**ABSTRACT**

Mood disorders are among the most common mental disorders encountered in clinical practice and divided into bipolar disorders and depressive disorders. The essential feature of these disorders is a major disturbance in mood. The aim of the study is to compare the efficacy of Citalopram and Escitalopram in the Major Depressive Disorder Patients during the first 8 weeks (acute phase) of treatment. Totally 20 patients are selected for each group randomly and enroll for this study. The rating scales used are Hamilton rating scale for depression (HAMD), Montgomery-Åsberg Depression Rating Scale (MADRS), Clinical Global impressions scale (CGIS). The percentage of changes in HAMD during the visits efficacy was significant (<0.05). The same efficacy in (MADRS) was significant (<0.05) in all visits. On assessment of the drug Escitalopram response using rate of global improvement 14(70%) patients were Much Improved and 3(15%) patients were very much improved, 3(15%) patients were not significant in the treatment in assessment of clinical response using the Clinical Global impressions scale (CGIS). On assessment of the drug Citalopram response using rate of global improvement 10(50%) patients were much improved, 10(50%) patients were not significant in the treatment in assessment of clinical response using the Clinical Global impressions scale (CGIS). This study shows that the new Selective serotonin reuptake inhibitor Escitalopram has better efficacy in the treatment of severe depression than Citalopram. This evidence clearly supports the use of Escitalopram as a legitimate first-line treatment for Major Depressive Disorder.

**Key words:** Citalopram, Escitalopram, Major Depressive Disorder.

**INTRODUCTION**

The term depression is reserved in psychiatry to describe a specific entity having biological and pharmacological implications. Studies show that the physical and social dysfunctions produced by depression outweigh most chronic medical conditions\cite{1}. The medical outcomes study demonstrated that the degree of impairment in depressed patients is comparable only to patients with chronic heart disease. In turn, the cost of care for depression produces a tremendous burden upon society\cite{2}. If co-morbid with a medical condition, and may even shorten life expectancy. Because of high prevalence and chronicity of depression, a complete antidepressant response remains an objective for clinicians and is still a key target for new drug developments. Approximately eight classes of antidepressants acting by different mechanisms are available for the physicians for treatment\cite{3}. Despite the similarity of Escitalopram and Citalopram, preclinical as well as various clinical studies (including double-blinded studies) have shown differentiated effects of Citalopram and Escitalopram, as well as a clinical superiority compared with a variety of other SSRIs, such as Paroxetine especially in severely depressed patients. A head-to-head comparison of Escitalopram with Duloxetine (Cymbalta) found Escitalopram to be both more tolerable and more effective. Compared with Venlafaxine and Sertraline, Escitalopram was shown to have similar efficacy\cite{4-9}.

**MATERIALS AND METHODS**

**Study Design:**
It is a prospective, randomized, interventional and comparative study of Citalopram and...
Escitalopram in the Major Depressive Disorder patients. This is an 8 week study. Participated patients shall be visiting the hospital for periodical review, for every 2 weeks. This study is conducted over a period of six months including the interpretation and analysis of results. Totally 20 patients are selected for each group randomly and enrolled for this study. The result will be calculated with the help of statistics, tables and graphs.

Materials:
40 patients attending the outpatient psychiatric department of M.S Chellamuthu Trust & Research Foundation, Madurai were independently evaluated by the psychiatrist who initially did the clinical interview and arrived at a diagnosis using the ICD-10 criteria for research.

Ethical Committee Approval:
Ethical committee approval was sought from Institutional Review Board, MS Chellamuthu trust and research foundation, Madurai, Tamilnadu.

Inclusion criteria:
- Patients who met DSM-IV criteria for major depressive disorder (MDD), a single major depressive episode or recurrent major depressive episode without psychotic features, MDD are primary mental disorder.
- Age from 18-65 Years old, male or female.
- HAMD-17 total score at least 20 at baseline and first item’s score at least 2
- MADRS score greater than or equal to 22 at baseline.
- CGI-S at least 4 at baseline
- Written informed consent provided by patient himself/herself.

