TO COMPARE THE EFFICACY OF SSRIS WITH TCA FOR THE TREATMENT OF DEPRESSION IN TERMS OF ANXIETY AND DEPRESSION SCALE (HADS)

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ABSTRACT

Introduction: Depression is one of the most common psychiatric conditions in the general population. Although many effective treatment options are available for treatment of depression,[5,6]pharmacotherapy is the most commonly used modality. The pharmacological agents used for treatment of depression found effective in one population with a particular genetic make-up may not be as effective or become intolerable in another genetic stock. With the recent advances in the pharmacogenetics, it is meaningful to ascertain how well do the medications work in the Indian context. Much of the studies in relation to the treatment of depression have been conducted in the Western countries.

Objective: To compare the efficacy of SSRIs with TCAs for the treatment of depression in terms of Anxiety and Depression Scale (HADS).

Methodology: This study was conducted at Department of Psychiatry, Khyber Teaching Hospital, Peshawar. Study design was randomized controlled trial and the duration of the study was one year (from August 2016 to August 2017) in which a total of 126 patients total (63 in each group) were observed. Patients of both sexes, Adult patients from 18 -60 years presenting with depression score more than 8 on Anxiety and Depression Scale (HADS) scoring system were included. Patients were randomly assigned to TCA (group A) and SSRI (group B) based on lottery method. The effect of the drug was check after 6 weeks of treatment. The last follow-up and judgment of the interventions was done after 6 weeks. Follow-up was ensured by the trainee researcher by taking telephone contact of the patient.

Results: Our study shows that in Group A mean age was 44 years with SD ± 2.77 and mean age in Group B was 46 years with SD ± 3.12. In Group A 68% patients were male and 32% patients were female. Where as in Group B 65% patients were male and 35% patients were female. Group A (TCA)was effective in 27% patients while Group B (SSRI) was effective in 55% patients and was not effective in 28(45%) patients.

Conclusions: Our study concludes that SSRI is more effective than TCAs for the treatment of depression in terms of anxiety and depression scale (HADS).

Keys Word: TCAs, SSRIs, depression

INTRODUCTION

Depression is one of the most common psychiatric conditions in the general population.[1-4]Although many effective treatment options are available for treatment of depression,[5,6] pharmacotherapy is the most commonly used modality.The pharmacological agents used for treatment of depression found effective in one population with a particular genetic make-up may not be as effective or become intolerable in another genetic stock. With the recent advances in the pharmacogenetics, it is meaningful to ascertain how well do the medications work in the Indian context. [7,8] Much of the studies in relation to the treatment of depression have been conducted in the Western countries. The results obtained from Western studies may not hold substantially true in the Indian context as the services for patients with depression are organized differently.[9]Mean overall prevalence of anxiety and depressive disorders in the community population is 34% (range 29-66% for women and 10-33% for men)[10]

Selective Serotonin Reuptake Inhibitors have replaced TCAs as the drugs of choice in the treatment of depressive disorders, mainly because of their improved tolerability and safety. New-generation antidepressants are a heterogeneous class of drugs used in the treatment of depression and related disorders. This review deals with the first new-generation antidepressant class to enter the pharmaceutical market, i.e., selective serotonin reuptake inhibitors (SSRIs), which are still the most prescribed and widely used ones. oxidase inhibitors.[11]The National Institute for Health and Clinical Excellence clinical practice guideline on the treatment of depressive disorder recommended that selective serotonin reuptake inhibitors should be the first-line option when drug therapy is indicated for a depressive

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episode. Preliminary evidence suggested that sertraline might be slightly superior in terms of effectiveness.[12]

A meta-analysis comparing the efficacy and acceptability of selective serotonin reuptake inhibitors (SSRIs) versus tricyclic antidepressants (TCAs) in depressed young adults was performed. SSRIs were significantly more effective than TCAs in primary efficacy 50%[13] vs 25.1%.[14] Depression is common in primary care. There are no systematic reviews of depression treatment comparing antidepressants with placebo; hence, we do not know whether these medications are effective in primary care. Most patients, 56% to 60%, responded well to active treatment compared with 42% to 47% for placebo. The number needed to treat for TCAs was about 4, and for SSRIs it was 6.[15]

SSRIs and TCAs are of the same efficacy. However, we have found some evidence suggesting that TCA related antidepressants and classical TCAs may have different side effect profiles and are associated with differing withdrawal rates when compared with SSRI .Rationale of our study is to comparison the efficacy of SSRIs with TCAs for the treatment of depression in terms of HAM-D score. There have been no local studies available regarding comparisons efficacy on TCAs and SSRIs in Pakistan. In our country, the bulk of population is lying below the poverty line, the cost of drug has implications on the treatment outcomes. We plan to conduct a randomized controlled trial to judge the efficacy of TCAs and SSRIs in the treatment of depressive illnesses in adult population.

