

DOI: <https://dx.doi.org/10.18203/2319-2003.ijbcp20261950>

Original Research Article

Comparative study of efficacy and safety of escitalopram versus opipramol in the treatment of major depressive disorder: one-year, prospective, open label, randomized and add on therapy in a tertiary care hospital

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Received: 21 March 2026

Revised: 05 May 2026

Accepted: 06 May 2026

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ABSTRACT

Background: A randomized, prospective, open label, comparative study was conducted to evaluate and compare the Efficacy and safety of escitalopram versus opipramol in patients suffering from major depressive disorder (MDD).

Methods: A total of 100 patients from psychiatry OPD diagnosed with major depression were included in the study after fulfilled the inclusion and exclusion criteria. The eligible participants were randomly allocated into one of the following two treatment groups after randomization block permutation method i. e., pharmacologically equivalent dose range of the two drugs as follows: group 1: Tab. escitalopram 10-20 mg OD for 6 weeks. Group 2: Tab. opipramol 50 mg-100 mg BD for 6 weeks. All patients were given the respective tablets for 2 week and were asked to come for follow up after 2nd, 4th and 6th week of treatment. At first visit baseline parameters like weight, BMI, CBC, LFTs, RFTs, lipid profile, blood glucose, ECG and use of concomitant medicines were recorded and subsequently measured again at the end of 4th and 6th week. Evaluation parameters were assessed by using HAM (D and A) scale and Naranjo causality assessment scale.

Results: Escitalopram group exhibited a better improvement in HAM-D score in comparison to Opipramol group. Escitalopram group exhibited a better improvement in CGI-SOI, CGI-GI, CGI-EI score in comparison to Opipramol group. On intergroup comparison, no statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment. It was observed that 32 patients in Escitalopram arm and 35 patients in opipramol group required the rescue treatment (tab. Clonazepam).

Conclusions: we conclude from our study that escitalopram group showed better improvement in management of symptoms of depression than opipramol.

Keywords: Depression, Escitalopram, Opipramol, HAM-A, HAM-D, CGI-severity of illness, Global improvement, Efficacy index

INTRODUCTION

Major depressive disorder is characterized by a depressed mood or loss of pleasure or interest for at least 2 weeks (American Psychiatric Association, 2013). Persistent depressive disorder in the Diagnostic and Statistical

Manual of Mental Disorders (DSM-5) is characterized by a depressed mood most of the time for at least 2 years, along with at least two of the following symptoms: feeling hopeless, insomnia or hypersomnia, overeating or poor appetite, fatigue or low energy, low self-esteem, and indecisiveness or poor concentration.^{1,2} Among various

treatment modalities, an antidepressant medication is the initial treatment of choice for patients with mild to moderate depression.^{3,4}

Escitalopram (SSRI) is widely used for treatment of depression and anxiety. It is a purer agent that can potentially offer an improved safety, efficacy and tolerability with minimal drug interactions as compared to others. Escitalopram is approved by the U. S. Food and Drug Administration (FDA) for treating major depressive disorder in adults and adolescents for both acute and maintenance phases.⁵⁻⁷ Opipramol, a potent sigma ligand with high affinity to sigma 1 and lower affinity to sigma 2 sites, play a key role in potentiating intracellular calcium mobilization, modulating calcium signaling, regulating ion channels, neurotransmitter release which include dopamine, serotonin, nor-epinephrine, glutamate and acetylcholine. It is this property which is responsible for the therapeutic benefit against anxiety and depression.⁸ The recommended dose for the adults is 50 mg in morning, 50 mg in the afternoon and 100 mg in the evening.

In context pertaining to our Indian set up, we were able to site only a limited number of studies which made direct head-to-head comparisons between escitalopram and opipramol in patients of depression and provision of any conclusive results regarding superiority of one over the other was also not retrieved. Furthermore, no such comparative study related to Escitalopram and Opipramol in MDD patients had been conducted in our region to the best of our knowledge.

