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Efficacy and Safety of Escitalopram in First Episode of Major Depressive Disorder - A Tertiary Care Indian Center Experience

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Abstract

Context: Major Depressive Disorder (MDD) is the most prevalent psychiatric illness and escitalopram is one of the most commonly used selective serotonin reuptake inhibitors (SSRI) for its treatment.

Aim: To study efficacy and safety of escitalopram in patients with first episode of MDD.

Materials and methods: This was a prospective, open label, eight weeks follow-up study. Eighty-four patients with first episode of MDD were selected using simple random sampling. Depression was diagnosed using DSM-5 diagnostic criteria for MDD. Montgomery-Asberg Depression Rating Scale (MADRS) was used to assess the severity of depression. Clinical Global Impression Severity (CGI-S) and Clinical Global Impression Improvement (CGI-I) were used to measure illness severity and global improvement. The Antidepressant Side-Effect Checklist (ASEC) was used to measure adverse reactions to antidepressants.

Results: The mean of MADRS total score at baseline was 32.08 which was decrease in subsequent follow up and at 8-week score was 11.24. 77% of patients responded (≥50% or more reduction of MADRS total score) and 64.9% remitted (≤12 score of MADRS) at 8 weeks. 22.9% of patients reported side effects during the 8-week treatment. 94.2% of patients got significant improvement with 10 mg dose of escitalopram. The common side effects were constipation (5.4%), nausea (5.4%), dry mouth (4.1%) and yawning (4.15%).

Conclusion: Escitalopram treatment was efficacious and well tolerated in patients with first episode of MDD. Nearly two third patients achieved remission at the end of eight week.

Keywords: Escitalopram; Depression; Response; Remission

Introduction

Major Depressive Disorder (MDD) is a chronic and disabling disorder and has highest lifetime prevalence among major psychiatric disorders. World Health Organization (WHO) states that globally, more than 300 million persons of all ages suffer from depression. It is one of the leading causes of disability worldwide and a major contributor to the overall global burden of disease [1,2]. Escitalopram is a selective serotonin reuptake inhibitor (SSRI) as produced by isolating the active S-enantiomer from Racemic-citalopram [3].

A number of clinical practice guidelines suggest SSRIs as first choice of treatment of MDD [4-6]. Some comparative studies reported escitalopram has equal and or better efficacy and tolerability in patients with MDD than other SSRI [7-9]. An Indian multicenter study of antidepressant prescriptions in patients with first episode of depression found escitalopram was widely prescribed as a first choice [10].

In India, limited research on efficacy and tolerability of escitalopram in patients with MDD found that escitalopram was effective and well tolerated [11]. Hence, this study was designed to evaluate efficacy and safety of Escitalopram in patients with first episode of MDD.

Materials and Methods

Study design

This was a prospective, open label, eight-week study of patients with first episode of MDD conducted in the Department of Psychiatry, M. P. Shah Govt. Medical College (MPSGMC), Jamnagar from October 2016 to September 2017. On an average, 900 adult patients with first episode of depression per year are consulting Psychiatry OPD for the past three year. A sample of 84 participants (18 to 60 years of age) of the 900 patients with first episode of MDD was selected through simple random sampling by random number table method. Study objectives were explained to participants and their written informed consent were obtained.

Subjects

A sample of 84 participants (18 to 60 years of age) with first episode of MDD attending OPD of Psychiatry was recruited. Patients with mild depression, bipolar disorder, schizophrenia, schizoaffective disorder, major neurocognitive disorders, neurological disease, imminent risk for suicide, pregnancy, refusal for consent were excluded. Study was approved by the Institutional ethics committee of MPSGMC, Jamnagar.

