



Effect of Baseline Severity on Antidepressant Efficacy of Escitalopram and Milnacipran at Tertiary Health Care Center

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Abstract

Background: The intent of this prospective, open labelled study was to determine the relationship between baseline depression symptom severity and treatment efficacy for Escitalopram selective serotonin reuptake inhibitors (SSRI) in comparison with Milnacipran, dual serotonin noradrenaline reuptake inhibitors (SNRI) in the treatment of major depressive disorder.

Methods: Outpatients (N=120) of Psychiatry with diagnosed ICD-10 major depressive episode and having score of ≥ 8 on 21-item Hamilton Depression Rating Scale (HDRS) were further divided according to their severity of depression as defined by 21-HDRS score of ≥ 23 as very severely depressed, 19-22 as severely depressed, 14-18 as moderately depressed and 8-13 as mildly depressed patients. These patients were assigned to receive escitalopram, 10–20 mg/day (54 patients) and milnacipran 50-100 mg (66 patients), for a 8 week treatment period with follow up at 2nd, 4th & 8th week of initiating the treatment. The patients with various grades of depression in each group were assessed and compared for efficacy in terms of response (decrease of $\geq 50\%$ in HDRS scores) and remission (HDRS score of ≤ 7).

Results: Escitalopram achieved highest response and remission among very severely depressed patients i.e. 94.18% and 76.40% respectively whereas Milnacipran showed maximum response and remission among patients with severe depression i.e. 85.7% and 50% respectively. Escitalopram showed comparable response in mild to moderate grades and greater response in severe grades of depression whereas remission was significantly higher with Escitalopram in all grades of depressed patients relative to Milnacipran.

Conclusion: Escitalopram is more efficacious than Milnacipran in all grades of depression.

Keywords- Escitalopram, Milnacipran, SSRI, SNRI, HDRS.

Introduction

Depression is a common, chronic and debilitating psychiatric disorder which encompasses a plethora of symptoms. The cause of depression is a

combination of disturbed brain chemistry, genetics and psychosocial environment. Depression affects about 7%-18% of the population at least once in their lives, before the age of 40.¹ In India, depression is the most widely prevalent psychiatric

disorder with a prevalence rate of 31.2 per 1000 individuals.²It also imposes a great economic burden on the society due to decreased productivity while at work called Presenteeism and depression related absenteeism. The worst consequence of unrecognized depression is that it is associated with suicide risk of approximately 15%.³

Various scales have classified depression into mild, moderate and severe types according to symptom severity and patient disability.

Patients with severe depression, mostly characterized by a high intensity and frequency of depressive symptoms, suffer from greater functional impairment, somatic complaints and risk for suicide and relapse compared to individuals with mild or moderate severity depression.^{4,5} Because of these reasons, patients with severe depression deserve prompt treatment.

Many studies have explored the relationship of antidepressant efficacy with baseline severity as assessed by various scales of depression but neither study has compared the efficacy of Escitalopram, a Selective serotonin reuptake inhibitor with Milnacipran, a dual reuptake inhibitor of noradrenaline and serotonin, in patients with various grades of depression. So the above study was planned.

Methods

This prospective, open labelled study included those outpatients between the ages of 18 and 60 years, who fulfilled ICD-10 criteria for a current episode of MDD with a baseline score of 8 on the 21-item Hamilton Depression Rating Scale (HDRS) and who agreed to give their written informed consent to participate in the study. Our study of 8 weeks duration was approved by institutional Ethics Committee. The patients who had other serious medical or psychiatric illnesses, bipolar depression, receiving any psychiatric medication, pregnant or breast feeding were excluded from the study. The patients fulfilling the inclusion criteria were randomly assigned to treatment with Escitalopram 10-20 mg (group A) and Milnacipran 50-100 mg (group B).The patients in each group were further

divided on the basis of severity of depression as defined by Hamilton Depression Rating Scale (HDRS). HDRS scores of ≥ 23 were defined as *very severely depressed*, 19-22 as *severely depressed*, 14-18 as *moderately depressed* and 8-13 as mildly depressed patients. Patients with various grades of depression in each group were assessed and compared for efficacy in terms of *Response*, defined by a decrease of $\geq 50\%$ in the HDRS Scores & *Remission*, as HDRS score of ≤ 7 . Follow up & Assessment was done at an interval of 2, 4 & 8 weeks of initiating the treatment. Statistical analysis was performed by using software Epicalc 2000 ec2v102. The response & remission in the two Groups were compared by Chi-square test. All means were expressed as mean \pm Standard deviation. The critical level of significance of the results were considered at 0.05 i.e. $P < 0.05$ was considered significant.

Result

A total of 120 patients were enrolled for the study, out of which 54 patients were assigned to receive Escitalopram 10-20 mg (Group A) and 66 patients for Milnacipran 50-100 mg (Group B). After a total drop out of 31 patients in both the groups, 48 patients from Group A and 41 patients from Group B completed the study

The mean age of patients of depression in our study was 33.27 with a female predominance of 64%. The maximum number of patients i.e. 29 (32.60%) had very severe depression, 28 patients (31.45%) had severe depression, 21 patients (23.70%) had moderate depression and 12.35% (11 patients) had mild depression. The patients were further divided in both the groups according to severity of depression (Table 1).

