International Journal of Basic & Clinical Pharmacology
Dhanalakshmi R et al. Int J Basic Clin Pharmacol. 2025 Sep;14(5):786-790
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20252577

Original Research Article

A comparative analysis of fluoxetine and amitriptyline in depression: assessing effectiveness and adherence in a rural hospital setting

Dhanalakshmi R.[1]*, Arunkumar K.[2], Thaslim Ridhwana Barakath Ali[3], Pari K.[3], Surya R.[3]

[1]Department of Pharmacology, E. G. S. Pillay College of Pharmacy, Nagapattinam, Tamil Nadu, India
[2]Department of Psychiatry, Government Medical College and Hospital, Nagapattinam, Tamil Nadu, India
[3]Department of Pharmacy Practice, E. G. S. Pillay College of Pharmacy, Nagapattinam, Tamil Nadu, India

Received: 13 June 2025
Revised: 12 July 2025
Accepted: 15 July 2025

***Correspondence:**
Dr. Dhanalakshmi R.,
Email: medresearchgroup25@gmail.com

ABSTRACT

Background: Fluoxetine and amitriptyline are commonly prescribed antidepressants. However, the superior option in terms of effectiveness and adherence remains unclear. Medication non-adherence significantly impacts treatment outcomes. This study aims to compare the two drugs in terms of effectiveness and adherence, and to assess their correlation.

Methods: This is a single-centered, prospective observational study, conducted in the psychiatric outpatient department (OPD) of the Government Medical College and Hospital, Nagapattinam, over six months (23 July 2024 to 22 January 2025). It included 126 patients newly diagnosed with depression. Patients receiving either fluoxetine or amitriptyline were enrolled. Effectiveness was measured using the 17-item Hamilton depression rating scale (HAM-D), calculating score reduction from baseline to endpoint. The four-item Morisky scale (MMAS-4) was applied to assess the medication adherence of the participants. Data were analysed with statistical package for the social sciences (SPSS) version 24, applying descriptive analysis, independent t-test and Pearson correlation as appropriate.

Results: Depression was more prevalent among women. Most participants were married and unemployed. Fluoxetine showed a greater mean reduction in HAM-D scores compared to amitriptyline. It also demonstrated higher medication adherence. A statistically significant positive correlation between effectiveness and adherence was observed for both drugs.

Conclusions: Better clinical outcomes were associated with higher medication adherence. Fluoxetine was superior to amitriptyline in both effectiveness and adherence. These findings highlight the importance of adherence in improving depression treatment outcomes.

Keywords: Depression, Fluoxetine, Amitriptyline, Adherence, MMAS-4, HAM-D-17

INTRODUCTION

Depression is a prevalent, debilitating emotional disorder, affecting 322 million people globally, increasing morbidity, mortality, and economic burden.[1,2] Despite its severity, depression often remains undiagnosed and untreated.[3] Fluoxetine, a selective serotonin reuptake inhibitor, and amitriptyline, a tricyclic antidepressant, are commonly prescribed treatments, but both require one to two weeks to show effect.[4,5] Medication adherence is crucial for achieving therapeutic success, yet only 50% of people maintain it.[6]

These concerns led to this study, which aims to observe the improvement in depressive symptoms, i.e., the effectiveness of the drug and patient medication adherence in a real-world medical setting.

METHODS

After obtaining institutional ethical committee approval, the study was carried out in the psychiatric outpatient department of the Government Medical College and Hospital, Nagapattinam, for a period of 6 months (23 July 2024 to 22 January 2025). This study was a pre-designed single-centered, prospective, observational study with a sample size of 126 patients. The sample size for this study was determined based on the number of patients diagnosed with depressive disorder presenting to the outpatient department of psychiatry. The patients were further divided into two groups; group A was given fluoxetine and group B was given amitriptyline.

