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Depression: Overview and its ADR with antidepressant drugs

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Abstract

Depression is a mental illness characterized by a persistent sense of sadness as well as a lack of enthusiasm for activities. Depression, also known as major depressive disorder (MDD) or clinical depression, affects a person's feelings, thoughts, behavior and can result in a wide range of emotional and physical issues. Major depression is a common illness that severely limits psychosocial functioning and diminishes quality of life. In 2008, WHO ranked major depression as the third cause of burden of disease worldwide and projected that the disease will rank first by 2030.

Depression is a major public health psychiatric problem that affects people all over the world, with a high lifetime incidence and severe disability. Depending on the severity and pattern of depression episodes over time, antidepressant (ADs) medication may be advised as one of the therapeutic methods. On the other hand, ADs medication may have adverse drug reactions (ADRs). ADRs reduce people's quality of life, which leads to poor adherence to ADs, longer hospital stays, higher healthcare costs, poor therapeutic outcomes, physical morbidity, stigma and also death in the worst-case scenario.

Keywords: Depression, Neurotransmitters, stress, therapy, antidepressants, Adverse drug.

Introduction

Depression (also known as depressive disorder) is a common mental disorder. It involves a depressed mood or loss of pleasure or interest in activities for long periods of time.

Depression is different from regular mood changes and feelings about everyday life. It can affect all aspects of life, including relationships with family, friends and community. It can result from or lead to problems at school and at work.

A prolonged sense of sadness and loss of interest are symptoms of depression, a mood illness.

[1-2]The Diagnostic and Statistical Manual of Mental illnesses, fifth Edition (DSM-5) of theAmerican Psychiatric Association divides depressive illnesses into:

- Disorder of disruptive mood dysregulation
- Depressive disease in adults
- Dysthymia, a persistent depressive disorder
- Dysphoria prior to menstruation
- Depression brought on by a different medical condition

According to WHO predictions, depression will overtake cardiovascular disease as the second most common cause of death in the world in next ten years. Currently, one in five women and twelve men worldwide suffer from depression. Not only do adults experience depression, but so do 2% of school-aged children and 5% of teenagers, most of whom go undiagnosed. The most frequent cause for people to visit a psychiatrist is depression, despite the fact that the general

Public believes that all psychiatric issues are depression. [3-4]The myth about depression is what is typically observed in patients. People continue to think that the condition stems from a personality flaw, that it can be treated on one's own, or that medication is only a temporary sedative.

All depressive disorders include the characteristics of sorrow, emptiness, or irritability with accompanying physical and cognitive alterations that have a major impact on the person's ability to function.[5]

Nearly 60% of persons with depression do not seek medical attention because of erroneous perceptions. Many people believe that the stigma associated with mental health disorders should not exist in our culture and may negatively impact both personal and professional lives. The majority of antidepressants are proven to be effective, but each person's response to medication may be different.

