Journal of Diseases
2018 Vol. 5, No. 2, pp. 33-42
ISSN(e): 2410-6550
ISSN(p): 2413-838X
DOI: 10.18488/journal.99.2018.52.33.42

DIFFERENTIAL RESPONSES TO COGNITIVE BEHAVIORAL THERAPY AND PHARMACOTHERAPY VERSUS COMBINED THERAPY IN YOUNG ADOLESCENTS WITH DEPRESSION

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Article History
Received: 24 May 2018
Revised: 2 July 2018
Accepted: 15 August 2018
Published: 10 October 2018

Keywords
Cognitive behavioral therapy
Pharmacotherapy
Depression
Students
Cognition
behavior

ABSTRACT

Background: Treatment of patients with major depression involves some problems and, an effective therapy, is still a debatable issue. The goal of this review was to provide a comprehensive survey on comparing three methods of Cognitive Behavioral Therapy, pharmacotherapy and combined therapy on treatment of depressed adolescents. Material and methods: this study was a randomized clinical trial with follow- up which was conducted in Isfahan city (2015). The statistical population included 330 middle school students (aged 13- 16 years) who had the criteria of depression disorder. Then 120 girls and boys were selected via cluster sampling. After that, they divided into 4 groups (3 experimental groups and 1 control group). 4 month after finishing the intervention, all groups were followed by the project. The research tool was the children's depression Inventory (CDI). Results: the results showed that all of the 3 experimental groups were significantly effective in the treatment of depression ($p<00.1$). In the post-test stage, the combination of pharmacotherapy and CBT, pharmacotherapy, CBT respectively were effective ($p<00.0$). But the findings illustrate that in the follow- up stage cognitive behavioral therapy had a long-term effect in compare to pharmacotherapy. Conclusion: at last the research results show significant efficacy of all three methods, with different priorities effect, at various stages, on improving the criteria for depression in adolescents.

Contribution/Originality: This study contributes to the existing literature to clarify the best therapy for depressive mood in adolescents. This study uses a new estimation methodology for comparative studies. This study originates a new formula for two kinds of therapy. This study is one of the very few studies which have investigated the differentiated responses to different therapies. The paper contributes the first logical analysis that why these therapies can be different. The paper's primary contribution is finding that in which condition we can use 3 different therapy. This study documents the proven sources in the use of various therapeutic approaches.

1. INTRODUCTION

Adolescence is a developmental period characterized by important changes in personality traits and mood. The changes in how adolescents think, reason, and Understand can be even more dramatic than their obvious physical changes [1]. From a psychosocial perspective, Erikson views adolescence as a period of identity formation and role

diffusion. An incoherent sense of self and values will result in the lack of a sense of identity. In essence, adolescence represents the second separation from adult caretakers, with the first having occurred when the youth attained the motor and cognitive ability to move away from the parents' constant watch. Adolescence marks the period where youth are biologically, albeit not usually psychosocially, capable of surviving on their own [2]. A healthy and stable self-image is of primary importance in healthy adolescent development. Problems in the formation of a positive sense of self-show significant correlations depression and mood instability [3]. Epidemiologic studies show that major depression is comparatively rare among children, but common among adolescents, with up to a 25% lifetime prevalence by the end of adolescence [4]. Depression is associated with significant morbidity, disability (loss of work days, reduced quality of life), increased medical comorbidity (cardiovascular disease and stroke), and mortality (increased risk for suicide and death from comorbid medical disorders) [5].

