Original Article

Role of fluoxetine and nortriptyline in major depressive disorders

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ABSTRACT

Objective

To assess the effectiveness and safety of fluoxetine and nortriptyline in major depressive disorders

Patients and Methods

This study was conducted in Sir Cowsee Jee Jehangie Institute of Psychiatry, Hyderabad in collaboration with Department of Pharmacology and Therapeutics Mohammad Medical College Mirpur Khas, from January 2009 to June 2009. Following a 1-week washout period, patients were randomly assigned to 12 weeks of parallel treatment with either fluoxetine (in a flexible daily dose of 20-80 mg) and nortriptyline (in a flexible daily dose of 25–100 mg) provided on a three times per day schedule. Clinical response was seen on weekly follow up basis.

Results

A total of 192 patients were included in this study. In the fluoxetine group, mean age was 38.2±8.8 years. In the Nortriptyline group, mean age was 39.5±11.6 years. At week-1, the gain in fluoxetine was - 55.4± 15.3 and in nortriptyline group it was - 35.4± 10.4 (P <

0.0001). Nausea and headache were common in nortriptyline 14.6% and 12.5% respectively and in Fuoxetine 4.2% and 4.2% respectively.

Conclusion

This study provides evidence in favor of efficacy and advantages of fluoxetine over Nortriptyline. Fluoxetine can be considered as first choice in pharmacological treatment of this disorder. Nausea and headache occurred more in nortriptyline than fluoxetine. (Rawal Med J 2011;36:38-40).

Key Words

Depression, fluoxetine, nortriptyline, SSRI.

INTRODUCTION

Depression can affect anyone.[1] The focus of attention on depression has shifted from the cause of depression to its effects on the afflicted people.[2] Symptoms can lead to thoughts of death or suicide.[3] Acute and chronic socioenvironmental stimuli, negative life events, and stressful situations may lead to depression.[4] WHO global burden of diseases, 2001 states that 33% of the years lived with disability (YLD) are due to neuropsychiatric disorders and depressive disorders were estimated to be the leading cause of disability in the world in 1990.[5,6]

Tricyclic antidepressants (TCA) raise the amount of chemical messengers in the brain but can take from few weeks to month to have the proper effect.[7] Fluoxetine is a Selective Serotonin Reuptake Inhibitor and has been widely prescribed to treat depression, obsessive-compulsive disorder, and bulimia nervosa.[8] Nortriptyline is a TCA and increases levels of norepinephrine and serotonin, two neurotransmitters, and blocks the action of acetylcholine, another neurotransmitter. It is believed that by restoring the

balance of these different neurotransmitters in the brain depression is alleviated.[9] The aim of this study was to assess the safety and efficacy of fluoxetine and nortriptyline in major depressive disorders.

PATIENTS AND METHOD

This study was conducted in Sir Cowsee Jee Jehangie Institute of Psychiatry Hyderabad in collaboration with department of Pharmacology and Therapeutic MMC January 2009 to March 2009. The patients aged 30 and 50 onward who met DSM-VI-R criteria for single-episode or recurrent major depression and whose 24-item Hamilton Depression Rating Scale (10) scores were ≥18 were included in the study. Patients with DSM-VI-R diagnosis of acute or chronic organic mental disorder, a Mini-Mental State examination (11) score <23, concomitant use of any psychotropic drug (except intermittent use of chloral hydrate or diazepam specifically for sleep), presence of another axis I psychiatric disorder, or any acute or unstable medical condition that might interfere with safety or the interpretation of results were excluded from the study.

Following a 1-week washout period, patients were randomly assigned to 12 weeks of parallel treatment with either fluoxatine (20-80 mg) or nortriptyline (25-100 mg) provided on a three times per day schedule. A double-dummy procedure was used to preserve the blind. Nortriptyline was initiated at a dose of 25 mg in the evening and could be titrated in increments of 25 mg per week. The maximal dose could be initiated as early as the end of week 3. Fluoxetine treatment was initiated at a dose of 20 mg in the evening and could be titrated in increments of 60 mg every 3 weeks. The maximal dose could be initiated as early as week 6.

Patients and caregiver/ relatives/ Guardians/ husband/ mother/ father/ fulfilled selection criteria for diagnosis of depressive participants and giving informed consent were enrolled in the study. They were enrolled for six week. Total two hundreds were enrolled, 100 for each drug. Four patients dropped from this grouping in 1st week of study;four did not follow the study protocol. Lorazepam was allowed in sleep disturbances. Assessments were done on day 07, 14, 20 and 42 through improvement in Hamilton rating depression Scale, Clinical Global impression-1 improvement scale .