The participants selected for observation were those who were newly diagnosed with depression, prescribed treatment of either fluoxetine or amitriptyline, and who agreed to sign the informed consent form. Patients of both genders, ranging from 20 to 60 years of age, were included. Patients who are already on medication of fluoxetine or amitriptyline, patients prescribed both fluoxetine and amitriptyline concomitantly, and patients who disagreed to sign the informed consent form fall under the exclusion criteria of this study.

Every participant was presented with a questionnaire of the 17-item Hamilton depression rating scale (HAM-D) when they were initially diagnosed with depression. The responses obtained from the participants were used to assess the severity of their depressive symptoms based on HAM-D scores (baseline). HAM-D scores were calculated using the standardized scoring instructions of the HAM-D scale. The subjects studied were followed up for eight weeks. After eight weeks of antidepressant treatment, the questionnaire was again presented to receive participants' responses over the therapy (end-point). The effectiveness of the individual medicine was studied by evaluating the reduction in the HAM-D scores from baseline to the endpoint. The medication adherence of the patients was also studied at the eighth week of treatment using the 4-item Morisky medication adherence scale (MMAS-4) questionnaire with a standard scoring method.[7-9]

The data collected was compiled in an Excel sheet. Results were obtained by several statistical tests, including descriptive statistics, independent t-test, and Pearson's coefficient. The statistical analysis was carried out using statistical package for the social sciences (SPSS) software of 2024.

RESULTS

Among the 126 patients recruited, everyone completed the eight-week treatment with no dropouts. The gender distribution between patients identified 42% of them to be males and 58% females. The age-wise distribution reveals 4% of subject fall under the age category of 20-29, 33% patients are within 30-39 years of age, majority of 34% are among 40-49 years old, and 29% range from 50 to 60 years. This study reported 67% of people were married, 14% unmarried, 13% widows, and 6% divorced.

There is a significant variation in the mean difference and standard deviation of reduced HAM-D scores analyzed by the independent t-test, between group A and group B patients. The p value is 0.044 and 95% confidence interval. The mean reduction is greater in fluoxetine [8.70] than in amitriptyline [7.24]. This denotes, subjects administering fluoxetine show higher improvement in their depressive symptoms, thereby proving its greater effectiveness.

There is a significant variation in the mean and standard deviation of patient medication adherence between the two groups under the treatment of fluoxetine and amitriptyline, respectively. The p value is 0.0016 with a 95% confidence interval. The results denote better adherence among people administering fluoxetine when compared to amitriptyline.

The Pearson's coefficient value correlating HAM-D score reduction and adherence in the group A subjects is 0.667, and in the group B subjects is 0.865. Both values confirm the positive correlation between the effectiveness of the drug and patient medication adherence, with the p value of 0.000 for both groups.

Table 1 discusses the demographical distributions of the participants involved in this study. According to this data, incidence of depression tends to be higher in females. Age group from 40-49 are highly affected. Married patients and unemployed members are affected highly by depression.

Table 1: Demographical data representing the participants of the study.

Demographic-al data of the participants	Fluoxetine partici-pants	Amitrip-tyline partici-pants	Percen-tage
Gender			
Male	25	28	42
Female	38	35	58
Age (years)			
20-29	3	2	4
30-39	20	22	33
40-49	22	21	34
50-60	18	18	29
Marital status			
Married	43	42	67
Unmarried	10	8	14
Widow	8	8	13
Divorced	2	5	6
Employment status			
Employed	30	27	45
Unemployed	33	36	55

The reduced mean of fluoxetine is greater than the reduced mean of amitriptyline with a significant p value of 0.044.

This result support fluoxetine in their relatively better effectiveness (Table 2).

When comparing two groups of people, the mean of better medication adherence is greater among those administering fluoxetine. The p value 0.0016 shows the statistical significance of this result (Table 3).

Figure 1 shows a positive correlation between the effectiveness of the drug and adherence among subjects administering fluoxetine.

Table 2: Comparison of endpoint effective analysis of group A and group B.

