ORIGINAL RESEARCH PAPER

Pharmacology

A PROSPECTIVE RANDOMISED OPEN LABEL COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ESCITALOPRAM VERSUS SERTRALINE IN MAJOR DEPRESSIVE DISORDER IN A TERTIARY CARE HOSPITAL

KEY WORDS: Depression, Escitalopram, Sertraline, HAM-D Score

Dr.Sharmi.V.J Asst Professor, Department of Pharmacology, Government Vellore Medical College Vellore.

Dr.K.Vijayarani* Associate Professor, & HOD ,Department of Pharmacology, Government Chengalpattu Medical College Chengalpattu.* Corresponding Author

ABSTRACT

BACKGROUND: Depression is a common mental illness affecting people irrespective of sects or area. Recent hike in incidence mandates the requirement of research in this disorder to find out the best possible treatment option among the antidepressant drugs with minimal side effects to ensure compliance to avoid the consequence of impaired quality of life and poor treatment schedules many times culminating in suicides. Aim: To compare efficacy and safety of Escitalopram and Sertraline in major depressive disorder. **Materials and Method:** 120 patients recruited, randomized to receive Escitalopram or Sertraline for 12 weeks . Hamilton depression rating scale at baseline, 12 weeks as a measure of efficacy. Safety assessed by adverse drug reaction reported and laboratory parameters. **Results:** Reduction of mean HAM-D score from 20.77 at baseline to 8.75 with Escitalopram, 20.96 to 8.65 with Sertraline. Statistically significant HAM-D score reduction within groups, but not between groups. Statistically significant (P=0.007) adverse reactions to sertraline than escitalopram. **Conclusion:** Both Escitalopram and Sertraline appropriate as first line drugs for MDD. Escitalopram was better tolerated .

INTRODUCTION: Depression is a long term health issue, recurrent, with remission and relapses ,ultimately results in suicide, and affecting people of all sectors. Major depressive disorder has significant impact on individual's quality of life. Selective serotonin reuptake inhibitors (SSRIs) drug of choice (1).But the variations within this class of drugs is not known(2). Hence this study aims to compare SSRIs.. MDD is diagnosed if any of the 5 out of the 9 symptoms described in DSM V (Diagnostic and Statistical Manual of Mental Disorders) is present. Major complication of depression is suicide.

HAM-D 17 (Hamilton Depression rating scale) used to measure depression severity .Severity is assessed before initiating therapy. Severity range by HAM-D score - 0-7 – Nil; 8-16-Mild; 17-23-Moderate; ≥24-Severe. On treatment, Score ≤7 for 2 consecutive weeks – remission. Relapse is reappearance of symptoms after remission(3). Recovery is remission for 6 consecutive months(4) ≥50% score reduction from baseline is responders, remitters ≤7 points on a post-baseline assessment(5)

Antidepressants - SSRIs, SNRIs, TCAs block NET, SERT (Norepinephrine or Serotonergic transporter, increase noradrenergic or serotonergic neurotransmission. Neurotransmitter receptor hypothesis in depression explains the time lag before therapeutic effect (6) SSRIs are the main stay of treatment for MDD(1). SSRIs have better tolerability, reduce 50% symptoms in 6-8 weeks . Mono Amine Oxidase Inhibitors(MAOIs) produce Serotonin Syndrome(7). Hyponatremia occurs in 0.5% to 32%, resolves on stopping SSRI in 2 weeks (8). SSRIs with shorter halflife produce "discontinuation syndrome"on sudden withdrawal after 6 weeks use. Both Escitalopram, S-enantiomer of citalopram and sertraline are SSRI. Escitalopram, first-line for MDD(9). Escitalopram and sertraline well tolerated in therapeutic dose. Pharmacotherapy is preferred in Severe depression. In poor responders treatment optimized with increased dose of antidepressant, adding ECT/second antidepressant. Continuation phase is to maintain response achieved . Patients are monitored for relapses after discontinuation.

MATERIALS AND METHODS: A Prospective, randomized, open labelled, study to compare the efficacy and safety of antidepressants escitalopram and sertraline in 120 patients for 3 months in Newly diagnosed Drug naive major depressive disorder patients attending Psychiatry Department of Chengalpattu Medical College and Hospital. After IEC approval and written informed consent, patients of 18- 60 years, both genders, recruited, screened, 120 enrolled, by simple randomization assigned to receive Tab. Escitalopram 10mg-20 mg or Tab. Sertraline. 50- 200mg .Dose titrated based on response after 4 weeks of continuous therapy.

Demographic details , history, Clinical examination, screening with HAM-D scale , lab investigations done at baseline and at end of 12 weeks. Both groups followed up for efficacy and safety.

RESULTS: Data analyzed using SPSS software 21 version according to per protocol analysis. 95% escitalopram , 91% sertraline group completed 12 weeks study (p=0.8). Hence the 112 patients who completed the 12 week study were analysed as follows.Percentage distribution of age and Gender by chi-square test, mean age distribution by student independent t'- test. No significant statistical difference in percentage age distribution between the groups. Sex distribution showed female predominance in both the groups.

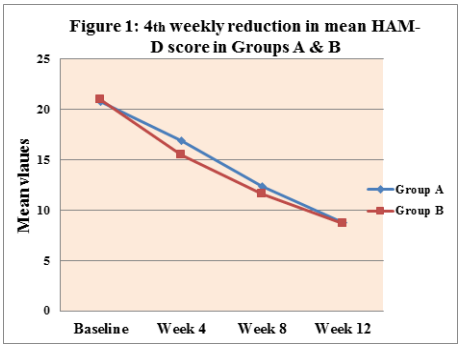

Figure 1 shows Baseline Severity of depression – distribution comparable between groups ,there is no significant difference by student independent t-test between the groups.

