Original Research Article

Evaluation and comparison of the effect of Escitalopram, Amitriptyline and Mirtazapine on psychomotor performance and cognitive functions in patient of depression

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Abstract

Background: Cognitive deficits are commonly reported by patients with depressive disorder (DD). Certain antidepressant drugs possess sedating and otherwise impairing side effects that can further degrade the patients' functional abilities. This study was carried out to evaluate and compare the effect of Eight-week administration of a commonly prescribed antidepressant amitriptyline, escitalopram and mirtazapine from different group on cognitive and psychomotor functions in patients of depressive disorder using a battery of simple tests. **Materials and Methods:** The study was open label, prospective observational study. Cognition level was measured using Test Your Memory (TYM) Questionnaire and psychomotor performance was measured using battery of tests including critical flicker fusion test (CFFT), hand steadiness test (HST), Arithmetic ability test, and reaction time monitoring. Depression assessed using Global severity depression scale by psychiatrist. Adherence was assessed at end of two months using Morisky 8-item medication adherence questionnaire. **Results and Conclusion:** In present study, within group analysis, amitriptyline showed statistically significant decrease in CFFT score but was not clinically relevant. Other parameters were not affected by amitriptyline, but there was decrease in the HST score by 31 which was not statistically significant (p=0.144) but can be clinically relevant, showing improved psychomotor performance. Escitalopram group showed no effect on cognitive and psychomotor performance. In Mirtazapine group, no meaningful conclusions can be drawn because of the less power. All the three drugs were independently efficacious at the end of two months ($p \leq 0.05$). Adherence score of amitriptyline (2.66) and escitalopram (2.36) was less than low adherence and compared to amitriptyline and escitalopram, adherence score of mirtazapine (5.0) was inferior ($p \leq 0.05$).

Key Word: Escitalopram, Amitriptyline Mirtazapine, Psychomotor, Cognitive, Depressive disorder Running title: Escitalopram vs Amitriptyline vs Mirtazapine on Psychomotor Performance and Cognitive Functions.

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INTRODUCTION

Mental disorders are common either as a primary disorder or co morbid condition. Statistic indicates that four out of ten most important causes of disease worldwide are psychiatric in origin.[1] Worldwide estimated number of people affected from depression is 350 million. One out of 10 people suffered from major depression and almost one out of five persons have suffered from this disorder during their lifetime (one-year prevalence is 10% and lifetime prevalence 17%).[2] According to the findings of the

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National Co morbidity Survey Replication study, the lifetime prevalence of any type of depression is 21 percent, or one in five persons. The incidence of depression is 50% higher in women than men.[3] Report on the global burden of disease has estimated the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women. And it would be the second leading cause of disability –adjusted life years.[4] Depressive disorder (DD) impact on a patient's social, physical and mental wellbeing and contribute to social burden in terms of direct and indirect healthcare costs.[5,6] The pathogenesis of depression includes monoamine hypothesis and receptor hypothesis. Monoamine hypothesis is traditional, in which lack of noradrenaline and serotonin implicates and in receptor hypothesis, upregulation of certain noradrenergic and serotonergic receptors is proposed. Most of the antidepressant agents act by increasing the concentration of the monoamines at neuronal synapses, particularly in locus coeruleus (noradrenaline) and raphe nucleus (serotonin).[5,7] In the last 20 years, newer antidepressant came into existence such as selective serotonin reuptake inhibitors (SSRIs) and selective serotonin norepinephrine reuptake inhibitors (SNRIs). TCA inhibits NA and 5-HT reuptake into neurons. Most prominent action of TCA is ability to inhibit nonepinephrine transporter (NET) and serotonin transporter (SERT) located at neuronal/platelet membrane at low and therapeutically attained concentration. It inhibits monoamine reuptake and interact with variety of receptor viz, muscarinic, α-adrenergic, histamine H1, 5-HT1, 5HT2 and occasionally D2 receptor. SSRIs selectively inhibits membrane associated SERT or both SERT and NET.[8] Mirtazapine is a noradrenergic and specific serotonergic antidepressant (NASSA)[9] acts by blocking α_2 auto (on NA neurons) and hetero (on 5-HT Neurons receptors enhancing both NA and 5-HT release. It is H1 blocker and quite sedative but not anticholinergic or dopaminergic.[8] However the studies which are showing above conclusions in Indian population are very much limited especially effect of SSRIs on cognitive and psychomotor functions. So, to show the effects of atypical antidepressant, SSRI and TCA on cognitive and psychomotor function, this study is being carried.

