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Efficacy of pharmacotherapy and psychotherapy in treating Depression and Anxiety Disorders

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EFFICACY OF PHARMACOTHERAPY AND PHYCHOTHERAPY IN TREATING DEPRESSION AND ANXIETY DISORDERS

by

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Abstract

Major depression is the most prevalent psychiatric disorder which affects 20% of the population in the united states, and the prevalence is twice as high in women than men (Porth, 2014). A literature review of the prevalence of major depression among ICU survivals revealed that being female increased the likelihood for major depressive disorder five times compared with men in the ICU (Asimakopoulou, 2014). There is also an increasing incidence in adolescents and children, and also a higher prevalence with people with family history of mood disorder. Major depression affects up to 37 percent of American adults and is more common among women than among men. In adolescence, girls are twice as likely as boys to be diagnosed with depression (Romanowski, 2004). There are many theories of the etiology of major depressive disorder (MDD), including evolutional theory, genetic influence, dysregulation of neurotransmitter model, psychosocial theories, and biological basis which includes abnormalities in brain chemistry. Dopamine is a neuromediator in the brain, it is located in the substantia nigra and ventral segmental area in the midbrain, derived from tyrosine. It is involved in motivation, thoughts, emotions. “Dopamine is thought to play a role in anhedonia (lack of pleasure in usual activities) which is often experienced by patients with depression” (Perese, 2012).

The patient in the case report presented with severe major depressive disorder, passive thoughts of death, with a comorbid substance use disorder. Upon further evaluation, pharmacotherapy was initiated to stabilize the patient and improve sleep. The Patient disposition after stabilization in inpatient psychiatry includes safe housing, connecting with an outpatient mental health provider which includes psychotherapy services. These actions appear to be in line with most recommendations for mental health professionals in the literature reviewed.

Background

Most adults with major depressive disorder (MDD) fail to achieve remission with index pharmacological treatment. Moreover, at least half will not achieve and sustain remission following multiple pharmacological approaches. The goal of treatment now is complete remission of symptoms, then maintaining a level of improvement so that depression does not relapse shortly after remission, nor does that patient have a recurrent episode in the future. The case presentation takes a look at a patient suffering from recurrent depression with chronic suicidal ideation, generalized anxiety with substance use disorder. The patient has seemed not to benefit from past treatment plans/ options modality and currently endorse severe episode of depression. Knowing the unlikelihood of achieving complete remission, and how it declines with each successive treatment attempt, the purpose of the report is to compare and contrast the efficacy of psychotherapy and pharmacotherapy in treating depression and anxiety disorders.

Case Report

Patient is a 55-year-old male with a past medical history significant for diabetes mellitus II, seizures, past suicide attempts, asthma, obstructive sleep apnea, personality disorder, traumatic brain injury (TBI), substance abuse who was admitted with altered mental status and suicide attempt by overdose by an unknown substance in an attempt to take his life. The patient psych history includes a number of inpatient psychiatric hospitalizations for depression, suicidal ideation when drinking, most recently twice within the past 2 months. Pt appears to be currently seeing an outpatient psych provider, and some engagement with psychotherapy per chart review. Upon interview with the patient, he reports that he has been feeling depressed lately due to the social stressors of losing his apartment, being homeless, and also stressors of living in environments like the public shelters, having his money and food stolen, and substance use to the point where he wants to commit suicide. Patient further reports that he currently is staying in a

