Psychotherapy Cognitive Behavioral Therapy and Pharmacotherapy in Depression Patients Evidence Base Case Report

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Abstract: Depression is a mental problem that generally occurs at various ages. Depression in children and adolescents is almost similar to conditions in adults in general. It is estimated that in 2030 according to the World Health Organization (WHO), depression can be a problem for middle to developed countries. A case of depression in a female patient aged 20 years received combination therapy with pharmacotherapy in the form of sertraline 50 mg/24 hours orally and Cognitive Behavioral Therapy (CBT). The aim of this study is to compare pharmacotherapy with CBT to increase the awareness of therapists to develop treatment for depression in patients in future studies. The search was conducted using the PubMed, Cochrane, Tripdatabase, Medscape databases using the search keywords Depression AND Pharmacotherapy AND Psychotherapy AND Cognitive Behavioral Therapy. The search was restricted to using a screening of journals published in the last 10 years, subject to human research. The results showed that SSRIs are suitable therapy combined with CBT in depressed patients. The study also found that the combined effect of CBT and pharmacotherapy can accelerate the healing effect and prolong remission in depressed patients.

Keywords: Depression; Pharmacotherapy; Psychotherapy; Cognitive Behavioral Therapy

Introduction

Unipolar depression is a problem that is now common at several ages, starting from childhood (age 5-10 years) at 0.3% then 2.7% in young adolescents (age 11-16 years) and 4.8% in adolescents nearing adulthood (age 17-19 years) and in adult the incidence of depression can vary between 5-20%. The main problem with this disorder is that the symptoms can vary with emotional problems, aggression and avoidance in the face of a problem (refusal to attend school). Depressive conditions can be exacerbated by continuous episodes, recurrent episodes or triggered by comorbid problems from other psychiatric disorders. According to a study carried out in the United States, the initial symptoms of depression appeared during adolescence with 48% of patients showed a tendency to commit suicide and in adulthood about 26% committed the act in which the adolescent tend to do something more fatal than adult patients. Further research from World Health Organization (WHO) assesses that by 2030

depression will become a disturbing problem for middle and high income countries because the problem of depression is not only assessed based on suffering, incapacity of a patient or worsening health conditions, but also raising health care costs and increase the length of hospitalization that can be exacerbated from depression itself. Evaluation is needed for the treatment of depression either with pharmacotherapy or psychological treatment. Many patients want psychotherapy as an addition to pharmacotherapy.

Over the past two decades, pharmacotherapy and psychological treatment have been widely used for the treatment of depression in both children and adults. The use of antidepressant medication in 2005-2012 in children alone increased from 1.3% to 1.6% in the United States and from 0.7% to 1.1% in the United Kingdom. In clinical practice, pharmacotherapy with tricyclic antidepressants, norepinephrine antidepressants, dopamine reuptake inhibitors and selective serotonin reuptake inhibitors (SSRIs) was found. Fluoxetine and Sertraline were introduced as pharmacotherapy in patients with depression, including patients with mixed depression with anxiety, depression with somatic complaints, and can also be given to patients with or without mania. Most of the antidepressants act on monoamine neurotransmitters that will affect the synapse and will then continue intracellular signalling and second messenger pathways. Although antidepressants can improve mood in patients, long-term effects on antidepressants can cause sexual disorders, weight gain, nausea and headaches. It has also been reported that the use of antidepressants that cause sedative effects cannot significantly improve the mood of depressed patients with anxiety or motor problems. Patients that only pharmacotherapy without psychological treatment (psychotherapy), experienced three times higher rates of discontinuation of treatment during therapy than patients with a combination of pharmacotherapy and psychotherapy.

