Research Article

Comparative evaluation of amisulpride and escitalopram on Hamilton Depression Rating Scale among depression patients in a tertiary care teaching hospital in Nepal

Vijay Kaul[1], Shaktibala Dutta[2], Mirza Atif Beg[2], Nand Kishore Singh[3], Shalu Bawa[2], Mohammad Anjoom[2], Srihari Dutta[4]

[1]Department of Psychiatry, Nepalganj Medical College, Nepalganj, Nepal.
[2]Department of Pharmacology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
[3]Department of Psychiatry, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
[4]Immunization Health Specialist, Unicef, New Delhi, India Country office, India.
Correspondence to: Mirza Atif Beg, E-mail: mabeg1997@gmail.com

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Abstract

Background: Depression is a considerable global public health problem and is a major cause of disability and premature death. It results in poor quality of life in patients and caregivers.

Objective: The present study was conducted to compare efficacy and safety of amisulpride and escitalopram, using Hamilton Depression Rating Scale (HAM-D) among depression patients in a tertiary care teaching hospital in Nepal.

Material and Methods: This study was conducted in the Department of Neuropsychiatry, Nepalganj Medical College, a tertiary care teaching hospital in Nepal, for a period of 1 year. A total of 117 depression patients were randomly selected and divided into two groups. Group I (58 patients) received amisulpride 50 mg/day orally and Group II (59 patients) were given escitalopram 10 mg/day orally. The patients were followed up at 4, 8, and 15 weeks. The efficacy of the drugs was calculated by HAM-D. Adverse drug reactions were monitored at every follow-up. GraphPad Instat, version 3.0, tool was used for statistical analysis and p-value <0.05 was considered significant.

Results: HAM-D score in the 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 ($p < 0.0001$). Intergroup comparison at 15 weeks was more significant for escitalopram ($p < 0.05$). Gastrointestinal disturbances, sexual disturbances, amenorrhoea lactation, agitation and insomnia were the commonly encountered adverse drug reactions.

Conclusion: The present study showed both amisulpride and escitalopram were highly effective in improving the HAM-D score and in the treatment of depression. But intergroup comparison showed greater reduction in HAM-D score in patients receiving escitalopram.

KEY WORDS: Depression, amisulpride, escitalopram, Hamilton Depression Rating Scale (HAM-D)

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Introduction

Depression is a considerable global public health problem and is a major cause of disability and premature death.[1] It can be defined as a mental state, which is characterized by feelings of sadness, loneliness, despair, low self-esteem, and self-reproach.[2] The report on Global Burden of Disease estimates the point prevalence of unipolar

depressive episodes to be 1.9% for men and 3.2% for women, and the 1-year prevalence has been estimated to be 5.8% for men and 9.5% for women. It is estimated that by the year 2020, if current trends for demographic and epidemiological transition continue, the burden of depression will increase to 5.7% of the total burden of disease and it would be the second leading cause of disability-adjusted life years (DALYs), second only to ischemic heart disease.[3] Antidepressant medications remain the mainstay of treatment for major depressive disorders especially for those with moderate to severe depression. Newer antidepressants including selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitors (SNRIs), and novel mechanism agents offer fewer side effects and are safer in overdose compared with tricyclic antidepressants and monoamine oxidase inhibitors. Hence, most clinical guidelines consider the newer generation antidepressants to be first-line medications for depression.[4–6] Escitalopram, the S-enantiomer of racemic citalopram, is an SSRI that has an additional modulatory effect at an allosteric binding site on the serotonin transporter protein.[7] Escitalopram has been demonstrated in many placebo controlled, randomized, trials to be an efficacious antidepressant for major depressive disorders.[8,9] 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.[10] Amisulpride is indicated for the treatment of acute and chronic schizophrenia with prominent positive and/or negative symptoms. Its effectiveness in the improvement of both the positive and negative symptoms is related to a dose-dependent blockade of dopamine receptors.[10,11] 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 humans in clinical studies in patients with dysthymia and/or major depression.[12] 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. Based on the above observations, the present study was done to compare efficacy and safety of amisulpride and escitalopram on Hamilton Depression Rating Scale (HAM-D) among depression patients in a tertiary care teaching hospital in Nepal.