Tools

Diagnostic and Statistical Manual of Mental diagnostic Disorders-5 (DSM-5) criteria for MDD was used to diagnosis [12]. Montgomery-Asberg Depression Rating Scale (MADRS) was used to assess the severity and treatment response. MADRS is the clinician-rated scale and it consists of 10-items. It is commonly used in clinical studies and practice. A score greater than 30 or 35 on the MADRS indicate severe depression, 50% reduction in the MADRS score was taken as response and a score of 10 or below as remission [13]. The sensitivity and specificity is 0.75 and 0.84, respectively and the validity of MADRS is 0.80. MADRS has been reported as equivalent to or more sensitive to the changes in symptoms over time than the Hamilton Rating Scale for Depression (HSRD). It does not assess all the core criterion symptoms (across depressive subtypes) used in DSM-5 to diagnose MDD as it lacks ratings of oversleeping and overeating, as well as interest though it assesses energy (though it assesses lassitude), self-criticism (guilt), and psychomotor changes [14]. Clinical Global Impression (CGI) scale was used to measure illness severity and global improvement. CGI is a 3-item observer-rated scale that measures illness severity (CGI-S), global improvement or change (CGI-I) and therapeutic response. The illness severity and improvement sections of the instrument are used more frequently than the therapeutic response in both clinical and research settings in many clinical drug trials, CGI has proven itself as a robust measure of efficacy. It is rated on a 7-point scale, with the severity of illness scale using a range of responses from 1 (normal) through to 7 (amongst the most severely ill patients) and with the improvement scale scores range from 1 (very much improved) through to 7 (very much worse). Each component of the CGI is rated separately; the instrument does not yield a global score [15,16].

Anti-depressant Side Effect Checklist (ASEC) self-reported instrument used to measure 21 adverse reactions to antidepressants. For each item, the participants rated the severity of the specific symptom on a four-point scale (0 absent; 1 mild; 2 moderate; 3 severe) and specified whether a symptom (if present) was likely to be a side effect of the antidepressant drug (yes or no) [17].

Procedure

Depression in the patients was diagnosed clinically by senior psychiatrist using DSM-5 diagnostic criteria. Escitalopram 10 mg once daily was started in patients with first episode of MDD and if no response (≥50% or more reduction of MADRS total score) to 10 mg in 4-weeks then the dose was increased to 20 mg. Clinical improvement and tolerability of escitalopram were evaluated once a week for first two weeks then every 2-week in subsequent follow-ups until 8-weeks. Assessment and scoring of severity of depression was done using MADRS, CGI and ASEC by a senior resident doctor who was not involved in treatment of the patients at each follow-up. Drug adherence was assessed by pill counting method and caregiver's confirmation at each follow-up.

Statistical analysis

Collected data was subjected to appropriate descriptive statistics of different variables using frequency and percentage, mean and standard deviation. Chi-square test was used for qualitative data and p-value of <0.05 was considered statistically significant. Paired samples t-test was used for quantitative data. Statistical Package for the Social Sciences (SPSS) version 15 was applied to analyse the data.

Results

Out of the total 84 patients, four withdrew consent and six were lost in follow-up and 74 completing the 8-week follow up were included for analysis. There was almost equal proportion of males (51.4%) and females (48.6%) with a mean age of 36.62 years.

The mean MADRS total score decreased on subsequent follow-up from the baseline of 32.08 and, was 24.11 at the end of one week, at the end of 2-week 20.22, at the end of 4-week 16.92, at the end of 6-week 13.86 and at the end of 8-week 11.24.

The percentage of responders (≥ 50% reduction in MADRS total score) in Figure 1 reflects a sharp increase from second to fourth week, followed by gradual increase from fourth to eighth week. No patient showed remission (≤10 score on MADRS) at the end of 1-week. Figure 2 shows result and pattern of improvement based on CGI-S and CGI-I score similar to the MADRS total score, which confirms the robustness of response to the treatment.

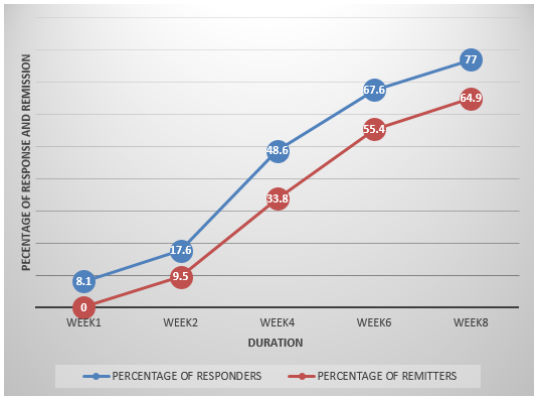

Figure 1: Percentage of response and remission for 8 weeks.