shelter and has been waiting for assistance with housing but it's going slow and he is tired of waiting. He reports frustration, sadness, helplessness, hopelessness, feeling worthless, poor sleep with racing thoughts, poor appetite, anxiety, and passive thoughts of death. Patient denies hallucinations, voices, mood swings, mania, and thoughts to hurt others. Prior to hospitalization, the patient stated he was on Zoloft and Trazodone which he avoids when he drinks and endorses using cocaine on occasions. The patient says he "drinks sometimes to kill my problems" and wants to take something that prevents him from "feeling so down all the time". On observation, the mood appears depressed, attention/concentration is slow, insight/judgement is poor, thought process and speech are slow, and the patient appears dysphoric. Pt is homeless, currently unemployed, the support system includes a brother, currently on probation for a felony conviction for domestic assault by strangulation, also has a history of armed robbery as a teenager, served three years in prison. Pt has been a victim of trauma in the past, history of stabbing to the abdomen, head injury due to assault, and a gunshot wound to the chest.
Patient has past psych medication trials which include but not limited to Depakote, Trazodone, Keppra, Lyrica, Celexa, and Zoloft, no history of ECT, no history of MI/CD commitment.
Patient has been in CD treatment about 5 times, endorsed poor choices while in treatment, and identifies alcohol use as the only dependency he believes she has trouble overcoming.
Working diagnoses at the moment are Alcohol use Disorder, Moderate, Cocaine Use Disorder, Moderate, Major Depressive Disorder, Recurrent episode vs Substance/Medication-induced Depressive Disorder, Rule out Post Traumatic Stress Disorder symptoms, Rule out personality disorders and malingering behaviors. The plan is to hospitalize patient in inpatient psychiatry for further stabilization, restart home meds that include Zoloft, Trazodone, Gabapentin, also consult to addiction medicine for recommendations, possible chemical dependency treatment social

work assistance with disposition, having financial counselors involved for financial assistance, and reconnecting patient back with an outpatient provider and individual therapy. Thus, leading to the comparing, contrasting the efficacy of pharmacotherapy, psychotherapy, or the combination of both in the treatment of depression and anxiety.

Literature Review

According to (Grieken et al., 2015), by the year 2030, depression is estimated to be the leading cause of burden of disease in high-income countries. The article describes a need for improvement from traditional evidenced based on depression management due to recurrent episodes. An approach to improvement is the addition of effective self-management strategies. Although self-management in general medicine is mostly related to coping with a chronic disease, it is interesting that in the case of depression, information on the Internet and in (self-help) books suggests that self-management could help in particular in the 'recovery from' instead of 'coping with' the disease (Grieken et al., 2015). The patients in the study agreed that the focus for recovery must be behavioral and cognitive strategies. Key findings in the article are the different number of self-management strategies from patients' perspective that contributes to their recovery. Some of these strategies include having a proactive attitude towards depression and treatment, daily life strategies and goals, being able to explain the disease to others, remaining socially engaged, engaging in activities, structured attention to oneself, contact with fellow sufferers. Self-management can be an alternative or supportive treatment introduced to depressed patients.

The article by Muneoka, 2009 looks into the effectiveness of duloxetine, an SNRI in the treatment of major depressive disorder and anxiety. Depression is associated with anxiety and physiological and psychological pain. In a 4 day in clinical trials by Muneoka, 2009 on rats, 20

mg/day of duloxetine induced a marked increase in Serotonin levels. A Longer-term (21-day) treatment of rats with duloxetine increased the electrically stimulated release of 5-HT and NA in the hippocampus and midbrain. The study also demonstrated an anxiolytic-like effect when treating the animals with duloxetine, "it significantly increased the time animals spent in open areas in the zero-maze suggesting an anxiolytic action of the drug" (Muneoka, 2009). Adverse effects of duloxetine were also taking into consideration, with trials on healthy people, ventricular repolarization when assessed by QT prolongation was not affected. Thus, showing duloxetine to be safe when administered within therapeutic dose range. In a short-term observation (7-9weeeks) of measuring its efficacy on MDD, duloxetine 60 mg/day was superior to placebo in reducing the score on the 17-item Hamilton Rating Scale for Depression (HAM-D-17) 2 weeks after administration began. "Reported remission rates were 43%–58% in the short-term studies" (Muneoka, 2009). Longer-term studies showed that patients had a significantly longer time to relapse while on duloxetine compared to placebo, and also shows a 70% – 75% remission rate. "Three short-term (10 weeks) placebo-controlled studies indicated the superior effects of duloxetine (60–120 mg/day) compared with placebo in reducing the Hamilton Anxiety Rating Scale (HAM-A) score" Muneoka, 2009). In a longer-term study with patients with GAD, it also shows a greater improvement of the quality of life when compared to the placebo. Implications for practice shows its effectiveness in treating MDD, dysthymia, GAD, and pain-related diseases such as fibromyalgia.