In the past forty years, at least two main developments existed concerning theories and treatment of depression. One of the most used Treatments of this disorder is pharmacotherapy which used drugs for sedating depression signs and the other was a cognitive behavioral therapy [6]. In pharmacotherapy of major depression, various drugs are employed, they include selective serotonin reuptake inhibitors (SSRIs), other agents with varied mechanisms of action (e.g., venlafaxine, mirtazapine), and older classes such as tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) [7]. SSRIs and other newer agents have become first-line treatments for most primary care physicians, psychiatrists, and other medical specialists because of their relative tolerability and ease of use in terms of dosing schedules. Nonetheless, many of the patients are reluctant to accept pharmacotherapy [8] and may be prone to drug side effects and drug-drug interactions. The most commonly studied psychotherapeutic treatment of depression is cognitive behavior therapy, which is focused on changing maladaptive patterns of thinking, feeling, and behaving [9]. The advantages of psychotherapy include the lack of drug side effects and drug-drug interactions. Given that psychosocial stressors may engender or exacerbate depressive episodes [10] the focus in psychotherapy of enhancing social supports, resolving interpersonal stressors, or increasing coping abilities may be useful and desirable [11]. An often mentioned disadvantage of psychotherapy relative to medication is the slower response [12] but there are structural disadvantages too, including language, financial, and transportation barriers and the lack of psychotherapists who are trained to work with Rucci, et al. [13].

The main aim in cognitive behavioral therapy is reducing mental pressure and improving functions which have been disturbed due to mental disorders. The thoughts, beliefs, and mental images patients experience are the main core of cognitive behavioral therapy [14]. Treatment content includes identification of thoughts and beliefs, reviewing the evidence and investigating thoughts and cognitions related to the mood and behavior [15]. The techniques used, include behavioral and cognitive techniques. Relaxation therapy through muscle relaxation (regular contraction and relaxation of all the major muscle groups), meditation and targeted imagination (imagining a quiet place and listening to the soothing sounds) reduce physical and mental stress [16]. Increasing number of research studies have been dedicated on this type of treatment since emergence of cognitive behavioral therapy. Many studies have been conducted on depression [17, 18] anxiety disorders [19, 20] eating disorders [21, 22] and insomnia [23, 24] in order to evaluate the therapeutic changes.

Keller, et al. [25] investigated the differences between nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. The result of their study showed the overall) 48 percent rate of response (both remission and satisfactory response in both the nefazodone group and the psychotherapy group, as compared with 73 percent in the combined-treatment group. Rush, et al. [26] also had a research on topic of "Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients"; they asserted that the dropout rate was significantly higher with pharmacotherapy (8 Ss) than with cognitive therapy (1 S). Even when these dropouts were excluded from data analysis, the cognitive therapy patients showed a significantly greater improvement than the pharmacotherapy patients. Follow-up contacts at three and

six months indicate that treatment gains evident at termination were maintained over time. Moreover, while 68%of the pharmacotherapy group re-entered treatment for depression, only 16%of the psychotherapy patients did so. In accordance with the previous researches, it becomes clear that most therapeutic interventions in the area of major depression have been performed on adults, while few researched have taken place on adolescents who are the vulnerable groups of society, particularly in Iran. Also, these few types of research on the adolescents suffering from major depression have not enjoyed a comprehensive look which covers all the potentialities of the combined therapies. Hence, given high rates of depression among the adolescents and its destructive impacts on the social, educational and personality growth and also the fact this disease is followed by some other psychological disorders like anxiety and conduct disorder and contradictory information in the superiority of treatment methods in the previous studies, this study was conducted with the aim of comparing the three methods of group therapy with the cognitive behavioral approach alone, pharmacotherapy alone and the combined therapy in the depressed adolescents.

2. METHODOLOGY

2.1. Subjects

With regard to the overall goal of this study, to compare the effectiveness of three methods of cognitive behavioral therapy, pharmacotherapy and combined therapy in the treatment of youth's depression; this experimental study was performed in Isfahan city, Iran, with pretest and posttest and a four-month follow-up in 2009. The Statistical Society was 330 depressed young adolescence, studying in one of the threesome grades of junior high school in Isfahan, who were identified due to the previous research entitled "Epidemiology of depression in adolescents in Isfahan". Based on that research person whose score was 19 or more in the Maria Cowax questionnaire as well as having diagnostic criteria for depression based on DSM-IV, such as frustration, depression, low motivation, irritability, changes in appetite, low self-esteem, social withdrawal and feelings of inferiority, determined as a depressed person.