Cognitive Behavioral Therapy (CBT) began to emerge in the 1960s after cognitive theory developed by Aaron Beck an expert in cognitive theory argued that negative thoughts contribute to symptoms of depression. CBT refers to intervention through family (cognitive, behavioral, developmental and social skills). Therapists who use CBT can assess from several trials such as on behavior, development and cognitive thoughts that appear in a person. CBT is most often used in outpatients who are required to come regularly and can be combined with pharmacotherapy. CBT is expected to encourage positive thinking in patients, CBT techniques include assigning tasks, homework, and role playing in difficult situations. In some studies, it was also found that patients with depression that tends to be chronic and resistant to the use of antidepressants will get a positive effect with CBT. CBT itself is one of the short-term dynamic psychotherapy (STDP) which is proven to provide efficacy for axis I and axis II. Tolin et all said that when CBT is compared with other psychotherapeutic techniques (taking psychodynamics as an example), CBT is the therapy of choice that can be used in a variety of psychiatric disorders. Although CBT itself does not show superiority over other psychotherapeutic techniques.

In some previous studies, it was found that the combination of CBT with pharmacotherapy has a good effect after 12-16 weeks of treatment. There is an improvement of about 30%-40% in achieving remission and can even reach 60% efficacy when therapy is combined. CBT as a stand-alone therapy is not recommended in patients with psychotic or bipolar depression. Meanwhile, pharmacotherapy alone tends to cause recurrent depressive symptoms and discontinuation of therapy. Major depressive disorder is a psychiatric problem that suffered by approximately 17.3 million adults in the United States, while in Indonesia it is found to be 6.2% in adolescence (15-24 years) and will show an increase following the age assessment of 8.9% at 75 years and above. (Figure 1). In the research summary, it will be a question whether pharmacotherapy is more effective than CBT or whether CBT is more effective than pharmacotherapy. It is believed that comparing pharmacotherapy with CBT might increase therapist awareness to develop better treatment for patients with depression in future research.

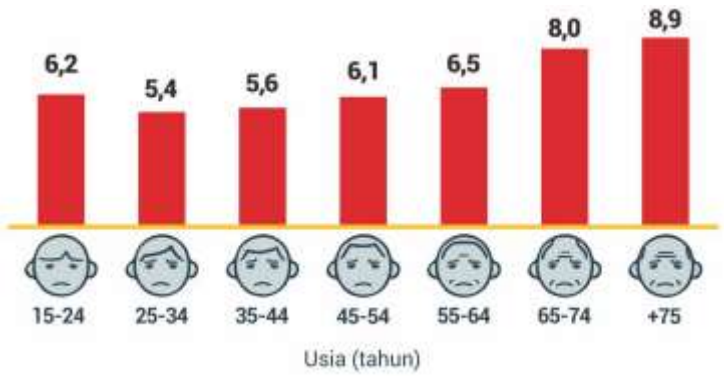


Figure 1: Prevalence of depression in the population over 15 years old by age group. Riskesdas 2018.

