ORIGINAL ARTICLE

The Efficacy of Cognitive Behavioral Therapy in Addition to Pharmacotherapy Versus Pharmacotherapy Alone in the Treatment of Major Depressive Disorder in the Pakistani Population

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ABSTRACT

Objective: To access the efficacy of cognitive behavioral therapy (CBT) in addition to pharmacotherapy versus pharmacotherapy alone in the treatment of major depressive disorder

Methodology: A case-control study was conducted at different psychiatric clinics in Pakistan between April 2019 to October 2020. All participants with depression were divided into two groups; Group A patients were treated in compliance with the current treatment guidelines for antidepressant pharmacotherapy whereas patients in Group B were managed with CBT which included 15 individual 45 minutes sessions in addition to pharmacotherapy. The efficiency of the treatment was assessed on PHQ-9, with treatment being considered successful in patients with a significantly improved score.

Results: 53.80% participants of Group A and 37.50% participants of Group B with moderate depression suffered a depressive episode within the last 12 months whereas 46.20% participants of Group A and 62.50% participants of Group B with moderate depression suffered a depressive episode the last 12 months. However, 49.50% participants of Group A and 83.30% participants of Group B with moderately severe depression suffered a depressive episode within the last 12 months whereas 50.50% participants of Group A and 16.70% participants of Group B with Moderately severe depression suffered a depressive episode the last 12 months. Escitalopram was the most common prescribed antidepressant (44.8%).

Conclusion: It was found that CBT in addition to Pharmacotherapy was more effective in moderate depression whereas Pharmacotherapy alone was much more effective in Moderately Severe depression.

Keywords: cognitive behavioral therapy, major depressive disorder, pharmacotherapy, CBT, PHQ-9

INTRODUCTION

Major depression is one of the critical public health crises in Pakistan, that significantly contributes to the loss of productive years, loss of healthy lives, and several other mental health issues [1]. Individuals who experience an intense depressive episode at some point are at risk for complications in the future, and the recurrence of such episodes elevates the likelihood of relapse substantially [2].

In context with treatment, a combination of medications and therapy is seemed to be efficacious and beneficial [3], however; when used separately, these approaches generally yield therapeutic efficacy of less than 50% [4].

Thus, to improve efficiency, a combination of pharmacotherapy and psychotherapy is advantageous. The sequenced treatment alternatives to relieve depression (STAR*D) trial demonstrated the need for supplementary treatment modalities. In the investigation, the findings revealed a recovery rate of 33% following the first therapeutic intervention and only 50% after the subsequent. However; after four treatment regimens, the cumulative remission rate was 70%.[5]. Consequently, the inability to obtain higher response rates is associated with

poor prognosis in the long term and thereby contributing to increased health care expenditures.

[6,7].

There are only limited studies from Pakistan exploring the effectiveness of pharmacotherapy in adjunction to Cognitive behavioral therapy in patients with depressed patients. Therefore, the present study assessed the efficacy of Cognitive behavioral therapy in addition to pharmacotherapy compared to pharmacotherapy alone for the treatment of major depressive disorder.

METHODS AND MATERIALS

A case-control study was conducted at different psychiatric clinics in Pakistan between April 2019 to October 2020. Ethical approval from the Institutional Review Board (IRB) was obtained prior to the study. Simple randomization technique was used to enroll participants. All patients diagnosed with major depressive disorder, above 17 years of age, and gave informed verbal and written consent to participate were included in the study. Only patients with a score of 18 or higher were included. Patients with a neurological disorder, Schizophrenic disorders, history of bipolar mood disorders, and those who recently suffered a traumatic brain injury were excluded from the study.

All patients presenting to the outpatients department will be assessed for unipolar depressive disorder. Depression assessment will be performed using International Diagnostic Checklists for ICD-10 (IDCL), enabling symptom-specific classification of depression based on the criteria of ICD-10 [8].

All patients with depression were assigned alternatively to either Group A - pharmacotherapy alone or Group B - Pharmacotherapy plus cognitive behavioral therapy (CBT).

