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Efficacy and tolerability of escitalopram and duloxetine in patients suffering from depression

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ABSTRACT

Introduction: Depression is a leading cause of disability worldwide, with significant treatment gaps in low-resource settings like Nepal. Escitalopram, a selective serotonin reuptake inhibitor (SSRI), and duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), are widely used antidepressants, but their comparative efficacy and tolerability in diverse populations remain understudied.

Objectives: This study aimed to compare the efficacy and tolerability of escitalopram and duloxetine in patients with moderate-to-severe major depressive disorder (MDD).

Methodology: A prospective, comparative study was conducted among 200 patients taking escitalopram (10–20 mg/day) or duloxetine (60 mg/day) at Nobel Medical College, Biratnagar. A convenience sampling technique was used to select the sample. Data collection was done from February 17, 2023, to February 16, 2024, after getting ethical approval from the Institutional Review Committee (IRC). Efficacy was assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS), while tolerability was evaluated through adverse event reporting and dropout rates.

Results: Duloxetine showed superior efficacy, with greater MADRS reduction (15.8 ± 2.9 vs. 14.2 ± 3.1; p value <0.05) and higher response (78% vs. 65%) and remission rates (55% vs. 42%). Escitalopram was better tolerated, with fewer adverse events (e.g., nausea: 12% vs. 34%) and lower dropout rates (6% vs. 16%).

Conclusion: Duloxetine is more effective for severe depression, while escitalopram offers better tolerability, making it suitable for elderly patients and those with comorbid conditions. These findings can guide treatment decisions in resource-limited settings.

Keywords: Depressive disorder; Duloxetine; Escitalopram

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INTRODUCTION

Depression remains one of the most common reasons people experience mental health challenges worldwide.[1] It is estimated that 300 million people are affected worldwide.[2] National Mental Health Survey of Nepal, in 2020, reported depression prevalence at 0.6% among adolescents and 1% in adults, with a lifetime prevalence of 2.9%.[3]

Management of depression is complex, as treatment response varies. Selective serotonin reuptake inhibitor, remain the first line of choice.[4] A double-blinded comparison of duloxetine and escitalopram has shown them to be equally effective over an 8-week.[5] fewer escitalopram-treated patients discontinued treatment due to adverse events.[5] An eight-week, trial demonstrated that duloxetine was not inferior to escitalopram.[7] Patients taking duloxetine experienced a higher rate of adverse effects, but the overall rate of discontinuation due to side effects was similar.[7] A comparative study showed that

Escitalopram was superior to duloxetine during acute treatment.[8] In a 6-week randomized trial, escitalopram was as effective as duloxetine for mild–to–moderate major depressive disorder and was better tolerated.[9]

Despite guidelines for 6–9 months of continuation therapy post-remission,[10] long-term outcomes data remain limited, particularly in Lower Middle-Income Countries where treatment discontinuation rate is high.[11] This study compares efficacy and tolerability of escitalopram and duloxetine at 8 weeks and 24 weeks of therapy.

METHODOLOGY

This prospective, comparative study was conducted at the Department of Psychiatry, Nobel Medical College and Teaching Hospital, Biratnagar, from February 17, 2023, to February 16, 2024. Ethical approval was obtained from the Institutional Review Committee (IRC) on January 5, 2023 (Reference No. 729/2023).

Adults aged 18–65 years diagnosed with moderate-to-severe major depressive disorder (MDD) were recruited from the outpatient department (OPD). Diagnosis was confirmed using the MADRS with a baseline score ≥22.[8,9] To ensure robustness, 200 participants were enrolled via convenience sampling.

Sample size calculation was based on a comparative efficacy study of antidepressants in MDD. The following assumptions were used:

Expected mean difference in MADRS score reduction between escitalopram and duloxetine group was considered. Effect Size is based on a prior study reporting a 60% response rate (defined as ≥50% reduction in MADRS scores) with antidepressants in MDD.[9] Statistical Parameters are Power (1-β): 80%. Significance level (α): 0.05 (two-tailed). Expected attrition rate: 15% (to account for dropouts). Using these inputs, the minimum required sample size was calculated as 85 participants per group (total N = 170). To enhance robustness and accommodate potential variability in response rates, we enrolled 200 participants (100 per group). Patients with comorbid psychiatric disorders (e.g., bipolar disorder, psychosis), severe medical illness (e.g., uncontrolled diabetes, cardiovascular disease), Pregnancy, lactation, hypersensitivity to study drugs and substance use disorder (past 6 months) were excluded from the study.