Methods

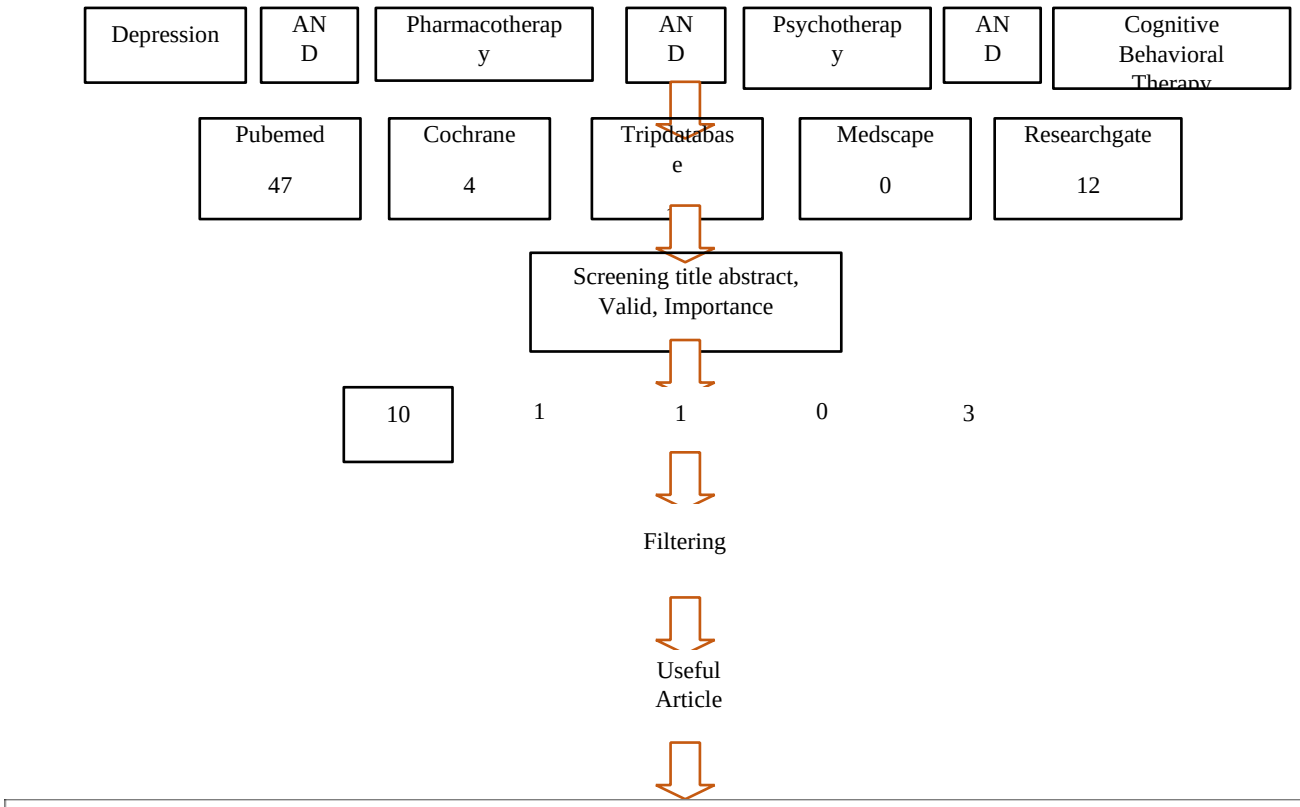
Searches were conducted with PubMed, Cochrane, Tripdatabase, Medscape, Researchgate databases using the keywords Depression AND Pharmacotherapy AND Psychotherapy AND Cognitive Behavioral Therapy. The search was restricted using a screening of journals published in the last 10 years, human research subjects. Clinical question formulation: How is the comparison of therapy efficacy in patients with depression using pharmacotherapy and cognitive behavioral therapy? The purpose of this question is to find out the best treatment through pharmacology or Cognitive Behavioral Therapy in patients with Depression.

P : Depression

I : Pharmacology and Cognitive Behavioral Therapy

C : Other Pharmacology and Psychotherapy

O : Effectiveness of symptom improvement with Pharmacology and Cognitive Behavioral Therapy



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Case Illustration

A 20-year-old woman complained of frequent dizziness and pain in the shoulder for the last 3 years. The symptoms was felt since her father decided to leave the house. She is the second of four children with all siblings being male. Every month, she switches places with her siblings to either be with their father or mother. The relationship between her and her mother is not very close. Every time there is an argument between her mother and father, she is usually the one who gets blamed. These family issues had caused her academic performance to drop during high school, prompting the school to call her parents. Her father came and tried to understand her, in which she felt a little better but the dizziness and shoulder pain were still there. She then asked by her father to see a neurologist and no abnormalities were found in her.

Around 1 month before the patient first saw a psychiatrist. She experienced difficulties with her thesis. She said there are difficulties in processing her data. She tried to tell her mother about her problem, but her mother said to not be too stressed about it. Hearing this response, she felt sad about her family condition. Her parents were living in a different house but were not divorced until the time she was examined. She often complains of dizziness and pain in her shoulder. When the condition become more stressful, she feels additional symptoms such as migraine. She also cried every night for the past 2 weeks thinking about her thesis and her family. She feels that her mother is unable to understand her, and she needs the attention given by her mother even though her father already care for her. She then tried to see a psychiatrist on the advice of her brother. Her father understood that she was seeking treatment. She choose not to inform her mother because she is afraid her mother will blame her for being too stressed. During the examination with the psychiatrist, she denied any excitement or elative mood for 1 week. She had never been treated before and she did not dare to self-diagnose her condition 3 years ago. She said that she didn't feel any emptiness and that she didn't have the urge to harm herself or think about suicide. She denies any strange things such as hearing whispering voices without a source or seeing shadows without a form.