Efficacy

1. Response- (Table- 2)

The highest response rate of Escitalopram was seen among very severely depressed patients (94.18%) whereas maximum response of Milnacipran was seen among patients with severe depression (85.7%). The difference in response rate among patients with

various grades of depression in the two groups was comparable.

2. Remission-(Table-3)

So like response, remission in Escitalopram group was also highest among cases who were very severely depressed i.e. 76.40% whereas in Milnacipran group, maximum number of remission i.e. 50% were seen in patients who were severely depressed. The difference in remission rate among patients with various grades of depression in the two groups was comparable.

3. Comparison of efficacy of Escitalopram and Milnacipran in patients with various grades of depression (Table-4)

The response rate was comparable in Escitalopram and Milnacipran group in patients with mild-moderate grades of depression whereas it was significantly higher in Escitalopram group as compared to Milnacipran in patients with severe to very severe depression.

The remission rate in Escitalopram group was found to be significantly greater in patients with mild to moderate as well as severe to very severe grades of depression as compared to Milnacipran.

Table No.1

Severity	Group A	Group B
Very Severe	17	12
Severe	14	14
Moderate	11	10
Mild	6	5

Table No. 2

Severity	Group A			Group B		
	No. of patients	Response		No. of patients	Response	
		No. of patients	Percent (%)		No. of patients	Percent (%)
Very Severe	17	16	94.2%	12	10	83.3%
Severe	14	13	92.8%	14	12	85.7%
Moderate	11	9	81.8%	10	8	80%
Mild	6	2	33.2%	5	1	20%

Table 3

Severity	Group A			Group B		
	No. of patients	Remission		No. of patients	Remission	
		No. of patients	Percent (%)		No. of patients	Percent (%)
Very Severe	17	13	76.4%	12	5	41.6%
Severe	14	8	57.1%	14	7	50%
Moderate	11	5	45.5%	10	1	10%
Mild	6	2	33.3%	5	1	20%

Table No.4

	Mild-moderate		Severe-very severe	
	Escitalopram (Group A)	Milnacipran (Group B)	Escitalopram (Group A)	Milnacipran (Group B)
Response	64.7 %	60.0 %	93.5 %	84.6 %
Remission	41.2 %	13.3 %	67.7 %	46.1 %

Discussion

This study was conducted with the aim of elucidating and comparing the efficacy of Escitalopram and Milnacipran in the treatment of patients with various grades of depression. 21 item Hamilton Depression Rating Scale (HDRS) was selected for gauging efficacy in terms of response and remission. The highest response and remission rates in Escitalopram group were seen among very severely depressed patients suggesting greater efficacy of Escitalopram in more severe forms of depression. This finding is consistent with earlier study done by Llorca et al in which they noticed greater superiority of Escitalopram in group of patients with greater severity of depression⁶ Other comparative studies have also confirmed linear relationship of efficacy of Escitalopram with baseline severity of depression.⁷ Similarly, Milnacipran has also shown greater response and remission in patients with severe depression in our study. This finding is supported by earlier studies on Milnacipran in which it has shown higher responders and remitters in a subset of severely ill depressed patients.⁸ So, both the antidepressants under study has shown maximum efficacy in severe to very severe grades of depression. It has been proved in previous studies that the magnitude of benefit of antidepressants is directly proportional to severity of depression symptoms.⁹ In our study we also compared the efficacy (in terms of response and remission) of Escitalopram and Milnacipran in patients with mild to moderate and severe to very severe depression in both the groups as defined by HDRS scale. The severely ill group showed significantly higher response rate with Escitalopram than Milnacipran while the response was comparable with both the drugs in mild to moderately depressed patients. The superiority of Escitalopram over citalopram has been reported in severely ill depressed patients¹⁰

but has not been compared with SNRIs to the best of author's knowledge. In our study, Escitalopram was found to be superior to Milnacipran in achieving remission in patients of all grades of depression. Previous studies comparing Escitalopram with other SSRIs have reported similar results¹¹. Studies comparing Milnacipran with SSRIs fluoxetine, fluvoxamine in moderately to severely depressed patients,⁸ reported significantly more responders with milnacipran than with the two SSRIs and a significantly higher remission rate. Another study, compared milnacipran with paroxetine in mildly depressed outpatients, and reported similar remission rates for the two antidepressants.¹² These findings are not consistent with the results of our study. The probable reason behind this disparity could be because Milnacipran has been compared with SSRIs other than Escitalopram. Moreover, the antidepressant efficacy and tolerability of Escitalopram have been shown to be comparable or superior to selective serotonin reuptake inhibitors fluoxetine, fluvoxamine,⁸ paroxetine,¹² and serotonin-norepinephrine reuptake inhibitor, venlafaxine.¹³

Finally, based on the findings in our study, it can be concluded that the efficacy of Escitalopram increases as the baseline severity of depression increases in relation to Milnacipran.

Escitalopram clearly emerges as a promising treatment option in patients with mild, moderate and severe grades of depression.

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