Participants were assigned to two groups: escitalopram 10–20 mg/day and duloxetine 30-60 mg/day. Semi-structured socio-demography form and adverse event checklist were used for tolerability assessment, and Case report forms were used for clinical data. Efficacy was assessed using MADRS score reduction at 24 weeks. Tolerability was evaluated by assessing adverse event reporting, documented at each visit (e.g., nausea, insomnia), and dropout Rates due to intolerable side effects. These tools were administered by psychiatrists themselves. Data analysis was performed using IBM SPSS Statistics for Windows, version 17 (IBM Corp., Armonk, NY, USA). An independent t-test was used to compare the mean score, a chi-square test was used for treatment response, and tolerability was assessed by regression analysis of adverse events.

RESULTS

The study included 200 patients diagnosed with MDD at Nobel Medical College Teaching Hospital, Nepal. Almost half of them, 90 (45%), were from the age group 41–50 years, with a male predominance of 115 (57.5%). Most of the participants, 192 (96%), were married, 175 (87.5%) lived in nuclear families, and 150 (75%) had completed grade 10 education. Socioeconomic status was predominantly lower-middle class, 100 (50%).

There was a significant reduction in MADRS score at 24 weeks of treatment in both groups; however, when comparing the scores between the two groups, the reduction was significantly higher in the duloxetine group (p-value <0.05). The mean reduction was higher in major depressive disorder group (Table 1).

Similarly, there was a significant reduction in HAM-D17 scores at 8 weeks of treatment in both groups. However, when comparing the scores between the two groups, the reduction was significantly higher in the duloxetine group (p-value) The mean reduction was higher in the severe MDD subgroup (Table 2).

Males are three times more likely to smoke and consume alcohol in comparison to females. The analysis of treatment outcomes based on smoking and alcohol consumption showed significant differences in efficacy, measured by response rates (≥50% reduction in MADRS scores). Non-smokers showed a higher response rate of 120 (72.7%) compared to smokers at 20 (57.1%), indicating that smoking may negatively impact treatment efficacy. Similarly, non-alcohol consumers had a higher response rate of 130 (72.2%) compared with alcohol consumers at 10 (50%), suggesting that alcohol consumption is also associated with reduced treatment effectiveness (Table 3).

Duloxetine demonstrated superior efficacy, with significantly higher response (78% vs. 65%) and remission rates (55% vs. 42%) compared to escitalopram (p-value <0.05, Table 4).

The analysis of tolerability, measured by dropout rates due to adverse events, shows that both smoking and alcohol consumption are associated with poorer treatment adherence. Smokers had a higher dropout rate of 8 (22.9%) compared to non-smokers at 20 (12.1%), indicating that smoking may increase the likelihood of discontinuing treatment due to adverse effects. Similarly, alcohol consumers had a significantly higher dropout rate of 6 (30%) compared to non-alcohol consumers at 22 (12.2%) , suggesting that alcohol use also negatively impacts treatment tolerability (Table 5).

Discontinuation due to adverse effects was significantly higher among the duloxetine group (16%) than the escitalopram group (6%), p-value <0.05. Escitalopram was better tolerated, with considerably lower rates of nausea (12% vs. 34%) and dry mouth (8% vs. 22%, Table 5). Also, Elderly Patients (≥60 years) receiving escitalopram had fewer adverse effects (14% vs. 28% , p-value <0.05, Table 6).

Table 1: Comparison of efficacy of two drugs 24 weeks after treatment

Outcome	Escitalopram group	Duloxetine group	p-value (between group comparison)
Mean reduction of MADRS in Severe MDD	16.1 ± 3.0	18.5 ± 2.4	0.01†
Overall mean reduction in MADRS score	14.2 ± 3.1	15.8 ± 2.9	0.02†
p-value	<0.001*	<0.001*	

p-value significant at <0.05=* paired t - test, † Independent t – test

Table 2: Comparison of efficacy of two drugs 8 weeks after treatment (HAM-D17)

Outcome	Escitalopram group	Duloxetine group	p-value (between group comparison)
Mean reduction of HAM-D17 in Severe MDD	13.2 ± 2.8	15.4 ± 2.3	0.01†
Overall mean reduction in HAM-D17 score	11.8 ± 3.0	13.3 ± 2.7	0.03†
p-value	<0.001*	<0.001*	

p-value significant at <0.05=* paired t-test, † Independent t-test

Table 3: Smoking and Alcohol Consumption among respondents and efficacy of drug.