MATERIAL AND METHODS

The study was open label, prospective observational study. Eligible subjects were of either gender who attended psychiatry outdoor clinic of a tertiary care hospital with clinical diagnosis of Depressive disorder as per Diagnostic and Statistical Manual of Mental Disorder, fourth edition.

Research plan: Patients visiting to psychiatry OPD, of a tertiary care hospital were interviewed by psychiatrist personally and those who were suffering from Depressive Disorder and Clinical Global depression severity score (as per psychiatrist rating) were assessed on a grading of no depression, mild, moderate and severe and would be assessed in every visit.

This study was started only after permission from Institutional ethics committee. The newly diagnosed patients of depression were recruited from Psychiatry OPD.

Inclusion Criteria:

1. Age of patient between 18-65 years
2. Newly diagnosed Patient of Depressive Disorder (DD) were recruited.
3. Patient who was on single antidepressant either amitriptyline or escitalopram or mirtazapine by treating psychiatrist
4. Patient who were willing to give written informed consent

Exclusion Criteria: (On history)

1. Pregnant and lactating Women
2. Patient with any other long-term treatment like antihypertensive, anti-diabetic, anti-tubercular drugs
3. Patient with neurologic disorders (dementia, seizures, stroke), obesity with functional impairment, serious or not stabilized organic disorder (neoplastic, cardiovascular, pulmonary, uncontrolled diabetes)

Study Design: Allocation to one of the two groups was done on the first day of examination immediately after it had been established that a participant fulfilled all the inclusion criteria and none of the exclusion criteria by treating psychiatrist. Patients satisfying inclusion criteria were prescheduled to any one of groups i.e. Escitalopram, Amitriptyline and Mirtazapine group by treating psychiatrist. Patients were kept on fixed doses till study duration. Baseline cognition level was measured using Test Your Memory (TYM) Questionnaire. Baseline psychomotor performance was measured using battery of tests including critical flicker fusion test (CFFT), hand steadiness test (HST), Arithmetic ability test, and reaction time monitoring. At end of 2 months, again cognitive function using TYM questionnaire and Psychomotor functions using the same methods employed previously were performed. Depression assessed using Global severity depression scale by psychiatrist. Adherence was assessed at end of two months using Morisky 8-item medication adherence questionnaire. Data was analysed using Graph Pad prism v. 5.01. Drug dose and administration

Drug	Dose
Escitalopram	10mg OD orally for two months
Amitriptyline	50mg OD orally for two months
Mirtazapine	7.5mg OD orally for two months

It was self-sponsored study. At the end of the study (at 8 week), the treatment was continued or modified as per decision of the psychiatrist.

Calculation of sample size: Sample size: 22 patients per treatment group Based on CFFT α= 0.05 and β=0.2, SD=1.8, change 1.2,(10) Paired data in each group n=20 considering 10% dropout the sample size was rounded to 22. Calculated by power and sample size (PS) program version 3. 1.2.

TESTS

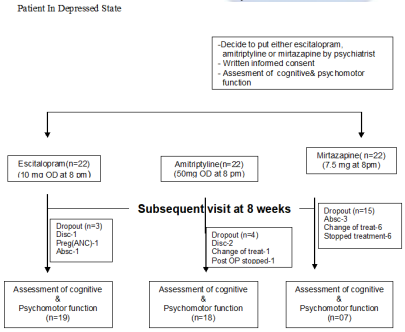
The Cognition function has following essential components -Memory- Test your memory

The psychomotor functions have following essential components[11, 12]

- The central integration and processing mechanism- Critical flicker fusion test, Arithmetic ability test
- Motor responses – Hand steadiness test
- Central integration and motor response. - Reaction time
- Subjective components –Global score grading by Psychiatrist

Antidepressant's efficacy: Global score of depression as assessed and graded by treating psychiatrist in depression patients by visits as no depression, mild, moderate and severe depression scored as 0, 1, 2 and 3 respectively.

