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## RESEARCH ARTICLE

**COMPARATIVE EVALUATION OF AMISULPRIDE AND ESCITALOPRAM ON SHEEHAN'S DISABILITY SCALE AMONG DEPRESSION PATIENTS IN A TERTIARY CARE TEACHING HOSPITAL IN NEPAL**Dr. Vijay Kaul<sup>1</sup>, Dr. Shaktibala Dutta<sup>2</sup>, \*Dr. Mirza Atif Beg<sup>3</sup>, Dr. Nand Kishore Singh<sup>4</sup>, Dr. Shalu Bawa<sup>5</sup>, Dr. Mohammad Anjoom<sup>6</sup>, Dr. Srihari Dutta<sup>7</sup><sup>1</sup>Department of Psychiatry, Nepalgunj Medical College, Nepal.<sup>2</sup>Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun<sup>3</sup>Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun<sup>4</sup>Department of Psychiatry, SGRRIM&HS, Patel Nagar, Dehradun<sup>5</sup>Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun<sup>6</sup>Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun<sup>7</sup>Immunization Health Specialist, Unicef, New Delhi, India Country Office India\*Corresponding Author's Email: [mabeg1997@gmail.com](mailto:mabeg1997@gmail.com)

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**ABSTRACT**

**Introduction and Aim:** Depression is an important global public health problem due to its relatively high lifetime prevalence and significant disability caused by it. The present study was conducted to compare improvement in functional outcome by Amisulpride and Escitalopram among depression patients using Sheehan's Disability Scaling.

**Material and methods:** The study was conducted in depression patients for 1 year in the Department of Neuropsychiatry, Nepalgunj Medical College & Teaching Hospital. A total of 117 depression patients were divided into 2 groups. Group I (58 patients) received Amisulpride tablet at a dose of 50 mg/day and Group II (59 patients) were given Escitalopram at a dose of 10 mg/day. The patients were required to follow up at 4, 8 and 15 weeks. The efficacy of the drugs was calculated by Hamilton depression rating scale (HAM-D). The improvement in functional outcome was compared between the two groups by using Sheehan's Disability Scale (SDS). Appropriate statistical tools using GraphPadInstat 3.0 were used for analysis. p value < 0.05 was considered significant.

**Results:** HAM-D score in group receiving Amisulpride at 0 and 15 weeks was 16.92±0.35 and 7.87±0.29 (p<0.0001). HAM-D score in group receiving Escitalopram at 0 and 15 weeks was 17.09±0.39 and 6.63±0.39 (p<0.0001). Sheehan's Disability Score in group receiving Amisulpride at 0 and 15 weeks was 20.35±0.31 and 11.08±0.60 (p<0.0001). SDS score in group receiving Escitalopram at 0 and 15 weeks was 21.53±0.55 and 11.49±0.46 (p<0.0001). Intergroup comparison at 15 weeks was insignificant (p>0.05). Gastrointestinal disturbances, sexual disturbances, amenorrhea, lactation, agitation and insomnia were the commonly encountered adverse drug reactions.

**Conclusion:** Both Amisulpride and Escitalopram showed improvement in Sheehan's Disability Scale at the end of study period. But intergroup comparison showed no significant difference in the two groups.

**Key words:** Depression, Amisulpride, Escitalopram, Sheehan's Disability Scale (SDS).

**INTRODUCTION:**

Depression is an important global public health problem due to its relatively high lifetime prevalence and significant disability caused by it. It accounts for almost 12% of the total years which were lived with disability worldwide<sup>1</sup>. The WHO defines depression as a pessimistic sense of inadequacy and a despondent lack of activity. It can be defined as a mental state which is characterized by feelings of sadness, loneliness, despair, low self-esteem, and self-reproach. The accompanying signs include psychomotor retardation or at times, withdrawal from interpersonal contact and vegetative

