

**Original Article****Comparative Analysis between Controlled Release Paroxetine and Extended-Release Venlafaxine for Treatment of Depression**

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Depression is a common condition seen in Psychiatry outpatient department. The treatment data suggest that the drugs that modulate the serotonergic neurotransmission are effective in the treatment of depression. Serotonin and nor Epinephrine re uptake inhibitors are also being used to treat depression. This study is aimed at comparing the results of a selective serotonin re-Uptake inhibitor (Paroxetine) to that of both Serotonin and Nor-Adrenaline re-Uptake inhibitor (Venlafaxine). Comparative analysis between the effects of Controlled release Paroxetine and extended-release Venlafaxine for treatment of depression in eastern Nepal.

**Materials and Methods**

It is a prospective, open and randomized comparison. One Hundred consecutive patients who attended the Psychiatry outpatient door of Nobel Medical College and Teaching Hospital and diagnosed as depression were enrolled for this study after being divided into 2 groups: Group 1 also being named as Paroxetine group while Group 2 as Venlafaxine group. The 100 patients were enrolled after being followed all the required protocols including Montgomery Asberg rating Scale readings and data were recorded on Day 0, Week 1, 2,3,4,6,8.


**Results**

According to the analysis of the Montgomery Asberg rating Scale scores at baseline and after completion of study at 8 weeks, both Paroxetine Controlled Release and Venlafaxine Extended-release treated patients improved similarly. But, many of the Venlafaxine-treated patients had nausea and constipation ( $p < 0.05$ ).

**Conclusion**

Paroxetine controlled released is better tolerated by patient though, the efficacy of both the drugs (paroxetine and venlafaxine) are similar for the treatment of Depression.

**Keywords:** Depression, Paroxetine, Venlafaxine

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## Introduction

According to the International classification of diseases 10<sup>th</sup> edition, it is a serious illness and can be recurrent or severe in intensity. They require treatment as it can even lead to suicide [1]. Current statistics state that 280 million people are affected by this illness, which is around 3.8% of the population and nearly 700 000 people die due to suicide every year. Suicide is the fourth leading cause of death in 15-29-year-olds [2]. Depression results from a complex interaction between many factors like psychological, social, and biological.

Substantial evidence is accumulated that drug naive depressed patients have abnormalities in brain 5-HT function. The evidence that serotonin contributes to the patho-physiology of depression comes from studies of tryptophan depletion, which show that lowering brain 5-HT levels can induce acute symptomatic relapse in recovered depressed individuals' reactions [3]. Due to these Studies currently the accepted modality of treatment is the selective Serotonin Reuptake Inhibitors and neither Serotonin nor epinephrine reuptake inhibitors [4]. Paroxetine, a phenylpiperidine derivative is an inhibitor of the reuptake of 5-hydroxytryptamine. It has also a property of weakly inhibiting norepinephrine uptake in the synapse [6]. On the otherhand Venlafaxine, a Phenylethylamine derivative is a major active metabolite, which is known as O-desmethylvenlafaxine. They both inhibit presynaptic reuptake of norepinephrine, 5-hydroxytryptamine and they cause weak dopamine reuptake. [5].

In our study we intend to compare the response of these two drugs (Paroxetine and Venlafaxine) in the treatment of depression.

## Materials and Methods

It is a prospective, open, randomized comparison of the efficacy and tolerability of Controlled release Paroxetine and Venlafaxine Extended release in the patients suffering from depression. The study was conducted after getting the approval from Institutional review committee, Nobel Medical College Teaching Hospital (NMCTH). A total of 100 consecutive patients who attended the Psychiatry department in NMCTH, diagnosed as depression, were enrolled for the study. Convenient sampling was done. Written consent was taken from the subjects.

The criteria for the sampling were 20 and 65 years of age, Montgomery and Åsberg Depression Rating Scale (MADRS) score >17, no comorbidity, written consents, where as a history of psychotropic medications, drug or alcohol abuse or dependence, Montgomery and Åsberg

Depression Rating Scale (MADRS) score < 17, pregnant or breast-feeding were not included.

The patient or informant was explained about the study & its advantages, disadvantages and procedures. Only after they agreed, they were included. The subjects were alternatively allotted into Group 1 (Paroxetine Group) and Group 2 (Venlafaxine Group). A study period was kept for 8 weeks. The initial dose of Venlafaxine XR was 37.5 mg whereas, for Paroxetine Controlled Release, 12.5 mg was prescribed. The patients were called on a regular follow up and the doses as per requirement could be titrated up to 150 mg of Venlafaxine and 37.5 mg of Paroxetine. The clinician had to decide the dosage according to the requirement on case basis. The data was recorded on Week 0 (Day 0), Week 1, week 2, week 3, week 4 week 6 & week 8. At each visit the vitals were monitored and the adverse drug reactions were assessed and noted down. Montgomery and Åsberg depression Rating Scales [7] were also recorded for assessing improvement.