The diagnosis according to ICD-10:

(F32.11) Moderate Depressive Episode with Somatic Symptoms

The therapy given was used to reduce the depressive mood disorder and somatic symptoms experienced by the patient. The patient received sertraline 50 mg/24 hours orally combined with Cognitive Behavioral Therapy in every meeting. The patient attended therapy and assessment once a week for three months. In the first session, she was not given any task and only explanation about her condition. The patient said that the dizziness had been felt for a long time, and she had been to the neurologist and internal medicine before she went to a psychiatrist. However, no abnormalities were found in the patient. The patient and family denied any history of high blood pressure, diabetes or heart disease. At the second session, the patient was given an assignment to write an essay about herself at least 1 page of paper. It

was discovered that she never confided in family members or other close friends about her problems since she thought it will only upset them over her behaviour. For the second to fifth session, she was asked to make a Daily Thought Record every time she experienced a symptom. She began to realize that her actions often tended to suppress her problem in the subconscious and causing physical symptoms to appear. Therapy began to try to modify dysfunctional beliefs and strengthen adaptive beliefs in the patients. For instance, she frequently fails to ask her mother's action when the latter is irritated due to tiredness from work. It will then cause the patient to thinks that her mother hates her. She then becomes sad and cause dizziness to arise. The patient was taught to ask directly to confirm whether the patient's negative thoughts were true or not, her mother said that she only wanted to rest and love the patient. The dizziness subsided and she started to feel more at ease. Therapy sessions with the CBT model continue for patient evaluation and become a new core belief that is more adaptive for the patient. The use of sertraline is aimed at reducing symptoms of depression and somatic complaints in the patients. She reported a decrease in somatic complains after three weeks use of sertraline. There were no side effects from the use of sertraline.

DISCUSSION

The patient was given SSRI therapy in the form of sertraline 50 mg/24 hours orally and psychological therapy in the form of CBT. In clinical practice, pharmacotherapy and psychotherapy are often used together. Sertraline was introduced as one of the SSRI pharmacotherapies that can be used to treat depression symptoms. Sertraline is often used in combination with CBT rather than other types of pharmacotherapy. From a study conducted by Wenliang et all, there were 12 searches from studies with the division of assessment from 2 groups which is before and after treatment. Using meta-analysis of depression assessment ($I2 = 96.3\%$, $P < 0.001$), with a combination of sertraline and CBT showed a significant reduction in the control group (SMD = 2.97, 95% CI: 3.64, -1.94). Patients with anxiety symptoms were also divided into two groups; before and after treatment ($I2 = 92.2\%$, $P<0.001$) and it was again found that there was a decrease in symptoms after sertraline and CBT in a controlled group (SMD = 1.22, 95% CI: -1.96-0.47). Although sertraline is most commonly used in adolescent to young adult patients, it has also been found that sertraline by cardiologists can be used as antidepressant pharmacotherapy in patients with cardiovascular history. 6,9 Studies have been done using other treatments like paroxetine, venlafaxine, and escitalopram in addition to sertraline. In a study conducted by Goldapple et al. using positron emission tomography (PET) on 14 depressed patients using paroxetine and CBT therapy, an increase in the hippocampus and dorsal cingulate, a decrease in the dorsal, ventral and media frontal cortex was found in 13 patients, which is a part that often increases in patients with

depression. Then in a study using venlafaxine with 24 outpatients; a decrease in metabolic blood sugar in the orbitofrontal cortex was found. Other than that, a decrease in the left medial prefrontal cortex and an increase in the right occipital side of the brain were also found using PET. The patients then become the control for cognitive assessment in patients with depression. A different research process was carried out in patients that used escitalopram. It is conducted on 38 patients who previously only use pharmacotherapy for 12 weeks without CBT. After no progress was found, CBT was carried out for the next 12 weeks with a combination of escitalopram administration. Metabolic decrease was found in the anterior region of the right insula when CBT was combined compared to when given escitalopram therapy alone.