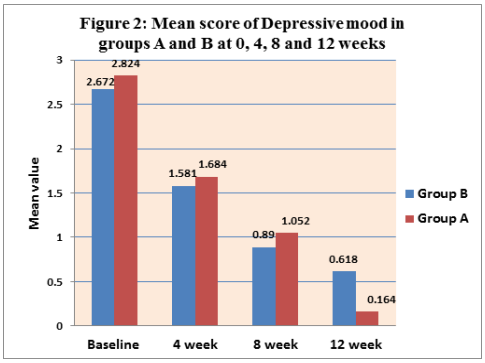

Figure 2 analysis of Depressive mood in HAM-D score within group by ANOVA is statistically significant difference within the group, but not significant between the groups.

TABLE 1 : NUMBER OF ADR IN GROUPS A & B

Groups	Adverse events		Total	Chi-square value	P value
	Present	Absent			
Group A	6	51	57	7.126	0.007
Group B	17	38	55		

Table 1.shows statistically significant difference in number of reported adverse events between group A & B as assessed by chi-sq test.

DISCUSSION: Attrition due to drop out was 5% in test group and 8% in control group. Study groups were comparable in Demographic characteristics. Data tabulated showed increase in prevalance of depression with age and in females 72% in group A and 67% in group B ,similar to prevalence studied by Maier et al(10).

HAM-D scoring distribution of grades of severity were comparable at baseline. After treatment with Escitalopram 10-20mg/day in group A. Sertraline 50-200mg/day in control group B, response assessed by HAM-D Scoring at 4,8,12 weeks. Dose titrated in 30% in escitalopram 38% in sertraline group. The mean baseline HAM-D score was 20.77 in group A and 20.96 in group B. difference was not statistically significant. Significant ($p<0.001$)reduction in depression score within group analysis from baseline till end of study period in both groups confirms that antidepressants take time to produce clinical benefit. Comparison between groups show equivalent therapeutic efficacy of drugs used in study and active control groups .

19% in escitalopram group , 24% in sertraline group reduction in score not achieved , but as per American Psychiatric Association, guidelines patient can be termed non responders only after continuous therapy for 6 months. Yet clinical trials suggest that three months therapy is adequate to ascertain efficacy Early response in terms of improvement in somatic symptoms of HAM-D, is predictive of achieving remission with active treatment but were not done due to limited study period.

Mild adverse effects headache followed by nausea, insomnia, diarrhoea and sexual dysfunction in sertraline group. Among escitalopram group headache and nausea had equal incidence followed by insomnia and sexual dysfunction Adverse effects in sertraline group statistically significant (P=0.007). higher than escitalopram group . No treatment emergent suicides. No serious adverse events, drop outs were due to other reasons.

Limitations: Smaller number of patients and short duration of study period. As Current guidelines to treat depression recommends 6-9 months anti depressant therapy, and follow up 6 to 9 months after achieving remission. is needed to compare efficacy of these drugs in preventing relapses requiring further studies. Effect of treatment on quality of life need to be analyzed further .Health care costs impacted by these drugs need to be

CONCLUSION

- Both Escitalopram and Sertraline are appropriate as first line drugs to treat depression.
- Efficacy profile was identical, but Escitalopram, the test drug is found to be Non inferior to the control Sertraline as measured by response (81% vs 76%) and remission rates (56% vs 54%)
- Escitalopram was better tolerated with statistically significantly less number of reported adverse events than sertraline.

REFERENCES

1. Ogle WO, Speisman RB, Ormerod BK. Potential of Treating Age-Related Depression and Cognitive Decline with Nutraceutical Approaches: A Mini-Review. Gerontology. 2013;59(1):23–31.
2. Kroenke K, West SL, Swindle R, Gilsenan A, Eckert GJ, Dolor R, et al. Similar Effectiveness of Paroxetine, Fluoxetine, and Sertraline in Primary Care: A Randomized Trial. JAMA. 2001 Dec 19;286(23):2947–55.
3. Gautam S, Jain A, Gautam M, Vahia VN, Grover S. Clinical Practice Guidelines for the management of Depression. Indian J Psychiatry. 2017 Jan;59(Suppl 1):S34–50.
4. Al-Harbi KS. Treatment-resistant depression: therapeutic trends, challenges, and future directions. Patient Prefer Adherence. 2012 May 1;6:369–88.
5. Versiani M, Moreno R, Ramakers-van Moorsel CJA, Schutte AJ, Comparative Efficacy Antidepressants Study Group. Comparison of the effects of mirtazapine and fluoxetine in severely depressed patients. CNS Drugs. 2005;19(2):137–46.
6. Stahl SM. Stahl's Essential Psychopharmacology. 4 edition. Cambridge University Press; 2013. 628 p.
7. Trevor BGKAJ, Katzung BG. Basic and Clinical Pharmacology 13th/2015. Mc Graw Hill; 2015.
8. Jacob S, Spinler SA. Hyponatremia associated with selective serotonin-reuptake inhibitors in older adults. Ann Pharmacother. 2006 Sep;40(9):1618–22.
9. Garnock-Jones KP, McCormack PL. Escitalopram : A Review of its Use in the Management of Major Depressive Disorder in Adults (Adis Drug Evaluation). CNS Drugs. 2009;24(9):769–96.
10. Maier W, Gänsicke M, Gater R, Rezaki M, Tiemens B, Urzúa RF. Gender differences in the prevalence of depression: a survey in primary care. J Affect Disord. 1999;53(3):241–52.