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| RESEARCH ARTICLE

Physical and Psychological Outcomes of Pharmacological Treatment for Depressive Disorder

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| ABSTRACT
Depressive disorder is one of the most prevalent psychiatric conditions, exerting wide-ranging effects on individual health, social functioning, and overall quality of life. The present study aims to examine the physical and psychological outcomes of antidepressant medications, including selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants (TCAs), in the treatment of depressive disorder. This descriptive–analytical research was conducted through the review and analysis of scientific books, peer-reviewed articles, and credible online sources. Findings indicate that antidepressants are generally effective in reducing depressive symptoms, improving mood, and enhancing patients' quality of life; however, each pharmacological class presents specific outcomes and limitations. SSRIs and SNRIs, due to their high efficacy and relatively favorable tolerability, are most often prescribed as first-line treatments but are associated with side effects such as nausea, sexual dysfunction, weight changes, sweating, and emotional blunting. MAOIs, although effective in treating atypical depression, are less commonly used because of the risk of hypertensive crisis and dietary restrictions. TCAs, while beneficial for mood and sleep improvement, are associated with side effects such as dry mouth, constipation, blurred vision, weight gain, and cardiotoxicity in overdose cases. In general, selecting an appropriate antidepressant should be based on symptom severity, patients' physical and psychological conditions, and the likelihood of side effects. Furthermore, combining pharmacotherapy with psychotherapy and lifestyle modification may maximize treatment effectiveness and minimize adverse outcomes.

| KEYWORDS

Depression; pharmacotherapy; physical outcomes; psychological outcomes; antidepressant medications

| ARTICLE INFORMATION

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Introduction

Depression is the most common psychiatric disorder. According to estimates by the World Health Organization, by 2010, after cardiovascular diseases, depression would become the second leading condition threatening human health and life worldwide. Due to its high prevalence among psychotherapy patients, it has been referred to as the "psychological common cold" (Kotler, 2006, as cited in Aghaei et al., 2012). Approximately two-thirds of patients with severe depression think about suicide, and 10–15% eventually end their lives in this way (Sadock & Sadock, 2009). Statistics further indicate that suicide ranks as the eighth most common cause of death in the United States (Rezaei et al., 2016).

Depression is classified as a mood disorder, in which individuals experience prolonged periods of sadness, low mood, and social withdrawal at certain stages of life, often linked to specific life events. Depressed individuals usually feel worthless, empty, and hopeless. In addition, several cognitive symptoms and ideas are strongly associated with depressive reactions, including pessimistic beliefs about their abilities. Emotionally, they experience negative affect and are often described by others as sad, distressed,

dejected, unmotivated, and discouraged. From a behavioral perspective, depressed individuals display slowed speech and activity, respond with short phrases, and exhibit physical inactivity. They may remain in bed for hours, appearing to expend excessive effort even for minor tasks (Ganji, 2020).

The exact cause of depression remains unknown; however, it is widely believed to result from a combination of genetic, biochemical, environmental, and psychological factors. Research has shown that depressive disorders disrupt brain functioning. Neuroimaging techniques such as magnetic resonance imaging (MRI) have demonstrated that the brains of individuals with depression differ structurally and functionally from those of non-depressed individuals (Hosseini & Mahdizadeh Ashrafi, 2011).

According to DSM-IV-TR, depressive disorders are classified into three general groups: major depressive disorder, dysthymic disorder, and depressive disorder not otherwise specified, with several subtypes within each category (Sadock, 2005, as cited in Sararoudi, Sanei, & Baghbanian, 2011). In this study, the primary objective is to examine the physical and psychological outcomes of pharmacological treatment for depressive disorder.

Methodology

This study employed a descriptive research design with an applied orientation. Data were collected through a comprehensive review of books, scientific articles, and other reliable academic sources. Descriptive research seeks to answer questions concerning the *nature* and *characteristics* of a phenomenon, variable, or subject matter, focusing on *what it is* and *how it functions*.

Descriptive studies serve both applied and theoretical purposes. From an applied perspective, the findings of such studies can be utilized to inform decision-making, policy development, and practical planning. From a theoretical standpoint, they contribute to a deeper understanding of the underlying structures and processes related to the phenomenon under investigation.

Depressive Disorder Due to Another Medical Condition

The diagnosis of depressive disorder due to another medical condition is considered appropriate when the symptoms can be directly attributed to an underlying medical illness. If the depressive symptoms result from the direct pathophysiological consequences of a medical condition (such as multiple sclerosis, traumatic brain injury, or hyperthyroidism), the diagnosis of *major depressive disorder* would not be suitable.

On the other hand, the role of ion channels, particularly potassium and calcium channels, has received increasing attention in psychiatric disorders, including depression. Potassium channels play a critical role in maintaining membrane potential. Their blockade can lead to contraction of smooth muscles and blood vessels, or affect the secretory activity of certain cells. Following cellular stimulation, these channels drive the membrane potential toward potassium equilibrium. In general, the closure of potassium channels causes depolarization, while their opening induces hyperpolarization of the membrane. These channels are widely involved in various physiological functions, including the regulation of cardiac rhythm, muscle contraction, neurotransmitter release, neuronal excitability, insulin secretion, and many other processes (Coetzee et al., 1999; Martens, Kwak & Tamkum; Pongs et al., 1999).