In the study by Hassan et al., 2017, they compared how patients with a dual diagnosis of opioid use disorder with mood and anxiety disorders can have variable prognosis due to receiving opioid agonist therapies (OAT). Thus, they embark on examining the efficacy of pharmacotherapy in the treatment of symptoms of depression or anxiety in patients on OAT.

"Patients with OUD have a high incidence of affective symptoms, such as depression and anxiety, also have poor outcomes, poor quality of life, severe substance abuse, and psychosocial impairment" (Hassan et al., 2017). Their study also shows that opioid agonist therapy can effectively treat OUD, but about a quarter of the patients did not experience improved mood after the therapy. An early RCT compared cognitive behavioral therapy (CBT) to non-directive group therapy in the treatment of 14 patients on methadone. Patients in the CBT group had a highly significant reduction in symptoms of depression and anxiety than patients in the control group. "In comparison to pharmacotherapy, treatment with psychotherapy consistently decreased symptoms of depression in patients with dual diagnosis. These results demonstrate that the use of psychotherapies is beneficial for patients in OAT in general. There were no significant differences between various psychotherapies in term of their effectiveness in alleviating either symptom of depression or anxiety" (Hassan et al., 2017). Their metanalysis of RCT's also shows that patients with persistent symptoms of depression responded better to TCA than SSRI treatment. Hassan et al. (2017) conclude on psychotherapy being more effective than pharmacotherapy in treating symptoms of depression and anxiety in patients on OAT due to decreasing the stress of the individual's negative environment, and also enhancing the therapeutic alliance by providing empathy, support, or acceptance of distressing thoughts. "In addition, targeting early maladaptive schemas might be beneficial to assist with symptoms of depression and anxiety in patients with OUD" (Hassan et al., 2017).

A case report demonstrating the efficacy of psychotherapy in treating depression and anxiety in polycystic ovarian syndrome (PCOS) shows a scarcity of available evidence-based study in the use of psychotherapy in this population. Correa et al., (2015) suggested the PCOS Workbook that uses the cognitive-behavioral framework in treating symptoms of anxiety,

depression, and problematic eating in a 19-year-old female previously diagnosed with PCOS. "Women with PCOS produce an elevated amount of androgens, causing hormone imbalances that could produce infertility, insulin resistance, and obesity, and also vulnerable to developing mental health problems due to hormone imbalances" (Correa et al., 2015). The use of CBT in treating these symptoms helps create cognitive restructuring that can help improve psychological functioning and also help in adopting lifestyle changes that may be necessary for managing the disorder. The subject of the case reports "change in problematic symptoms, as well as body weight, throughout the course of therapy. The participant experienced a consistent, significant reduction in BDI-II scores and BAI scores during the course of treatment. Scores on both measures dropped from the severe range at intake to the normal range at termination and remained in the normal range 6 months after termination" (Correa et al., 2015). The participant also stated that the cognitive restructuring was very helpful, and it contributed to her long-term success. Though PCOS workbook shows an effectiveness in helping with depression and anxiety symptoms, the authors felt a need for a more rigorous randomized clinical trials against active controls, such as other empirically supported interventions are needed.

Meaney-Tavares & Hasking, 2013 conducted a study to analyze the efficacy of a pilot program, aimed at treating college students with a borderline personality disorder (BPD) using short-term, modified group dialectical behavior therapy at an Australian college counseling service. Since remission in BPD takes about 1 -3 years of therapy before significant clinical improvements, a preliminary pilot of a modified (DBT) group named "Coping and Regulating Emotions" (CARE) was created with the hope the CARE program could result in a decrease in self-reported anxiety, depression, and BPD criterion-related behaviors and an increase in adaptive coping skills. It consisted of the 4 DBT modules; includes conceptual frameworks, such

as the neurobiological underpinnings of emotion and behavior, and language and examples relevant to college students. Seventeen enrolled college students aged between 18 and 28 (76.5% female), with a diagnosis of BPD completed the program between November 2009 and November 2010. Eight 2-hour group therapy sessions were held, and participants were assessed for levels of depression, anxiety, BPD traits, and coping strategies, at commencement and completion of the program. “Over the 8-week period, the mean scores indicated a decrease from the lower end of a severe range of depressive symptoms (29–63) to the upper end of a mild range of symptoms (14–19)” (Meaney-Tavares & Hasking, 2013”. With a reduction in symptoms of depression and BPD traits, and an increase in adaptive coping skills, including problem-solving, and constructive self-talk, it shows the modified DBT can be effective in minimizing the distress caused to this population through difficulties in obtaining an appropriate external referral.