The data so collected was tabulated and analyzed using descriptive analytical tools. Statistical analysis was done using the SPSS software package. The treatment group 1 and Group 2 were compared for efficacy and safety using of Student's t test.

## Results

A total of 100 patients were recruited for the study 50 each to Group 1 (Paroxetine Cr) and Group 2 (venlafaxine XR).

**Table 1: Socio-demographic profile of study participants**

Characteristics	Group 1 (n = 50)	Group 2 (n = 46)
Age	46 ± 15	49 ± 13
Male	19 (38%)	21 (46%)
Female	31 (62%)	29 (63%)
Weight	72 ± 19	69 ± 15

There were no clinically relevant differences at baseline between the two treatment groups. At baseline, 56.4% of patients in the Group 1 and 52.9% of patients in the Group 2 were suffering from moderate depression. The number of patients who withdrew due to adverse events was 4 in the group 2 which is 8%. The adverse event with the highest incidence that led to withdrawal was nausea and constipation.

A total of 73% of the patients in Group 1 and 82% of the patients in the Group 2 had their dose of antidepressant increased. The mean daily dose a week 8 was 25.79 mg for Paroxetine CR and



113.86 mg for venlafaxine XR.

**Table 2: Group 1(Paroxetine CR) Pre & post treatment scores of MADRS.**

Characteristics	Group1(n)	Mean(±SD)	Difference	p value
MADRSSCORES Pre-Treatment	50	28.60±3.2	-	
Post-Treatment	50	9.02±8.0	19.94	<0.001*

The mean MADRS total score decreased substantially over time for patients in both treatment groups. The pre treatment MADRS score of Group 1 was 28.60 and Group 2 was 29.01. At week 8 the end of the study period the MADRS scores on Group 1 was 8.68, The P value of the pre and post treatment MADRS scores of Paroxetine CR group was <0.001\*, which was statistically significant.

**Table 3: Group 2 (Venlafaxine XR) pre & post treatment scores of MADRS**

Characteristics	Group2 (n)	Mean(±SD)	Difference	pValue
MADRS SCORES Pre-Treatment	50	29.01±9.23	-	
Post-Treatment	46	8.60±2.12	20.33	<0.001*

Comparable results of Paroxetine CR and venlafaxine XR were achieved in change of mean in between Day 0 and Week 8 in MADRS total score.

In Group 2 the post treatment MADRS score was 8.60. The P value of the pre and post treatment MADRS scores of Venlafaxine XR group was <0.001\* was statically significant.

**Table 4: Estimated mean change from baseline in MADRS total scores in both the groups**

Characteristics	Group1	Change	Group2	Change
Week 0	28.60	-	29.01	-
Week 1	24.32	-4.28	24.36	-4.65
Week 2	18.8	-9.80	20.05	-8.96
Week 3	15.17	-13.43	16.33	-12.86
Week 4	12.33	-16.27	13.42	-15.59
Week 6	11.04	-17.56	11.38	-17.63
Week 8	8.66	-19.94	8.68	-20.33

Vital Signs, weight was taken. There were no apparent trends within or between treatment groups with respect to weight (mean loss of 0.2 kg for Paroxetine XR -treated patients vs. 0.3kg for venlafaxine XR-treated patients). For vital signs, there was a statistically significantly higher increase in pulse rate from baseline to last assessment for venlafaxine treated patients (2.3bpm vs. 0.8 bpm for Paroxetine treated patients; p = 0.04).

## Discussion

This is a prospective, open, randomized comparison of the efficacy of Controlled release Paroxetine with Extended-Release Venlafaxine in the treatment of Depression. The result showed clear treatment-related improvements in MADRS scores in both treatment groups during the study. The efficacy of Paroxetine CR was similar to venlafaxine XR, in Outpatients, but there were more adverse effects in the Venlafaxine group than Paroxetine group.

This is in line with results seen in study by Eduard Vieta, Anabel Martinez-Araneta. comparing Paroxetine and venlafaxine in the treatment of bipolar affective disorder current episode depression. They found that both are equally effective and safe in the treatment of depressive episodes in bipolar affective disorder. Significant Hamilton Rating Scale for Depression (HAM-D) scores changes were seen in both paroxetine- and venlafaxine-treated patients (p<.0001). There were no significant differences noted in efficacy and safety of the 2 drugs. 43% (N=13) of patients taking paroxetine and 48% (N=14) taking venlafaxine were considered to be responders. The sample size of this study was very small. Much smaller than our study [8] Smajkic, A., Weine, S., Djuric-Bijedic, Z. et al. in a study conducted on refugees in 2001, Three antidepressants were used in treating Depressive illness with posttraumatic stress disorder in those patients. All received open trials of Sertraline (n = 15), Paroxetine (n = 12), or Venlafaxine (n = 5). It was concluded that Sertraline and Paroxetine produced significant changes in 6 weeks. Venlafaxine produced improvement in PTSD, but not in depressive disorder, and had a high rate of side effects. The higher rate of side effects seen in this study are similar to side effects seen in our study with Venlafaxine [9].