17-item HAM-D scores (n=126)	Group – A (fluoxetine)		Group – B (amitriptyline)	
	Mean	Standard deviation	Mean	Standard deviation
Baseline	21.98	4.814	22.14	4.439
Endpoint analysis	13.29	5.389	7.24	4.362
Reduced mean and standard deviation	8.70±3.675		7.24±4.362	

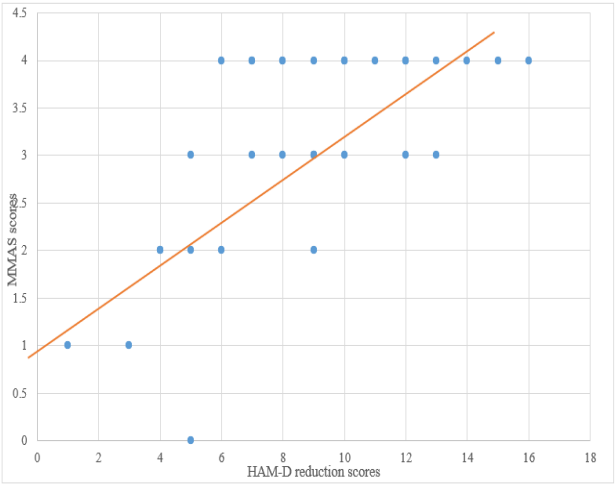

Figure 1: Scatter plot correlating baseline-endpoint reduction and adherence among subjects of fluoxetine group.

Figure 2 shows a positive correlation between the effectiveness of the drug and adherence among subjects administering amitriptyline.

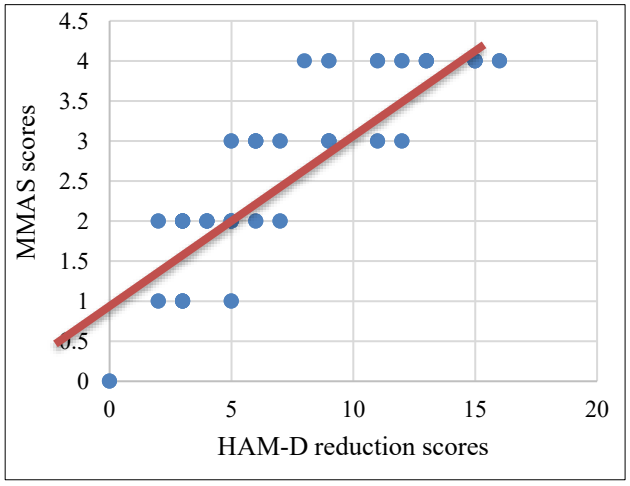

Figure 2: Scatter plot correlating baseline-endpoint reduction and adherence among subjects of amitriptyline group.

Table 3: Comparison of patient medication adherence in group A and group B.

MMAS-4 item scores (n=126)	Mean	Standard deviation
Group A (fluoxetine)	3.08	1.082
Group B (amitriptyline)	2.60	1.115

DISCUSSION

Though the findings of this study develop a hypothesis on the distribution of depression among individuals, depression tends to be a behavioral disorder conquering the minds of several individuals irrespective of gender, age, employment status and marital status.

After surveying 34,802 depressed patients across twelve states of India, Aravind et al discovered women between 40-59 years had the highest prevalence of depression, which correlates with the findings of this study. Of 126 individuals participated, 58% belonged to female category.[10] Nevertheless, the findings of Zang et al in his study involving randomly selected 1428 elderly adults failed to reveal any relationship between gender and depressive symptoms.[11]

Torre et al reported age groups between 45 to 59 experience high rate of depression when studied the prevalence and age distribution in United Kingdom whereas Aravind et al discovered women between 40-59 years had the highest prevalence in depression according to his multisite research on prevalence and socioeconomic factors in India.[10,12] Both this finding somewhat relates to this study. Of the 126 individuals diagnosed with depression, females between 40-49 years and males between 30-39 years shows greater incidence of depression.