2.2. Research Design

After determination of statistical society, 120 male and female students were selected from different areas as the sample of this research based on cluster random sampling. And then randomly divided into four groups of 30 patients. Each group consists of 15 girls and 15 boys. It is noteworthy that at first, for a 12 people group of boys the cognitive behavioral therapy was conducted by way of pilot in order to identify the shortcomings of the administrative method of the research and dominance in applying the therapeutic methods, wherein vertical flashes were used, however, it was not a perfect protocol. Also, in this group, most students were present with low average scores and educational status which caused problems for cooperation and enough comprehension of the material presented. In addition, there were some accompanying disorders such as learning disorder or hyperactivity-inattention that led the researchers to a conclusion that for participating in cognitive behavioral sessions, it is imperative for people to have at least an average score of higher than 15 so that they enjoy enough thinking abilities and enough participation in this treatment and avoid some other disorders that would reduce the adolescents" cooperation for concentrating on cognitive material. Then, this protocol was completed and was translated from a book by Munoz and Miranda [20] and transformed into some PowerPoint slides. This protocol was employed for increasing the attention of the junior school students who were energetic and the tendency for these discussions among them was weak.

2.3. Inclusion Exclusion Criteria

The criteria for entering the research were: 1. The students suffering from major depression based on the DSM-IV diagnostic criterion determined in-depth psychological screening interview, 2. Age between 13-16 and at

the junior school level, 3. Educate in Isfahan, 4. Students' written disclaimer for participating in the program based on active presence till the end of the research, 5. An average score of 15 at least, and 6. A lack of accompanying disorders. Also, the criteria for exiting the research were 1. Severe mental disorders, 2. An absence of more than two sessions, 3. Lack of interest among people to continue education.

2.4. Interventions

Therapeutic programs for each group were executed as follow:

Group 1: cognitive behavioral therapy, twice a week and each session for 45 minutes; Group 2: pharmacotherapy that includes 20 milligrams of *Fluoxetine* as prescribed by a specialist doctor for 8 weeks and Group 3: pharmacotherapy with cognitive behavioral therapy for 8 weeks. Pharmacotherapy interventions were performed by a psychiatrist and cognitive behavioral therapy was done by a professional therapist. It should be noted that the group cognitive behavioral therapy period of 12 sessions included 4 sessions about the relationship between thought and feeling, 4 sessions about the relationship between feeling and daily activities an 4 sessions of relationship between feeling and social relations. Slides prepared in the cognitive behavioral and combined therapy groups were displayed and were read by the research subjects and explained by the therapist. Also, participants in the research explained their own views and states while implementing therapeutic programs. A briefing of cognitive behavioral therapy sessions is presented in table, 1.

Table-1. A brief Description of Cognitive Behavioral Therapy Sessions

Part	Session	Subject matter of the sessions content
First: effects of modifying thoughts on depressive mood	1	Familiarity with one another, explanation of depression disorder, effects of modifying thoughts on depressive mood,
	2	Identification of depressed thoughts, introduction of daily mood scale, identification of positive and negative thoughts
	3	Recognition of thinking errors, replacing negative thoughts with positive thoughts
	4	Practice of A-B-C-D method
Second: effects of a change in the daily activities on the depressive mood	1	Review of goals, definition of depression, reciprocal effects of daily activities on depressed mood
	2	Identification of enjoyable activates, prediction of satisfaction with activities, personal contracts
	3	Training planning for attain the goals and enjoyable activities
	4	Improvement of internal word (thoughts) and external world (behaviors) and their effects on the depressed mood
Third: effects of improved social relations on the depressive mood	1	Quality of the effects of social relations in the depressed mood
	2	Role of thoughts, expectations, conducts and feelings in reciprocal communications
	3	Training building confidence-based relations, decisive treatment
	4	Ways for improving communications (listening actively, giving feedbacks and….). More exercise

2.5 Research Tools

a) Demographic questionnaire: the required demographic information of this research was age, gender and educational average score.