Category	Smoking n (%)	Non-Smoking n (%)	Alcoholic n (%)	Non-Alcoholic n (%)
Sex				
Male	29 (25)	86 (75)	17(15)	98 (85)
Female	9(10)	76(90)	4 (5)	81 (95)
Response rate				
(≥50% Reduction) in MADRS	20 (57.1)	120 (72.7)	10 (50)	130 (72.2)
No response	15 (42.9)	45(27.3)	10 (50)	50 (27.8)

Table 4: Treatment response and remission rates among both groups

Outcome	Escitalopram (%)	Duloxetine(%)	p-value
Response rate (≥50% reduction	65	78	0.03‡
Remission rate (MADRS ≤10)	42	55	0.04‡

p-value significant at <0.05= ‡Chi-Square test

Table 5: Smoking, Alcohol Consumption and tolerability of drugs

Category	Dropout Rate (Due to Adverse Effects) n (%)	No Dropout n (%)
Smoking	8 (22.9)	27 (77.1)
Non-Smoking	20 (12.1)	145 (87.9)
Alcoholic	6 (30)	14 (70)
Non-Alcoholic	22 (12.2)	158 (87.8)

Table 6: Tolerability Outcomes in terms of adverse events of drug and dropout

Adverse Effect	Escitalopram (%)	Duloxetine (%)	p-value
Nausea	12%	34%	0.001*
Dry Mouth	8%	22%	0.005*
Insomnia	18%	16%	0.65
Dizziness	10%	18%	0.08
Dropout rates	6%	16%	0.01

DISCUSSION

This study compared the efficacy and tolerability of escitalopram and duloxetine in patients with moderate-to-severe major depressive disorder (MDD) over a 24-week period. The findings highlight important differences between the two antidepressants, providing valuable insights for clinical practice, particularly in resource-limited settings like Nepal.

Duloxetine demonstrated superior efficacy, with a significantly greater reduction in Montgomery-Åsberg Depression Rating Scale (MADRS) scores (15.8 ± 2.9 vs. 14.2 ± 3.1, p-value = 0.02) and higher response (78% vs. 65%) and remission rates (55% vs. 42%) compared to escitalopram. Additionally, at 8 weeks, duloxetine showed a significantly greater reduction in Hamilton Depression Rating Scale-17 (HAM-D17) scores (13.3 ± 2.7 vs. 11.8 ± 3.0, p-value = 0.03), with a more pronounced effect in patients with severe MDD (15.4 ± 2.3 vs. 13.2 ± 2.8, p-value = 0.01). These results align with previous studies suggesting that serotonin-norepinephrine reuptake inhibitors (SNRIs) like duloxetine may offer enhanced efficacy in severe depression due to their dual mechanism of action[2,3]. The greater reduction in both MADRS and HAM-D17 scores in the duloxetine group, particularly in severe cases, likely reflects its noradrenergic effects, which address both emotional and physical symptoms of depression[2].

However, escitalopram, a selective serotonin reuptake inhibitor (SSRI), also showed significant efficacy, with substantial reductions in both MADRS (14.2 ± 3.1, p-value < 0.001) and HAM-D17 scores (11.8 ± 3.0, p-value < 0.001), consistent with its established role as a first-line treatment for MDD[4]. Its allosteric binding properties enhance serotonin reuptake inhibition, making it effective for a broad range of patients[3]. While duloxetine was more effective in severe cases, escitalopram remains a viable option for moderate depression, especially in settings where cost and tolerability are critical considerations.

Escitalopram was better tolerated, with significantly lower rates of nausea (12% vs. 34%) and dry mouth (8% vs. 22%) compared to duloxetine. These findings are consistent with the result of a study done in 2007, which reported that escitalopram's favorable side-effect profile makes it a preferred choice for patients prone to adverse events[3]. The higher dropout rate in the duloxetine group (16% vs. 6%) further underscores its tolerability challenges, particularly in populations with comorbid medical conditions or elderly patients, where side effects like nausea and dizziness can be particularly burdensome[5]. In patients with severe MDD (MADRS ≥30), duloxetine showed a larger reduction in both MADRS (18.5 ± 2.4 vs. 16.1 ± 3.0; p = 0.01) and HAM-D17 scores (15.4 ± 2.3 vs. 13.2 ± 2.8; p = 0.01), reinforcing its utility in treatment-resistant or severe cases. Conversely, escitalopram was better tolerated in elderly patients (≥60 years), with fewer adverse events (14% vs. 28%; p = 0.02). This aligns with guidelines recommending SSRIs like escitalopram for older adults due to their lower risk of drug interactions and side effects.[4,5]

This study has several limitations. First, the use of convenience sampling may limit the generalizability of the findings. Second, the open-label design could introduce bias, although efforts were made to standardize assessments. Third, the 24-week follow-up period may not capture long-term outcomes, such as relapse rates or delayed side effects. Future studies should address these limitations by employing randomized, double-blind designs with longer follow-up periods.

CONCLUSION

This study highlights the efficacy of duloxetine in severe depression and the tolerability of escitalopram, particularly in elderly patients and those with comorbid conditions. In resource-limited settings like Nepal, where mental health resources are scarce, these findings can guide clinicians in tailoring treatment to individual patient needs. Duloxetine should be considered for severe or treatment-resistant cases, while escitalopram

remains a first-line option for moderate depression and vulnerable populations. Future research should explore long-term outcomes and cost-effectiveness to inform clinical practice and policy further.

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