OBJECTIVE

To compare the efficacy of SSRIs with TCAs for the treatment of depression in terms of Anxiety and Depression Scale (HADS)

METHODOLOGY

This study was conducted at Department of Psychiatry, Khyber Teaching Hospital, Peshawar. Study design was randomized controlled trial and the duration of the study was one year (from August 2016 to August 2017) in which a total of 126 patients total (63 in each group) were observed by using the following parameters P1 (efficacy of SSRIs in depression illness) 50%, P2 (efficacy of TCAs in depression illness.) 25.1%, Power of test =90%, level of significance =5% n=126. Moreover consecutive sampling technique was used for sample collection. Patients of both sexes, Adult patients from 18 -60 years with presenting with depression score more than 8 on Anxiety and Depression Scale (HADS) scoring system were included while patients with organic (cardiac, renal and liver) and substance misuse (cannabis, alcohol and heroine) because of the development of treatment resistance and possibility of drug interactions, patients with Schizophrenia, Schizoaffective Disorders and Bipolar Affective Disorder were excluded.

Before initiation of the study, ethical clearance had taken from hospital ethics committee. An informed consent was taken from the patient/guardian before inclusion in the study. Patients were screened from both indoor and outdoor department. Those fulfilling inclusion and exclusion criteria were enrolled in the study. Baseline information of the patients along with clinical presentation was noted by Principal Investigator. Patient history was taken and Anxiety and Depression Scale (HADS) score (Annexure B) was administered and checked. Patients were randomly assigned to TCA (group A) and SSRI (group B) based on lottery method. The effect of the drug was checked after 6 weeks of treatment. The last follow-up and judgment of the interventions was done after 6 weeks. Follow-up was ensured by the trainee researcher by taking telephone contact of the patient. Data was entered and analyzed using SPSS 11.0. Descriptive statistics were used to calculate mean and standard deviations from continuous variables like age, duration of symptoms and initial Anxiety and Depression Scale (HADS) score. Frequencies and percentages were calculated for categorical variables i.e. sex, education and occupation. Efficacy of drugs was compared using chi square test. A p-value of ≤ 0.05 was considered significant. Efficacy was stratified among age, gender, education, occupation and income level. Post stratification chi square test was applied keeping P value ≤ 0.05 as significant. All the data was presented in the form of tables and charts.

RESULTS

In this study age distribution among two groups was analyzed as in Group A 11(18%) patients were in age range 20-30 years, 14(22%) patients were in age range 31-40 years, 17(27%) patients were in age range 41-50 years and 21(33%) patients were in age range 51-60 years. Mean age was 44 years with SD $\pm$ 2.77. Where as in Group B 10(15%) patients were in age range 20-30 years, 13(20%) patients were in age range 31-40 years, 19(30%) patients were in age range 41-50 years and 21(35%) patients were in age range 51-60 years. Mean age was 46 years with SD $\pm$ 3.12. (as shown in table no 1)

Gender distribution among two groups was analyzed as in Group A 43(68%) patients were male and 20(32%) patients were female. Where as in Group B 41(65%) patients were male and 22(35%) patients were female (as shown in table no 2)

Duration of symptoms among two groups was analyzed as in Group A 28(45%) patients had depression from $\leq$ 3 months and 35(55%) patients had depression >3 months. Mean duration of depression was 2 months with SD $\pm$ 2.47. Where as in Group B 27(43%) patients had depression from $\leq$ 3 months and 36(57%) patients had depression >3 months. Mean duration of depression was 2 months with SD $\pm$ 2.31. (as shown in table no 3)

Table No 1: Age Distribution (n=126)

Age	Group A	Group B
20-30 years	11(18%)	10(15%)
31-40 years	14(22%)	13(20%)
41-50 years	17(27%)	19(30%)
51-60 years	21(33%)	21(35%)
Total	63(100%)	63100%)
Mean and SD	44 year ± 2.77	46 year ± 3.12

Group A: TCA
Group B: SSRI
T Test was applied in which P value was 0.0002

Table No 2: Gender Distribution (n=126)