Adherence of antidepressant regimen: Adherence score (AS) as assessed by morisky 8- item medication adherence questionnaire at end of 2 month. Score, 0= high adherence, 1 or 2 = medium adherence, >2= low adherence



Disc- discontinued from study, preg- pregnancy / anc during study period, absc- abscond from study, Post OP stopped- post operation stopped treatment, change of treat- patients changed treatment from other class of drug due to noncompliance.

OBSERVATIONS AND RESULTS

The cognitive functions and psychomotor functions were assessed in 66 adult patients of both genders having depression, out of which 44 completed the study. Age range for the patients was 18-65 years, mean age 38.52 ±14.56, of which 22 were men and 22 women. No statistically significant change in memory, Critical flicker fusion score, hand steadiness, arithmetic ability and reaction time in all three groups at baseline (table no.1). In present study, within group analysis, amitriptyline showed statistically significant decrease in critical flicker fusion score but is not clinically relevant. Other parameter like memory, arithmetic ability test and reaction time were not affected by amitriptyline. But there was decrease in the hand steadiness test score by 31 which was not statistically significant (p=0.144) but can be clinically relevant, showed improvement in psychomotor performance (table no.2). Escitalopram showed no statistically significant change in memory, Critical flicker fusion score, hand steadiness, arithmetic ability and reaction time at end of two months (table no.2). Mirtazapine group which was having small sample size of 07 although showed the tendency to decrease memory score and increase clinically relevant reaction time with some drop in the critical flicker fusion test and hand steadiness test, none of these changes were statistically significant. No meaningful conclusions can be drawn because of the less power (power < 80% on all parameter) due to high number of dropouts in this group (table no.2). Analysis between the two groups showed that escitalopram and amitriptyline were equivalent for all parameters (TYM, CFFT, HST, AAT and reaction time) at the end of 2 months (table no.3). The comparison between mirtazapine and other two groups showed no significant results but conclusion cannot be drawn because of less power due to high dropouts in mirtazapine group (table no.3). Global score for antidepressant efficacy as judged by treating psychiatrist as no depression, mild, moderate and severe were scored as 0,1,2 and 3 respectively. All three drugs were independently efficacious at the end of two months ($p \leq 0.05$) but antidepressant efficacy for amitriptyline and escitalopram was highly significant while that of mirtazapine was significant (table no.4). Adherence score as assessed by Morisky 8-item medication adherence questionnaire at end of two months of Amitriptyline treatment is 2.66 and escitalopram is 2.36, which was less than low adherence and mirtazapine was 5.0, which was very less than low adherence. Score, 0= high adherence, 1 or 2 = medium adherence, >2= low adherence (table no.5).

Table 1: Baseline demographic and clinical characteristics of amitriptyline, escitalopram and mirtazapine

	Amitriptyline Group	Escitalopram Group	Mirtazapine Group	P Value
Mean age	**42.22±13.19**	**37.47±16.31**	**31.86±8.80**	**-**
M:F	**0.5**	**1.71**	**1.33**	**-**
TYM	34.22±3.75	36.53±3.85	34.57±2.50	0.1004
CFFT	36.61±4.12	36.89±3.348	39.64±3.72	0.1722
HST	155.9±77.76	169.5±169.2	100.3±84.36	0.1417
AAT	15.56±5.13	17.37±5.39	12.57±5.85	0.1258
RT	701.8±173.5	669.1±185.6	583.9±89.27	0.2507

ES-Escitalopram, AM- Amitriptyline, MIR- Mirtazapine, P ≤0.05- significant, Values of scores are expressed as mean ± standard deviation, Test- Kruskall Wallis test.