Substance/Medication-Induced Depressive Disorder

In order to differentiate this disorder from *major depressive disorder*, it is essential to determine whether a substance (e.g., drugs of abuse, medications, or toxins) is the etiological factor underlying the mood disturbance. For instance, a depressed mood that emerges exclusively during cocaine withdrawal is diagnosed as *cocaine-induced depressive disorder* (American Psychiatric Association, 2022).

The lifetime prevalence of depression is estimated to be approximately 17–21%. Among patients with depression who undergo treatment, about 10–15% fail to respond, where treatment response is defined as at least a 50% reduction in symptoms (Rajabi, 2015). The risk of developing substance-induced depressive disorder appears to be similar across both genders (American Psychiatric Association, 2022).

In an experimental study entitled *The Role of the L-Arginine/Nitric Oxide Pathway in the Antidepressant Effect of Lithium in the Forced Swimming Test (FST)*, Ghasemi and colleagues (2007) investigated the effects of co-administration of sub-effective doses of nitric oxide synthase (NOS) inhibitors and lithium. The findings revealed that concurrent administration of low doses of NOS inhibitors (L-NPA or L-NAME) and lithium, which individually had minimal impact on immobility time in the FST, produced a significant antidepressant-like effect, markedly reducing immobility time in mice. These results suggest that neuronal nitric oxide (NO) may play a role in the antidepressant effects of lithium in the FST paradigm (Ghasemi et al., 2007).

Pharmacotherapy

Depression is often associated with deficits or imbalances in neurotransmitters such as dopamine, serotonin, and norepinephrine. For most individuals with major depressive disorder, relapse following recovery is a common phenomenon. Although the primary objective of treatment is the remission of depressive symptoms, maintaining long-term mental health stability remains a major

challenge. Both naturalistic and clinical studies of major depression consistently emphasize the high rate of relapse following remission (Gonzales & Keller, as cited in Hosseini, 2018). Moreover, the risk of relapse increases with the number of prior depressive episodes.

Pharmacotherapy is one of the most widely used approaches to treatment. Antidepressant medications, first introduced in the 1960s, achieved considerable success in managing depressive symptoms (Ghanji & Ghanji, 2020). Currently, the United States Food and Drug Administration (FDA) has approved 26 different antidepressants for the treatment of depression (Finley & Lee, 2013). The four main classes of antidepressant drugs are:

Tricyclic antidepressants (TCAs): such as imipramine, amitriptyline, desipramine, and nortriptyline. These agents are more effective in alleviating biological symptoms of depression such as appetite loss and insomnia.

Monoamine oxidase inhibitors (MAOIs): such as phenelzine and tranylcypromine, which exert their effects by inhibiting the enzyme monoamine oxidase.

Selective serotonin reuptake inhibitors (SSRIs): including fluoxetine, sertraline, fluvoxamine, paroxetine, trazodone, citalopram, and bupropion.

Serotonin-norepinephrine reuptake inhibitors (SNRIs): such as duloxetine, venlafaxine, and desvenlafaxine (Ghanji & Ghanji, 2020; Moradi & Moradi, 2023).

TCAs, MAOIs, and SNRIs increase the levels of both serotonin and norepinephrine in the brain, whereas SSRIs selectively inhibit the reuptake of serotonin, thereby enhancing serotonergic transmission at the synapse. All of these drug classes facilitate neurotransmission by increasing the availability of monoamine neurotransmitters between neurons (Ghanji & Ghanji, 2020).

A study conducted by Semnani, Saeedi, and Zad-Mashinchi (2002) examined the prescribing patterns of antidepressants in insurance prescriptions of patients attending pharmacies in Anzali city. Results showed that 70.7% of prescriptions included TCAs, 23.2% included MAOIs, and 6.1% included SSRIs. Among these, imipramine (a TCA) and tranylcypromine (a MAOI) were the most frequently prescribed drugs.

Numerous reports indicate that depression is commonly associated with decreased levels of monoamine neurotransmitters, particularly serotonin, norepinephrine, epinephrine, and dopamine in the brain. Most antidepressant drugs—including TCAs, MAOIs, and SSRIs such as fluoxetine—reduce depressive symptoms primarily by increasing the levels of these neurotransmitters (Hillhouse, 2015).

Antidepressant Effects of Royal Jelly and the Clinical Role of Tricyclic Antidepressants in the Elderly

In a study conducted by Parandin and Abbasi (2023) entitled *"The Antidepressant Effects of Royal Jelly on Reserpine-Induced Depression in Laboratory Mice"*, the results indicated that reserpine-induced depression significantly reduced the antioxidant capacity of the brain and markedly increased malondialdehyde (MDA) levels, a marker of lipid peroxidation. Administration of royal jelly at concentrations of 200 and 400 mg/kg, similar to fluoxetine, significantly enhanced the antioxidant capacity of the brain and decreased MDA levels in reserpine-treated mice (Parandin & Abbasi, 2023).