Types of Depression

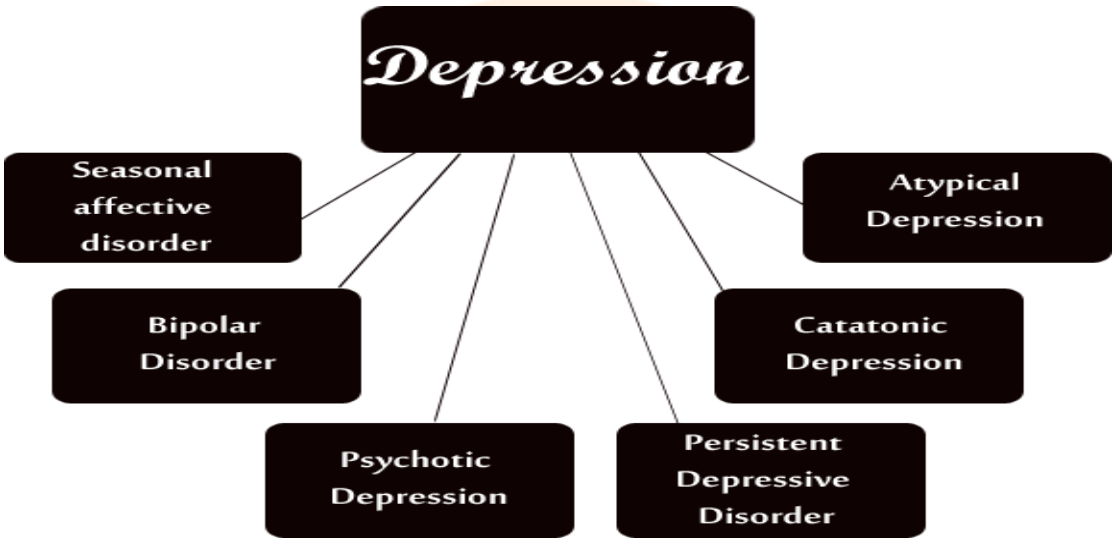

Figure 1: Types of Depression

Etiology

Major depressive illness has a complex aetiology, involving both hereditary and environmental variables. Although depression can strike individuals without a history of the condition, first- degree relatives of depressed persons are around three times more likely to experience depression than the general population. [6-7]

1) Biological factors, including the presence of antidepressants and their effects on brain neurotransmission, as well

as hormonal elements that may indicate the genesis of depression.

2) Genetic considerations, since research suggests that first-degree relatives with depression have risks that are two to three times higher. However, research involving homozygotic twins did not demonstrate a concordance of 100 percent, allowing us to draw the conclusion that psychosocial factors are significant. [8-9]

3) Psychosocial aspects and the person's lifestyle, such as leisure time, physical exercise versus inactivity, smoking, diet, family time, and personal hobbies, are among the determining factors.
[10-11]

Epidemiology

Major depressive illness affects about 7% of people over the course of a year, with substantial variances by age group. Compared to people 60 years of age and older, the frequency is three times higher in people aged 18 to 29. From early adolescence forward, females have 1.5 to 3 times the rates of boys. Nearly 17 million adults in the US suffer from depression, yet these figures are vastly understated because many of them have not even sought medical help.

Symptoms and patterns

A person has a depressed mood (feeling sad, irritated, or empty) during a depressive episode. They can experience a decrease in enjoyment or interest in activities.

A depressive episode is distinct from sporadic mood swings. For at least two weeks, they last practically every day for the majority of the day. [12-14]

Other symptoms are also present, which may include:

- poor concentration
- feelings of excessive guilt or low self-worth
- hopelessness about the future
- thoughts about dying or suicide
- disrupted sleep
- changes in appetite or weight
- feeling very tired or low in energy
- persistent sad, anxious or empty mood
- loss of interest or pleasure in hobbies and activities that you once enjoyed, including sex
- persistent physical symptoms that do not respond to treatment
- such as headaches, digestive disorders and chronic pain