Table 2: Intragroup analysis of amitriptyline, escitalopram and mirtazapine on test your memory (TYM), critical flicker fusion test (CFFT), hand steadiness test (HST), arithmetic ability test (AAT) and reaction time (RT) scores

TEST		TYM	CFFT	HST	AAT	RT
AM (n=18)	**BL**	34.22±3.75	36.61±4.12	155.9±77.76	15.56±5.13	701.8±173.5
	2M	34.44±4.01	35.19±2.39	124.8±63.74	15.06±4.70	698±143.4
	p	0.8843	0.0103	0.144	0.2554	0.6013
ES (n=19)	**BL**	36.53±3.85	36.89±3.348	169.5±169.2	17.37±5.39	669.1±185.6
	2M	36.63±4.84	36.74±3.12	154±125.2	17.89±5.18	642.1±141.2
	p	0.8268	0.7528	0.7475	0.7821	0.4326
MIR (n=07)	**BL**	34.57±2.50	39.64±3.72	100.3±84.36	12.57±5.85	583.9±89.27
	2M	33.43±2.29	29.14±2.61	88.57±49.88	13.14±4.88	678.1±91.52
	p	0.2905	0.7344	0.8125	0.8501	**0**.2359

ES-Escitalopram, AM- Amitriptyline, MIR- Mirtazapine, BL- Baseline, 2M- 2 months. P ≤0.05- significant, DIFF- Difference, Values of scores are expressed as mean ± standard deviation, Test- Wilcoxon signed rank test.

Table 3: Between group analysis of amitriptyline, escitalopram and mirtazapine on changes in score at two months of test your memory (TYM), critical flicker fusion test (CFFT), hand steadiness test (HST), arithmetic ability test (AAT) and reaction time (RT)

TEST/DRUG	ES (change at 2 months)	AM (change at 2 months)	MIR (change at 2 months)	P
TYM	0.10±3.81	0.22±3.65	-1.14±2.85	0.7279
CFFT	-0.15±2.672	-1.41±2.9	-0.50±4.61	0.6303
HST	-14.79±79.54	-31.14±61.72	-11.71±107.2	0.2626
AAT	0.52±3.06	-0.50±1.65	+5.71±2.76	0.6852
RT	-27.05±12.08	-3.22±137.60	+94.29±149.0	0.1620

ES-Escitalopram, AM- Amitriptyline, MIR- Mirtazapine, P ≤0.05- significant, Values of scores are expressed as mean ± standard deviation, Test- Kruskall Wallis test

Table 4: Intragroup global score of depression as assessed and graded by treating psychiatrist in depression patients by visits in escitalopram, amitriptyline and mirtazapine groups.

GROUP/VISIT	BL	2M	P	DIFF
ES	2.52±0.51	0.52±0.84	0.0001	-2.0
AM	2.66±0.48	0.61±0.77	0.0002	-2.05
MIR	2.71±0.48	1.0±0.81	0.019	-1.71

ES-Escitalopram, AM- Amitriptyline, MIR- Mirtazapine, BL- Baseline, 2M- 2 Months. P ≤0.05- Significant, DIFF- Difference, Values of scores are expressed as mean ± standard deviation, Test- Wilcoxon signed rank test.

Table 5: Comparison of mean difference in Adherence score as assessed by morisky 8- item medication adherence questionnaire in escitalopram, amitriptyline and mirtazapine groups.

Group	MEAN±SD	
ES	2.36±1.16	
AM	2.66±1.32	
MIR	5.00±1.15	
Comparison between	**Difference of adherence Score**	**p**
AM-ES	1.92	ns
AM-MIR	-17.44**	p≤0.001
ES-MIR	-19.37**	p≤0.001

ES-Escitalopram, AM- amitriptyline, MIR- Mirtazapine, ns- nonsignificant, Test- Kruskall-Wallis test, followed by Dunn's multiple comparisons test.

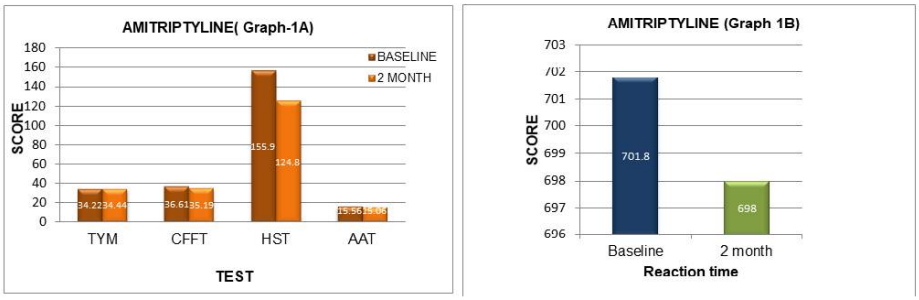


Figure 1: Intragroup analysis of amitriptyline on test your memory (TYM), critical flicker fusion test (CFFT), hand steadiness test (HST), arithmetic ability test (AAT) and reaction time (RT) scores (n=18)

TYM- Test your memory, CFFT- Critical flicker fusion test, HST-Hand steadiness test and AAT- Arithmetic ability test, Values of scores are expressed as mean ± standard deviation, Test- Wilcoxon signed rank test.

