Available on line at : www.eijppr.com

International Journal of Pharmaceutical and Phytopharmacological Research

(ICV-5.09)

ISSN (Online) 2249 – 6084

ISSN (Print) 2250 – 1029

Int.J.Pharm.Phytopharmacol.Res. 2012, 2(3): 216-221

(Research Article)

Comparative Study of Safety and Efficacy of Duloxetine Versus Escitalopram : A Randomised Control Trial

Mohit Trivedi[1]*, Ajay Kholi[2] ,V.K Verma[3], R. K. Dixit[4]

** [1]Junior Resident, Pharmacology, E.L.M.C., Lucknow, India*
[2]Professor and Head, Dept. of Psychiatry, E.L.M.C., Lucknow, India
[3]Professor, Pharmacology, E.L.M.C., Lucknow, India
[4]Professor, Pharmacology and Therapeutics, K.G.M.U., Lucknow, India

Received on: 30/12/2012 ***Accepted on:*** 31/12/2012

ABSTRACT

Duloxetine (SNRI) and Escitalopram (most selective SSRI) were compared to evaluate the safety in mild to moderate depressive disorder. A 6-week, double blind, randomized, parallel-group study in collaboration with Departments of pharmacology and psychiatry, Era'S Medical College and Hospital, Lucknow (n= 60 patients) on patients suffering from depression single episode (▲ F 32.0 or ▲F 32.1 A/T ICD X), recurrent depressive disorder (▲ F 33.0 or ▲F 33.1 A/T ICD X) was conducted. Scoring on MADRS was kept as primary end point. Subjects were randomly assigned (1:1) into two different groups (Duloxetine 40-60 mg/day (flexibly dosed) and to escitalopram 10-20mg/day) i.e. Group A and Group B with the step-up dosing pattern. The primary efficacy variable was change from baseline at week 6 in MADRS total score and DOTES . A significantly greater proportion of escitalopram-treated patients completed the 6-week study compared with duloxetine-treated patients. At week 6, Duloxetine treatment resulted in slightly lesser improvement, more drop outs, and more adverse effects compared with escitalopram, however the differences were not clinically significant. These findings suggest that SSRI, Escitalopram is better tolerated and at least as effective as the SNRI, Duloxetine in the treatment of major depressive disorder with mild to moderate severity.

Key word: Duloxetine, Escitalopram, Depression, Antidepressants

INTRODUCTION

Depression is a complex diagnostic construct, applied to individuals with a particular set of symptoms among which the essential ingredients are depressed mood and loss of interest[1, 2]. Across the world, 10.07% of disability can be attributed to unipolar major depression. It contributes to nearly 20% of disease in women aged from 15 to 44years. W.H.O. expects that by the year 2020, unipolar major depression will be the second leading cause disease burden in the world. Aggregate burden of disability associated with depression of mild severity may be greater than the disability associated with the smaller number of people with the more severe depression [3]. Depressive symptoms are not recognized in around 50% of attending patients and aggregate disability is more in them, so sample was drawn from mild to moderate depressed patients [4].

Antidepressants that act via modifying both serotonergic and noradrenergic neurotransmission SNRIs may have an advantage compared with antidepressants that primarily affect only one of these neurotransmitter systems like SSRIs, particularly in patients with both depression and physical symptoms. Depressive disorders are also associated with a constellation of physical or somatic symptoms and the link between depression and somatic symptoms which resolve better with SNRIs. Studies have demonstrated significantly greater remission (HAM-D $\leq$ 7) rates with the SNRI venlafaxine as compared with SSRIs [5,6,7]. There is controversy whether the newer, better tolerated, and safer Serotonin norepinephrine reuptake inhibitors are more efficacious than SSRIs. The studies related to comparision of Duloxetine versus selected SSRIs are limited. So in the current study we aim to compare the efficacy and safety of Duloxetine and Escitalopram in mild to moderate depressed patients.

MATERIAL AND METHODS

This study was a randomized, comparative and step up dosing design and was carried out in outdoor patients in the department of Psychiatry, Era's Medical College and Hospital, Lucknow after clearance from Institutional Ethical Committee. Systematic Random Sampling was applied and concealment was done by envelop method. Statistician had generated allocation sequence and assigned participants to their respective groups. Psychiatrist had enrolled participants, administered scales and assessed the clinical

outcomes. Side effect monitoring was done by a pharmacologist and a psychiatrist.

