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ANTIDEPRESSANT USE AND SIDE EFFECTS AMONG ADOLESCENTS: AN INTEGRATED REVIEW

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ABSTRACT:

Introduction: Depression is a pervasive psychological condition impacting individuals of all ages, with particularly severe implications for young people and children, affecting their social, academic, and familial functioning. This study investigates the intake of antidepressants and associated side effects among adolescents.

Methods: An integrated review approach was employed, utilizing databases such as PubMed, SciELO, VHL, and LILACS. Keywords including Depression, adolescence, mental health, and antidepressant medications were used to retrieve relevant English-language human research published within the last 20 years.

Results: Pharmacotherapy plays a vital role in managing depressive disorders in adolescents, according to existing findings and debates. However, it must be part of a comprehensive therapeutic approach rooted in thorough mental health assessments. Despite the importance of antidepressant medication, there remains a scarcity of research on its safety and efficacy in children and young adults.

Conclusion: While antidepressant medication is an essential component of treating Depression in adolescents, its safety and efficacy warrant further investigation. There is a pressing need for more studies to fill the gap in the literature and provide comprehensive guidelines for the use of antidepressants in this vulnerable population.

KEYWORDS: Depression; Adolescence; Medicine; Mental Health.

INTRODUCTION:

In recent decades, the use of antidepressants by adolescents has been increasing. This significant increase is mainly due to cases of depressive and anxiety disorders, which affect children and adolescents and have serious consequences, both on a psychological and general health level. Depression is a psychiatric disorder whose main symptoms are a recurrent state of sadness and apathy characterized by social isolation and impairment of social and family life (Videtta, Squarcina, Prunas, Brambilla, & Delvecchio, 2024).

Given the current context, Depression is considered the disease of the century, as it affects a large number of people around the world, especially children and adolescents, and it represents an increased risk of suicide in this age group. To alleviate risks and mitigate Depression, doctors are increasingly recommending the use of medications to relieve symptoms, and these medications are also recommended for adolescents, highlighting the crucial role of the pharmacist in guiding effective treatment (Beck et al., 2024).

In the literature, there are classifications of the types of Depression, described as reactive Depression, which can be caused by stressful and psychosocial factors linked to some event in which the individual will have to reorganize their life. Endogenous or melancholic Depression occurs without a psychogenic trigger and has a biological genesis. Bipolar Depression is based on loss of interest in daily activities, episodes of euphoria, and difficulty sleeping, causing numerous challenges for adolescents (Viduani et al., 2024).

Studies show that family support associated with psychotherapy so that adolescents can understand their role in treatment, maintain a healthy diet, and regularly engage in enjoyable activities, such as going out with friends, maintaining contact with nature, increasing the production of endorphins, dopamine and the serotonergic hormones responsible for the feeling of well-being, as they assist pharmacotherapy, are excellent allies for reducing the severity of Depression (Yang et al., 2024).

Pharmacotherapy is widely recognized as a crucial pillar in the treatment of Depression, especially in adolescents. However, there are several unknowns related to the use of antidepressant agents in this age group, fueling intense debates in academia and among healthcare professionals. This is due to the potential triggering of adverse brain reactions, which increases the risk of suicidal behavior. The importance of research on the medicalization of Depression in adolescents is fundamental, contributing to a scientifically based debate. Wagner underlines the need for theoretical foundations to support these approaches, highlighting the importance of research in this field (Zhang, 2024).

It is imperative to promptly identify and treat Depression in childhood and adolescence, considering the morbidity and increased mortality associated with this condition. Diagnosis and treatment in an ethical and timely manner require consideration of the specificities of this age group. Da Silva and Lacerda point out those depressive symptoms can manifest in different ways in children, requiring adaptations in mental status examination for a more accurate diagnosis, having stated that the goal of this study is to examine the usage of antidepressants during adolescence while emphasizing the need for research on the medical treatment of Depression and its treatment modalities. The intention is to encourage fruitful dialogue on treatment strategies for kids and teenagers with depressive diagnoses (Binaqail et al., 2024; Mehta & Tyagi, 2024).