symptoms such as anorexia and insomnia. Depression is associated with marked personal, social and economic morbidity affecting 9.5% of population worldwide<sup>2</sup>. A recent American survey found the prevalence of current depression to be 9% and the rate of current major depression to be 3.4%<sup>3</sup>. Over the past several decades, pharmacologic management of depressive disorders has evolved substantially. Despite the introduction of many new antidepressant medications and a continually advancing understanding of their individual strengths and weaknesses, selecting the best possible treatment

for each individual patient remains a significant challenge for general practitioners and psychiatrists. Response and remission are key goals in the management of depression. Acceptability is also an important step towards achieving these goals, since patients require long-term (often life-long) pharmacotherapy. First-line pharmacotherapy for depressive disorders typically chosen from among the “newer antidepressants”— either a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI)<sup>5</sup>. Escitalopram, the S-enantiomer of citalopram, is a selective serotonin reuptake inhibitor (SSRI) antidepressant that is the most selective of the SSRIs<sup>6</sup>. The efficacy of escitalopram has been demonstrated in major depressive disorder (MDD) in both primary care and specialist settings<sup>7-9</sup>. Amisulpride is a substituted benzamide derivative structurally related to sulpiride. It belongs to the second-generation antipsychotic that preferably binds to dopamine D2/D3 receptors in limbic rather than striatal structures<sup>10</sup>. Amisulpride is indicated for the treatment of acute and chronic schizophrenia with prominent positive and/or negative symptoms due to a dose-dependent blockade of dopamine receptors<sup>10,11</sup>. In addition to antipsychotic effects, preliminary reports suggest that Amisulpride may have antidepressant effects in dysthymia. Amisulpride has been shown to be as effective as comparator in clinical studies in patients with dysthymia and/or major depression<sup>12</sup>. The presumed selectivity of amisulpride for D2 and D3 dopamine receptors has led to the prevailing hypothesis that modulation of dopaminergic signaling is responsible for its antidepressant efficacy. Recent evidence suggests that primary-care providers do not decide on drug treatment or referral for depression on the basis of questionnaire scores alone, and that they consider practical wisdom and clinical judgment to be more important than objective assessments<sup>13,14</sup>. Assessment of function may, therefore, provide additional, important efficacy information over and above that provided by measuring response and remission. In this regard, emerging data show that escitalopram has an ability to improve functional outcomes in depression patients<sup>15, 16</sup>. Based on the above observations, the present study was conducted to compare efficacy of Amisulpride and Escitalopram by HAM-D and improvement in functional outcomes by Sheehan’s Disability Scale (SDS) among depression patients in a tertiary care teaching hospital in Nepal.

#### MATERIAL AND METHODS:

This study was conducted in the Department of Neuropsychiatry, Nepalgunj Medical College &

Teaching Hospital, Nepalgunj, for a period of 1 year from January 2013 to December 2013. Institutional Ethics Committee approval and written informed consent from the patients or legal guardians were taken prior to the commencement of the study. Inclusion Criteria: (a) All drug naive patients attending the Neuropsychiatry OPD, of both sexes who were diagnosed as F 34.1, according to ICD 10 (World Health Organization, 2008). (b) Score  $\geq 14$  points on the Hamilton Depression Rating Scale (1980) on the first screening visit. Exclusion Criteria: (a) Use of psychoactive substances (b) any systemic illness (c) lactating and pregnant women (d) known case of psychiatric illness as described by ICD 10 (World Health Organization, 2008), (e) History of Drug reaction.

**Study Design:** The study was an open label study conducted from January 2013 to December 2013. A total of 117 patients diagnosed with depression were randomly divided in two groups: Group I (58 patients) received tablet Amisulpride 50 mg/day orally and Group II (59 patients) were given tablet Escitalopram 10 mg/day orally. Drug compliance was monitored rigorously, but no drug blood levels were monitored due to lack of any such facility locally. The patients were followed up at 4, 8 and 15 weeks. Adverse drug reactions were monitored at every follow up. Appropriate statistical tools using GraphPad InStat 3.0 were used for analysis. p value  $< 0.05$  was considered significant.