The patients were included in the study after fulfilling the inclusion/ exclusion criteria and only after obtaining full informed consent as diagnosed in psychiatry OPD of Era's Medical College.

All subjects gave informed consent for the study. The patients diagnosed to be suffering from depression as per diagnostic criteria of ICD-10 were randomly allocated to either Duloxetine or Escitalopram group. The study was carried out from March 2010 to July 2011.The sample size consisted of 30 patients for each mild to moderate depressed patients which were drawn from OPD, Department of Psychiatry, Era's Medical College and Hospital, Lucknow. A sample group was taken up for the study . Subjects above 18 years of age of either gender, diagnosed to be suffering from depression (▲ F 32.0 or ▲F 32.1 as per ICD - 10)(International classification of Diseases) with or without somatic symptoms or recurrent depressive disorder (▲ F 33.0 or ▲F 33.1 as per ICD -10) with or without somatic symptoms, duration of current depressive episode is to be between 4 weeks to 12 months, and scoring >6 and ≤ 34 on MADRS(Montgomery Asberg Depression Rating scale), CGI-S(Clinical global impression)>3 and <5 on the initial visit were enrolled in the study. Patients having Axis I or Axis II disorder other than depressive disorder, scoring > 4 on MARDS items number 10 (suicidal thoughts) at screening or baseline, history of non response to an adequate (6 week) trial of three or more antidepressant (with or without mood stabilizers) during the current episode, with imminent risk of suicide or injury to self, others, or property, pregnant, lactating women or women not using medically accepted method of contraception were excluded. Besides patients with current clinically significant neurological, metabolic (including type1 diabetes), hepatic, renal hematological, pulmonary, cardiovascular, gastrointestinal, and / or urological disorder such, as unstable angina, congestive heart failure (uncontrolled), or centre nervous system (CNS) infection that would pose a risk to the subject if they were to participate in the study or that might confound the results of the study ,subjects with human immunodeficiency virus (HIV) seropositivity (or history of seropositivity) , history of malignancy, or any chronic incapicitaing illness were excluded. Besides subjects with history of substance abuse excluding tobacco use were excluded. Patients satisfying the selection criteria and eligible were provided with informed consent form and those who were desirous were enrolled in the study. A detailed baseline assessment was done as per the semi structured proforma which included psychiatric and medical history, physical examination and detailed mental status assessment. Baseline investigations (Hb, TLC, DLC, ESR, Blood Sugar, Liver Function Tests and Blood Urea) were carried out. Dosage Schedule was random allocation of Duloxetine 60mg(Group A) and Escitalopram 20mg(Group B) belonging to study population were done.Dosage was one capsule twice daily (20mg of Duloxetine for first 2 weeks and 30mg of Duloxetine for next 4 weeks) and Escitalopram 10mg in the morning for first two weeks and 20mg for next four weeks and 1 capsule in the evening which was placebo. However the investigator would not know the type of capsule being given to the patient due to double blind nature of the study. Patients were evaluated every second week as per schedule mentioned earlier. Concomitant medication like Lorazepam 2 mg were given as and when required (only night time), records of which were maintained. The addition of Lorazepam, in the depressive symptom study was considered for the final analysis. Instruments used were

- Semistuctured proforma for socio demographic details.
- Details of psychiatric history and examination
- Montgomery As berg Depression Rating Scale (MADRS) [8]
- Clinical global impression (CGI-I)[9]
- Dosage Record Treatment Emergent Symptom Scale (DOTES)[10]

At every visit depressive symptoms were measured by using Montgomery-Asberg Depression Rating Scale (MADRS). At initial visit severity of symptoms were assessed by CGI-S. At visits space between every two weeks Clinical global impression – improvement (CGI-I) were given to the subjects. Adverse effects were also either recorded by the patient, reported by the patient, observed by the therapist or either elicited by the therapist on each visit. Drug naive patients were taken in the study. If the patients were on any medication, then they were kept drug free for a period of at least 15 days for complete elimination of the drug from the body prior to randomization. Treatment with prior psychotropic medications (e.g., antipsychotic agents, antidepressants and mood stabilizers) were discontinued as tolerated and clinically appropriate at least 15 days prior to randomization. Prior to the study the power of the study estimated was about 90% but during the execution of the study the power came out be (Calculated using G*Power software) 92.9%.