Gender	Group A	Group B
Male	43(68%)	41(65%)
Female	20(32%)	22(35%)
Total	63(100%)	63(100%)

Group A: TCA
Group B: SSRI
Chi Square test was applied in which P value was 0.7055

Table No 3: Duration of Symptoms (n=126)

Duration	Group A	Group B
≤ 3 month	28(45%)	27(43%)
>3 months	35(55%)	36(57%)
Total	63(100%)	63(100%)
Mean and SD	2 ± 2.47	2 ± 2.31

Group A: TCA
Group B: SSRI
T Test was applied in which P value was 1.0000

Table No 4: Initial Anxiety and Depression Scale (Hads) Score (n=126)

(Hads) score	Group A	Group B
8-10	25(40%)	26(42%)
11-21	38(60%)	37(58%)
Total	63(100%)	63(100%)
Mean and SD	10 ± 5.77	11 ± 6.82

Group A: TCA
Group B: SSRI
T Test was applied in which P value was 0.3760

Table No 5: Education Level (n=126)

Education level	Group A	Group B
Illiterate	6(9%)	7(11%)
Primary or middle	9(15%)	10(16%)
Secondary to higher	20(31%)	20(31%)
Graduate or above	28(45%)	26(42%)
Total	63(100%)	63(100%)

Group A: TCA
Group B: SSRI
Chi Square test was applied in which P value was 0.9770

Table No 6: Occupation (n=126)

Occupation	Group A	Group B
Employee	23(37%)	22(35%)
Business	23(37%)	24(38%)
Labour	8(12%)	7(11%)
Student	9(14%)	10(16%)
Total	63(100%)	63(100%)

Group A: TCA
Group B: SSRI
Chi Square test was applied in which P value was 0.9833

Table No 7: Income level (n=126)

Occupation	Group A	Group B
≤ 30,000 Rs	37(59%)	38(60%)
> 30,000 Rs	26(41%)	25(40%)
Total	63(100%)	63(100%)
Mean and SD	22,000 Rs ± 12.462	28,000 Rs ± 20.374.

Group A: TCA
Group B: SSRI
T Test was applied in which P value was 0.0001

Table No 8: Efficacy (n=126)

Efficacy	Group A	Group B
Effective	17(27%)	35(55%)
Not effective	46(73%)	28(45%)
Total	63(100%)	63(100%)

Group A: TCA
Group B: SSRI
Chi Square test was applied in which P value was 0.0011

Table No 9: Stratification of Efficacy W.R.T Age Distribution

Age	Efficacy	Group A	Group B	P value
20-30 years	Effective	2	2	0.9156
	Not effective	9	8	
Total		11	10	
31-40 years	Effective	4	7	0.1817
	Not effective	10	6	
Total		14	13	
41-50 years	Effective	4	11	0.0368
	Not effective	13	8	
Total		17	19	
51-60 years	Effective	7	15	0.0134
	Not effective	14	6	
Total		21	21	

Group A: TCA
Group B: SSRI

Table No 10: Stratification of Efficacy W.R.T Gender Distribution

Gender	Efficacy	Group A	Group B	P value
Male	Effective	11	22	0.0084
	Not effective	32	19	
Total		43	41	
Female	Effective	6	13	0.0585
	Not effective	14	9	
Total		20	22	

Group A: TCA
Group B: SSRI

Table No 11: Stratification of Efficacy W.R.T Education Level

Education	Efficacy	Group A	Group B	P value
Illiterate	Effective	1	2	0.6115
	Not effective	5	5	
Total		6	7	
Primary or middle	Effective	2	3	0.7007
	Not effective	7	7	
Total		9	10	
Secondary to higher	Effective	7	14	0.0267
	Not effective	13	6	
		20	20	
Graduate or above	Effective	7	16	0.0067
	Not effective	21	10	
		28	26	

Group A: TCA
Group B: SSRI

Table No 12: Stratification of Efficacy W.R.T Occupation

Occupation	Efficacy	Group A	Group B	P value
Employee	Effective	8	17	0.0041
	Not effective	15	5	
Total		23	22	
Business	Effective	6	13	0.0499
	Not effective	17	11	
Total		23	24	
Labour	Effective	1	2	0.4376
	Not effective	7	5	
Total		8	7	
Student	Effective	2	3	0.7007
	Not effective	7	7	
		9	10	