Primary care providers now are now expected to be able to assess and treat depression as it is a leading cause of global disease burden and tends to be managed in primary care settings in many places around the world. Arroll et al, 2016 looks into the effectiveness of antidepressants in primary care, also examining the efficacy of different individual agents. They argued that most current practice guidelines show studies done in secondary and tertiary settings, and in situations where patients were mostly moderate- severely depressed, and a need for updated guidelines for mild depression mostly encountered in primary care. Thus, they embarked on assessing the effectiveness of all classes of antidepressants versus placebo in primary care patients. Results suggested “antidepressants are effective when compared with placebo for depression in primary care. There were four broad medication groups, including TCA, SSRI, SNRI, and NaSSA, and all had evidence of efficacy in the current review of participants with mild to moderate severity

in primary care" (Arroll et al., 2016). Implications for practice showed evidence in some individual agents such as amitriptyline, mianserin, sertraline, escitalopram, venlafaxine due to evidence, but does not necessarily means more effective than other agents that lacked research evidence. The article did specify on the need to conduct more studies on agents that lacked evidence in the treatment of depression in primary care.

In treating major depressive disorders, questions have always arisen on what the initial treatment should be. Markowitz (2008) argues that clinicians often do not think carefully before deciding and that psychotherapy may be overlooked too often as a first treatment option. Also, treatment bias by clinicians tends to influence or determine which interventions they select for their patients rather than by treatment guidelines or the empiric outcome research literature. "The choice of initial treatment is hardly trivial; it consigns a patient to a particular mode of therapy for a period of weeks or months" (Markowitz, 2008). If treatment choice is ineffective, the patient may become increasingly hopeless in their condition and may drop out of other treatment options that may alleviate their symptoms. In patients with mild depression, antidepressants may not be needed, as "psychotherapy- CBT, interpersonal therapy, and dynamic psychotherapy- has been found to be equivalent to the use of antidepressant medications" (Perese, 2012). The author suggested the indication for psychotherapy in practice should be a patient preference, symptom severity, nature of symptoms, prior treatment history, psychosocial context, and contraindication to pharmacotherapy. Significant psychosocial stressors, intrapsychic conflict, interpersonal difficulties, or a comorbid Axis II disorder complicates treatment, and thus psychotherapy may be more beneficial. The author concludes combined treatment is the treatment of choice for patients with chronic or severe depressive episodes, but also that psychotherapy is only as good as their therapists. Thus, the choice of a good empirically supported psychotherapy and a good

therapist can improve mild to moderate depressive symptoms, and "psychotherapy may keep on working even after acute treatment has been terminated as a result of learned new skills" (Markowitz, 2008).

Perese (2012), estimated that about two-thirds of patients with depressive disorder experience some improvement following treatment with the first antidepressant that is used- that is, they experience at least a 50% reduction of their symptoms; however, less than 50% of patients achieve remission. SSRIs are usually the first line agent for the treatment of depression, and it is also helpful in treating a number of anxiety disorders, eating disorders, premenstrual dysphoric disorder. Preliminary evidence suggested that sertraline might be slightly superior in terms of effectiveness. Cipriani et al., 2010, looks into the effectiveness of Sertraline versus other anti-depressive agents for depression. In their study, they found evidence favoring sertraline over some other antidepressants for the acute phase treatment of major depression, either in terms of efficacy (fluoxetine) or acceptability/tolerability (amitriptyline, imipramine, paroxetine, and mirtazapine). However, some differences favoring newer antidepressants in terms of efficacy (mirtazapine) and acceptability (bupropion) were also found" (Cipriani et al., 2010). The author also highlighted that participants experienced a higher rate of diarrhea while sertraline but was also highly favored in a systematic review in terms of efficacy and tolerability. Sertraline appears to be well tolerated, had proven efficacy and is a recommended first line of antidepressant for clinicians.