Group A patients will be treated in compliance with the current treatment guidelines for antidepressant pharmacotherapy according to current guidelines [9]. The patients in Group B will be managed with CBT in addition to pharmacotherapy.

All participants in group B were assigned to the Cognitive-behavioral therapy offering at least 15 individual 45-minute sessions. These sessions were scheduled weekly. Therapists followed the procedures outlined in the CBT Manual for Depression (CBT Manual for Depression) [10]. This manual is based on Beck's original treatment manual, with some adaptations designed to address the cultural characteristics of Japanese patients, such as their emphasis on interpersonal relationships and consideration of the family as an essential part of treatment.28

The efficacy of the treatment was determined using scores of PHQ-9 [11]. In patients with significantly improved PHQ-9 scores, the treatment was considered as successful. The PHQ-9 was used to assess the severity of the depressive symptoms and was set as the tool to assess the efficacy of the treatment i.e. primary outcome.

All data was entered and analysed using SPSS V.26. All continuous variables were presented as mean and standard deviation while all categorical variables were presented as frequency and percentages. Efficacy of treatment were calculated as differences of mean scores of PHQ-9 before and after treatment in both groups.

RESULTS

Table 1 shows distribution of antidepressants prescribed to the study population. Escitalopram was the most frequently prescribed with a frequency of 278 (44.8%).

Table 1: Distribution of Antidepressants

TCAs		
Amitriptyline	49 (7.9%)	
Amoxapine	3 (0.5%)	
Clomipramine	22 (3.5%)	
Doxepin	16 (2.6%)	
Imipramine	9 (1.5%)	
Nortriptyline	5 (0.8%)	
SSRIs		
Citalopram	13 (2.1%)	
Escitalopram	278 (44.8%)	
Fluoxetine	87 (14%)	
Paroxetine	75 (12.1%)	
Sertraline	110 (17.7%)	
SNRIs		
Duloxetine	8 (1.3%)	

Milnacipran	2 (0.3%)			
Venlafaxine	17 (2.7%)			
Venlafaxine (Extended release form)	4 (0.6%)			
CBT + Pharmacotherapy				
Combined	83 (13.4%)			

83 (13.4%) patients were prescribed both pharmacotherapy as well as cognitive behavioral therapy. When frequency of depressive episodes were assessed after initiating the treatment according to the groups, it was found that most of the individuals on both CBT and pharmacotherapy suffered from depressive episodes within the last 12 months albeit the difference was statistically insignificant (table 2).

Table 2: Number of last episodes in CBT and Pharmacotherapy vs. Pharmacotherapy alone

	Within the last 12 months	Before last 12 months	p- value	
CBT + Pharmacotherapy	29 (64.40%)	16 (35.60%)		
Only Pharmacotherapy alone	181 (52.60%)	163 (47.40%)	0.134	

Stratification on the basis of severity of data was done to find out the efficacy of both treatments on patients with different grades of depression. It was found that CBT + Pharmacotherapy is more effective in moderate depression. Pharmacotherapy alone is much more effective in Moderately Severe depression.

Table 3: Number of last episodes in CBT and Pharmacotherapy vs. Pharmacotherapy alone in different severities of depression.

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Moderate Depression		Within the last 12 months	Before last 12 months	p- value		
	CBT + Pharmacother apy	3 (37.50%)	5 (62.50%)	0.470		
	Pharmacother apy alone	42 (53.80%)	36 (46.20%)			
		Within the last 12 months	Before last 12 months	p- value		
Moderately Severe	CBT + Pharmacother apy	5 (83.30%)	1 (16.70%)	0.207		
	Pharmacother apy alone	54 (49.50%)	55 (50.50%)			
Severe Depression		Within the last 12 months	Before last 12 months	p- value		
	CBT + Pharmacother apy	21 (67.70%)	10 (32.30%)	0.173		
	Pharmacother apy alone	85 (54.10%)	72 (45.90%)			

DISCUSSION

Multiple studies have revealed that cognitive-behavioral therapy is as effective as pharmacotherapy alone for the management of major depressive disorder. [11] Some

studies also reported that the use of cognitive-behavioral therapy in addition to antidepressant medications enhanced the results of treatment. [12]

The significance and benefit of cognitive-behavioral therapy combined with pharmacotherapy for the effective management of major depressive disorder have long been studied. Though some researchers have supported the use of combination therapy and reported positive results, [13] other studies found no such advantage of combination therapy [14] or mindfulness therapies over pharmacotherapy alone [15] for the treatment of depression.