THEORETICAL FOUNDATION:

DEPRESSION IN ADOLESCENCE:

Depression is an illness that causes a series of psychological disorders that are reflected in emotional, social, and family behaviors, bringing countless negative consequences to the life of the person who suffers from it. The World Health Organization (WHO) states that Depression poses a significant threat to the health of the world's population. It is characterized as a chronic mental illness that arises from a complex interplay of social, psychological, and biological factors (Virtanen et al., 2024).

Symptoms of Depression include sadness, a lack of interest or happiness, feeling guilty or low self-esteem, disturbed sleep or appetite, fatigue, and difficulty concentrating. In its most extreme form, it can result in suicide. It also can limit or impair an individual's functional abilities, social interactions, and ability to manage daily duties. An estimated 350 million individuals worldwide suffer from

Depression, and the illness is thought to be the cause of almost one million suicides (Boström et al., 2024).
In recent years, adolescents have been recognized as a high-risk group for Depression, and, as a result, the need to prescribe antidepressant medications for this population has increased. Depressive disorder in children and adolescents can continue into their adult life and culminate in other psychiatric pathologies if it is not diagnosed correctly and within a considered period, raising the alarm about the possibility of other more severe diseases in adulthood (Morphett et al., 2024).

In situations of morbidity, it is essential to highlight that these conditions entail substantial social costs, constituting a significant challenge to public health. This problem affects different strata of society. In this context, adolescents with suspected Depression must undergo appropriate professional care to begin the correct treatment. In the vast majority of cases, treatment consists of psychotherapeutic monitoring and the use of antidepressant drugs (Vöckel et al., 2024).
Given the morbidity and mortality caused by Depression in childhood and adolescence, it must be promptly recognized and treated through correct psychiatric methods and medications. To achieve this objective, it is necessary to consider a series of specificities regarding diagnosis and treatment in this age group. That is, many depressive symptoms can present in other ways in children, as in adolescence in particular, self-harm, hostility, drug use, running away from home, as well as fits of anger are common (Dauchot et al., 2024).
In this context, the relevance of investigations focusing on the medicalization of Depression in adolescents and its healthcare approaches emerges, which aim to stimulate constructive debates on issues relating to treatment strategies for children and adolescents diagnosed with Depression. Treatments for people diagnosed with Depression are usually psychotherapy, the use of psychotropic drugs, and transcranial magnetic stimulation. The interventions applied to this individual diagnosed with Depression should preferably be understood in a globalized way, considering the biological, psychological, and social; therefore, interventions and care practices must also cover all these aspects (Ayvaci et al., 2024).
Specifically, the treatment aimed at depressed adolescents requires a different perspective on the part of the professional since, in this phase of life, the adolescent's brain structures are in the process of being formed and structured. In many cases, the use of antidepressants causes various damage by damaging the cellular structures of the brain and, instead of alleviating the problem, can even worsen it. During this delicate period of physiological and cognitive development, the brain produces neurobiological changes, some of which may last longer than the course of treatment. If taken during the neurodevelopmental period, such as childhood and adolescence, it may represent a problem, as has been proven in several studies (Bennett et al., 2024).

In addition to the pharmacological approach, there are equally relevant psychotherapeutic treatments. Among these, cognitive-behavioral therapy, interpersonal therapy, group sessions, and family therapy stand out. Adolescence is when the brain undergoes significant structural, physiological, and cognitive changes. This period of neurological development is associated with the individual's lifelong risk of experiencing affective disorders; with this peak at the age of 14, we speak of Major Depression, a disorder that remains prevalent throughout life, starting from childhood and adolescence. They are more vulnerable (Lineham, Avila-Quintero, Bloch, & Dwyer, 2024).