#### RESULTS:

Out of a total of 117 patients which were included in the study, 18 patients dropped out from the study due to varying reasons: 6 patients were lost to follow up, 6 patients decided to withdraw from the study due to adverse drug reactions, 3 patients were lost due to lack of cost effectiveness, 2 patients requested therapy change and 1 patient was uncooperative. Overall, 99 patients completed the study: 48 patients in Amisulpride group and 51 patients in Escitalopram group. The mean age of the patients in the study drug groups was  $46.84 \pm 1.10$  years. The male: female percentage was 41(41.41%) and 58(58.59%). In our study, 31(31.31%) patients were residing in urban areas and 68(68.69%) patients were residing in rural areas. A total of 47(47.47%) patients were illiterate and 52(52.53%) patients were literate. 65(65.66%) patients were farmers, 23(23.23%) patients were employed and 11(11.11%) belonged to others category (table 1&2).

**Table 1: Demographic Profile of study group**  
(All the values are expressed in Mean ± SEM)

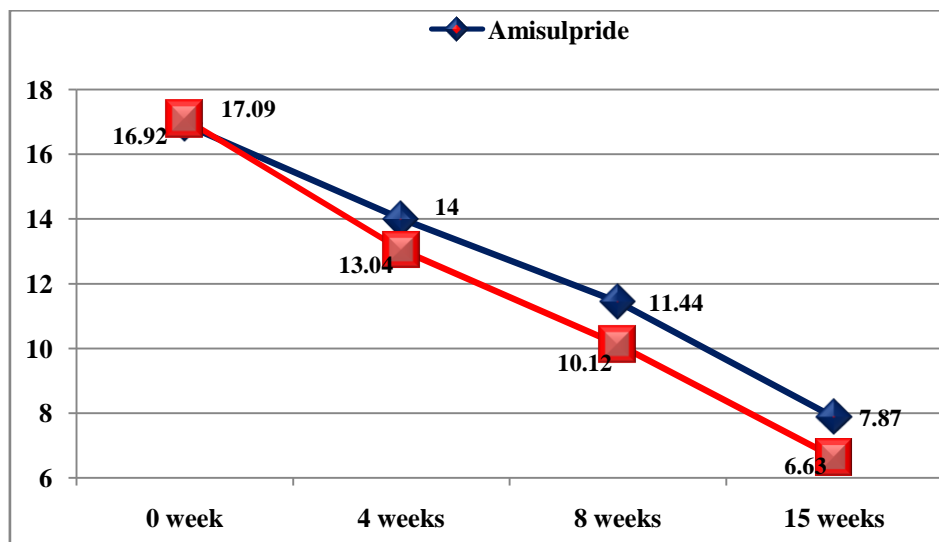
Variables	Total
Age (Mean)	46.84± 1.10
Sex (M:F)	41(41.41%): 58(58.59%)
Urban: Rural	31: 68 (31.31%, 68.69%)
Illiterate: Literate	47:52 (47.47%, 52.53%)
<b>Occupation:</b>	
Farming	65 (65.66%)
Employed	23 (23.23%)
Others	11 (11.11%)

**Table 2: Drop Outs**

Variables	Amisulpride n=58	Escitalopram n=59	Total n=117
Total Drop Outs	10	08	18
<b>Reasons:</b>			
Lost to follow up	03	03	06
Un Cooperative	00	01	01
Adverse drug reaction	03	03	06
Requested therapy change	01	01	02
Lack of cost effectiveness	03	00	03
Total completed study	48	51	99

The efficacy of the drugs was calculated by Hamilton depression rating scale (HAM-D) and improvement in functional outcomes was measured by Sheehan’s Disability Scale(SDS). All values were expressed in Mean ± SEM. At the beginning of the study, the HAM-D Score in Amisulpride group was 16.92±0.35 and in the

Escitalopram group was 17.09±0.39 respectively. There was no significant difference between the two groups at the start of study (p >0.05). Patients were followed up at 4, 8 and 15 weeks. Progressive improvement was seen in both the groups over the study period (figure 1).