Exclusion criteria:
- Severe suicide attempt.
- Any unstable medical illness would affect study or increase patient’s risk to participate this study, including disease of heart, lung, liver, kidney, cardiovascular system, eyes, nervous system, endocrine system, hematological system etc.
- History of epilepsy (except children febrile seizure/convulsion).
- Known history of high intraocular pressure or angle closure glaucoma.
- Psychoactive substance abuse or dependences within 1 year prior enrollment.
- Depressive episode due to other mental disorders or physical diseases.
- Bipolar disorder, rapid cycling/ circulation.
- Female patient during their pregnant and lactation period or childbearing potential during study.
- History of severe drug hypersensitivity.
- Patients cannot administrate drug according to medical order.
- HAMD total score decreased more than 25% from screening to baseline.
- Use of Electroconvulsive therapy within half year prior enrollment.
- Known lack of efficacy to Escitalopram by treatment before.

Scales:
Hamilton rating scale for depression$^{[10,11]}$, Montgomery-Åsberg Depression Rating Scale$^{[12]}$, Clinical Global impressions scale$^{[13]}$.

Method of collection of data:
The patients satisfying the inclusion criteria were assessed for the severity of the illness using, (1) HAM-D scale which assess the score of the 17 symptoms of the disease and (2) CGI scale which classifies the patients onto different groups on the basis of the severity of the disease, (3) MADRS was originally a subscale of the Comprehensive Psychopathological Rating Scale.

RESULTS
In this group A patients had a Mean value of 27.5 and SD value of 2.2 for HAMD scale. Mean value of 32.4 and SD value of 3.46 for MADRS scale. Group B patients had a Mean value of 29.9 and SD value of 4.7 for HAMD scale. Mean value of 34.75 and SD value of 3.67 for MADRS scale. P value for both groups in HAMD scale is 0.0227 and MADRS scale is 0.0220. These results were shows us that both the drugs in baseline visit had no significant effects(Table 1).

Table 1: Efficacy of the Drugs Citalopram 20mg and Escitalopram 10mg baseline Values:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>HAMD</th>
<th></th>
<th>MADRS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN</td>
<td>SD</td>
<td>MEAN</td>
<td>SD</td>
</tr>
<tr>
<td>Citalopram (Group A)</td>
<td>27.75</td>
<td>2.2</td>
<td>32.4</td>
<td>3.46</td>
</tr>
<tr>
<td>Escitalopram (Group B)</td>
<td>29.7</td>
<td>4.7</td>
<td>34.75</td>
<td>3.67</td>
</tr>
</tbody>
</table>
Comparison of both the drugs:
In HAMD rating scale percentage change in the mean value of Citalopram had no significant value during 1st and 2nd visits but it was improved from 3rd visit onwards. During second visit the change was 9.17%, and then it will be gradually increased as 16.66%, 18.13%, 18.48%, during 3rd, 4th, 5th visits respectively. In Escitalopram groups percentage change in the mean value was improved from 3rd visit onwards but the percentage values were greater than Citalopram groups. During second visit the value was 19.78% but third visit onwards the values were 43.27% for 3rd visit, 52.01% for 4th visit and 53.08% for 5th visit. Those results were gave us Escitalopram had a great efficacy compare than Citalopram groups.

In MADRS rating scale percentage change in the mean value of Citalopram had no significant value during 1st and 2nd visits but it was improved from 3rd visit onwards. During second visit the change was 7.05%, and then it will be gradually increased as 15.95%, 16.93%, 17.81%, during 3rd, 4th, 5th visits respectively. In Escitalopram groups percentage change in the mean value was improved from 3rd visit onwards but the percentage values were greater than Citalopram groups. During second visit the value was 13.43% but third visit onwards the values were 39.88% for 3rd visit, 53.88% for 4th visit and 54.75% for 5th visit. Those results were gave us Escitalopram had a great efficacy compare than Citalopram groups (Table 2).

Assessment of Clinical Response Using the Clinical Global Impressions Scale (CGI Scale):
Escitalopram 10mg showed a good response to the treatment. An assessment of the response using rate of global improvement, 14 (70%) patients were Much Improved and 3 (15%) patients were very much improved, 3 (15%) patients were not significant in the treatment. Citalopram 20mg showed a good response to the treatment. On assessment of response using rate of global improvement 10 (50%) patients were much improved, 10 (50%) patients were not significant in the treatment (Table 3&4).