Our study found that cognitive-behavioral therapy in combination with pharmacotherapy was more effective in the management of moderate depression, while moderately severe depression was best treated with pharmacotherapy alone

A similar study was conducted by Kamenov et al., which revealed very different results. The efficacy of combination therapy and pharmacotherapy was studied, and it was noted that combination therapy was more beneficial in terms of treatment outcomes as compared to pharmacotherapy alone. [16] Studies have shown that the long-term benefits of psychotherapy are more pronounced as compared to the short-term effects, [17] which can explain why cognitive behavioral therapy is associated with better long-term treatment outcomes. The results obtained can be attributed to various factors, such as better availability of resources in the form of health personnel and that behavioral therapy is a more economically friendly mode of treatment. [18]

In a similar study, a six-month treatment response was evaluated in patients on combined psychotherapy and pharmacotherapy and patients receiving only pharmacotherapy. The results were inconsistent with our findings and revealed that combined therapy was more beneficial in the management of depression in the six months. The results implied that combination therapy had a stronger enduring effect as compared to medical therapy alone, for the management of major depressive disorder. [19]

In a randomized control trial, a comparison was made between treatment efficacy using psychotherapy, pharmacotherapy, and combination therapy. The results indicated that all modes of therapy yielded similar results in terms of subjective, cognitive, and biological markers of depression. [20]

Though pharmacotherapy alters the neurochemical pathways to limit negative emotions, [21] cognitive behavioral therapy supports the process by allowing patients to build the skills to counter the negative emotions, [22] thereby having a significant long-term impact on the patient's mental well-being.

The study was associated with certain limitations. The absence of a control group did not allow us to compare the efficacy of the treatment. Furthermore, the small sample size did not facilitate the identification of minor differences between the study groups.

CONCLUSION

It was found that CBT in combination with Pharmacotherapy was more effective in moderate

depression whereas Pharmacotherapy alone was much more effective in Moderately Severe depression.

REFERENCES

- McTernan WP, Dollard MF, LaMontagne AD. Depression in the workplace: An economic cost analysis of depressionrelated productivity loss attributable to job strain and bullying. Work & Stress. 2013 Oct 1;27(4):321-38.
- Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, Segal ZV. Metacognitive awareness and prevention of relapse in depression: empirical evidence. Journal of consulting and clinical psychology. 2002 Apr;70(2):275.
- Schonfeld WH, Verboncoeur CJ, Fifer SK, Lipschutz RC, Lubeck DP, Buesching DP. The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder. Journal of affective disorders. 1997 Apr 1;43(2):105-19.
- Arroll B, Macgillivray S, Ogston S, Reid I, Sullivan F, Williams B, Crombie I. Efficacy and tolerability of tricyclic antidepressants and SSRIs compared with placebo for treatment of depression in primary care: a meta-analysis. The Annals of Family Medicine. 2005 Sep 1;3(5):449-56.
- Trivedi MH, Fava M, Wisniewski SR, Thase ME, Quitkin F, Warden D, Ritz L, Nierenberg AA, Lebowitz BD, Biggs MM, Luther JF. Medication augmentation after the failure of SSRIs for depression. New England Journal of Medicine. 2006 Mar 23:354(12):1243-52.
- Fekadu A, Wooderson SC, Markopoulo K, Donaldson C, Papadopoulos A, Cleare AJ. What happens to patients with treatment-resistant depression? A systematic review of medium to long term outcome studies. Journal of affective disorders. 2009 Jul 1;116(1-2):4-11.Zimmerman M, Martinez JH, Young D, Chelminski I, Dalrymple K. Severity classification on the Hamilton depression rating scale. Journal of affective disorders. 2013 Sep 5;150(2):384-8.
- Cuijpers P, Berking M, Andersson G, Quigley L, Kleiboer A, Dobson KS. A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. The Canadian Journal of Psychiatry. 2013 Jul;58(7):376-85.
- Köhler S, Hoffmann S, Unger T, Steinacher B, Dierstein N, Fydrich T. Effectiveness of cognitive-behavioural therapy plus pharmacotherapy in inpatient treatment of depressive disorders. Clinical psychology & psychotherapy. 2013 Mar;20(2):97-106.
- Piek E, van der Meer K, Nolen WA. Guideline recommendations for long-term treatment of depression with antidepressants in primary care—a critical review. The European journal of general practice. 2010 Jan 1;16(2):106-12.
- Naeem F, Waheed W, Gobbi M, Ayub M, Kingdon D. Preliminary evaluation of culturally sensitive CBT for depression in Pakistan: findings from Developing Culturallysensitive CBT Project (DCCP). Behavioural and cognitive psychotherapy. 2011 Mar;39(2):165-73.
- Ahmad S, Hussain S, Akhtar F, Shah FS. Urdu translation and validation of PHQ-9, a reliable identification, severity and treatment outcome tool for depression. J Pak Med Assoc. 2018 Aug 1;68(8):1166-70.
- Cuijpers P, Sijbrandij M, Koole SL, Andersson G, Beekman AT, Reynolds III CF. Adding psychotherapy to antidepressant medication in depression and anxiety disorders: a meta-analysis. Focus. 2014 Jul;12(3):347-58.
- 13. Keller MB, McCullough JP, Klein DN, Arnow B, Dunner DL, Gelenberg AJ, Markowitz JC, Nemeroff CB, Russell JM, Thase ME, Trivedi MH. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. New England Journal of Medicine. 2000 May