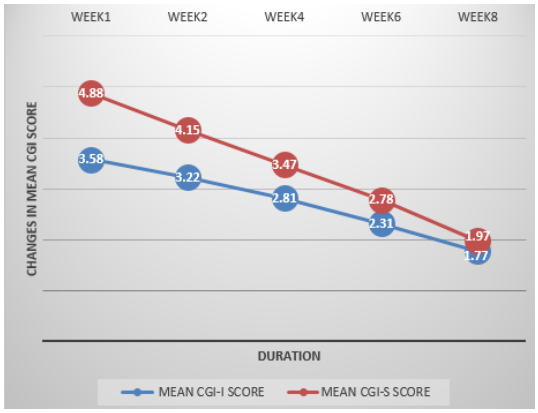

Figure 2: Mean change in CGI score from baseline to 8 weeks.

In this study, at the end of 8-weeks, out of 59 patients with very much/much improvement, 94.92% (55) of patients received 10 mg of escitalopram. While, in the 13 patients with minimal improvement 69.23% (7) received 20 mg. Distribution between dosages of escitalopram and improvement in CGI-I score at eight weeks was statistically significant (Table 1).

Dose of Escitalopram	Improvement at 8 week using CGI X_2=33.194, p<0.001		
	Very much/ much improved n=59 (%)	Minimally improved n=13 (%)	No change n=2 (%)
10 mg	56 (94.92)	4 (30.77)	1 (50)
20 mg	3 (5.08)	9 (69.23)	1 (50)

Table 1: Association between dose of escitalopram and improvement at 8-week using CGI.

Patients with moderate depression showed 86% response and 76% remission at the end of 8-weeks on escitalopram while in the patients with severe depression, 58.33% showed response and 41.67% showed remission. Patients receiving escitalopram 10 mg daily dosage showed 85.24% response and 75.41% remission while, those receiving 20 mg daily showed 38.46% response and 15.25% remission. Distribution of patients with response and remission at 8-weeks using MADRS scores, daily dose of escitalopram and severity of depression was statistically significant (Tables 2 and 3).

Response at 8-week using MADRS	Dose of Escitalopram X_2=13.255, p<0.001		Major depression X_2=7.015, p=0.008	
	10 mg n=61 (%)	20 mg n=13 (%)	Moderate n=50 (%)	Severe n=24 (%)
Responded	52 (85.24)	5 (38.46)	43 (86)	14 (58.33)
Not responded	9 (14.75)	8 (61.53)	7 (14)	10 (41.66)

Table 2: Association between response at 8-weeks using MADRS, dose of escitalopram, and severity of depression.

Remission at 8-week using MADRS	Dose of Escitalopram X_2=16.942, p< 0.001		Major depression X_2=8.387, p=0.004	
	10 mg n=61 (%)	20 mg n=13 (%)	Moderate n=50 (%)	Severe n=24 (%)
Not remitted	15 (24.59)	11 (84.61)	12 (24)	14 (58.33)
Remitted	46 (75.41)	2 (15.39)	38 (76)	10 (41.67)

Table 3: Association between remissions at 8 weeks using MADRS, dose of escitalopram and severity of depression.

22.9% patients reported side effects with treatment of escitalopram with ASEC. No patients reported any serious adverse reactions, 5.4% of patients reported constipation and nausea, 4.1% of patients reported yawning and dry mouth, 2.7% of patients reported headache and 1.4% of patients reported palpitation.