### Table 2: Comparison of Citalopram and Escitalopram

<table>
<thead>
<tr>
<th>HAM-D Percentage of changes at</th>
<th>Citalopram</th>
<th>Escitalopram</th>
<th>(\beta)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN</td>
<td>SD</td>
<td>MEAN</td>
</tr>
<tr>
<td>Second visit</td>
<td>9.17</td>
<td>10.82</td>
<td>19.78</td>
</tr>
<tr>
<td>Third visit</td>
<td>16.66</td>
<td>14.65</td>
<td>43.27</td>
</tr>
<tr>
<td>Fourth visit</td>
<td>18.13</td>
<td>15.07</td>
<td>52.01</td>
</tr>
<tr>
<td>Fifth visit</td>
<td>18.48</td>
<td>14.75</td>
<td>53.08</td>
</tr>
<tr>
<td>MADRS Percentage of changes at</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MEAN</td>
<td>SD</td>
<td>MEAN</td>
</tr>
<tr>
<td>Second visit</td>
<td>7.05</td>
<td>13.36</td>
<td>13.43</td>
</tr>
<tr>
<td>Third visit</td>
<td>15.95</td>
<td>16.16</td>
<td>39.88</td>
</tr>
<tr>
<td>Fourth visit</td>
<td>16.93</td>
<td>17.1</td>
<td>53.88</td>
</tr>
<tr>
<td>Fifth visit</td>
<td>17.81</td>
<td>16.92</td>
<td>54.75</td>
</tr>
</tbody>
</table>

### Table 3: Assessment of Clinical Response of Escitalopram

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Global Improvement</th>
<th>No of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
<td>Minimaly improved</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Much improved</td>
<td>14</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td>Very much improved</td>
<td>3</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>3</td>
<td>15%</td>
</tr>
</tbody>
</table>

### Table 4: Assessment of Clinical Response of Citalopram

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Global Improvement</th>
<th>No of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>Minimaly improved</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Much improved</td>
<td>10</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Very much improved</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>10</td>
<td>50%</td>
</tr>
</tbody>
</table>
DISCUSSION
The study attempted is comprehensive because it included all trials in which the maximum dose for Escitalopram (20 mg) can be administered. According to the cut-off point taken to define severe depression based on the MADRS TOTAL SCORE (30), 40 patients were considered as severely depressed patients and so included in this study. Among them, 20 administered Escitalopram 10mg, and 20 administered Citalopram 20mg. The primary efficacy parameter was the mean change from baseline to end of treatment in MADRS TOTAL SCORE between Escitalopram and Citalopram groups, based on last-observation-carried-forward method. The change from baseline to endpoint of the Hamilton rating scale for Depression (HAM-D) and the Clinical Global Impression of Improvement and Severity (CGI-I and CGI-S) were also analyzed as secondary criteria.

Results showed that the mean change from baseline in the MADRS total score was significantly higher in the Escitalopram group compared with the Citalopram group (15.95±9.91 Vs 26.3±4.6; p=0.001, P<0.05). Response rates were significantly higher for Escitalopram than for Citalopram (85% vs. 50% respectively). A borderline significant difference was found for remission rate in the observed-cases analysis (54.75% ±25.51 vs. 17.81% ± 16.92 respectively, p=0.0001).

Analyses of the HAM-D total score was significantly higher in the Escitalopram group compared with the Citalopram group (13.25±6.77 vs 22.5±4.16; p=0.0001, P<0.05). Response rates were significantly higher for Escitalopram than for Citalopram (85% vs. 50% respectively). A borderline significant difference was found for remission rate in the observed-cases analysis (53.08% ±26.94 vs. 18.48% ± 14.75 respectively, p=0.0001).

CGI-I and CGI-S scores revealed consistent results. In CGI-S 14(70%) patients were Much Improved and 3(15%) patients were Very much improved in Escitalopram 10mg group, but in Citalopram only 10(50%) patients were got improvement.

Escitalopram is significantly more effective than Citalopram, and is associated with lower healthcare costs. This prospective economic analysis demonstrated that Escitalopram is a cost-effective first-line treatment option for major depressive disorder.

This study shows that the new Selective serotonin reuptake inhibitor [14] (SSRI) Escitalopram has better efficacy in the treatment of severe depression than Citalopram, its racemic parent. Mean differences between treatments groups were in favour of Escitalopram for all scales. The benefits of Escitalopram compared with Citalopram, as demonstrated by both magnitude of effect and time of onset, are superior to the benefits of Citalopram, an antidepressant drug with proven efficacy. This evidence clearly supports the use of Escitalopram as a legitimate first-line treatment for Mood depressive disorder15 (MDD).

REFERENCES
1. Wills KB, The functioning and wellbeing of depressed patients.JAMA; 262:914.
8. Ventura D, Armstrong EP, Skrepnek GH, Haim Erder M, Escitalopram versus...