**Figure 1: Progressive change of HAM-D score over study period**

At the end of the study, the HAM-D score in Amisulpride group was 7.87±0.29 and in the Escitalopram group was 6.63±0.39 respectively. Intragroup comparison was done between baseline and 15 weeks and highly significant improvement was seen in both groups (p<0.0001). At the end of study period intergroup comparison was made between the two groups which was insignificant (p>0.05) (table 3). At

the beginning of study, the Sheehan’s Disability Scale (SDS) in Amisulpride group was 20.35±0.31 and in Escitalopram group was 21.53±0.55 respectively. Intergroup comparison was insignificant (p>0.05). At the end of study, SDS score in Amisulpride group was 11.08±0.60 and in Escitalopram group was 11.49±0.46 respectively. Intragroup comparison was done between baseline and 15 weeks which was highly significant in

both the groups ( $p < 0.0001$ ). Intergroup comparison at the end of study was insignificant ( $p > 0.05$ ) (table 4). A total of 44 adverse drug reactions (ADRs) were seen during the study period. 25 ADRs were seen in patients in Amisulpride group and 19 ADRs were seen in Escitalopram group. Gastrointestinal disturbances were seen in 5 patients in Amisulpride group and 9 patients in Escitalopram group followed by Delayed orgasm in 5 patients in Amisulpride group and 2 patients in

Escitalopram group, Amenorrhoea in 4 patients in Amisulpride group, dryness of mouth in 03 patients in Amisulpride group and 02 patients in Escitalopram group, erectile dysfunction in 02 patients in Amisulpride group and 01 patient in Escitalopram group, agitation in 02 patients in both groups, giddiness, insomnia and weight gain in 1 patient in each group and lactation in 1 patient in Amisulpride group (table 5).

**Table 3: Efficacy as per HAM-D**

(All the values are expressed in Mean  $\pm$  SEM)

Drug	0 weeks	15 weeks	p- value
Amisulpride	16.92 $\pm$ 0.35	7.87 $\pm$ 0.29	<0.0001
Escitalopram	17.09 $\pm$ 0.39	6.63 $\pm$ 0.39	<0.0001
p- value	> 0.05	>0.05	

**Table 4: Functional outcomes as per SDS**

(All the values are expressed in Mean  $\pm$  SEM)

Drug	0 weeks	15 weeks	p- value
Amisulpride	20.35 $\pm$ 0.31	11.08 $\pm$ 0.60	<0.0001
Escitalopram	21.53 $\pm$ 0.55	11.49 $\pm$ 0.46	<0.0001
p- value	> 0.05	>0.05	

**Table 5: Adverse Drug Reactions**

Variables	Amisulpride ----- n=48	Escitalopram ----- n=51
Total patients with ADR	25(59%)	19(42.2%)
Gastrointestinal disturbances	05	09
Delayed orgasm	05	02
Amenorrhoea	04	00
Dryness of Mouth	03	02
Erectile Dysfunction	02	01
Agitation	02	02
Giddiness	01	01
Insomnia	01	01
Weight gain	01	01
Lactation	01	00

**DISCUSSION:**

Depressive disorders lead to significant dysfunction, disability and poor quality of life in sufferers and pose a significant burden on the caregivers<sup>17, 18</sup>. In the present study there was a higher prevalence of depression in females which was in accordance with previous studies by Sethi et al and Ramachandran et al depicting that women were more commonly suffering from depression<sup>19, 20</sup>. The greater prevalence of depression among women is not fully understood, although potential contributors include different responses to stressful life events, genetic predisposition and hormonal differences<sup>21</sup>. The mean age group in our study was 46.84 $\pm$ 1.10 years which was comparable with previous studies by Dutta et al and Grover et al where incidence of depression was seen predominantly in 30-51 years age group<sup>22, 23</sup>. More depression patients were