Therefore, when identifying any changes in the adolescent's development and behavior that lead to a possible case of Depression, professional assistance is essential for diagnosis and appropriate treatment. In the case of Depression in adolescence, an integrated treatment is recommended, where the use of antidepressant drugs is combined with psychotherapeutic support (Lombardo et al., 2024).

BIOCHEMICAL DISORDERS IN DEPRESSION:

Although recent evidence indicates the association between Depression, neurodegeneration, and reduced neurogenesis in the hippocampus, it is expected to find deficits in cognitive functions.

Disorders related to anxiety and Depression often have both genetic and environmental roots, as highlighted by Rang et al. Studies have highlighted several anatomical changes in the brain, in the area of the prefrontal cortex, which is closely linked to the paralympic pathways and is also related to the pump of recapitulation, which degrades in excess, causing a deficiency in the quantity of norepinephrine, serotonin, dopamine, and glutamate causing a lower sensitivity of neurons in carrying out stimuli between neurotransmitters (Sarakbi et al., 2024).

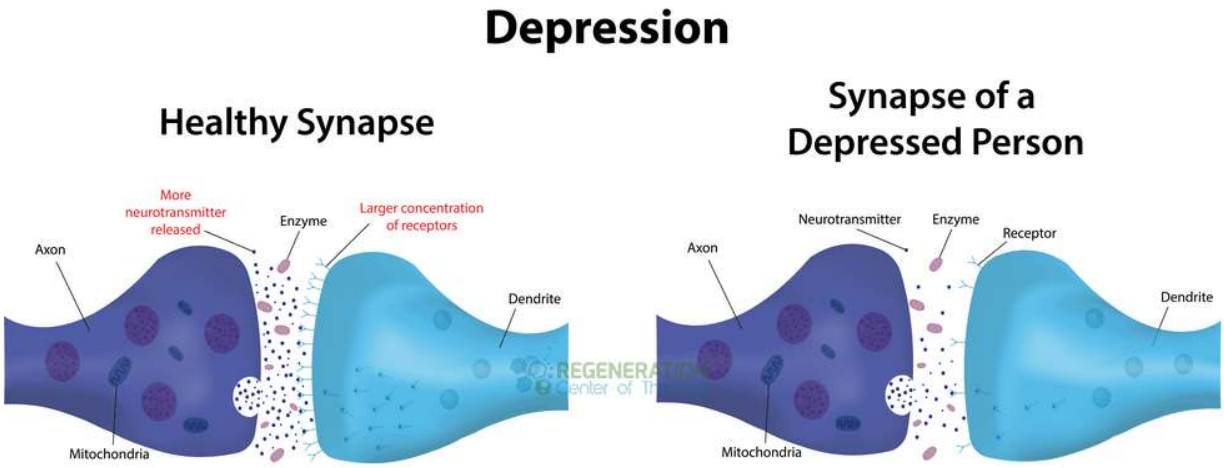

Figure 1- *Neurotransmitters Linked to Depression*

TYPES OF DEPRESSION:

Reactive Depression	Endogenous Depression	Bipolar Depression
Caused by an acute reaction to stress, it is characterized by onset immediately after the traumatic event, such as bereavement. To be compatible with ICD-10 and to aid in the early discovery of cases, this new category was added to the DSM-IV to represent acute reactions to excessive stress.	An emotional state of sadness, apathy, and hopelessness characterizes Depression. Its origin distinguishes it, as it does not require a specific external trigger; it emerges from internal factors, such as alterations or structural changes in brain biochemistry. These changes may or may not be hereditary in origin, making it considered the most severe form of this mental condition.	It is characterized by the alternation, sometimes sudden, of Depression and euphoria of varying intensity. Furthermore, the reasoning is not linear; it depends on what you want to say but never reaches the goal. In depressive episodes, the main symptoms are: decreased disposition towards life, increased need for sleep, retraction and isolation, deep sadness, and lack of willingness to carry out pessimistic activities and thoughts of lesser value, which lead to a worsening and risky environment.