METHODS

We conducted this randomized, prospective, open label, comparative study after approval by Institutional Ethics committee no IEC/GMC/2019/764 Dated 26/11/2019 in the Department of Pharmacology in collaboration with the Department of Psychiatry, GMC Jammu for period of 1 year (November 2019 to December 2020). A total of 100 patients from psychiatry OPD diagnosed with major depression were included in the study after fulfilled the inclusion criteria.

Inclusion criteria

Patients with age group 18-65 years, sex both male and female, WHO meet DSM-V criteria for depression (American Psychiatric Association,1994) A minimum total score of 18. On the 24-item Hamilton scale for depression (Hamilton, 1960). Non pregnant females. No co morbid conditions like DM, HT, and IHD were included in the study.

Exclusion criteria

Patients with age group <15 and >65 (years), severe suicidal depression and patient opting for ECT /hospitalization. Severe co morbid conditions like DM, HT, and IHD. Patient who had taken any antidepressant

the last 6 weeks. Intake of any drug which causes depressive state, psychosis or anxiety. Pregnancy/lactating mothers. Any chronic ailment which leads to depression. The eligible participants were randomly allocated into one of the following two treatment groups after randomization block permutation method i. e., pharmacologically equivalent dose range of the two drugs as follows: group 1: Tab. Escitalopram 10-20 mg OD for 6 weeks. Group 2: Tab. Opipramol 50 mg-100 mg BD for 6 weeks. The dose selection for both the drugs was based on dose used by various clinical studies and also the dose most commonly used clinical practice.⁹ All patients were given the respective tablets for 2 week and were asked to come for follow up after 2nd, 4th and 6th week of treatment were excluded.

Assessments

Evaluations were conducted at screening, baseline, and after two weeks, four weeks and six weeks of study treatment.

Efficacy assessments were-HAM-D (Hamilton scale of rating depression), HAM-A (Hamilton scale of rating anxiety) and CGI (Clinical global impression).

At first visit baseline parameters like weight, BMI, CBC, LFTs, RFTs, Lipid Profile, Blood Glucose, ECG and use of concomitant medicines were recorded and subsequently measured again at the end of 4th and 6th week.

Safety assessments

Safety assessments were done by observing vital signs, blood pressure, heart rate, pulse, ECG, BMI, waist circumference, use of concomitant medication. Adverse event monitoring was done by using Naranjo-Scale.^{10,11}

RESULTS

Effect on HAM-D

The mean HAM-D score in opipramol group gradually reduced to at 2 weeks, at 4 weeks and at 6 weeks of treatment. Similarly, the mean HAM-D score also decreases in Escitalopram group from at a baseline to 2 weeks, at 4 weeks and at 6 weeks of treatment. Escitalopram group exhibited a better improvement in HAM-D score in comparison to opipramol group. No statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment.

Effect on HAM-A

The mean HAM-A score in opipramol group gradually reduced to at 2 weeks, at 4 weeks and at 6 weeks of treatment. Similarly, the mean HAM-A score in escitalopram group reduced at 2 weeks, 4 weeks and at 6 weeks of treatment. Escitalopram group exhibited a better improvement in HAM-a score in comparison to opipramol

group. No statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment.

Effect on CGI (Severity of illness)

Escitalopram group exhibited a better improvement in CGI-SOI score in comparison to Opipramol group. No statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment.

Effect on CGI (Global improvement)

Opipramol group exhibited a better improvement in CGI-GI score in comparison to escitalopram group.

P value was significant at 2 weeks in opipramol group only i. e., ($p = 0.02$). No statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment.

Table 1: Demographic parameters.