RESULTS

Table-1 summarizes the events from the point of screening to randomization of patients. Sociodemographic variables of the subjects enrolled in the study are presented in table-2. Different clinical variables considered in the study are presented in table-3. Mean change in MADRS score from baseline in two groups are present in table-4. Change in CGI Score from baseline among the patients are presented in table-5. Side effects assessed by DOTES are presented in table-6. Side effect either reported by the patient, observed by the clinician or elicited by the therapist are presented in table -7.

Figure-1 summarizes the main side effects reported by the patients of both the groups.

Table-1: Summarizing the events from the point of screening to randomization of patients

1	TOTAL NO. OF PATIENTS WITH TENTATIVE DIAGNOSIS OF DEPRESSION SCREENED IN O.P.D	175
2	NO. OF PATIENTS EXCLUDED REASONS FOR EXCLUSION	103
I	Not fulfilling the diagnostic criteria	80
II	Unwilling to give informed consent	03
III	Unwilling to come for Scheduled follow up visits	04
IV	Unwilling to accept oral drugs	02
V	Already taken antidepressant for the current episode	12
VI	Did not report to collect the drugs after	02

	screening	
3	NO. OF PATIENTS INCLUDED IN THE STUDY	72
4	TOTAL NO. OF DROP OUT PATIENTS	12
A	In Duloxetine group	09
VII	Did not report on the scheduled day/absent	00
VIII	Refused to Continue in the study due to any cause(side effect,poor compliance,etc	07
IX	Did not report on assigned visit or follow the systems of medication	02
B	In Escitalopram Group	03
I	Did not report on the Scheduled scheduled day/absent	00
II	Refused to continue in the study due to any cause(side effect,poor compliance,etc	02
III	Did notreport on the assigned visit or follow the system of medication	01
5	NO. OF PATIENTS WHO COMPLETED THE TRIAL	60
a	Duloxetine group	30
b	In Escitalopram Group	30

Table-2: Depicts the sociodemographic variables of the 60 subjects enrolled in the study

VARIABLES	DULOXETINE GROUP (n=30)		ESCITALOPRAM GROUP (N=30)		X^2	d.f.,p
	N	%	N	%		
AGE (in yrs)						
Upto 30	3	10.0	1	3.3	0.02	1,0.89
31-45	27	90.0	29	96.7		
SEX						
Male	12	40.0	15	50.0	0.61	1,0.43
Female	18	60.0	15	50.0		
MARITAL STATUS						
Married	28	93.3	28	93.3	0.00	1,1.00
Single	2	6.7	2	6.7		
RELEGION						
Hindu	25	83.3	23	76.7	0.42	1,0.52
Muslim	05	16.7	07	23.3		
Others	00		00			
INCOME GROUP (in Rs. /month)						
> 5000	6	20.0	3	10.0	2.74	2,0.25
5000-7499	14	46.7	11	36.7		
7500 and above	10	33.3	16	53.5		
EDUCATION						
Primary	8	26.7	6	20.0	0.47	2,0.79
Secondary	12	40.0	12	40.0		
Higher Secondary/PUC	10	33.3	12	40.0		
OCCUPATION						
Housewives	16	53.3	14	46.7	0.29	2,0.86
Farmers/Manual labourers /Skilled labourers	10	33.3	11	36.6		
Clerical	04	13.3	05	16.7		

Regarding socio demographic variables like age ,sex, marital status ,distribution as per religion, and income distribution, education and occupation both Duloxetine and Escitalopram groups had no significant difference in the age, sex marital status, religion of the two groups ,education and occupation i.e. both the populations were similar in nature.