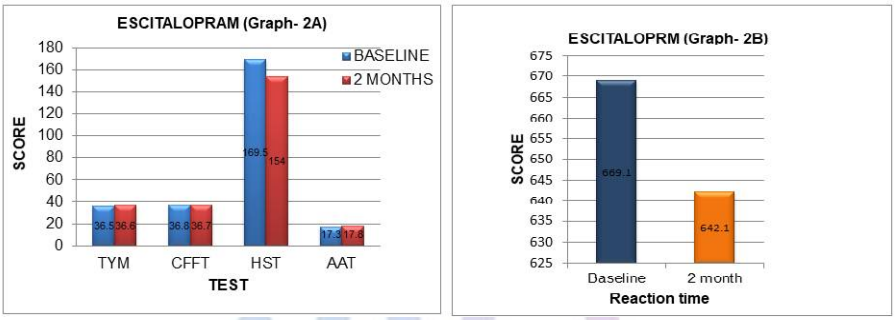


Figure 2: Intragroup analysis of escitaloprm on test your memory (TYM), critical flicker fusion test (CFFT), hand steadiness test (HST), arithmetic ability test (AAT) and reaction time (RT) scores (n=19)

TYM- Test your memory, CFFT- Critical flicker fusion test, HST-Hand steadiness test and AAT- Arithmetic ability test, Values of scores are expressed as mean ± standard deviation, Test- Wilcoxon signed rank test.

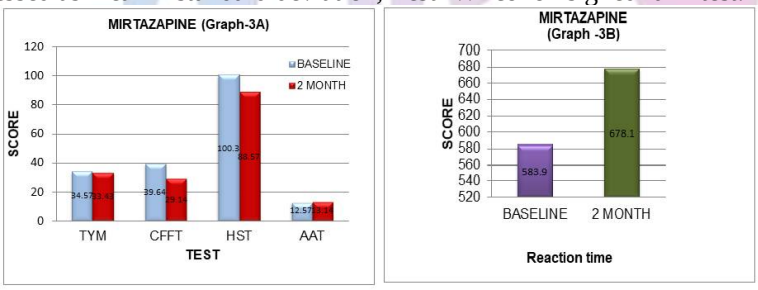


Figure 3: Intragroup analysis of mirtazapine on test your memory (TYM), critical flicker fusion test (CFFT), hand steadiness test (HST), arithmetic ability test (AAT) and reaction time (RT) scores (n=7)

TYM - Test your memory, CFFT - Critical flicker fusion test, HST-Hand steadiness test and AAT- Arithmetic ability test, Values of scores are expressed as mean ± standard deviation, Test- Wilcoxon signed rank test.

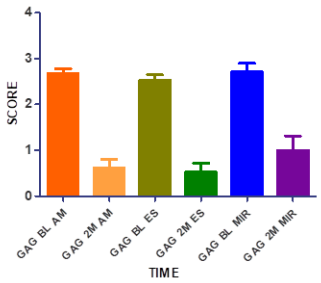


Figure 4: Global antidepressants grade efficacy of amitriptyline, escitalopram and mirtazapine