RESULTS

A total of 192 patients were included in this study. Demographic characteristics of both groups were not significant (Table 1).

Table 1. Demographic characteristics of study population (n=192).

	Fluoxetine	**Nortriptyline**	P-values*
Age (years) Mean± SD = 38.3± 10.4	Mean± SD = 38.2± 8.8	Mean± SD = 39.5± 11.6	
20-39	56 (58.3%)	58 (60.4%)	0.767
40-59	40 (41.7%)	38 (39.6%)	
Gender (M: F = 1.6: 1)	M: F = 1.6: 1	M: F = 1.5: 1	
Male	60 (62.5%)	58 (60.4%)	0.769
Female	36 (37.5%)	38 (39.6%)	

*Chi-Square test of Association

Weekly improvement showed that at week-1 and week-6 the gain in Fluoxetine were significant (Table 2).

Table 2. Mean change of score (gain) on PANSS (n=192).

Time in study	Fluoxetine n = 96 Mean± SD	Nortriptyline n = 96 Mean± SD	P-Values*
Week 1	- 55.4± 15.3	- 35.4± 10.4	< 0.0001**
Week 2	- 49.4± 10.1	- 48.4± 10.9	0.51 (ns)
Week 3	- 51.7± 12.3	- 50.3± 11.3	0.513 (ns)
Week 4	- 48.4± 9.3	- 46.9± 9.4	0.268 (ns)
Week 5	- 45.9± 11.1	- 44.8± 11.9	0.064 (ns)
Week 6	- 54.8± 13.5	- 40.5± 12.3	< 0.0001**

*By Independent Sample T-test, ** Significant difference, ns = Not Significant

Similar improvement was seen on clinical global impression scale (CGI) (Table 3).

Table 3. Clinical global impression scale at different time of treatment (n=192).

Time in study	CGI Scale	Fluoxetine	Nortriptyline	P-Values*
1st week	CGI-1 n = 43	31 (72.1%)	12 (27.9%)	0.004
2nd week	CGI-1 n = 34	20 (58.8%)	14 (41.2%)	0.303 (NS)
3rd week	CGI-1 n = 7	7 (100%)	0	NA
	CGI-2 n = 23	10 (43.5%)	13 (56.5%)	0.532 (NS)
4rth week	CGI-2 n = 25	12 (48%)	13 (52%)	0.841 (NS)
5th week	CGI-2 n = 14	8 (57.1%)	6 (42.9%)	0.593 (NS)
	CGI-3 n = 6	2 (33.3%)	4 (66.7%)	0.414 (NS)
6th week	CGI-3 n = 40	6 (15%)	34 (85%)	< 0.0001

*Chi-Square test of Proportions, NA = Not Applicable, NS = Not Significant

Nausea and headache were the most common adverse effect in Nortriptyline (14.6% and 12.5% respectively) and in Fluoxetine (4.2% and 4.2% respectively). Other adverse effects were insignificantly different between two drugs (Table 4).

Table 4. Adverse Effects between two groups (n=192).

Adverse effects	Drug of study		P-values*
	Fluoxetine	Nortriptyline	
Dry mouth	3 (3.1%)	6 (6.3%)	0.317
Headache	4 (4.2%)	14 (14.6%)	0.018
Diarrhea	2 (2.1%)	3 (3.1%)	0.655
Nausea	4 (4.2%)	12 (12.5%)	0.046
Insomnia	3 (3.1%)	4 (4.2%)	0.705
Somnolence	1 (1.04%)	4 (4.2%)	0.18

* Chi-Square test of proportions

DISCUSSION

This study matched the study by Fabre who reported average total scores on the Hamilton Rating Scale for Depression (HAM-D) for both treatment groups declined from 22-23 at baseline to 11.5 at 5-week period. At Week 5, 71% of nortriptyline patients and 65% of fluoxetine patients were improved and Fluoxetine was more frequently associated with nausea while nortriptyline was associated with dry mouth.[10] Another study reported that the efficacy of nortriptyline was superior to fluoxetine and no significant differences were observed between dropout rates in the two groups but anti-cholinergic side-effects were significantly more frequent with Nortriptyline than with Fluoxetine.[11] In our study, gain score in Fluoxetine was better than Nortriptyline.

Adverse effect of nausea and headache were seen more often Nortriptyline in our patients. The general conclusion of this study was in favor of efficacy and advantages of Fluoxetine over Nortriptyline. Fluoxetine can be considered as first choice in pharmacological treatment this disorder. Adverse effects nausea and headache occurred more in Nortriptyline.

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