Table 3: Shows different clinical variables considered in the study

VARIABLES	DULOXETINE GROUP (N=30)		ESCITALOPRAM GROUP (N=30)		X^2	d.f.,p
	N	%	N	%		
DURATION						
<1 Months	08	26.7	06	20.0	0.39	2,0.82
1-6 Months	16	53.3	17	56.7		
> 6 Months	06	20.0	07	23.3		
ONSET						
Insidious	14	46.7	13	43.3	0.07	1,0.79
Acute	16	53.3	17	56.7		
EPISODE						
1^{ST}	24	0.0	23	76.7	0.10	1,0.75
>1	06	0.0	07	23.3		
FAMILY HISTORY OF SIMILAR ILLNESS						
Present	06	20.0	08	26.7	0.37	1,0.54
Absent	24	80.0	22	73.3		

Pertaining to clinical variables like duration of illness, type of onset, episodicity and family history of similar illness statistical analysis revealed there was no significant different in duration, onset, episode and family history between the two groups.

Table – 4: Mean change in MADRS score from baseline in two groups

Change from baseline	Duloxetine (n = 30) Mean	SD	Escitalopram (n = 30) Mean	SD	Significance 't'	d.f.	p
After 2 weeks	4.93	2.15	5.30	15.79	0.76	58	0.450
After 4 weeks	8.90	4.03	9.83	2.95	1.02	58	0.312
After 6 weeks	13.36	6.20	14.50	4.52	0.81	58	0.421

Significant at $p< 0.05$ (d.f = 58), hence above stated values are not significant.

Changes in mean in MADRS scores in the Duloxetine group biweekly from the base line revealed significant reductions in MADRS score at end of 2 ,4 and 6 weeks (p=0.000). Similarly mean reduction in MADRS scores in the Escitalopram group from base line i.e. Also had significant reduction of MADRS score at the end of 2, 4 and 6 weeks (p=0.000).When comparison was drawn between the two groups with consideration of MADRS scores. Escitalopram group had slightly more reduction of MADRS scores than Duloxetine group however not clinically significant. (p=0.421).

Table – 5: Change in CGI Score from Baseline

Change from baseline	Duloxetine (n = 30)			Escitalopram (n = 30)			
	Same	Decrease	Increase	Same	Decrease	Increase	
N	12	16	2	12	16	2	X^2= 0.00
After2weeks %	40.0	53.3	6.7	40.0	53.3	6.7	d.f.=1 p=1.00
N	7	21	2	5	24	1	X^2=0.52
After4weeks %	23.3	70.0	6.7	16.7	80.0	3.3	d.f.=1 p=0.4
N	7	23	--	2	28	--	X^2=3.22
After6weeks %	23.3	76.7	--	6.7	93.3	--	d.f.=1 p=0.07

Significant at $p< 0.05$ (d.f = 1), hence above stated values are not significant.

Overall there was more reduction in CGI scores in Escitalopram group as compared to Duloxetine group at the end of 4 and 6 weeks however it was not statistically significant (p=0.07).

Patient discontinued more in duloxetine group as compared to escitalopram group.Pertaining to Central Nervous System side effects Insomnia (20%vs6.6%), headache (26.4%vs6.6%) was more in duloxetine group. Somnolence,(6.6 % vs 0), tremors(3.3% vs 0%), lethargy, dream abnormality and yawning (3.3%vs 0%), orgasmic abnormality (6.6% vs3.3%), ejaculation disorder(10%vs6.6%) was more in escitalopram group. Pertaining to G.I.T and autonomic. Symptoms; Constipation (10%vs3.3%), increased sweating (6.6% vs 0%),nausea (20% vs 13.2%), hot flushes (3.3% vs 0%), weight gain (3.3%vs 0%), decreased appetite (6.6% vs 0%), hot flushes (3.3%vs0%), increased salivation (6.6%vs 0%), vomiting (6.6% vs 3.3%), blurred vision (6.6% vs 0%), palpitation (3.3% vs 0%) were more increased in duloxetine group. Influenza like symptoms (6.6% vs 0%), rhinitis (6.6% vs 3.3%), sinusitis (3.3% vs 0%), neck shoulder pain (3.3%vs 0%) were more in escitalopram group. Escitalopram is having a better tolerated drug as compared to duloxetine. In the present study on initial dosage of study medication less side effect were reported but on increasing dosage more subjects in duloxetine group.(83.3% vs 63.3%) had side effects however didn't reach point of clinical significance. Concomitant medication-Lorazepam 2 m.g. was required in 02 patients (6.6%) in Escitalopram group and in 06 patients (20.0%) in Duloxetine group as insomnia was more in duloxetine group.