- 18;342(20):1462-70.
- 14. Wiersma JE, Van Schaik DJ, Hoogendorn AW, Dekker JJ, Van HL, Schoevers RA, Blom MB, Maas K, Smit JH, McCullough Jr JP, Beekman AT. The effectiveness of the cognitive behavioral analysis system of psychotherapy for chronic depression: a randomized controlled trial. Psychotherapy and psychosomatics. 2014;83(5):263-9.
- Michalak J, Schultze M, Heidenreich T, Schramm E. A randomized controlled trial on the efficacy of mindfulnessbased cognitive therapy and a group version of cognitive behavioral analysis system of psychotherapy for chronically depressed patients. Journal of consulting and clinical psychology. 2015 Oct;83(5):951.
- Kamenov K, Twomey C, Cabello M, Prina AM, Ayuso-Mateos JL. The efficacy of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in depression: a meta-analysis. Psychological medicine. 2017 Feb:47(3):414-25.
- Health Quality Ontario. Psychotherapy for major depressive disorder and generalized anxiety disorder: a health technology assessment. Ontario health technology assessment series. 2017;17(15):1.

- Karyotaki E, Smit Y, Henningsen KH, Huibers MJ, Robays J, De Beurs D, Cuijpers P. Combining pharmacotherapy and psychotherapy or monotherapy for major depression? A meta-analysis on the long-term effects. Journal of Affective Disorders. 2016 Apr 1;194:144-52.
- Iftene F, Predescu E, Stefan S, David D. Rational-emotive and cognitive-behavior therapy (REBT/CBT) versus pharmacotherapy versus REBT/CBT plus pharmacotherapy in the treatment of major depressive disorder in youth; a randomized clinical trial. Psychiatry Research. 2015 Feb 28;225(3):687-94.
- Ma Y. Neuropsychological mechanism underlying antidepressant effect: a systematic meta-analysis. Molecular psychiatry. 2015 Mar;20(3):311-9.
- Beck AT, Haigh EA. Advances in cognitive theory and therapy: The generic cognitive model. Annual review of clinical psychology. 2014 Mar 28;10:1-24.
- Leichsenring F, Steinert C, Hoyer J. Psychotherapy versus pharmacotherapy of depression: What's the evidence?.
 Zeitschrift für Psychosomatische Medizin und Psychotherapie. 2016 Jan 1:190-5.