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Comparative study of efficacy of amitriptyline and fluoxetine in patients presenting with mixed anxiety and depression

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Abstract
Aim: To analyse the comparative study of efficacy and tolerability of amitriptyline and fluoxetine in patients presenting with Mixed-Anxiety and Depression.
Introduction: Mixed anxiety and depression is a condition where both the symptoms of anxiety and depression are present. Globally, depression is the top cause of illness and disability among young and middle-aged populations, while suicide ranks second among causes of death for the same age groups. Depression increase the mrotality because it worsens many medical conditions such as cardiovascular disease and diabetes and increase risk of suicide.
Methodology: A prospective observational study was conducted for a period of 6 months in OPD of Jayanagar General Hospital, Bengaluru and BBMP Public health camps. Patient aged between 19-59 years with mixed anxiety and depression (as defined by ICD 10) were equally divided randomly in fluoxetine and amitriptyline groups. Patients assessment was done at 1st visit, 2nd week, 4th week and 8th week for efficacy and safety parameters such as HAM-A and HAM-D. Student t-test was performed on efficacy measure.
Results: In the total of 62 patients, 25 (40.32%) were male and 37 (59.68%) were female. On HAM-A the percentage improvement (reduction in the mean score) for fluoxetine group was and 92.37%, while that for the amitriptyline group was 89.21% on 8th week. HAM-D the percentage improvement (reduction in the mean score) for fluoxetine group was 92.34%, while in amitriptyline group 89.29% on 8th week.
Conclusion: Our study shows Fluoxetine apparently working faster than Amitriptyline. Fluoxetine being an SSRI claimed to be equally effective as TCA in treating Mixed Anxiety and Depression with least adverse effects and better tolerability.

Keywords: amitriptyline, Fluoxetine, anxiety, depression, mrotality

Introduction

More than one lakh lives are lost every year to suicide in India. Majority of studies note that around 90 % of those who die by suicide have a mental disorder. 1 Several studies reveal that the presence of anxiety and depressive disorder increases the risk of suicide attempts and completed suicide. Moreover, patients with severe anxiety and depression symptoms more often were recurrent attempters than patients with moderate symptoms. 2 Globally, depression is the top cause of illness and disability among young and middle-aged populations, while suicide ranks second among causes of death for the same age groups. 1 The risk is higher among the poor, homeless, the unemployed, persons with low education, victims of violence, migrants and refugees, indigenous populations, children and adolescents, abused women and the neglected elderly. 3 In India, it is estimated that 4.5% (i.e 57 million) of the population is suffering from depressive disorder, and 3.0% (i.e 3.8 million) from anxiety. Depressive disorders led to a total of 1 million (i.e 7.1%), and anxiety disorders led to a total of 35 lakh (i.e 2.5%) Years Lived with Disability (YLD) in 2015. 4 The basic obstacle in the treating anxiety and depression is that patient do not asked for helps from the institution responsible for protection of mental health as well as that many cases of anxiety and depression are not recognised in the primary health care institutions. Patients with anxiety and depression are often not in a state to correctly apply the prescribed pharmacological therapy which leads to cessation/disruption of therapy, in adequate treatement of depression, frequent hospitalizations, incapability to work and frequently feeling of suicide. 5 The better choice of drug for the treatment is necessary to cope all these conditions.

To overcome these shortcomings, a large number of newer antidepressants have been developed since 1980s. The most significant of these are the selective serotonin reuptake inhibitors (SSRIs). Though, none of the newer drugs has surpassed older tricyclic anti-depressants (TCAs) in overall efficacy, some patients not responding to one type of drug may respond to the other. 6 Though wide ranges of anti-depressants are prescribed in private practice, amitriptyline and fluoxetine are most commonly

used in the psychiatric outpatient department in government hospitals and Mental health camps conduted by BBMP for treating Mixed Anxiety and Depression, so they were selected to be candidate drug. Both are competitive to each other and we aim to compare the efficacy between these two drugs since fluoxetine is comparable to amitriptyline in all efficacy measure except HAM-D sleep factor. The principle of efficacy comparision is to rationalize the treatment and induce effective health outcome with least advervse effects in the government hospital setup.