DISCUSSION

The present study was framed to evaluate and compare the effect on cognitive and psychomotor performance of amitriptyline (TCA), escitalopram (SSRI) and mirtazapine (NASSA) in the treatment of depression. The lack of head to head comparison studies of these antidepressants belonging to different categories, prompted us to go for such a study. The study was open label, prospective observational study carried out in patients suffering from depression. Standardized tests used to assess psychomotor effect were Test your memory test for evaluation of memory and cognitive effect was assessed in the form of central integration and processing mechanism by using critical flicker fusion test, Arithmetic ability test, motor response was assessed by hand steadiness test, central integration and motor responses using reaction time, subjective components were assessed by global score for assessment and grading of depression for antidepressant efficacy of amitriptyline, escitalopram and mirtazapine drugs as judged by treating psychiatrist. Patients were evaluated at the time of enrolment and at 8 weeks (2 months) post treatment. Amitriptyline group: Within group analysis, amitriptyline had statistically significant decrease in critical flicker fusion score but was not clinically relevant. No statistically significant change in memory, hand steadiness, arithmetic ability test and reaction time. Hand steadiness showed improvement in performance. In the McNair DM *et al*[13] study, double-blind to equipotent doses of amoxapine or amitriptyline in a 12-week double-crossover of 3-week periods of active agent and placebo. The above study showed amitriptyline was associated with faster reaction time and reduced accuracy on attention tasks and impaired long-term memory. In present study amitriptyline impaired accuracy in attention tasks like critical flicker fusion test score, improvement in hand steadiness score and reaction time was seen, although statistically not significant. Spring B et a1[15] Study here, depressed outpatients received double-blind placebo (n = 15), amitriptyline (n = 10), or clovoxamine fumarate (n = 10), a serotonin reuptake inhibitor. The above study showed that amitriptyline impaired performance on test of memory producing a significant decrement. They also mention that this impairment could be due to anticholinergic property of amitriptyline. The results of the present study were not in accordance with results of the above study, we felt that it was may be due to the evaluation of memory at different time intervals i.e. 4 weeks in the above study was having less sample size (n=10) whereas in the present study memory was evaluated at 8 weeks having sample size(n=22). J. S. Kerr *et al*[15] study was a double- blind 10-way crossover study. The volunteers received reboxetine 0.5 mg, 1 mg or 4 mg, amitriptyline 25 mg or matched placebo. The above study demonstrates that amitriptyline decreased critical flicker fusion threshold and increased reaction time and slowed short term memory. In present study also amitriptyline lowered critical flicker fusion score, but no effect on reaction time. Reason-may be due to different population and evaluation time i.e. in the above study only healthy volunteers were evaluated at 9 hours and in present study patients with depression were evaluated at 8 weeks. In Iwamoto K *et al*[16] in this double-blinded, 3-way crossover trial, 17 healthy males received acute doses of 10mg paroxetine, 25mg amitriptyline, and placebo. Above study showed that amitriptyline significantly impaired psychomotor performance in the form impaired road tracking and car-following performance. In the present study there was impaired psychomotor performance in the form of decreased critical flicker fusion test score, although clinically not relevant. Escitalopram group: Escitalopram had no statistically significant change in memory, critical flicker fusion test, hand steadiness, arithmetic ability and reaction time. Joshua D Rosenblat *et al*[17] Study was a review and meta-analysis to assess the pooled efficacy of antidepressants on various domains of cognition in MDD. The above study showed that escitalopram had a positive effect on psychomotor speed and delayed recall. With no statistical significance on cognitive control, but present study showed no significant effect on psychomotor and cognitive tests. Beheydt LL1 *et al*[18] in this study 28 non-demented elderly unipolar depressive patients on 5-20mg escitalopram were compared to 20 matched healthy elderly through three months escitalopram treatment on Cognitive and psychomotor. The above study showed that escitalopram did not affect cognitive and psychomotor performance. In present study also showed no impairment of Cognitive and psychomotor function. Zhenhe Zhou *et al*[19] in this study author detected the event-related potential mismatch negativity (MMN) of 30 depression patients and compared to 30 age, gender, and education-matched healthy controls. The above study showed that impairment of cognitive function with escitalopram but present study shows no such effect. Mirtazapine group: Mirtazapine group which was having small sample size of 07 although showed the tendency to decrease memory score and increase clinically relevant reaction time with some drop in the critical flicker fusion test, none of these changes are statistically significant. No meaningful conclusions can be drawn because of the power < 80% on all parameter and high number of dropouts in this group. Ramaekers JG *et al*[20] study showed that mirtazapine impaired psychomotor performance in the form of car-driving present study results also showed impairment on psychomotor