Discussion

Escitalopram was found to be efficacious and well-tolerated in the first episode of MDD in this study. In the present study, the response rate of 77% and remission rate of 64.9% were achieved at the end of 8 weeks, the result and pattern of improvement based on CGI score was consistent to MADRS total score that confirms the clinical relevance of the response and remission to treatment. An open-label, multi-center study found a response rate of 76.9% and a remission rate of 66.7% in patients with MDD [11]. A review of escitalopram efficacy in MDD showed that escitalopram was superior to placebo, and nearly equal or superior to other SSRIs and serotonin-noradrenaline reuptake inhibitors (SNRI) [18]. Similar findings were found with the randomized double-blind comparative study of escitalopram and citalopram in patients with MDD [19]. A pooled analysis of four Chinese clinical trials found, an overall response and remission rates after escitalopram monotherapy were 68.4% and 46.4%, respectively at the end of 7-weeks [20]. A multicenter, randomized, double-blind, fixed-dose trial of escitalopram in patients with MDD found 80% response and remission rate at the end of 8-weeks [21]. The differences in response and remission rates were due to different in study design, populations and duration of the trial.

In our study, at the end of 8-weeks mean of total MADRS score changed by -20.8. This finding was consistent with the findings of double blind and open label, prospective, multicenter studies in Chinese population [21-24]. A placebo-controlled study in depression at primary care found mean total MADRS score changed by -16.3 in escitalopram group compared to -13.6 in the placebo group [22]. A double-blind, comparative study in patients with MDD found a change in MADRS total score at 8 weeks -13.7 ± 10.0 in escitalopram group, -14.2 ± 9.9 in paroxetine group and -10.7 ± 9.5 in placebo group [23]. A randomized, double-blind study of escitalopram versus citalopram

in patients with MDD found mean change in MADRS total score at the end of 8 weeks was -16.8 in the escitalopram group [19].

In the present study, response and remission rates were significantly higher in moderate depression compare to severe depression. This finding was consistent with a pooled analysis of four Chinese clinical trials of escitalopram in patients with MDD [20]. In opposite to this study, Tianmei Si et al. found a higher response and remission rate in severe depression, which may due to escitalopram given in patients with severe depression [24].

In the present study, significant number of patients remitted at the 10 mg dose relative to 20 mg dose of escitalopram which suggest that escalation of dose of escitalopram may not require in treatment responded patients. A randomized double blind study in primary care patients with MDD found 76% of patients remitted with 10 mg dosage of escitalopram [19]. A fixed dose trial of escitalopram in outpatients with depression found escitalopram, at both 10 and 20 mg doses produced significant improvement at 8 weeks relative to placebo which may due to 10 mg and 20 mg dosage of escitalopram was given in separate groups while in the present study, 20 mg escitalopram was given to patients who did not responded to 10 mg in 4-weeks [25]. In opposite to our study, an open label pilot study found 57% patients achieved sustain remission with 20 to 50 mg dose escitalopram [26].

In this study, side effects with escitalopram were mild, tolerable and no one had reported severe side effects. The most common side effects were constipation and nausea followed by dry mouth, yawning, headache, and palpitation. This finding is consistent with the multicenter study of escitalopram in patients with depression in India and China [11,21,25]. An open-label pilot study of efficacy and tolerability of escitalopram in patients with MDD reported escitalopram was well tolerated up to 40 mg dose per day [26]. A randomized, double-blind, comparative, eight-week study in patients with MDD found low drop-out due to adverse effects in the escitalopram group compared to citalopram group (4% versus 11.2%) at the end of 8 weeks [19].

Conclusion

Escitalopram was effective and tolerable in patients with first episode of MDD. Nearly two third patients achieved remission with escitalopram at the end of 8-weeks. Three fourth of the patients with MDD achieved remission with 10 mg dose at the end of 8-weeks who showed response during 4-weeks. Escalation of dose of escitalopram is not required in many treatments responded patients with MDD till 8-weeks rather it increases cost of treatment and issues of tolerability in some patients. No patients had any serious adverse reactions with escitalopram during 8-week. Nausea and Constipation were most commonly reported side effects followed by dry mouth, yawning, headache and palpitation.

Strength of Study

Efficacy of Escitalopram was assessed by changes in MADRS and CGI scale at each follow up in good number (84 patients, Margin of error 10.9%) of patients.

Limitation of Study

This was a single center, open label study without any control group.

Future Implications

A multi-centric, longer duration, prospective, comparative study with larger sample size will require to establish efficacy and safety of Escitalopram in patients with MDD.

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None.

Conflict of Interest

There is no conflict of interest.

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