seen in rural areas as compared to urban areas in the present study. This was comparable with previous studies by Paritala et al, Giel et al and Gautam et al where rural back ground subjects were found to be somatising more than the urban subjects<sup>24-26</sup>. In our study more number of literates was suffering from depression which was comparable with previous study by Paritala et al and Barsky et al<sup>24, 27</sup>. Farmers were the major sufferers of depression which was in accordance with previous studies by Roberts and Lee<sup>28</sup> which was, based on data from the Epidemiologic Catchment Area (ECA) Program, found ‘farming, fishing and forestry’ to have the highest lifetime risk for major depression. Other studies have also shown increased suicide rates among farmers<sup>29, 30</sup>.

A comparative evaluation of Escitalopram and Amisulpride was done in depression patients by

measuring improvement in functional outcome using Sheehan's Disability Scale in this 15 week study. Escitalopram is an allosteric selective serotonin reuptake inhibitor (SSRI) with some indication of superior efficacy in the treatment of major depressive disorders. The results of our study revealed highly significant improvement in HAM-D in depressive patients over the study period. Intragroup comparison was made between baseline and 15 weeks in Escitalopram group, highly significant improvement was seen ( $p < 0.0001$ ). This was comparable with previous studies where efficacy of escitalopram has been proven<sup>8, 9, 31</sup>. Amisulpride, a selective D2/D3 receptor second generation antipsychotic is indicated for the treatment of acute and chronic schizophrenia<sup>32</sup>. The presumed selectivity of Amisulpride for D2 and D3 dopamine receptors has led to the prevailing hypothesis that modulation of dopaminergic signaling is responsible for its antidepressant efficacy. In the present study the antidepressant effect of Amisulpride was compared at baseline and at 15 weeks in depressive patients, highly significant improvement was observed ( $p < 0.0001$ ). This was comparable with previous studies by Ravizza L et al and Lecrubier Y et al where antidepressant role of Amisulpride has been proven<sup>33-34</sup>. Amisulpride has some selectivity for presynaptic dopamine autoreceptors, and exhibits limbic versus striatal selectivity, particularly at low doses, and it has been suggested that this might account for its therapeutic profile<sup>35</sup>.

The improvement in functional impairment was measured by SDS. In the present study highly significant improvement was seen in both Escitalopram and Amisulpride groups. Previous studies by Cipriani et al. and Wade et al, have also shown favorable outcomes in SDS for Escitalopram<sup>36, 15</sup> and study by Smeraldi et al has shown improvement in SDS by Amisulpride, which is comparable to the present study. Proving that patients who take medications that are efficacious and acceptable have a better chance of achieving superior functional improvements compared to those who take

agents that are less efficacious and/or not as well accepted<sup>35</sup>. At the end of the study period, intergroup comparison was made between Escitalopram group and Amisulpride group which revealed no significant difference ( $p < 0.05$ ), indicating both the drug were equally efficacious in improving depression and in improving functional outcome.

Safety analysis was done for both the groups and adverse drug reactions were assessed at each follow up. Gastrointestinal disturbances were seen most commonly with both the groups and have been proven in earlier studies<sup>37, 38</sup>. Endocrinological effects like Amenorrhoea and lactation were seen in Amisulpride group and have been seen in previous studies<sup>39</sup>. Other side effects like insomnia, agitation and dryness of mouth were seen similarly in both groups and were comparable with previous studies<sup>40, 41</sup>.

**Study Limitations:** The study was an open label study. Both doctors and patients were aware of the treatments. Hence there could be chances of bias. Sample size was small and the patients were followed up for only 15 weeks.

### CONCLUSION:

Both Escitalopram and Amisulpride were highly effective in improving functional outcome in depression patients. But intergroup comparison revealed no significant difference between the two groups. A double blind study with larger sample size and longer duration of follow up can substantiate the findings of the present study.

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