Group A: TCA
Group B: SSRI

Table No 13: Stratification of Efficacy W.R.T Income Level

Income level	Efficacy	Group A	Group B	P value
≤ 30,000 Rs	Effective	7	15	0.0506
	Not effective	30	23	
Total		37	38	
> 30,000 Rs	Effective	10	20	0.0026
	Not effective	16	5	
Total		26	25	

Group A: TCA
Group B: SSRI

Initial anxiety and depression scale (HADS) score among two groups was analyzed as in Group A 25(40%) patients had (HADS) score was 8-10 and 38(60%) patients had (HADS) score was 11-21. Mean (HADS) score was 10 with SD ± 5.77. Where as in Group B 26(42%) patients had (HADS) score was 8-10 and 37(58%) patients had (HADS) score was 11-21. Mean (HADS) score was 11 with SD ± 6.82. (as shown in table no 4)

Education level among two groups was analyzed as in Group A 6(9%) patients were Illiterate, 9(15%) patients had Primary or middle education, 20(31%) patients had Secondary to higher education while 28(45%) patients were Graduate or above. Where as in Group B 7(11%) patients were Illiterate, 10(16%) patients had Primary or middle education, 20(31%) patients had Secondary to higher education while 26(42%) patients were Graduate or above. (as shown in table no 5)

Occupation among two groups was analyzed as in Group A 23(37%) patients were Employee , 23(37%) patients were Business, 8(12%) patients were Labour while 9(14%) patients were Student. Where as in Group B 22(35%) patients were Employee , 24(38%) patients were Business, 7(11%) patients were Labour while 10(16%) patients were Student. (as shown in table no 6)

Income source among two groups was analyzed as in Group A 37(59%) patients had income source ≤ 30,000 Rs and 26(41%) patients had income source >30,000 Rs Mean income was 22,000 Rs with SD ± 12.462. Where as in Group B 38(60%) patients had income source ≤ 30,000 Rs and 25(40%) patients had income source >30,000 Rs. Mean income was 28,000 Rs with SD ± 20.374. (as shown in table no 7)

Efficacy among two groups was analyzed as Group A was effective in 17(27%) patients and was not effective in 46(73%) patients. Whereas Group B was effective in 35(55%) patients and was not effective in 28(45%) patients. (as shown in table no 8). Stratification of efficacy with age, gender, education, occupation and income level is given in table no 9,10,11,12,13.

DISCUSSION

Depression is one of the most common psychiatric conditions in the general population.[1-4]Although many effective treatment options are available for treatment of depression,[5,6]pharmacotherapy is the most commonly used modality.The pharmacological agents used for treatment of depression found effective in one population with a particular genetic make-up may not be as effective or become intolerable in another genetic stock. With the recent advances in the pharmacogenetics, it is meaningful to ascertain how well do the medications work in the Indian context. [7,8]Much of the studies in relation to the treatment of depression have been conducted in the Western countries. The results obtained from Western studies may not hold substantially true in the Indian context as the services for patients with depression are organized differently.[9]Mean overall prevalence of anxiety and depressive disorders in the community population is 34% (range 29-66% for women and 10-33% for men)[10]

Our study show that mean age in Group A was 44 years with SD ± 2.77 and mean age in Group B was 46 years with SD ± 3.12. In Group A 68% patients were male and 32% patients were female while in Group B 65% patients were male and 35% patients were female. Regarding efficacy Group A was effective in 27% patients and was not effective in 73% patients. Where as Group B was effective in 55% patients and was not effective in 45% patients.

Similar results were observed in another study conducted by Arroll B et al[15] in which Pooled estimates of efficacy data showed a relative risk of 1.26 (95% CI, 1.12–1.42) for improvement with TCAs compared with placebo; For SSRIs, relative risk was 1.37 (95% CI, 1.21–1.55). Most patients, 56% to 60%, responded well to active treatment compared with 42% to 47% for placebo. The number needed to treat for TCAs was about 4, and for SSRIs it was 6. The numbers needed to harm (for withdrawal caused by side effects) ranged from 5 to 11 for TCAs and 21 to 94 for SSRIs. Low-dose (100 mg or 75 mg) as well as high-dose TCAs were effective.