Paroxetine and venlafaxine are potent serotonin transporter antagonists and weaker Nor Adrenaline transporter antagonists. Using a blood assay that estimates CNS transporter occupancy, Owens, M., Krulewicz, S., Simon, J. et al estimated the relative serotonin transporter and nor Adrenaline transporter occupancy of paroxetine and venlafaxine in humans to assess these serotonin transporter antagonists and noradrenaline transporter inhibition quantity. 86 Outpatients, suffering from depression were enrolled in 8 weeks multicenter, randomized, double-blind, parallel group study. Subjects were treated by forced dose program of paroxetine CR (12.5–75 mg/day) or venlafaxine XR (75–375 mg/day). At week 8 MADRS total score with paroxetine was 16.7 and venlafaxine-treated patients 17.3. The





antidepressant effects were not significantly different from each other (95%CI-3.42, 4.54,  $p=0.784$ ). These results clearly prove that paroxetine and venlafaxine have similar improvement in depression patients. These results are reflected in our study also [10].

In 1999 a study to compare the efficacy and safety of venlafaxine and paroxetine in 122 patients by Poirier, M.F. and Boyer, P., with non-chronic treatment-resistant depression having a baseline HAM-D score 18 were included with a history of resistance to two previous antidepressant treatments and a CGI improvement score of 3 at the initiation of therapy. Doses were adjusted to 200–300 mg/day for venlafaxine and 30–40 mg/day for paroxetine. It was concluded that Venlafaxine showed some evidence of superiority to paroxetine in this difficult-to-treat patient population. The response rate was 51.9% for venlafaxine and 32.7% for paroxetine ( $P=0.044$ ) and a remission was achieved in 42.3% of venlafaxine-treated and 20.0% of paroxetine-treated patients ( $P=0.01$ ). The incidence of adverse effects was comparable between treatment groups [11] which is different from our study.

M.P.G. Broen, A.F.G. Leentjens et al, studied differential responses to anti depressant treatment in affective, somatic and cognitive domains of depression. Patients were treated for twelve weeks with placebo, venlafaxine or paroxetine as part of the Study of antidepressants in Parkinson's disease randomized controlled trial. Depressive symptoms were evaluated with three commonly used ratings scales. All symptom domains improved during the study period, There was a significant placebo effect, especially in the first two weeks that had diminished by week 12. In depressed Parkinson disease patients treated with venlafaxine or paroxetine, affective symptoms improved first, then somatic symptoms and later cognitive symptoms [12].

Ballús C et al A 24-week, double-blind, randomized trial was performed to compare the efficacy and tolerability of venlafaxine and paroxetine in patients with major depression or dysthymia. Day 0 Score of 17 on Hamilton Depression Rating Scale (HAM-D) were included. Patients were randomly divided into venlafaxine, 37.5 mg, or paroxetine, 20 mg, in the morning and placebo in the evening, which could be increased to venlafaxine, 75 mg twice daily, or paroxetine, 20 mg, for four weeks. Efficacy of the therapy was assessed using HAM-D, MADRS, HAM-A and the Clinical Global Impressions Scale (CGI). Forty-one patients were put in

venlafaxine group and forty-three to paroxetine. At week 6, improvement was observed in 55% of patients on venlafaxine and 29% on paroxetine ( $P = 0.03$ ) after 12 weeks, significantly ( $P = 0.011$ ) increased patients in the venlafaxine group had a HAM-D remission score of 8 or less (59% versus 31%). 16 (39%) patients on venlafaxine and 11 (26%) on paroxetine discontinued the therapy. A consistently higher proportion of patients had improvement on venlafaxine than on paroxetine. The result of this study was different from our study [13].

## Conclusion

In our study we were comparing the SSRI Paroxetine (12.5–37.5 mg/day) with SNRI venlafaxine XR (75–150 mg/day) in Nepali population. The efficacy of Paroxetine CR (12.5–37.5 mg) was similar to that of venlafaxine XR (37.5–150 mg) in the treatment of outpatients with Depressive illness. Discontinuation occurred in the patients on venlafaxine XR (37.5–150 mg) which was 8% due to adverse drug reaction. Thus, both drugs can be taken as having same efficacy but, Paroxetine as better tolerated drug.

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**Conflict of interest:** None

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