b) Maria Cowax depression in children questionnaire (CDI): In this questionnaire, 27 questions are designed that would provide various feelings and thoughts. The way this questionnaire is scored is like the Beck depression questionnaire and is 0, 1 and 2. The score range is between 0-54. The cutting off point and determining the depressed people is a score of higher than 18. A score of 0-8 is healthy, 9-19 means depression signs, but without depression disorder while 20 and higher is labeled depressed. The more people's score in this questionnaire, the more the depression level will be. To measure the CDI scale validity, the concurrent validity with teachers' assessment was applied where it indicated a validity

coefficient of 0.193, being statistically significant [27]. Ostovar and Razvye reported the divergence validity of the questionnaire along with the social anxiety scale for the adolescents (SAS-A) as 0.35 (10). Saylor et al, by using the Cronbach's alpha reported the internal consistency of the questionnaire as ranging from 0.71 to 0.94 (11). Also, Ostovar and Razavye reported the reliability of the questionnaires as 0.91 by using a retest with a time interval of two weeks (10).

3. FINDINGS

The participating groups in the research were the same in terms of gender, age and educational status variables and there was no need for equivalence. To analyze the data, at the first stage, prior to the comparison of the three therapeutic methods, first the effects of each therapy (pharmacotherapy, cognitive behavioral therapy and combined therapy) were individually evaluated on treating the patients suffering from major depression. For this purpose, using the twin t test, scores of pretest-posttest and those of pretest-follow up were separately compared.

In the first group who were placed under the cognitive behavioral therapy, the statistical test having been implemented, given the p-value=0.001 it was determined this method was found to be significantly effective for treating major depression. The average difference of the scores of pretest-posttest was 11.70 while the rate for those of pretest-follow up was 13.20.

The second group being under the pharmacotherapy measures, after the implementation of the related test with the p-value=0.001, it was determined that this method was significantly effective in reducing the scores. In other words, it was significantly effective in treating depression. The average difference of the scores of pretest-posttest was 13.27 while the same rate for and those of pretest-follow up was 12.30.

The third group being under the combined therapy measures, after the implementation of the related test with the p-value=0.001, it was determined that this method like its predecessors was significantly effective in reducing the scores. In other words, it was significantly effective in treating depression. The average difference of the scores of pretest-posttest was 14.80 while the same rate for and those of pretest-follow up was 15.03.

Table-2. The average difference of the scores of pretest-posttest and average score of the pretest-follow up in three cognitive behavioral, pharmacotherapy and combined therapy methods.

	Stage	Average difference of scores before and after the test	SD	Confidence distance 95% score difference		P value
				Low margin	High margin	
Cognitive behavioral therapy	Posttest	11.70	7.16	9.02	14.37	0.001
	Follow up	13.20	6.53	10.76	15.64	0.001
Pharmacotherapy	Posttest	13.27	5.82	11.09	15.44	0.001
	Follow up	12.30	5.96	10.07	14.52	0.001
Combined therapy	Posttest	14.82	6.34	12.43	17.17	0.001
	Follow up	15.03	6.18	12.73	17.34	0.001

Source: Output from SPSS 18 software

After investigating the significance of therapeutic methods separately, in the second stage, the three therapeutic methods were compared. The test used in this stage was the covariance analysis.

Table-3. A summary of covariance analysis results relating to the comparison of average treatment scores in experimental groups at the posttest and follow up stage

Source of changes	Stage	Square sum	Freedom degree	Average square	F	Significance	Effects size	Statistical power
Pretest	Posttest	1156.62	1	1156.62	38.66	0.001	25.5	1.000
	Follow up	1006.03	1	1006.03	40.10	0.001	26.2	1.000
Group membership	Posttest	3714.47	3	1238.15	41.38	0.001	52.4	1.000
	Follow up	4159.66	3	1386.55	55.27	0.001	59.5	1.000

Source: Output from SPSS 18 software

Covariance analysis results set forth in table 3 indicate that by eliminating the effects of the pretest scores, a significant difference was seen between the modified average depression score of the students based on group membership (three pharmacotherapy, combined therapy and cognitive behavioral therapy groups) at the posttest and follow up stage (P<0.05). Hence, it is concluded that therapies provided have an effect on depression. The difference rate suggests that 52.4% of the depression score variance at the posttest stage and 59.5% of the depression score variance at the follow up stage are because of the group membership. The statistical power of 1 indicates a high statistical accuracy of this test and sufficiency of the sample size. Totally, there is a significant difference between the three therapeutic methods. For investigating these differences, the LSD test was used in more details.