Though 55% of individuals included in our study tends to be unemployed, employed individuals who cover the remaining 45% was also affected by depressive disorder challenging the relation between work status and depression. This study's findings, unemployment individuals experience higher incidence of depression was

validated by the study conducted by Rizvi et al using two sizable databases of Canada for studying the depression and work status in primary entertainment care setting of Canada. Rizvi et al reveals relationship between depression and unemployment.[13]

Jia et al investigation on the link between depressive symptoms and marital status among 15,586 middle aged and older natives of China led to the finding that married population is less likely affected by depression.[14] However, our study's findings contradict the above-mentioned investigation by informing 67% of depressed patients were married, 14% unmarried, 13% widow and 6% divorced.

Answer for the superior one among Fluoxetine and amitriptyline, in terms of efficacy, has always been in dilemma. Some studies point fluoxetine; some points out amitriptyline, and some studies show equal efficacy in both these drugs. Sandanapitchai et al is one of the researchers who conducted a study to compare the efficacy of fluoxetine and amitriptyline in two group of people administering fluoxetine and amitriptyline respectively. Both groups contained 40 depressed patients. The student t-test was utilized to analyze the data, and the results obtained were not statistically significant. This study arrived at a conclusion that both fluoxetine and amitriptyline are equally efficacious.[2] Similar conclusions was obtained by Laakmaan et al and Hosak et al.[15,16] Lader reviewed certain studies. Two among them showed amitriptyline to be superior in efficacy with marginally significant results and one proved fluoxetine to be the superior one.[17] However in this study involving 126 patients (63 receiving fluoxetine and 63 receiving amitriptyline) fluoxetine was identified to be the superior one with statistical significance.

Demyttenaere et al studied the pattern of adherence in patients receiving amitriptyline or fluoxetine for depression therapy. Sixty-six patients were included in this nine-week double blind RCT. This study identified that Hamilton score was significantly lowered in patients receiving amitriptyline who followed better treatment adherence and longer duration of treatment. Unfortunately, no such trends were observed in patients receiving fluoxetine.[18] The contradiction began when our study showed positive linear regression between both the treatment group's final HAM-D scores and MMAS scores, associating effectiveness of the drug and patient adherence in real life practice. This investigation also revealed amitriptyline had the higher risk of severe adverse events and dropout rate. Despite no dropouts among these 126 patients, agreement with the results of Demyttenaere was found when our study's result showed better adherence among people administering fluoxetine.

These strong conclusions are yet to be evaluated as this study involves certain limitations like the involvement of depressed patients only in our locality (single-centered study), self-reported adherence, minimum exploration in the reasons of medication non-adherence and lack of MMAS-8 item scale use.

CONCLUSION

The primary motto of this study was to enhance scientific and clinical knowledge, by evaluating and comparing the two antidepressants, amitriptyline and fluoxetine in terms of effectiveness and patient medication adherence. Despite the noticeable reduction in HAM-D scores of patients receiving either fluoxetine or amitriptyline, the real-life evidences and statistical analysis proved fluoxetine to be superior. The extent of patient medication adherence was also greater in the group of 63 administering fluoxetine. The importance of medication adherence still remains under the rag among most of the public. Positive correlation between the effectiveness of the drug and the patient adherence is proved through this study, highlighting the importance of medication adherence to achieve appropriate therapeutic outcomes. This study also enhances our knowledge by highlighting the importance of medication adherence in effective treatment outcome. Continuous monitoring and promoting the awareness of medication adherence must be strictly regulated to achieve better outcomes even in psychiatric patients.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. S. Lakshmi Sabapathy, Pharm. D., Associate Professor, E. G. S. Pillay College of Pharmacy, for his mentorship and unwavering support throughout study. They would also like to thank Dr. Donald Morisky for his invaluable contributions to the field of medication adherence research, particularly the development of the MMAS-4 item scale which played an important role in enriching this research. Finally, they are thankful to Mr. Philip Morisky for kindly granting the permission to use the MMAS-4 item scale for this research purpose.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Vashisht E, Singh G, Vats V, Dhiman A, Singla C. An update on epidemiology of depression: a major concern. Ann Rom Soc Cell Biol. 2021:616-24.
2. Sandanapitchai V, Ramasamy S, Pichai E. Prospective study to evaluate the efficacy of fluoxetine in comparison with amitriptyline in patients with depression. Int J Basic Clin Pharmacol. 2016;5(6):2552-5.
3. Iyer K, Khan ZA. Depression – a review. Res J Recent Sci. 2012;1(4):79-87.
4. Lexicomp. Fluoxetine: drug information. 2024. Available at: https://online.lexi.com/lco/action/doc/