Despite the introduction of newer antidepressant agents over the past decades, tricyclic antidepressants (TCAs) continue to maintain a clinical role in the management of depression among older adults. This persistence is largely due to the availability of robust clinical evidence, well-documented efficacy, and the ability to monitor serum drug levels in clinical practice. Among TCAs, second-generation (secondary amine) compounds exhibit lower frequency and severity of adverse reactions compared to tertiary amines.

Nortriptyline, in particular, is considered by many researchers and clinicians as the "gold standard" TCA for elderly patients because of its defined therapeutic window, favorable safety profile, and broad efficacy across late-life depressive syndromes. However, due to age-related changes in pharmacokinetics and pharmacodynamics, older adults are more susceptible to TCA-related adverse effects. Consequently, effective management in geriatric populations often requires lower doses compared to younger adults.

To minimize the risk of side effects, initiation of TCAs in older patients should begin at the lowest possible dose, with gradual titration based on tolerability. Dose tapering by approximately 10–25% every 1–2 weeks is recommended to prevent withdrawal syndromes in elderly patients.

Prior to initiating TCA therapy, comprehensive medical evaluation is essential, particularly with respect to cardiovascular conditions (e.g., conduction abnormalities), glaucoma, and prostatic hypertrophy. During treatment, ongoing monitoring is necessary,

including orthostatic blood pressure, electrocardiogram (ECG), electrolytes, renal and liver function tests, as well as plasma drug levels following dose adjustments or the addition of interacting medications.

Importantly, the use of TCAs is contraindicated in elderly patients with Alzheimer's disease, ischemic heart disease, cardiac conduction disorders, congestive heart failure, or narrow-angle glaucoma, due to the potential exacerbation of underlying conditions.

The Impact of Antidepressant Medications on Male Sexual Function

Certain serotonergic and anticholinergic antidepressants stimulate serotonin receptors, ultimately leading to elevated prolactin levels (Chaiseh & Kang et al., 2010; Coker & Taylor, 2010). Increased prolactin inhibits the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary, and gonadal hormones from the testes, thereby impairing fertility (Sigman, 2007).

However, it cannot always be concluded that antidepressants reduce fertility solely through hyperprolactinemia. A study conducted on men treated with clomipramine demonstrated that levels of prolactin, LH, FSH, testosterone, and estradiol remained unchanged within normal ranges. The findings suggested that the sexual side effects of clomipramine are not hormonally mediated, but rather occur through direct effects on spermatogenesis and sperm motility (Salmani & Bozrafshan, 2013).

Since the precise mechanism of antidepressant action on spermatogenesis and sperm motility is not fully understood, several hypotheses have been proposed. Antidepressants may alter sperm function by affecting seminal pH or viscosity, modifying nitric oxide levels (an inhibitor of sperm activity), or influencing gamma-aminobutyric acid (a physiological regulator of sperm motility) (Bian, Zhang, et al., 2002).

In addition, another group of antidepressants, including fluoxetine, venlafaxine, and clomipramine, indirectly affect male fertility by reducing libido, delaying orgasm, impairing erectile function, or diminishing ejaculatory capacity (Osis & Bishop, 2010; Gocmez et al., 2010).

Discussion

The findings of the present study indicate that pharmacological treatment of depressive disorder not only alleviates psychological symptoms such as sadness, hopelessness, and lack of motivation, but also produces significant physical outcomes. From a psychological perspective, the use of antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs), plays a crucial role in improving mood, enhancing quality of life, and gradually restoring functional capacity in patients. These results are consistent with previous studies that have confirmed the efficacy of antidepressants in reducing depressive symptoms and preventing relapse.

Nevertheless, the physical consequences and adverse side effects of these treatments should not be overlooked. Some patients experience weight gain or loss, sleep disturbances, gastrointestinal issues, headaches, or reduced sexual desire during treatment, all of which may affect medication adherence and treatment continuity. This underscores the importance of continuous medical monitoring, dose adjustment, and, in some cases, combining pharmacotherapy with psychotherapeutic interventions.

Overall, the psychological benefits of pharmacological treatment in reducing the severity of depression and improving patients' social and occupational functioning are considerable. However, the physical side effects and potential health risks necessitate careful management to maintain a balance between therapeutic efficacy and the preservation of physical well-being.

Conclusion

Pharmacological treatment of depressive disorder can significantly reduce psychological symptoms and improve patients' quality of life. However, alongside these benefits, potential physical side effects should not be overlooked. An optimal approach appears to be the adoption of a comprehensive treatment plan that integrates pharmacotherapy with patient education, regular monitoring of adverse effects, psychotherapy, and lifestyle modifications. Such an approach can enhance therapeutic efficacy while minimizing the risk of relapse or physical complications associated with medication use.

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