Material and Methods

This study was conducted by the Department of Neuropsychiatry, Nepalganj Medical College, a tertiary care teaching hospital in Nepal, for a period of 1 year from January 2013 to December 2013. Inclusion criteria were: (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) who scored ≥14 points on the (HAM-D) (1980) on the first screening visit. Exclusion criteria were: (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), and (e) history of drug reaction. Prior to study approval from the institutional ethics committee, written informed consent from each patient/legal guardian of patients was obtained after the full explanation of study protocol.

Study Design

The study was an open-label study done 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 required to follow up at 4, 8, and 15 weeks. Adverse drug reactions (ADRs) were monitored at every follow-up. Statistical analysis was done by using (analysis of variance test) GraphPad Instat, version 3.0, tool, and p-value < 0.05 was considered significant.

Results

Out of 117 patients who were included in the study, 18 patients dropped out from the study due to varying reasons: six patients were lost because they were not followed up, six patients were lost due to ADRs, three patients were lost due to lack of cost effectiveness, two patients requested therapy change, and one 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 ± 1.10 years. The male/female %age was 41 (41.41%) and 58 (58.59%). According to the residence, 31 (31.31%) patients were residing in urban areas and 68 (68.69%) patients were residing in rural areas. 47 (47.47%) patients were illiterate and 52 (52.53%) patients were literate. According to occupation,

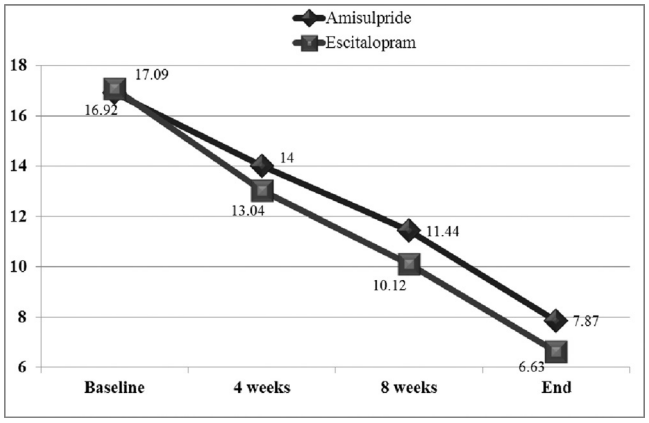

Figure 1: Progressive change of HAM-D score over study period.

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%)
Residence (Urban/Rural)	31:68 (31.31%, 68.69%)
Education	
Illiterate	47 (47.47%)
Literate	52 (52.53%)
Occupation	
Farming	65 (65.66%)
Employed	23 (23.23%)
Others	11 (11.11%)

Table 2: Dropouts

Variables	Amisulpride, *n* = 58	Escitalopram, *n* = 59	Total, *n* = 99
Total dropouts	10	08	18
Reasons			
Lost to follow up	03	03	06
Uncooperative	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

65 (65.66%) patients were farmers, 23 (23.23%) patients were employed and 11 (11.11%) belonged to others category [Tables 1 and 2].

The efficacy of the drugs was calculated by HAM-D. All values were expressed in mean ± SEM. At the beginning of the study, the score in amisulpride group according to HAM-D was 16.92 ± 0.35 and in the escitalopram group, was 17.09 ± 0.39. 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]. 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. 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 significant ($p < 0.05$) [Table 3]. A total of 44 ADRs were seen during the study period. Twenty-five ADRs were seen in patients in amisulpride group and 19 ADRs were seen in escitalopram group. Gastrointestinal disturbances were seen in five patients

Table 3: Efficacy as per HAM-D (all the values are expressed in mean ± SEM)