Table 1- *Main types of Depression*

PHARMACOLOGICAL TREATMENT OF DEPRESSION:

The effectiveness of drug treatment for Depression has been demonstrated in numerous studies conducted around the world since 1950. Antidepressant drugs help reduce morbidity and minimize the effects of Depression to promote significant improvement in case rates. Despite being essential elements in the treatment of Depression, the use of antidepressant drugs must be based on considerations and restrictions since some limitations in terms of effectiveness may occur, keeping in mind that Depression is not treated abstractly but rather in a context involving their social, cultural, biological and psychological environment since at least one in five depressed patients in treatment are refractory to various and different antidepressants in adequate doses (Ballard et al., 2024; Bruze et al., 2024).

When addressing the use of antidepressants in adolescence, it is essential to consider several elements that require the attention of both the professionals responsible for monitoring this individual and his family. The family must remain attentive to indicative signs to mitigate the risks of more serious developments. This is justified by the increased risk of mental disorders associated with the use of these drugs, transforming them into a risk factor for suicide in this age group (Yoshida et al., 2024).

Antidepressants, which block MAO's ability to destroy neurotransmitters or inhibit their reuptake, are typically used to treat Depression. This increases the amount of neurotransmitters in the synaptic cleft and, as a result, restructures the patient's mood. After starting treatment with antidepressants, it is expected to observe a period of therapeutic delay, generally 3-4 weeks, before a measurable response occurs. It should be noted that this interval is an average, as some patients may respond to treatment before this period, while others may require more than eight weeks to achieve adequate therapeutic improvement (Vidal et al., 2024).

There are currently several antidepressant substances on the market. The choice of antidepressant is based on the effectiveness of the drug based on the clinical characteristics of the depressive episode, the side effects of the drug, and the personal or family history of previous responses to a specific substance. In specific populations, such as children, adolescents, the elderly, and pregnant women, particular attention should be paid to the choice of treatment (Li et al., 2024).

In the treatment of Depression in adolescence, the administration of drugs is a very relevant concern, as the pediatric population presents specific developmental characteristics of a physiological and psychological nature, and these peculiarities are often not taken into consideration when choosing drugs. While on the one hand, drugs have the possibility of solving the problem of Depression by controlling the symptoms of this pathology, on the other hand, if misused, they can lead to the onset of adverse effects or drug interactions, which can sometimes worsen significantly the condition of the pre-existing disease (Li et al., 2024).

Since psychotropic drugs have a lag time before the onset of their therapeutic effects and the onset of side effects occurs at the beginning of the treatment, the user often misuses the drugs again or ends up abandoning the therapy, which in the case of adolescents undergoing treatment since Depression represents a risk factor for the onset of other more severe complications, such as suicide attempts (Noetel et al., 2024).

Antidepressants in adolescence must be used with caution and adequate professional monitoring, given the adverse effects they can have on the body and especially on the brain. Overstimulating the central nervous system can result in convulsions in the event of an overdose, excitement, tremors, and sleeplessness. The medication may need to be stopped because of the severe appetite increase that results in weight gain (Galler et al., 2024).

A large number of drug interactions lead to contraindications for simultaneous use with MAO inhibitors. Central nervous system (CNS) depressants, other narcotics, alcohol, and anesthetic agents should not be used with MAOIs. In general, other antidepressants, such as TCAs and bupropion, should also be avoided in patients taking MAOIs (Dragon & Obuchowicz, 2024).

When necessary, the drug administration should follow appropriate guidelines. Although medications can be effective in treating various health conditions and controlling some pathology, it is imperative to consider that antidepressants can have potential permanent effects on the brain, which in this age group is still in development. Furthermore, adverse effects may occur that worsen the patient's situation. Although there is no conclusive evidence of these impacts, it is essential to pay attention and thoroughly assess the balance between the risks and benefits of this type of treatment (Chrenek et al., 2024).