Table-4. Pair comparison of the average differences of the groups under study after the treatment and posttest stages

Groups		Average difference	Average deviation error	Sig.
Cognitive behavioral therapy	Combined therapy	1.85	1.44	0.20
	Pharmacotherapy	3.59	1.44	0.01
	Control	-10.76	1.43	0.001
Pharmacotherapy	Cognitive therapy	-3.58	1.44	0.01
	Combined therapy	-1.73	1.45	0.23
	Control	-14.35	1.43	0.001
Combined therapy	Cognitive therapy	-1.86	1.44	0.20
	Pharmacotherapy	1.73	1.44	0.23
	Control	-12.62	1.41	0.001
Control	Combined therapy	12.62	1.41	0.001
	Pharmacotherapy	14.35	1.43	0.001
	Cognitive therapy	10.76	1.43	0.001

Source: Output from SPSS 18 software

Table, 4results indicate that between the average difference of the two cognitive behavioral therapy and pharmacotherapy groups at the posttest is a significant difference (P<0.01). Thus, observing the average differences is indicative of the advantage of the pharmacotherapy over the cognitive behavioral therapy at the posttest. However, there is no significant difference between the average differences of the two cognitive behavioral and combined therapy groups (P<0.20). Also, there is no significant difference between the two combined and pharmacotherapy groups (P<0.23).

Table-5. Pair comparison of the average differences of the groups under study after the treatment and follow up

Groups		Average difference	Average deviation error	Sig.
Cognitive behavioral therapy	Combined therapy	2.53	1.32	0.05
	Pharmacotherapy	0.969	1.31	0.46
	Control	-12.29	1.31	0.001
Pharmacotherapy	Cognitive therapy	-0.969	1.31	0.46
	Combined therapy	1.56	1.32	0.24
	Control	-13.26	1.31	0.001
Combined therapy	Cognitive therapy	-2.53	1.31	0.05
	Pharmacotherapy	-1.56	1.32	0.24
	Control	-14.12	1.29	0.001
Control	Combined therapy	12.29	1.31	0.001
	Pharmacotherapy	14.82	1.29	0.001
	Cognitive therapy	13.26	1.31	0.001

Source: Output from SPSS 18 software

Table, 5 results indicate that no significant difference between the average difference of the two cognitive behavioral therapy and pharmacotherapy groups (P<0.46). Thus, observing the average differences is indicative of

the advantage of the combined therapy over the cognitive behavioral therapy and the pharmacotherapy. However, there is no significant difference between the average differences of the two cognitive behavioral and combined therapy groups (P<0.24). Also, there is a significant difference between the two combined and pharmacotherapy groups (P<0.05). Also, the effectiveness of the cognitive behavioral therapy at the follow up stage was higher than the pharmacotherapy. This tells that the CBT needs more time for leaving effects.

4. DISCUSSION

The current paper aimed to determine the effects of three methods of cognitive behavioral therapy, pharmacotherapy and combined therapy on the depressed adolescents Isfahan. Results indicated that there is a significant difference between the average depression scores of the three groups in the posttest and follow up stages compared t the pretest (P<0.001).In other words, all the three therapeutic treatments resulted in a significant reduction of the subjects' depression. Also, the highest depression improvement rate was achieved in the group with the combined therapy, because in this method the average difference of the scores of the pretest-posttest was 14.80 and while it was 15.03 in the follow-up stage, and resulted in reduced depression rate among the adolescents more than other methods. Therapeutic methods used in the major depression disorder are varied and most studies suggest that a combination of cognitive behavioral therapy and pharmacotherapy are the most effective treatment in treating the depression disorder [12].

