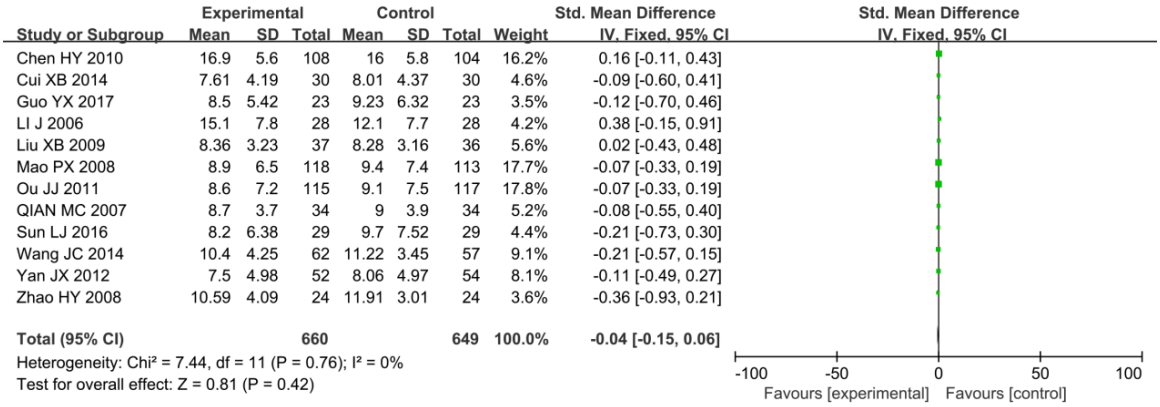

Figure 5: Forest plot of the HAMD score.

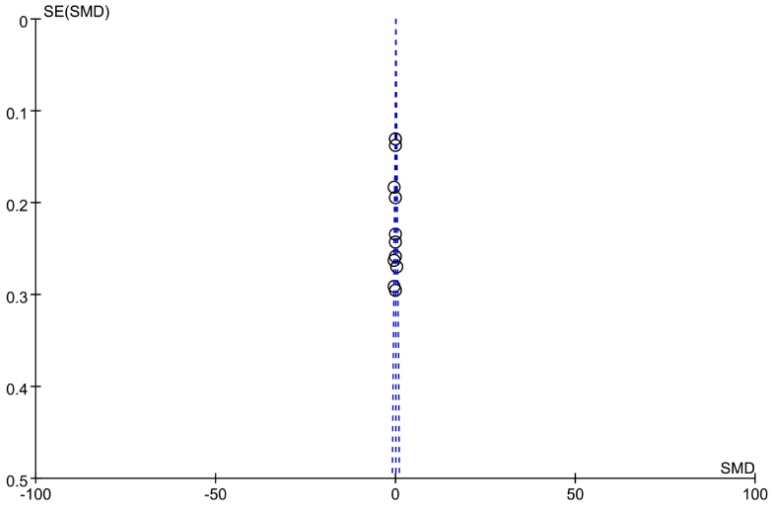

Figure 6: Funnel plot of the HAMD score.

4. Discussion

Kirino [15] demonstrated that escitalopram was markedly better than placebo in the treatment of depression and superior to other SSRIs (e.g., citalopram, paroxetine, fluoxetine, and sertraline) and serotonin and noradrenaline reuptake inhibitors (SNRIs) such as loxetine and venlafaxine or those with similar efficacy. In addition, escitalopram exhibited good tolerance, and adverse reactions were usually mild and temporary.

This study reviewed the efficacy and safety of escitalopram in the treatment of depression in China. Previously, several studies on antidepressants could not precisely evaluate the therapeutic effect because of their small sample size. Thus, a meta-analysis of RCTs can provide the best therapeutic effect evaluation.

This meta-analysis reviewed 12 RCT studies on patients with depression in China, revealing that the efficacy and safety of escitalopram were similar to those of other antidepressants (e.g., paroxetine, citalopram, flumipramine, fluoxetine, sertraline, and venlafaxine); however, escitalopram was the most cost-effective drug overall.

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