Methodology

The prospective, observation study was conducted for a period of six month with the assistance of psychiatrist in the OPD of jayanagar general hospital and BBMP Public health camps. Patients with anxiety and depression having the target symptoms were selected. Then the patients were subjected to the questionnaire (i.e HAM-A and HAM-D as per the diagnosis) 7,8. Follow-up was done after every second week, fourth week (i.e 30 days) and eighth week (i.e 56 days). On every follow-up the patients were subjected to the questionnaire and also with Hogan Drug Attitude Inventory for the patient adherence which also helped to review the effects of the medication. A total of 3 follow-ups were done. Also the patient was reviewed in between and whenever the patient develops the adverse event or poor improvement on the medication.

Inclusion Criteria

1. OPD patients.
2. Prescription containing fluoxetine and amitriptyline.
3. Age group of 19-60 years of both sex.

Exclusion Criteria:

1. Prescription which does not contain fluoxetine and amitriptyline.
2. Pregnancy and lactation patients.
3. Patients with cardiac disease, diabetes mellitus, hypothyroidism, and obesity.
4. Acute or chronic renal problems.
5. Tuberculosis, HIV/AIDS, leprosy.

Patients are permitted to discontinue at any time during the study, and when the patient is found to develop another illness or worsening of existing illness or require additional drugs,
they are withdrawn from the study.

Discussion

Both amitriptyline and fluoxetine are effective for the treatment of Mixed anxiety and depression as shown by the statistically significant decrease in total score of HAM-A and HAM-D from baseline to the end point. It is likey to be due to decrease in depressive or anxiety disorders. On head to head comparision between these two anti-depressants, none of these two drugs was found to have statistically superior results. The clinical benefits obtained is faster for the fluoxetine group compared to amitriptyline group from week 2 to week 8. Although amitriptyline is more frequently associated with adverse effects than fluoxetine, no serious side effects were observed and both the agents were well tolerated.

62 patients of Mixed anxiety and depression were included in the study, 32.26 % patients were in the age group of 30-39 years, out of it majority were females (59.68%) than males (40.32%).

Epidemiological studies have clearly shown a higher prevalence of Mixed anxiety and depression disorder under the age group of 30-39 years. We have found that Mixed anxiety and depression is more in female than male. Also study by MM welshman and Molfson has shown the prevalence of depression is approximately twice more common in women than man by studying the epidemiological data on depression worldwide. 9 The difference in the efficacy between two groups was tested using student t-test and the results were statistically significant (P<0.05). The efficacy of the both drug was evaluated and found that the fluoxetine group had efficacy rate of 92.35% and 92.34% in HAM-A and Depression HAM-D respectively, which was slightly more than amitriptyline group 89.21% and 89.29% in the HAM-A and HAM-D respectively at 8 th week with p< 0.0001 and 95% CI of 1.363 to 0.9572. Our study had the small sample size and the canididate drugs were the drug which was supplied freely by government.

Conclusion

Our study shows that both Amitriptyline and Fluoxetine are significantly effective in treating Mixed Anxiety and Depression. Fluoxetine apparently working faster than Amitriptyline. We have found Amitriptyline was prescribed more than Fluoxetine in severe cases as per the analysis of HAM-D. Amitriptyline appears to be associated with adverse effects more frequently than Fluoxetine. Though the efficacy of Amitriptyline is well established in severe depression, its usages have declined because of its adverse effects. Fluoxetine being an SSRI claimed to be equally effective as TCA in treating Mixed Anxiety and Depression with least adverse effects and better tolerability.

Table 1: Comparision of reduction of HAM-D score between Amitriptyline and Fluoxetine treatment group from graphpad prism

Reduction of HAM-D Score	t-test	df	P value	Mean Difference	Standard Error Difference	95% Confidence interval of the difference	
						Lower	Upper
Baseline	4.701	60	<0.0001	4.840	1.02942	6.9104	2.7696
2 weeks	9.334	60	<0.0001	5.620	0.602	6.8132	4.4268
4 weeks	12.953	60	<0.0001	3.650	0.282	4.2126	3.0874
8 weeks	11.266	60	<0.0001	1.160	0.103	1.3628	0.9572

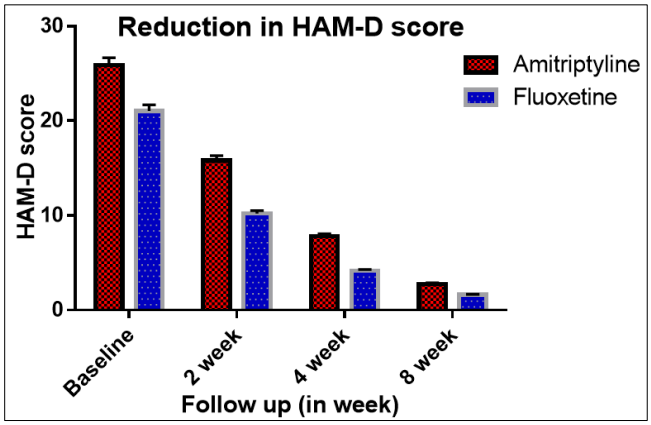

Fig 1: Reduction in HAM-D Score

Table 2: Comparision of reduction of HAM-A score between Amitriptyline and Fluoxetine treatment group from Graphpad prism.