Parameters	Category	Escitalopram, n=46 (%)	Opipramol, n=48 (%)	Percentage
Age (in years)	<35	14 (30.4)	21 (43.75)	37.2%
	35-40	6 (13.0)	9 (18.75)	15.9%
	41-45	5 (10.8)	6 (12.5)	11.7%
	46-50	9 (19.5)	6 (12.5)	15.9%
	51-55	2 (4.3)	2 (4.1)	4.2%
	56-60	5 (10.8)	1 (2.8)	6.3%
	60-65	2 (4.3)	5 (10.5)	7.4%
Sex	Male	25 (50)	23 (50)	48.9%
	Female	23 (50)	25 (52.1)	51.0%
Socio economic status	APL	20 (43.4)	31 (64.5)	54.2%
	BPL	26 (56.5)	17 (35.4)	45.7%
Family history of depression	Positive	27 (58.6)	21 (43.7)	43.6%
	Negative	19 (41.3)	27 (56.2)	56.3%
	Literate	17 (36.9)	12 (25)	30.8%

Table 2: Comparison of two groups i. e., opipramol versus escitalopram with respect to HAM-D scales.

Parameters	Duration in weeks	Opipramol, mean±SD	Escitalopram, mean±SD	T value	P value	95% confidence interval
HAM- D	2 weeks	11.44±2.40 ^{###}	10.96±1.80 ^{###}	1.09	0.277	(-.39-1.35)
	4 weeks	8.92±1.89 ^{###}	8.48±1.56 ^{###}	1.22	0.244	(-.27-1.15)
	6 weeks	6.88±1.77 ^{###}	6.26±1.63 ^{###}	1.75	0.083	(-.08-1.31)

*The data is shown as Mean±S.D showing Paired t test in comparison to respective baselines # $p < 0.05$, ## $p < 0.001$, ### $p < 0.0001$, NS Not significant and showing comparison between the groups at baseline, 2 weeks, 4 weeks and 6 weeks using student unpaired t test which were non significant throughout the study period.

Table 3: Comparison of two groups i. e., opipramol versus escitalopram with respect to HAM-A scale.

Parameters	Duration in weeks	Opipramol, mean±SD	Escitalopram, mean±SD	T value	P value	95% confidence interval
HAM-A	0 weeks	14.77±3.11	15.28±2.90	-0.82	0.412	(-1.74-.72)
	2 weeks	12.21±3.00 ^{###}	12.11±3.23 ^{###}	0.16	0.877	(-1.18-1.38)
	4 weeks	9.60±2.73 ^{###}	9.39±2.88 ^{###}	0.37	0.714	(-.94-1.36)
	6 weeks	9.60±2.73 ^{###}	9.41±2.89 ^{###}	0.33	0.742	(-.96-1.34)

*The data is shown as Mean±S.D showing Paired t test in comparison to respective baselines # $p < 0.05$, ## $p < 0.001$, ### $p < 0.0001$, NS Not significant and showing comparison between the groups at baseline, 2 weeks, 4weeks and 6 weeks using student unpaired t test which were non-significant throughout the study period.

Effect on CGI (Efficacy index)

Escitalopram group exhibited a better improvement in CGI-EI score in comparison to opipramol group.

On intergroup comparison, no statistically significant difference ($p < 0.05$) was seen between the groups at 6 weeks of treatment.

Rescue treatment

In our study a provision for using Tab. Clonazepam 0.5 mg as and when required was kept. It was observed that 32 patients (69.57%) in Escitalopram arm and 35 patients (72.92%) in opipramol group required the rescue treatment. On intergroup comparison, the significant difference was not statically significant.

The most common ADR seen in Opipramol group was sedation followed by fatigue, headache, tachycardia, Impotence and weight gain. Whereas in Escitalopram group the most common adverse drug reaction was headache followed by fatigue, sedation and nausea, drowsiness, impotence and weight gain and loss of appetite. On between group comparison, it was seen that headache was the most common ADR in escitalopram group while sedation was the frequently encountered ADR in opipramol group and p value was significant in sedation ($p=0.04$) in opipramol group and was significant in nausea ($p=0.04$) in escitalopram group.

DISCUSSION

The results of our study with respect to demographic parameters are consistent with Aryal et al who revealed that depression is common in age group 16-35 years which were similar to our current study.¹² Adults are twice likely (37.2%) to be diagnosed with MDD as compare to older age group 50-65 years (17.9%). Females are suffering more from depression (51.0%) as compare to males (48.9%). Females more likely to be diagnosed with MDD as compared to their male counterparts regardless of age group. Patients with positive family history are more prone to depression (58.5%) as compare to those with negative family history (41.4%).