performance but this could not be concluded because of less power due to high dropouts. Analysis between the two groups showed that escitalopram and amitriptyline were equivalent for all parameters (TYM, CFFT, HST, AAT and reaction time) at the end of 2 months. The comparison between mirtazapine and other two groups had shown no significant results but conclusion cannot be drawn because of high dropout and less power of mirtazapine group. The results of amitriptyline and escitalopram group in the present study were similar to those evidenced in previous studies. Antidepressants efficacy of study drug i.e. amitriptyline, escitalopram and mirtazapine: Global score for antidepressant efficacy as judged by treating psychiatrist as no depression, mild, moderate and severe were scored as 0, 1, 2 and 3 respectively. All the three drugs were independently efficacious at the end of two months ($p \leq 0.05$) but antidepressant efficacy for amitriptyline and escitalopram were highly significant while that of mirtazapine was significant. In present study, Global score for antidepressant efficacy as judged by treating psychiatrist of all the three drugs were independently efficacious at the end of two months($p \leq 0.05$) but antidepressant efficacy for amitriptyline group and escitalopram group were highly significant while that of mirtazapine group was significant. Anand Mathur *et al*[21] study –A Double blind clinical trial comparing escitalopram with amitriptyline in India. To evaluate the efficacy and safety of the newer antidepressant escitalopram in the treatment of major depression. The above study showed that escitalopram was effective in the treatment of major depression and its efficacy was equivalent to that of standard tricyclic antidepressants such as amitriptyline similar to the results of the present study. Anand Mathur *et al*[(22)] study was a clinical trial undertaken to evaluate the anti-depressant efficacy of newer antidepressant mirtazapine in the treatment of major depression in 39 patients as compared to that of amitriptyline. The above study showed that mirtazapine was effective in the treatment of major depression and it had efficacy equivalent to that of the amitriptyline similar to the results of the present study. Leinonen E *et al*[23] - Study aimed to compare the antidepressant and anxiolytic effects, tolerability and effects on quality of life of mirtazapine and Ecitalopram in a randomized, double-blind, multicentre, 8-week study. In this study, mirtazapine and Ecitalopram were equally effective in reducing symptoms of depression and anxiety. In the present study also both the drugs were equiefficacious. Adherence of antidepressant regimen: Adherence score as assessed by Morisky 8-item medication adherence questionnaire at end of two months of Amitriptyline and escitalopram, which were less than low adherence and mirtazapine which was very less than low adherence. Compared to amitriptyline and escitalopram, adherence score of mirtazapine was inferior to both. Shigemura J *et al*[24] Conducted a Internet-based survey among 1151 Japanese individuals with major depressive disorder. Adherence was similar between those on selective serotonin reuptake inhibitors/serotonin-noradrenaline reuptake inhibitors and tricyclics, in present study also adherence score as assessed by Morisky 8-item medication adherence questionnaire at end of two months of Amitriptyline and escitalopram, which were less than low adherence and mirtazapine, which was very less than low adherence. Amitriptyline and escitalopram showing similar adherence with no significant difference which was in accordance with above study. But Compared to amitriptyline and escitalopram, adherence score of mirtazapine was inferior to both.

Limitations

Results of the present study need cautious interpretation as number of patients in mirtazapine group is less.

Implications

a) Results of our study were helpful to choose the safest drug i.e. drugs affecting psychomotor function minimally, for the treatment of depression.
b) Results of this study were also guide psychiatrist to choose the drug affecting cognitive functions minimally.

SUMMARY AND CONCLUSIONS

Present study suggests that amitriptyline impairs the critical flicker fusion score but impairment is not clinically significant, but it was safe on all parameters. Escitalopram was safe for all parameters and does not have any adverse effect on all the psychomotor and cognitive functioning of the brain. In case of mirtazapine, there was a tendency to impair memory, critical flicker fusion threshold and reaction time but these findings need to be explored in separate set of studies. The reasons for the high dropout and low adherence in mirtazapine group needs to be investigated separately. When compared with each other amitriptyline and escitalopram were equiefficacious as antidepressant. Amongst escitalopram and amitriptyline choice depends on patient's profile and requirement of sedation.

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