Studies about antidepressant combination effects have been conducted in patients from adolescents to young adults with 88 randomized participants with average age of 15. The study used SSRIs as the main therapy and benzodiazepine as additional therapy. Exclusion criteria were bipolar patients, illicit drug use and antipsychotic drug use. The study was conducted for a minimum of 16 weeks with evaluations conducted every 2 weeks. The results of the study, which were described in the Child Depression Inventory (CDI) and Profile of Mood States (POMS) assessments, showed the course of each effect was different from the use of antidepressants alone, CBT alone or in combination. Assessments were also made based on cognitive levels through the Automatic Thoughts Questionnaire (ATQ). As well as looking at the chemical effects of norepinephrine and serotonin. (Table 1). As the result, it was found that the effects of combination therapy were balanced with the use of medication alone and CBT therapy alone. The improvement of depression symptoms tend to be faster for the first 8 weeks of pharmacotherapy then stagnate once it post-treatment stage. On the other hand, CBT tends to be slower in reducing depressive symptoms compared to pharmacotherapy but gives a better effect on post treatment. This is supported by the CDI results in assessing depressive symptoms in patients with children, adolescents and young adults. Using ATQ assessment for cognitive patients, combination therapy tends to be more stable than monotherapy. The effect of combination therapy is not too different from pharmacotherapy monotherapy on serotonin or norepinephrine.

	Pre-treatment	8 weeks	Post-treatment	Time-treatment interaction, *P* value	Time effect (pre-post), *P* value	Pre-post effect size (Cohen's *d*)	% Pre-treatment participants higher than the average Post-treatment participant
CDI total score							
REBT/CBT	23.60 (5.82)	21.12 (6.67)	15.92 (6.49)	$F(2, 82) = 0.543$;	$F(1, 82) = 71.059$;	1.201	88
Medication	24.78 (6.33)	20.10 (8.55)	15.39 (8.76)	$p = 0.583$	< 0.001	1.179	88
Combined	23.48 (5.14)	21.75 (7.29)	16.80 (8.78)			0.845	79
POMS (distress)							
REBT/CBT	75.91 (31.07)	61.97 (25.97)	37.44 (25.06)	$F(2, 82) = 1.402$;	$F(1, 82) = 55.622$;	1.311	90
Medication	70.45 (36.10)	44.93 (25.86)	42.00 (33.77)	$p = 0.252$	< 0.001	0.791	79
Combined	61.85 (33.98)	51.84 (35.48)	38.30 (34.51)			0.664	76
ATQ							
REBT/CBT	46.21 (11.52)	41.14 (11.78)	27.78 (9.52)	$F(2, 82) = 1.078$;	$F(1, 82) = 104.751$;	1.670	76
Medication	45.51 (11.89)	32.89 (10.52)	31.09 (15.72)	$p = 0.345$	< 0.001	0.991	82
Combined	43.14 (13.32)	36.80 (14.79)	29.46 (12.64)			1.017	84
Serotonin							
REBT/CBT	248.42 (113.70)	-	174.17 (125.63)	$F(2, 72) = 0.693$;	$F(1, 72) = 16.856$;	0.599	73
Medication	210.92 (113.18)	-	115.42 (117.29)	$p = 0.503$	< 0.001	0.805	79
Combined	274.00 (288.07)	-	113.09 (91.37)			0.441	66
Norepinephrine							
REBT/CBT	358.16 (178.15)	-	292.35 (188.43)	$F(2, 72) = 0.797$;	$F(1, 72) = 8.928$;	0.347	62
Medication	406.49 (199.25)	-	320.52 (140.37)	$p = 0.454$	0.004	0.480	69
Combined	450.29 (251.55)	-	295.10 (131.58)			0.685	76

Table 1. Standard deviation of before treatment, 8 weeks and after treatment 16 weeks.

In a study with 292 outpatient adults (171 women and 121 men) with an average age of 45.1 years, it was found that 137 patients who received monotherapy alone with the same pharmacotherapy as young adults were found to have a lower value in maintaining the patient's remission period, while 155 patients who followed combination therapy tended to maintain a better remission condition than pharmacotherapy monotherapy (Figure 1).