Table – 6: Side effects assessed by DOTES

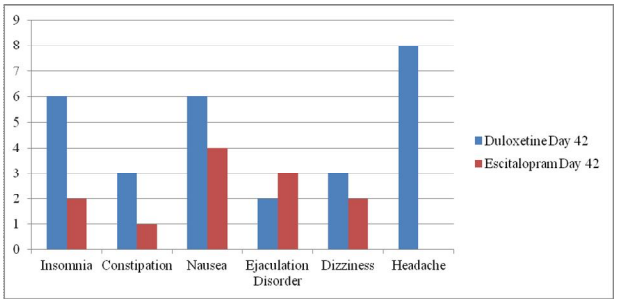
	Duloxetine(N=30)				Escitalopram(N=30)			
	DAY				DAY			
	0	14	28	42	0	14	28	42
a. BEHAVIOURAL TOXICITY								
1. Toxic confessional state	-	-	-	-	-	-	-	-
2. Excitement/ Agitation	-	-	-	-	-	-	-	-
3. Increased Motor activity	-	-	-	-	-	-	-	-
4. Decreased Motor activity	-	-	-	-	-	-	-	-
5. Insomnia	-	1	2	6	-	1	2	2
6. Drowsiness	-	-	-	-	-	-	-	-
1. Abnormal Urine Test	-	-	-	-	-	-	-	-
b. NUROLOGICAL								
1. Rigidity	-	-	-	-	-	-	-	-
2. Tremors	-	1	1	1	-	-	-	-
3. Dystonic symptoms	-	-	-	-	-	-	-	-
4. Akathisia	-	-	-	-	-	-	-	-
c. AUTONOMIC and GIT								
1. Dry mouth	-	1	1	1	-	1	1	1
2. Nasal Congestion	-	1	2	2	-	-	-	-
3. Blurred vision	-	-	1	2	-	-	-	-
4. Constipation	-	1	2	3	-	-	1	1
5. Increased Salivation	-	-	-	-	-	1	1	2
6. Sweating increased	-	-	1	2	-	-	-	-
7. Nausea	-	2	4	6	-	2	3	4
8. Diarrhoea	-	1	2	2	-	1	2	2
d. OTHERS								
1. Dermatologic								
2. Weight gain	-	-	1	1	-	-	-	-
3. Weight loss	-	-	-	-	-	-	-	-
4. Anorexia/decreased appetite	-	-	1	2	-	-	-	-
5. Tardive dskinesia	-	-	-	-	-	-	-	-

Table – 7: Side effect either reported by the patient, observed by the clinician or elicited by the therapist

Side Effects observed	Duloxetine (N=30) DAY					Escitalopram (N= 30) DAY		
	0	14	28	42	0	14	28	42
1. Flatulence	-	-	-	-	-	1	1	1
2. Paresthesia	-	-	1	2	-	-	-	-
3. Somnolence	-	-	-	-	-	1	1	2
4. Decreased libido	-	-	1	1	-	-	1	1
5. Anxiety	-	-	-	-	-	-	1	1
6. Orgasmic Abnormality	-	1	1	1	-	1	2	2
7. Lethargy	-	-	-	-	-	1	1	1
8. Dream Abnormality	-	-	-	-	-	1	1	1
9. Yawning	-	-	-	-	-	1	1	1
1. Vomiting	-	-	1	1	-	-	1	2
2. Palpitation	-	-	-	-	-	1	1	1
3. Hot Flushes	-	-	1	1	-	-	-	-
4. Mucosal dryness	-	-	-	-	-	-	-	-
5. Indigestion	-	-	1	1	-	-	1	1
6. Abdominal Pain	-	-	1	1	-	-	1	1
7. Influnza like symptoms	-	-	-	-	-	1	1	2
8. Hypertension	-	-	-	-	-	-	-	-
9. Fatigue	-	1	1	2	-	-	1	2
10. Ejaculation Disorder	-	1	1	2	-	1	2	3
11. Impotence	-	-	1	1	-	-	1	1
12. Anorgasmia	-	-	1	1	-	1	1	1
13. Rhinitis	-	-	1	1	-	-	2	2
14. Snusitisi	-	-	-	-	-	-	1	1
15. Dizziness	-	1	2	3	-	-	1	2
16. Decreased appetite	-	-	1	1	-	-	1	1
25.Headache	-	3	5	8	-	1	2	-

