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Original Research Article

Prospective, Comparative Assessment of Efficacy of Amitriptyline and Fluoxetine in Patients Presenting with Mixed Anxiety and Depression

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Abstract

Aim: To analyze the comparative study of efficacy and tolerability of amitriptyline and fluoxetine in patients presenting with Mixed Anxiety and Depression.

Material & Methods: The prospective, comparative study was conducted for a period of 12 months in the Department of Psychiatry, Government Medical College, Bettiah, Bihar, India. Patients with anxiety and depression having the target symptoms were selected. The patients were subjected to the questionnaire (i.e. HAM-A and HAM-D as per the diagnosis). Follow-up was done after every second week, fourth week (i.e. 30 days) and eighth week (i.e. 56 days). A total of 100 patients from hospital OPD were selected for the study.

Results: Mean Difference in Reduction of HAM-D Score at baseline was 4.523 [CI-95%, 7.8201-2.5281] and at the end of 8 weeks was 1.201 [CI-95%, 1.2810 -0.9261]. It was found to be statistically significant [p=<0.001].92.51% improvement with reference to baseline in HAM-D score was seen with Fluoxetine and 91.03% in Amitriptyline at the end of 8 weeks.

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, mortality

Introduction

Psychiatric disorders account for 22・8% of the global burden of diseases.[1] The leading cause of this disability is depression, which has substantially increased since 1990, largely driven by population growth and ageing.[2]

Grouped into various classes of drugs with slightly different mechanisms of action, antidepressants are widely used treatments

for major depressive disorder, which are available worldwide. However, there is a long-lasting debate and concern about their efficacy and effectiveness, because short-term benefits are, on average, modest; and because long-term balance of benefits and harms is often understudied. [3]

The mean effects of antidepressants for major depressive disorder compared with pill placebo (Hedges g 0・21 for selective serotonin reuptake inhibitor [SSRI] and 0・16 for serotonin –norepinephrine reuptake inhibitor [SNRI]) have been more modest than those found for treatment of other youth problems, including anxiety disorder (Hedges g 0・71 for SSRI and 0・41 for SNRI) and obsessive-compulsive disorder (Hedges g 0・39 for SSRI). [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 recognized 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 treatment 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.

Thus, we aim to analyze the comparative study of efficacy and tolerability of amitriptyline and fluoxetine in patients presenting with Mixed Anxiety and Depression.

Material & Methods:

The prospective, observation study was conducted for a period of 12 months in the Department of Psychiatry, Government Medical College, Bettiah, Bihar, India. Patients with anxiety and depression having the target symptoms were selected.

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.

Methodology

The patients were subjected to the questionnaire (i.e. HAM-A and HAM-D as per the diagnosis). 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.

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.

Results:

A total of 100 patients from hospital OPD were selected for the study.

Mean Difference in Reduction of HAM-D Score at baseline was 4.523 [CI-95%, 7.8201-2.5281] and at the end of 8 weeks was 1.201 [CI-95%, 1.2810 -0.9261]. It was found to be statistically significant [p=<0.001]. [Table 1]

Table 1: Comparison of reduction of HAM-D score between Amitriptyline and Fluoxetine treatment group from graph pad prism

Reduction of HAM-D Score	P value	Mean Difference	Standard Error Difference	95% Confidence interval of the difference	
				Lower	Upper
Baseline	<0.001	4.523	1.00368	7.8201	2.5281
2 weeks	<0.001	5.816	0.582	6.5290	4.3870
4 weeks	<0.001	3.725	0.339	4.1839	3.0793
8 weeks	<0.001	1.201	0.110	1.2810	0.9261

HAM-A score between Amitriptyline and Fluoxetine treatment group from Graph pad prism was statistically significant at 4 weeks and 8 weeks [p=<0.001]. [Table 2]

Table 2: Comparison of reduction of HAM-A score between Amitriptyline and Fluoxetine treatment group from Graph pad prism.

Reduction of HAM-A SCORE	P value	Mean Difference	Standard Error Difference	95% Confidence interval of the difference	
				Lower	Upper
Baseline	0.0259	2.083	0.968	3.8629	0.6747
2 weeks	0.001	2.572	0.682	3.7198	1.3670
4 weeks	<0.001	2.628	0.572	3.3721	2.5859
8 weeks	<0.001	0.981	0.080	1.685	0.7794

90.53% improvement with reference to baseline in HAM-A score was seen with Fluoxetine and 88.33% in Amitriptyline at the end of 8 weeks. [Table 3]

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

HAM-A	Mean±SME		Percentage of Improvement	
	Amitriptyline	Fluoxetine	Amitriptyline	Fluoxetine
Baseline	22.72±0.87	20.57±0.70	0%	0%
2 weeks	13.73± 0.52	11.44±0.52	37.72%	41.62%
4 weeks	7.62±0.20	4.52±0.20	66.81%	74.48%
8 weeks	2.51±0.07	1.61±0.05	88.33%	90.53%

92.51% improvement with reference to baseline in HAM-D score was seen with Fluoxetine and 91.03% in Amitriptyline at the end of 8 weeks. [Table 4]

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

HAM-D	Mean±SEM		Percentage of Improvement	
	Amitriptyline	Fluoxetine	Amitriptyline	Fluoxetine
Baseline	25.52±0.81	21.04±0.68	0%	0%
2 weeks	15.79±0.67	10.20±0.48	39.01%	48.62%
4 weeks	7.88±0.39	4.19±0.17	70.25%	80.38%
8 weeks	2.72±0.08	1.77±0.06	91.03%	92.51%

Discussion

Estimated differences between drugs were smaller in placebo-controlled trials than in head-to-head studies. There are several potential explanations, as many factors have been associated with higher placebo response rates, such as randomization ratio and the expectation of receiving an active treatment, the therapeutic setting, or the frequency of study visits. [6]

Moreover, for the same drug and the same probability of receiving placebo, larger all-cause dropout rates were associated with a lower response to treatment. The use of the last observation carried forward (LOCF) approach for imputing missing outcome data might have affected the estimates of treatment effect. [7] Depressive symptoms tend to spontaneously improve over time and this phenomenon contributes to the high percentage of placebo responders in antidepressant trials. [8]

Researchers and clinicians should recognize the potential biases in published studies, especially with regard to the potential barriers that have led to inaccurate reporting of harm outcomes. [9] Sixth, antidepressants with different doses might produce different treatment effects. [10] Although we included antidepressants without therapeutic dose ranges, we should consider the potential dose effects in this review. Moreover, various antidepressants have a wide range of half-lives, from 5 h to 5 days. Antidepressants with a long half-life (i.e., fluoxetine and paroxetine) need to be titrated over 3 or 4 weeks, whereas antidepressants with a short half-life (i.e., venlafaxine) do not. [11]

Some of the adverse effects would also be expected in psychotherapy trials, including the emergence of new symptoms and strains in the patient-therapist relationship,[12] however, few psychotherapy trials report data on adverse events and suicidality. [13,14]

Conclusion

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.

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