Drug	At beginning	At the end	*p*-value
Amisulpride	16.92 ± 0.35	7.87 ± 0.29	<0.0001
Escitalopram	17.09 ± 0.39	6.63 ± 0.39	<0.0001
p-value	>0.05	<0.05	

Table 4: 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
Amenorrhea	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

in amisulpride group and nine patients in escitalopram group followed by delayed orgasm in five patients in amisulpride group and two patients in escitalopram group, Amenorrhoea in four patients in amisulpride group, dryness of mouth in three patients in amisulpride group and two patients in escitalopram group, erectile dysfunction in two patients in amisulpride group and one patient in escitalopram group, agitation in two patients in both groups, giddiness, insomnia, and weight gain in one patient in each group and lactation in one patient in amisulpride group [Table 4].

Discussion

Depressive disorders lead to significant dysfunction, disability, and poor quality of life in sufferers and pose a significant burden on the caregivers.[13,14] In the present study, there was a higher prevalence of depression in females which was in accordance with previous studies by Sethi and Prakash[15] and Ramachandran et al.[16] depicting that women were more commonly suffering from depression. 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.[17] The mean age group in our study was 46.84 ± 1.1 year which was comparable with previous studies, by Dutta et al.[18] and Grover et al.,[19] in which incidence of depression was seen in 30–51 years age group. 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.,[20] Geil and Harding,[21] and Gautam and Kapur,[22] in which rural back ground subjects were found to be somatising more than

the urban subjects. In this study, more number of literates were suffering from depression, which was comparable with previous study by Paritala et al.[20] and Barsky.[23] In present study majority of the patients were farmers, which was in accordance with previous studies by Roberts and Lee,[24] 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 shown increased suicide rates among farmers.[25,26]

A comparative evaluation of escitalopram and amisulpride was done in depression patients using HAM-D in this 15 week study. Escitalopram is an allosteric 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 and highly significant improvement was seen ($p < 0.0001$), this was comparable with previous studies in which efficacy of escitalopram has been proved.[8,9,27] Amisulpride, a selective D2/D3 dopamine receptor antagonist, is indicated for the treatment of acute and chronic schizophrenia.[28] In addition to antipsychotic effects, preliminary reports suggest that amisulpride may have antidepressant effects. 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 and highly significant improvement was seen ($p < 0.0001$). This was comparable with previous studies by Lecrubier,[29] Boyer et al.,[30] Ravizza,[31] and Smeraldi[32] in which antidepressant role of amisulpride has been proved.

The unique therapeutic profile of amisulpride has proved difficult to explain in light of its known pharmacological profile. There is some evidence that amisulpride has some selectivity for presynaptic dopamine auto-receptors and it exhibits limbic versus striatal selectivity, particularly at low doses, which suggests that this might account for its therapeutic profile.[33]

At the end of the study period, intergroup comparison was made between escitalopram group and amisulpride group, which revealed significant difference ($p < 0.05$) suggesting more improvement in patients in escitalopram group. Because escitalopram is an established drug for treatment of depression, many pooled analyses and meta-analyses by Kennedy et al.[34] and Kasper et al.[35] have found superior efficacy of escitalopram as compared to other antidepressents.

Safety analysis was done for both the groups and ADRs were assessed at each follow-up. Gastrointestinal disturbances were seen most commonly with both the groups and had been proved in earlier studies.[36,37] Endocrinological effects like Amenorrhoea and lactation were seen in amisulpride group and had been seen in previous studies.[38] Other side effects like insomnia, agitation, and dryness of mouth were seen similarly in both groups and were comparable with previous study.[39]

Study Limitations

The study was an open-label study. Both doctors and patients were aware of the treatments. Hence, there could be chances of biasing. Also the patients were followed up to only 15 weeks. A longer duration of follow-up could have yielded different results.

Conclusion

Both escitalopram and amisulpride were highly effective in the treatment of depression patients during the study period. But intergroup comparison showed greater reduction in HAM-D score in patients receiving escitalopram. Furthermore, more clinical studies with longer follow-up duration are needed to substantiate the antidepressant effects of amisulpride.

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