Note: Number in the table indicates the number of patients complaining of side effects

Figure-1: Main side effects reported by the patients of both the groups



Number on y axis denote the number of patients

DISCUSSION

Studies comparing SSRI and SNRIs conclude dual re-uptake inhibition confers greater efficacy than inhibition of serotonin re-uptake alone[11,12,13,14]. Studies have demonstrated that duloxetine is a significantly more potent norepinephrine reuptake inhibitor than venlafaxine and a significantly more potent serotonin reuptake inhibitor than milnacipran[15,16]. Controlled clinical trials of escitalopram in depressed outpatients have established its efficacy in depression significantly, escitalopram has evidence of efficacy in a primary care study[17,18] . Selective serotonin reuptake inhibitors (SSRIs) have broadly replaced the older tricyclic antidepressant-type drugs as the first-line treatment for depression.. They combine good efficacy with their key advantage, a favourable adverse event profile . Escitalopram is the most selective antidepressant[19].

Earlier study summarized results that significantly greater proportion of escitalopram-treated patients completed the 8-week study compared with duloxetine-treated patients, MADRS total scores with Escitalopram had significantly greater improvement compared with duloxetine with significantly fewer escitalopram-treated patients discontinued because of adverse events compared with duloxetine (2% vs 13%, respectively; $p < 0.01$)[20].

Pigott_et al.,(2007) concluded that both drugs demonstrated similar remission rates over the course of the study, however the entire 8-month study, discontinuation rates differed significantly for duloxetine (62%) compared with escitalopram (55%; $p = 0.02$)[21].

Wade et al., (2002) concluded at week 8, the proportion of responders was 69% (escitalopram) and 58% (duloxetine) ($p < 0.05$) The overall withdrawal rates were 22% (escitalopram) and 25% (duloxetine) (NS). The withdrawal rate due to adverse events was lower for escitalopram (9%) compared to duloxetine (17%) ($p < 0.05$) and significantly more patients treated with duloxetine reported insomnia (12.6% vs. 4.9%) and constipation (8.6% vs. 2.8%)[17].

Nierenberg et al.,(2007) concluded that there is no differences between duloxetine, escitalopram, and placebo rates of remission or response at 8 weeks. Adverse events that occurred significantly more frequently among duloxetine-treated patients when compared with those receiving escitalopram were nausea, dry mouth, vomiting, yawning, and irritability. The rate of discontinuation due to adverse events did not differ significantly between treatment groups Lack of placebo arm, however earlier studies have concluded that Escitalopram and Duloxetine have higher efficacy than placebo[22].

This study did not compare the long term efficacy or safety of Duloxetine and Escitalopram . Finally, the study population is typical of the patient population recruited for the outpatient clinical studies in MDD, and the result may not generalize to the patients with MDD in an outpatient clinical practice who have co morbid medical or psychiatric condition that would have excluded them from participation in this study that is generalizability of the results to real world clinical practice can be a potential concern because of exclusion criteria as it was randomized control trial. Future studies that compare dual action antidepressants with SSRIs should probably start at the best tolerated initial dose and increase to maximally tolerated safe and effective dose should be undertaken.

Concluding, both showed significantly greater improvement on the primary efficacy measure.Sleep subscale of the MADRS which deteriorated with duloxetine. There were more drop outs in the duloxetine group as compared to escitalopram group.Escitalopram is better tolerated and at least as effective as the serotonin-norepinephrine reuptake inhibitor duloxetine in the treatment of major depressive disorder.