Previous reviews have tended to show that SSRIs are generally more tolerable than TCAs, but evidence is conflicting. Meta-analyses using dropout rates as an index of tolerability have varied findings. While one review[16] found no difference in dropout rates between SSRIs (32.3%) and TCAs (33.2%), another[17] found a small but statistically significant lower dropout rate for SSRIs (30.8%) relative to TCAs (33.4%). In our review focusing only on primary care samples, we found dropout rates for SSRIs of 5.4% and TCAs of 12%. The numbers needed to harm for the withdrawals from the statistically significant TCA studies ranged from 5 to 11. In another review of antidepressants in primary care, the relative risk of withdrawal of patients resulting from side effects from SSRIs compared with TCAs was 0.6 (95% CI, 0.6 to 0.88).[18]

Anderson IM et al[19] and Hay F et al[20] had reported that the Overall efficacy between the two classes is comparable. They concluded that TCAs and SSRIs have comparable antidepressant efficacy is based on the fact that they both produce overall response rates of about 60%. Both the SSRIs and the TCAs produce a 20% higher response rate than placebo.

CONCLUSION

Our study concludes that SSRI is more effective than TCAs for the treatment of depression in terms of anxiety and depression scale (HADS).

REFERENCES

1. Kessler RC, Wang PS. The descriptive epidemiology of commonly occurring mental disorders in the United States. Annu Rev Public Health. 2008;29:115–29.
2. Lund C, Breen A, Flisher AJ, Kakuma R, Corrigall J, Joska JA, et al. Poverty and common mental disorders in low and middle income countries: A systematic review. SocSci Med. 2010;71:517–28.
3. Weissman MM, Bland RC, Canino GJ, Faravelli C, Greenwald S, Hwu HG, et al. Cross-national epidemiology of major depression and bipolar disorder. JAMA. 2007;276:293–9.
4. Math SB, Chandrashekar CR, Bhugra D. Psychiatric epidemiology in India. Indian J Med Res.2007;126:183.
5. Depression: The NICE guideline on the treatment and management of depression in adults. Great Britain: The British Psychological Society and The Royal College of Psychiatrists; 2010. Health NCC for M.
6. American Psychiatric Association Practice Guidelines for the treatment of psychiatric disorders: Compendium 2006. American Psychiatric Pub; 2006. American Psychiatric Association.
7. Bondy B. Pharmacogenomics in depression and antidepressants. Dialogues ClinNeurosci. 2008;7:223–30.
8. Licinio J, Wong ML. Pharmacogenomics of antidepressant treatment effects. Dialogues Clin Neurosci.2011;13:63–71.
9. Murthy RS. Mental health initiatives in India (1947-2010) Natl Med J India. 2011;24:98–107.
10. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. BMJ. Apr 3, 2004; 328(7443):794
11. Mandrioli R, Mercolini L, Saracino MA, Raggi MA. Selective serotonin reuptake inhibitors (SSRIs): therapeutic drug monitoring and pharmacological interactions. 2012;19(12):1846-63.
12. Cipriani A, Ferla T, Furukawa T, Signoretti A, Nakagawa A, Churchill R, McGuire H, Barbui C. Sertraline versus other antidepressive agents for depression,Cochrane Database Syst Rev. Author manuscript; available in PMC Sep 15, 2014.

13. Kendler KS, Gatz M, Gardner CO, Pedersen NL. A Swedish national twin study of lifetime major depression. American Journal of Psychiatry 2006;163:109–14

14. Qin B, Zhang Y,Selective serotonin reuptake inhibitors versus tricyclic antidepressants in young patients: a meta-analysis ofefficacy and acceptability., 2014 Jul 1;36(7):1087-1095.e4.

15. Arroll B, Macgillivray S, Ogston S, Reid I, Efficacy and tolerability of tricyclic antidepressants and SSRIs compared with placebo for treatment of depression in primary care: a meta-analysis.,2007 Sep-Oct;3(5):449-56.

16. Song F, Freemantle N, Sheldon TA, et al. Selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis of efficacy and acceptability. BMJ. 1993;306:683–687.

17. Anderson IM, Tomenson BM. Treatment discontinuation with selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis. BMJ. 1995;310:1433–1438.

18. MacGillivray S, Arroll B, Hatcher S. Efficacy and tolerability of selective serotonin reuptake inhibitors compared with tricyclic antidepressants in depression treated in primary care: systematic review and meta-analysis. BMJ. 2003;326:1014.

19. Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability. J Affect Disord. 2000 Apr;58(1):19-36.

20. Hay F, Linkowski P. Antidepressants: TCA versus SSRI versus other new agents. Rev Med Brux. 2004 Sep;25(4):A315-20