RESULTS AND DISCUSSION:

The treatment of Depression in adolescence occurs in an integrated manner through psychotherapeutic monitoring combined with the use of antidepressants, which aims to improve the symptoms and thus avoid more significant damage from a psychological, social, and emotional point

of view. Antidepressant medications such as selective reuptake inhibitors of serotonin (SSRIs) and selective reuptake inhibitors of norepinephrine (SNRIs) are used to treat Depression in patients (Oliva et al., 2024).

Generally speaking, the same strategy is used for anxiety instances that call for medication; however, it may differ significantly according to the various clinical problems that are being treated. Depending on the individual's characteristics, these drug classes and other therapies may result in side effects. If antidepressant drugs have the possibility of solving various health problems and controlling some psychological pathology such as Depression, on the other hand, if misused, they can lead to the appearance of adverse effects and pharmacological interactions (Ho et al., 2024).

Fluoxetine is the most used drug in the treatment of Depression; its active ingredient improves the symptoms; although it is not well understood, its mechanism of action seems to occur through SSRIs, and drugs with this mechanism are more effective in the treatment of Depression In childhood and adolescence; however, it is necessary to take into account the adverse effects that may occur during use (Costa et al., 2024).

Serotonin is a neurotransmitter that works in the brain, establishing communication between nerve cells. SSRIs increase the extracellular concentration of the neurotransmitter serotonin in the body and brain, which is why drugs of this class are represented in 55.60% of prescriptions. NICE does not advise antidepressant medications for the initial management of moderate Depression in children. According to revised guidelines, fluoxetine may be used in conjunction with psychological treatments tailored specifically for young people (12 to 18 years old) as the first line of treatment for moderately to severe Depression (Bouquillon et al., 2024).

When considering the use of fluoxetine in conjunction with psychological treatment for children (ages 5 to 11), care should be used, and psychological therapy should be completed within 4-6 sessions. According to Goodman and Gilman, the classes of antidepressants that present the most side effects, being particularly harmful to adolescents, are TCAs, especially cardiac effects. This is due to the low specificity for NET and SERT receptors, which affects other receptors, including muscarinic cholinergic receptors, histamine receptors, and α-adrenergic receptors. Actions on these receptors contribute to its antidepressant effects but are responsible for numerous adverse effects (Slater et al., 2024).

Selective serotonin reuptake inhibitors (SSRIs) show less intense and less frequent side effects than tricyclic antidepressants (TCAs). This occurs because SSRIs exert a potent and selective inhibition of serotonin reuptake in the presynaptic neuronal terminal, demonstrating a low affinity for cholinergic, noradrenergic, and histamine receptors, as observed by Scivoletto and Tarelho. The most frequent adverse effects of this category of drugs concern manifestations in the gastrointestinal tract and, in certain situations, effects of a sexual nature. However, it is essential to emphasize that concerns about sexual effects are not significant for children and adolescents (Yrondi et al., 2024).

Selective serotonin-norepinephrine reuptake inhibitors (SNRIs) have a similar side effect profile to SSRIs. The effects mentioned include nausea, constipation, insomnia, headache, drowsiness, dry mouth, dizziness, nervousness, asthenia, anxiety, anorexia, and blurred vision. However, special attention to gastrointestinal effects should be highlighted in this list of possible adverse reactions. Bupropion is recognized for its tendency to have few side effects, attributed to its lower interaction with histamine and cholinergic receptors, acting more selectively on noradrenergic and dopamine receptors. This contributes to better tolerability. However, it is critical to note that among the more severe side effects are agitation, seizures, and possible gastrointestinal disorders associated with this drug (Liu et al., 2024).

MAOIs are antidepressants with few frequent side effects, but these effects are serious and require medical treatment. The main side effect is severe orthostatic hypotension, causing dizziness and dizziness, which can lead to serious falls. The diagnosis of Depression in childhood and adolescence is made difficult by the presence of comorbidities. The most common are anxiety, hyperactivity, insomnia, and irritability, as well as headaches (Lv et al., 2024).