In this area, Jonghe De, et al. [28] argues that a combination of pharmacotherapy and cognitive behavioral therapy in the patients suffering from major depression disorder is more effective than the pharmacotherapy and the cognitive behavioral therapy individually, where these findings are in line with those of this research [28]. In this research three cognitive behavioral therapy, pharmacotherapy and combined therapy methods were assessed. Results indicated that in the pharmacotherapy method the students' depression under study was reduced after prescription, such that the Maria Cowaks average depression difference (CDI) of them was statistically significant before and after the pharmacotherapy. Also, the findings revealed that the effectiveness of the pharmacotherapy at the posttest was higher than that of the cognitive behavioral therapy. On the other hand, the cognitive behavioral therapy (CBT) was effective in treating major depression disorder and a statistical test analysis is indicative of a significant difference. In fact, the CBT is a useful way for treating depression in the past five years [29]. Also, research results in the follow up stage indicated that cognitive therapy not only maintains its reliability in the course of time but it also overtakes the pharmacotherapy in terms of effectiveness (13.20 vs. 12.30).

Some researchers, following depressed patients undertaking the CBT method for six years concluded that cognitive therapy tactics would reduce considerably the risk of depression relapse [28]. This finding is in line with the present paper. Research results suggest a reduction of pharmacotherapy at the follow up stage, indicating pharmacotherapy needs a longer treatment period of time and in case drugs consumption is stopped, there is a possibility of a relapse of the disease. This finding is in line with Paykel researches who writes in this regard: despite the taking of antidepressants, the problem of depression relapse still remains and using the CBT substantially reduces the relapse of this patience [30]. In this regard, Scott et al, write over the effectiveness of the CBT over the depression disorder: the depressed patient undertaking cognitive therapy measures had a substantial low relapse level compared to the control group (47%) [29]. Research findings by Paykel and Scott et al reaffirm those of the current paper with respect to a combination of the CBT with the pharmacotherapy in order to avoid the relapse. Because in this a sense, the CBT by the therapist through altering thoughts and changing daily and social activities of the affected will break down a vicious cycle of negative automatic thoughts and unpleasant emptions among the patients and hereby, it will result in the improvement of the patients [31]. Hence, the effectiveness of the CBT can be justified in treating the major depression and its stability in the course of time based of the Beck theory.

All in all, Due to the hormonal changes of adolescence, it was assumed that pharmacotherapy can have a greater impact on the mood and treating depression in adolescents compared to cognitive behavioral therapy. But as a result of this study, we got to this point, that cognitive behavioral therapy is more effective in improving symptoms of depression in adolescents. Piaget's theory can be cited to explain this result. As he say, from the concrete, black-and-white thinkers, adolescents become able to think abstractly and in shades of gray. They are now able to analyze situations logically in terms of cause and effect and to entertain hypothetical situations and use symbols, such as in metaphors, imaginatively [32]. This higher-level thinking allows them to think about the future, evaluate alternatives, and set personal goals [33]. Although there are marked individual differences in cognitive development among youth, these new capacities allow adolescents to engage in the kind of introspection and mature decision making that was previously beyond their cognitive capacity. Cognitive competence includes such things as the ability to reason effectively, problem solving, think abstractly and reflect, and plan for the future. So as mentioned before it can be deduced that the impact of cognitive behavioral therapy was great in youth as a result of cognitive development in them and more involvement to the cognitive tasks more than before.

At the end a noteworthy point in this research is that the range of therapeutic method was extended to the junior school level from the hospital arena and from adults to the adolescents. Also, the researchers maintain that for treating the major depression, it is better to combine the therapeutic method instead of solely relaying on one method.

Funding: The authors would like to thank all Participants of this study and Also Dr. Raziye Izadi for their assistance in running the project.
Competing Interests: The authors declare that they have no competing interests.
Contributors/Acknowledgement: F.SH contributed in the concepts, design and statistical analysis and also she is the guarantor, agreed for all aspects of the work. M.E contributed in the Definition of intellectual content, Clinical studies & Data acquisition and agreed for all aspects of the work. N.B contributed in Literature search, Manuscript preparation, Manuscript editing, Manuscript review and agreed for all aspects of the work. F.Y contributed in Experimental studies & Data analysis and agreed for all aspects of the work.

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