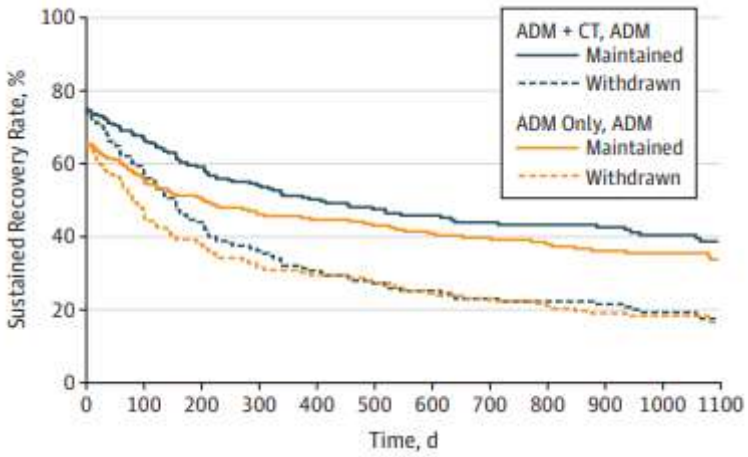

Figure 1. Patient's condition maintaining remission period.

The condition of the application of combined pharmacotherapy with CBT is also related to the patient's condition at the beginning of therapy (pre-treatment). According to research by Eddinton et al., patients with pessimistic features may seems to worsen for the first three to ten weeks of therapy. The patient motivation to mend themselves plays an important role in the treatment process of depression. 13 CBT can also be compared with other psychotherapy methods. Based on the Effect Size (ES) with a standard assessment of -0.02 to 0.25 as an assessment of the CBT effect, it was found that CBT was

superior to Behavioral Activation, psychodynamic psychotherapy, and other psychotherapies. However, when viewed using the Beck Depression Inventory (BDI) questionnaire, it was found that supportive psychotherapy had a range value of 0.26 and psychodynamic therapy of 0.27. It has a better range of assessment when BDI is used.

Apart from its optimal effect on patients, CBT combined with medication can have positive outcomes in terms of improving health fund for both the patients and the government. In nations where insurance system is in place, CBT can lessen the long-term consequences of hospital stays. Additionally, CBT can increase patient motivation to live for at least half to one day. Then hospitalization will decrease by 1.4% to 1.6% based on Canadian health technology research. CBT may increase the cost by up to twice as much as standard pharmacological treatment. However, the government's role is still necessary in addition to increasing hospital and healthcare facility revenue. This is because conducting CBT with health worker ratio of 1:48 (one health worker can treat 48 people) requires an increase of fund in order to improve health quality through psychotherapy.

Not every patients using CBT experience positive effects. In another study with 1700 depressed patients, 13% of patients felt worsening of negative symptoms. After each session, mild worsening may worsen by 5-7% or adding 1 point of BDI score. Moderate worsening can add 9 BDI points; and severe worsening can add patient's points up to a maximum BDI score of 31. To prevent this, combination therapy using pharmacotherapy is needed when CBT failed to provide a prominent effect for patients with depression. The main cause of this decline is the therapist. When the therapist immediately judge the patient's faults and chastised the patient in therapy, the patient becomes more depressed. Psychotherapy that immediately assesses the pathology of the patient without looking at the cause of the symptoms makes the patient a victim and the psychotherapist a criminal. To overcome these problems, it is hoped that a psychotherapist can control themselves and additional pharmacotherapy is given to reduce the negative effects of CBT.

Conclusion

Therapy using pharmacotherapy and psychotherapy is recommended in patients with depression. Children, adolescents, and young adults' patients benefit from SSRI therapy and it is even more beneficial when CBT is added. CBT tends to correlate with pharmacotherapy, especially SSRIs, as it can help reduce depressive symptoms and patient cognition symptoms. However, CBT alone cannot be considered superior in the treatment of depression. Other psychotherapies such as supportive psychotherapy and psychodynamic psychotherapy can be another alternative in conducting psychotherapy in patients.

Conflict of Interest

No potential conflict of interest was reported by the authors.

Acknowledgemnt

We would like to express our deepest gratitude to several parties who have helped in completing this research, for my patient, my students dr. Yudo and those whose names i can't mention, The contributions and time given by them are invaluable and have helped in obtaining accurate data.

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