The associated cost to society and health care systems of depressive disorders are well documented. Qaseem, A., Barry, M. J., & Kansagara, D. (2016) in their article estimated the economic burden associated with depression was $83.1 billion in 2000 and is higher today. The effectiveness of pharmacology and non-pharmacology are well documented in the literature,

publications, and practice guidelines. The authors discussed practice guidelines based on systematic review of RCTs for pharmacologic and non-pharmacologic treatment of adult patients with major depressive disorder. In their review, monotherapy of second-generation antidepressants when compared to CBT shows no difference in response in patients with MDD after 8 to 52 weeks of treatment. Also, combined therapy of both showed no difference in response or remission when compared to monotherapy in patients with MDD after 12 to 52 weeks of treatment. Qaseem, A., Barry, M. J., & Kansagara, D. (2016) summarized that most patients do not achieve remission after initial treatment with SGAs, in which case switching therapies or augmenting with additional interventions such as non-pharmacologic treatment may be warranted. An implication for practice is the strong consideration of CBT as a reasonable approach for an alternative treatment to SGAs where available due to adverse effects and or risk of discontinuation.

Cuijpers et al., (2013) compared the efficacy of psychotherapy and antidepressant medications in treating in all types of depressive, anxiety disorders, and whether all types of psychotherapy and antidepressants are equally efficacious for each disorder. The authors argued it remains unclear whether all types of psychotherapy and all types of antidepressant medications have comparable effects. In one previous meta-analysis, “they found that treatment with selective serotonin reuptake inhibitors (SSRIs) was somewhat more effective than treatment with psychotherapy, whereas tricyclic antidepressants (TCAs) and psychotherapy were equally effective” (Cuijpers et al., 2013). A re-analysis of those data, however, showed that there were no significant differences between psychotherapy and SSRIs after adjusting for differential drop-out from both treatments. Another meta-analysis confirmed that psychotherapy and SSRIs were equally effective when only *bona fide* psychotherapies were included. In providing stronger

evidence, Cuijpers et al., (2013) compared systematic search results of 67 randomized trials, including 5,993 patients that met inclusion criteria, 40 studies focusing on depressive disorders and 27 focusing on anxiety disorders. In conclusion, they found both psychotherapy and pharmacotherapy to have comparable effects in anxiety and depressive disorders, except in OCD and dysthymia. Evidence suggested that psychotherapy was significantly more efficacious in OCD and that pharmacotherapy was significantly more efficacious in dysthymia.

Patients value and prioritize functioning and quality of life over symptoms management. Meaning a depressed patient having a relative relief from their depressive symptoms from pharmacotherapy and an adverse effect of sexual dysfunction might not adhere to that treatment regimen due to loss of quality of life. Furthermore, improvement in functioning and quality of life has been considered the ultimate outcome measure that indicates whether certain treatments have succeeded. With the quality of life as a priority, Kamenov et al., (2016) metanalysis of RCTs was to determine the absolute and relative effects of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in patients with depression. In conclusion, Kamenov et al., (2016) provide comprehensive evidence that existing psychological and pharmacological interventions are efficacious for improving functioning and quality of life in depression. In comparing psychotherapy v. pharmacotherapy in functioning and quality of life, there was no significant difference. There is no robust evidence that one of the interventions is superior, although psychotherapy appears slightly superior to medication when both are compared to controlled conditions.

Implications

While pharmacotherapy and psychotherapy are both equally effective in the treatment of depressive and anxiety disorders, major difference seems to be in determining when it is

appropriate to initiate either or both therapy. The literature reviewed showed no evidence in the superiority of a therapy choice over the other over an extended period of time. The combination of both combined therapy against either treatment alone appears to be significantly better for both quality outcomes. The literature also shows psychotherapy to be adequate in treating mild to moderate depression, some anxiety disorders, in mild to a moderately depressed patient that prefers non-pharmacologic interventions, or in situations where pharmacological side effects are intolerable. The modest effects suggest that future research should focus on tailoring therapies to better cover the needs of individuals, thus implication for clinicians to tailor treatment based on evidence, patient's acuity, and patient preference.

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