According to Silva, when choosing an antidepressant, it is necessary to take into account the clinical manifestations of those children and adolescents present in case of Depression, as well as the other

comorbidities existing in this population. Depressed children and adolescents have some symptoms, including physical symptoms, such as pain in the head and abdomen, psychomotor agitation, insomnia, and irritability (Hernandez et al., 2024).

To mitigate the adverse effects of antidepressant treatment in adolescence, it is essential to adopt a combined approach that involves not only the use of drugs but also psychotherapeutic monitoring. This strategy aims not only to reduce the potential side effects of drugs but also to provide psychological support to the adolescent. This support is critical to mitigating risks, including suicide, by offering broader, more holistic support throughout treatment (Bojanić, 2024).

The findings of this study highlight the vital need for an in-depth evaluation of healthcare professionals' decision-making regarding the use of antidepressants in adolescents. This decision is often influenced by family circumstances and opinions and difficulties related to available or unavailable treatment resources in healthcare systems. These limitations may significantly impact the therapeutic options available for these young people, highlighting the importance of a comprehensive clinical approach (Samosir, Keliat, & Hargiana, 2024).

It indicates the need to integrate into clinical practice the understanding of the context in which the adolescent is inserted, trying to satisfy not only the needs expressed by parents or guardians but also what individuals of this age group understand that the use of antidepressants causes changes in sleep, weight changes, among other things, so they can understand the origin of the problem and the type of treatment they want (Zhao et al., 2024).

Pharmaceutical practice centered on clinical pharmacy carries with it the idea that medicine is a means to achieve a result, focusing attention on the patient. In this way, the pharmacist must act to ensure that the correct drugs are taken to benefit the patient and that those not necessary for use are removed or replaced with another more suitable alternative, the pharmacist being the professional of a most qualified multidisciplinary team in this context. In this action, the pharmacist must use an interdisciplinary team to continuously monitor the patients' drugs and their effects (positive or otherwise) that can influence the patient (Orsolini et al., 2024).

In this way, it is notable how the work of a multidisciplinary team can benefit the promotion and protection of the patient's health and consequently reduce the economic impacts that the practice of self-medication can generate in the public health system. As a word of caution, it is worth pointing out that antidepressants, when used correctly, save lives and that the worst threat to a depressed child's well-being would be to receive no treatment at all (Walaszek et al., 2024).

CONCLUSION:

As discussed in this study, Depression in adolescence requires special attention, as these individuals are going through a period of significant changes, both neurobiological and social. Family and people involved in the social circle of adolescents must be attentive to signs of behavioral changes, noticing the first symptoms of Depression as early as possible so that they are treated correctly and without the immediate introduction of drugs.

When necessary, drugs must and can be used following the appropriate recommendations. Still, if, on the one hand, drugs have the possibility of solving various health problems and controlling some pathologies, on the other, it cannot be excluded that treatment with Antidepressants can cause permanent brain problems in children and adolescents who are still developing or present adverse effects that can worsen the patient's situation. Even if there is unclear evidence, caution must be exercised, carefully evaluating the risk-benefit ratio.

In this sense, the ideal would be a treatment involving a multidisciplinary team, as it can provide better coverage of aspects related to symptoms and adequate treatment for each individual. The patient accompanied by the pharmacist monitoring the treatment, adjacent to various interventions, guarantees greater therapeutic efficacy and lower risk of disease recurrence.

Furthermore, it is up to the professionals involved in the treatment to provide clarifying information, each in their field of activity, so that the guidelines are followed correctly, as well as providing information on the rights guaranteed by the State so that the individual can be treated free of charge

for the disease, ensuring care for patients suffering from Depression, thus showing an alternative for those who do not have the means to obtain private treatment and monitoring.

Over the years, pharmacotherapy in the treatment of Depression has improved, creating the expectation that with the use of improving technologies, it will become possible to discover new drugs that can enhance human capabilities. Research in neuroimaging, molecular biology, and neurophysiology is necessary to improve our understanding of the fundamentals of brain function and to design more potent therapies.

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