retrieve/docid/multinat_f/4669729. Accessed on 28 October 2024.
5. Lexicomp. Amitriptyline: drug information. Lexicomp Online. Wolters Kluwer Clinical Drug Information, Inc. 2024. Available at: https://online.lexi.com/lco/action/doc/retrieve/docid/multinat_f/4668901. Accessed on 29 October 2024.
6. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. Oman Med J. 2011;26(3):155-9.
7. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence and long-term predictive validity of blood pressure control. Med Care. 1986;24(1):67-74.
8. Morisky DE, Malotte CK, Choi P, Etrata R, Davidson P, Rigler S, et al. A patient education program to improve rate with antituberculosis drug regimens. Health Educ Q. 1990;17:253-68.
9. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: final response. J Clin Epidemiol. 2011;64(3):262-3.
10. Arvind BA, Gururaj G, Loganathan S, Booth A, Sathyanarayana Rao TS, Kokane AM, et al. Prevalence and socioeconomic impact of depressive disorders in India: multisite population-based cross-sectional study. BMJ Open. 2019;9(6):e027250.
11. Zhang B, Li J. Gender and marital status differences in depressive symptoms among elderly adults: The roles of family support and friend support. Aging Ment Health. 2011;15(7):844-54.
12. Arias de la Torre J, Vilagut G, Ronaldson A, Serrano-Blanco A, Fernandez A, Dregan A, et al. Prevalence and age patterns of depression in the United Kingdom: a population-based study. J Affect Disord. 2021;279:164-72.
13. Rizvi SJ, Cyriac A, Grima E, Tan M, Lin P, Gallaugher LA, et al. Depression and employment status in primary and tertiary care settings. Can J Psychiatry. 2015;60(1):14-22.
14. Zhao L, Zhang K, Gao Y, Wu J, Wang Y, Chen Y, et al. The relationship between gender, marital status and depression among Chinese middle-aged and older people: mediation by subjective well-being and moderation by degree of digitization. Front Psychol. 2022;13:923597.
15. Laakmann G, Blaschke D, Engel R, Jahnke S, Wittchen HU, Essau C. Fluoxetine vs amitriptyline in the treatment of depressed out-patients. Br J Psychiatry. 1988;153(3):64-8.
16. Hosák L, Tůma I, Hanuš H, Libiger J, Beran V. Costs and outcomes of use of amitriptyline, citalopram, and fluoxetine in major depression: exploratory study. Acta Med (Hradec Králové). 2000;43(4):133-6.
17. Lader M. Fluoxetine efficacy vs comparative drugs: an overview. Br J Psychiatry. 1988;153(3):51-8.
18. Demyttenaere K, Mesters P, Boulanger B, Despiegel N, Dewe W. Adherence to treatment regimen in depressed patients treated with amitriptyline or fluoxetine. J Affect Disord. 2001;65(3):243-52.

Cite this article as: Dhanalakshmi R, Arunkumar K, Ali TRB, Pari K, Surya R. A comparative analysis of fluoxetine and amitriptyline in depression: assessing effectiveness and adherence in a rural hospital setting. Int J Basic Clin Pharmacol 2025;14:786-90.