Similar results were found by Li et al in their study where Escitalopram is one of the most commonly used SSRIs among medicare beneficiaries.¹³ Although escitalopram has shown better acceptability and fewer discontinuations than other antidepressants (such as duloxetine, fluvoxamine, paroxetine, reboxetine, and venlafaxine).

Another study done by Li et al has been reported that escitalopram has better efficacy than other SSRIs and is either better than or equivalent to SNRIs in the treatment of MDD.¹⁴ The efficacy of escitalopram in the treatment of MDD in Chinese patients as demonstrated in this pooled analysis was consistent with that reported in other populations. According to the CGI, 86.7% of patients achieved good/excellent improvement at the end of study.

Escitalopram and desvenlafaxine were found to be comparable in their efficacy in reducing depression in adult patients of depression in a study conducted by Gupta et al which is differed from the results of our study.¹⁵ Even though both the drugs showed significant differences in the HAM-D scores from their respective baselines, they failed to show any statistical difference at 3 and 6 weeks of treatment on inter group comparison.

On neck-to-neck comparison the efficacy and safety of both drugs i. e., opipramol and escitalopram in treating generalised anxiety disorders, findings similar to our study were observed in a study by Manjunath et al.¹⁶ The opipramol proved to be equally effective in the treatment of GAD compared to escitalopram in terms of efficacy. In our current study patients who were on opipramol for a

duration of 6 weeks were well tolerated. The study showed that opipramol is as effective as escitalopram in terms of efficacy, with a better tolerability profile than escitalopram.

Similar results were also found by Krysta et al in their study.¹⁷ They found that opipramol is an efficient drug in general anxiety disorders along with SSRI's, SNRI's, buspirone and pregabalin having an efficacy better than placebo.

Furthermore, studies done by Urade et al also reported similar finding wherein, within group and inter group comparison of the mean HAM-D scores in the escitalopram and agomelatine groups showed statistically significant changes ($p<0.0001$) in the escitalopram group, suggesting that escitalopram was superior to agomelatine in efficacy due to its early response, early remission and better relief of symptoms from MDD in adults.¹⁸

Similar to our observations, the comparative effects opipramol versus trifluoperazine in the treatment of anxiety and depression was also studied by Barritt et al where in the results showed that as far as depression as a symptom was concerned, there was no significant difference in the relief afforded by the two drugs but a wider selection of cases might have produced an improvement in the response to opipramol.¹⁹

Carpene et al treatment with several antipsychotic drugs exhibits a tendency to induce weight gain and diabetic complications.²⁰ Surprisingly, only opipramol exhibited substantial antilipolytic properties in the micromolar to millimolar range. An opipramol antilipolytic effect was evident against isoprenaline or atrial natriuretic peptide-stimulated lipolysis. Opipramol did not impair insulin activation of glucose transport but inhibited monoamine oxidase (MAO) activity to the same extent as antidepressants recognized as MAO inhibitors.

Limitations

It was a short duration study. The results may vary in larger general population because of relatively small number of patients. When we start our study, COVID-19 pandemic started so we get a smaller number of patients. Opipramol, limited data available in our country. No attempt was made to study the mechanism of action and dose response relationship.

CONCLUSION

Within the escitalopram group a significant improvement in HAM-D scale was recorded at 2, 4 and 6 weeks interval with a significant p value whereas in Opipramol group also similar findings were observed. While in intergroup comparison between escitalopram and opipramol it was noticed that escitalopram showed a better improvement over opipramol.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhagat V, Sadiq S, Banal R, Gupta MB. Comparative study of efficacy and safety of escitalopram versus opipramol in the treatment of major depressive disorder: one-year, prospective, open label, randomized and add on therapy in a tertiary care hospital. *Int J Basic Clin Pharmacol* 2026;15:651-5.