REFRENCES

1) Klerman G. - Overview of affective disorders. In comprehensive text books of psychiatry, 3rd edition vol 2nd (Eds. H.L. Kalpen, A.H. freddman, B.J. Sodok), Williamsand wilkins, Bltimore, 1980, 1305-1319
2) Kendell R.E. : Mood (affective) disorders. In comparison to psychiatric studies: 5th edition (Eds. R.E. Kendell, A.K. Zealley) Churchill Living stone, London,1993:427-457
3) Broadhead WE, Blazer D, George L, Tse C. Depression, disability days and days lost from work. *JAMA* 1990; 264: 2524–8.
4) Freeling P, Rao BM, Paykel ES, Sireling LI, Burton RH. Unrecognised depression in general practice. *BMJ* 1985; 290: 1880–3.
5) American psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC; American Psychiatric Association Press; 2000.
6) Greden JF. Physical symptoms of depression: unmet needs. J Clm psychiatry 2003;64 (suppl 7) : 5-11.
7) Stahl SM, Entsuah R, Rudolph RL. Comparative efficacy between venlafaxine and SSRIs: a pooled analysis of patients with depression. Biol Psychiatry 2002 Dec 15; 52 (12): 1166-74.
8) Montgomery SA, Asberg M. "A new depression scale designed to be sensitive to change". British Journal of Psychiatry 1979; 134 (4): 382–89
9) Guy W: Clinical Global Impressions (CGI) Scale. Modified From: Rush J, et al: Psychiatric M
10) National Institute of Mental Health. (1985). DOTES (Dosage record and treatment emergent symptom scale). Psychopharmacology Bulletin, 22, 347-381
11) Williams JWJ, Mutrow CD,Chiquette E, Noel PH, Aguilar C, Coornell J. A systematic review of newer pharmacotherapies for depression in adults: evidence report summary. Ann Intern Med 2000; 132: 743-56easures, APA, Washington DC, 2000.
12) Puech A, Motgomery SA, Prost JF, Solles A, Briley M. Milnacipran, anew serotonin and noradrenaline re-uptake inhibitor: an overview of its antidepressan activity and clinical tolerability. Int Clin Psychopharmacol 1997; 12: 99-108
13) Anderson IM. Meta-analyses of antripressant drugs: selectivity versus multiplicity. In: den Boer JA, Westenberg HGM. (eds) Focus on Psychiatry; Antidepressants: Selectivity or Multiplicity? Amsterdam: Syn-Thesis, 2001.
14) Thase ME. Are SNRIs More Effective than SSRIs? A Review of the Current State of the Controversy. Psychopharmacol Bull. 2008;41:58-85
15) Master FP, Dreshfield - Ahmad LJ, Threlkeld PG, et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin receptor subtypes, and other neuronal receptors. Neuropsychopharmaclogy 2001; 25:87-880.
16) Bymaster FP, Lee TC, Knadler MP, Detke MJ, Iyengar S. The dual transporter inhibitor duloxetine:a review of its preclinical pharmacology, pharmacokinetic profile, and clinical results in depression.*Curr Pharm Des*. 2005;11:1475-1493
17) Wade A, Lemming MO, Hedegaard BK. Escitalopram 10 mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. Int Clin Psychopharmacol 2002;17:95–102.
18) Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. J Clin Psychiatry 2002;63:331–336.

19) Sanchez C, Gruca P, Papp M. R-citalopram counteracts the antidepressant-like effect of escitalopram in a rat chronic mild stress model. Behav Pharmacol 2003b;14:465–470.
20) Khan A, Schwartz K . "Suicide risk and symptom reduction in patients assigned to placebo in duloxetine and escitalopram clinical trials: analysis of the FDA summary basis of approval reports". Ann Clin Psychiatry 2007; 19 (1): 31–6
21) Pigott TA, Prakash A, Arnold LM, Aaronson ST, Mallinckrodt CH, Wohlreich MM. Duloxetine versus escitalopram and placebo: an 8-month, double-blind trial in patients with major depressive disorder. Curr Med Res Opin. 2007;23:1303-1318.
22) Nierenberg AA, Greist JH, Mallinckrodt CH, et al. Duloxetine versus escitalopram and placebo in the treatment of patients with major depressive disorder: onset of antidepressant action, a non-inferiority study. Curr Med Res Opin. 2007;23:401-416.

***Corresponding Author:**
Dr. Mohit Trivedi,
B-8, Sector A, MahaNagar,
Lucknow- 226006, India.
E-mail: *mohittrivedi108@gmail.com*