Reduction of HAM-A SCORE	t-test	df	P value	Mean Difference	Standard Error Difference	95% Confidence interval of the difference	
						Lower	Upper
Baseline	2.165	60	0.0344	2.070	0.956	3.9826	0.1574
2 weeks	4.261	60	0.0001	2.390	0.561	3.5202	1.2598
4 weeks	10.139	60	<0.0001	2.730	0.269	3.2673	2.1927
8 weeks	9.615	60	<0.0001	0.860	0.089	1.0424	0.6776

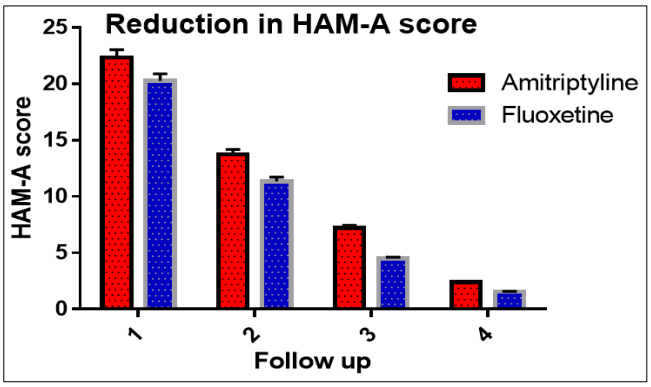

Fig 2: Reduction in HAM-A Score

Table 3: Comparision of percentage of improvement with reference to baseline in HAM-A score

HAM-A	Mean±SME		Percentage of Improvement	
	Amitriptyline	Fluoxetine	Amitriptyline	Fluoxetine
Baseline	22.32±0.71	20.25±0.64	0%	0%
2 weeks	13.74± 0.43	11.35±0.36	38.44%	43.95%
4 weeks	7.21±0.23	4.48±0.14	67.70%	78.00%
8 weeks	2.41±0.08	1.55±0.04	89.21%	92.35%

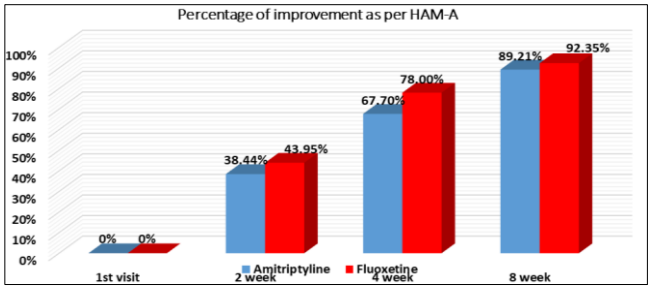

Fig 3: Percentage of improvement with reference to baseline in HAM-A score.

Table 4: Comperision of percentage of improvement with reference to baseline in HAM-D score

HAM-D	Mean±SEM		Percentage of Improvement	
	Amitriptyline	Fluoxetine	Amitriptyline	Fluoxetine
Baseline	25.87±0.79	21.03±0.66	0%	0%
2 weeks	15.81±0.51	10.19±0.32	38.89%	48.45%
4 weeks	7.81±0.25	4.16±0.13	69.82%	80.22%
8 weeks	2.77±0.09	1.61±0.05	89.29%	92.34%

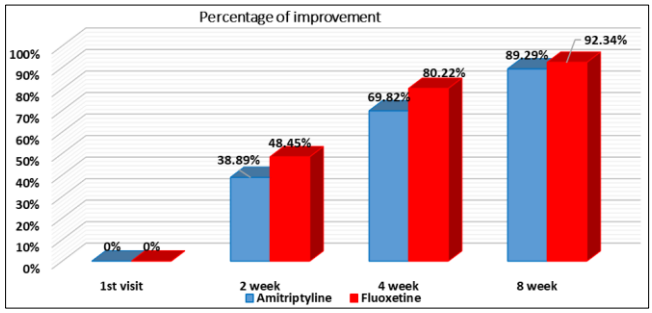

Fig 4: Percentage of improvement with reference to baseline in HAM-D score.

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