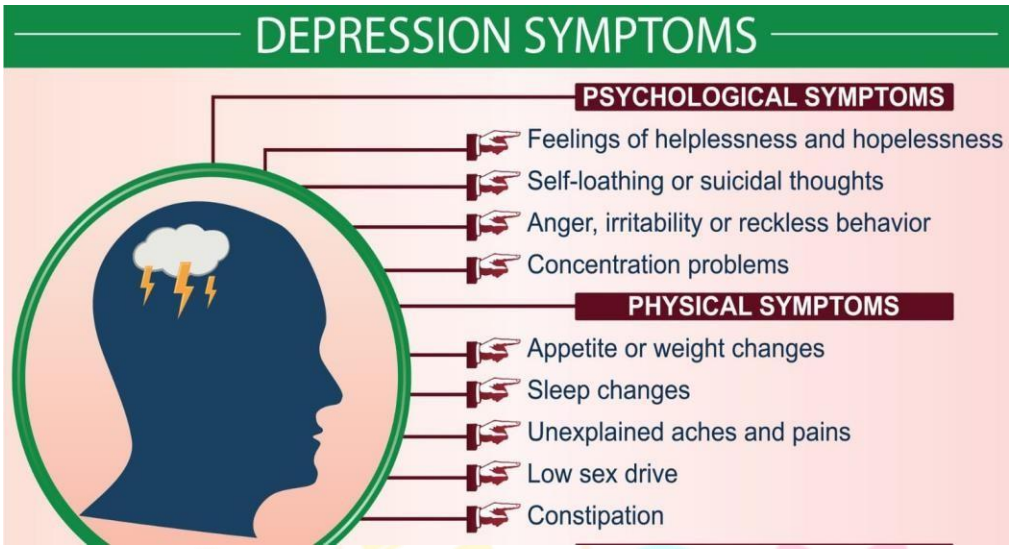

Figure 2: Symptoms of Depression

Depending on the frequency and severity of symptoms, the effect on the person's functioning,and other factors, a depressive episode can be classified as mild, moderate, or severe. [15-16]

All patients with depression should be evaluated for suicidal risk. Any suicide risk must be givenprompt attention which could include hospitalization or close and frequent monitoring.

- Single episode depressive disorder, meaning the person's first and only episode;
- Recurrent depressive disorder, meaning the person has a history of at least two depressiveepisodes; and
- Bipolar disorder, meaning that depressive episodes alternate with periods of manic symptoms, which include euphoria or irritability, increased activity or energy, and other symptoms such as increased talkativeness, racing thoughts, increased self-esteem, decreased need for sleep, distractibility, and impulsive reckless behaviour.

Diagnosis and treatment

Depression can be effectively treated. These include medicine and psychological therapy. If youare experiencing depression symptoms, get help.

Doctor may determine a diagnosis of depression based on:

- Physical exam. Your doctor may do a physical exam and ask questions about your health. In some cases, depression may be linked to an underlying physical health problem.
- Lab tests. For example, your doctor may do a blood test called a complete blood count or test your thyroid to make sure it's functioning properly.

- Psychiatric evaluation. Your mental health professional asks about your symptoms, thoughts, feelings and behavior patterns. You may be asked to fill out a questionnaire to help answer these questions.
- DSM-5. Your mental health professional may use the criteria for depression listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), published by the American Psychiatric Association.

The initial depression therapies are psychological ones. In cases of moderate and severe depression, they can be used in conjunction with antidepressant medicines. For moderate depression, antidepressant medicines are not necessary.[17]

New ways of thinking, coping, or interacting with others can be learned through psychological therapy. They might consist of supervised lay therapists and professional talk therapy. Both in- person and online talk therapy are options. Access to psychological therapy is possible via self- help books, websites, and applications.

Effective psychological treatments for depression include:

- Behavioural activation
- Cognitive behavioural therapy
- Interpersonal psychotherapy
- Problem-solving therapy.

Antidepressant medications include selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine.

Health-care providers should keep in mind the possible adverse effects associated with antidepressant medication, the ability to deliver either intervention (in terms of expertise, and/or treatment availability), and individual preferences. Antidepressants should not be used for treating depression in children and are not the first line of treatment in adolescents, among whom they should be used with extra caution. Different medications and treatments are used for bipolardisorder.[18]

Self-care

Self-care has a significant impact on controlling depressive symptoms and enhancing general wellbeing.

What we can do

- try to keep doing activities you used to enjoy
- stay connected to friends and family
- exercise regularly, even if it's just a short walk
- stick to regular eating and sleeping habits as much as possible

- avoid or cut down on alcohol and don't use illicit drugs, which can make depressionworse
- talk to someone you trust about your feelings
- Seek help from a healthcare provider. [19-20]

If you have thoughts of suicide:

- Remind yourself that you are not alone and that many people have experienced similarcircumstances to yours and recovered.
- Share your feelings with someone you trust.
- Consult a health professional, such as a doctor or counsellor.
- Consider joining a support group. [21]

Evaluation

The diagnosis of depression is based on history and physical findings. No diagnostic laboratory tests are available to diagnose major depressive disorder. Laboratory studies are, however, useful to exclude medical illnesses that may present as major depressive disorder.[22-24]

These laboratory studies might include the following:

- Blood alcohol level
- Blood and urine toxicology screen
- Arterial blood gas (ABG)
- Complete blood cell (CBC) count
- Thyroid-stimulating hormone (TSH)
- Vitamin B-12
- Rapid plasma reagin (RPR)
- HIV test
- Electrolytes, including calcium, phosphate, and magnesium levels
- Blood urea nitrogen (BUN) and creatinine
- Liver function tests (LFTs)
- Dexamethasone suppression test (Cushing disease, but also positive in depression)
- Cosyntropin (ACTH) stimulation test (Addison disease)
- Computed tomography (CT) scanning or magnetic resonance imaging (MRI) of the brain should be considered if organic brain syndrome or hypopituitarism is included in the differential diagnosis

Treatment / Management

Depressive symptoms can be alleviated by medication and brief psychotherapy (interpersonal therapy, cognitive-behavioral therapy) alone. Additionally, combination therapy has been linked

to significantly higher rates of treatment compliance, improved quality of life, and reductions indepressed symptoms. Empirical evidence also supports CBT's potential to stop relapse. [25-27]

Electroconvulsive therapy is useful for patients who are not responding well to medications orare suicida.[28-29]

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin/norepinephrine reuptake inhibitors (SNRIs)
- Atypical antidepressants

- Serotonin-Dopamine Activity Modulators (SDAMs)
- Tricyclic antidepressants (TCAs)
- Monoamine oxidase inhibitors (MAOIs)
- Selective serotonin reuptake inhibitors (SSRIs): SSRIs have the advantage of ease of dosing and low toxicity in overdose. They are also the first-line medications for late-onsetdepression.
- SSRIs include: Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vilazodone, vortioxetine
- Serotonin/norepinephrine reuptake inhibitors (SNRIs): SNRIs, which include venlafaxine, desvenlafaxine, duloxetine, and levomilnacipran can be used as first-line agents, particularly in patients with significant fatigue or pain syndromes associated with the episode of depression. SNRIs also have an important role as second-line agents in patients who have not responded to SSRIs.
- Atypical antidepressants: Atypical antidepressants include bupropion, mirtazapine, nefazodone, and trazodone. They have all been found to be effective in monotherapy in major depressive disorder and may be used in combination therapy for more difficult to treat depression.
- Serotonin-Dopamine Activity Modulators (SDAMs): SDAMs include brexpiprazole and aripiprazole. SDAMs act as a partial agonist at 5-HT1A and dopamine D2 receptors at similar potency, and as an antagonist at 5-HT2A and noradrenaline alp Brexpiprazole is indicated as adjunctive therapy for major depressive disorder (MDD).
- Tricyclic antidepressants (TCAS): TCAs include the following: Amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine. TCAs have a long record of efficacy in the treatment of depression. They are used less commonly because of their side-effect profile and their considerable toxicity in overdose.
- Monoamine oxidase inhibitors (MAOIs): MAOIs include isocarboxazid, phenelzine, selegiline, and tranylcypromine. These agents are widely effective in a broad range of affective and anxiety disorders. Because of the risk of hypertensive crisis, patients on these medications must follow a low-tyramine diet. Other adverse effects can include insomnia, anxiety, orthostasis, weight gain, and sexual dysfunction.

Electroconvulsive Therapy (ECT)

ECT is a highly effective treatment for depression. Onset of action may be more rapid than thatof drug treatments, with benefit often seen within 1 week of commencing treatment. A course of ECT (usually up to 12 sessions) is the treatment of choice for patients who do not respond to drug therapy, are psychotic, or are suicidal or dangerous to themselves. Thus, the indications for the use of ECT include the following:[30-32]

- Need for a rapid antidepressant response Failure of drug therapies
- History of a good response to ECT
- Patient preference
- High risk of suicide
- High risk of medical morbidity and mortality

Although advances in brief anesthesia and neuromuscular paralysis have improved the safety and tolerability of ECT, this modality poses numerous risks, including those associated with general anesthesia, postictal confusion, and, more rarely, short-term memory difficulties.

Psychotherapy

Cognitive Behavior Therapy and Interpersonal Therapy are evidence-based psychotherapies that have been found to be effective in the treatment of depression.

Cognitive-behavioral therapy (CBT)

CBT is a structured and didactic form of therapy that focuses on helping individuals identify and modify maladaptive thinking and behavior patterns (16 to 20 sessions). It is based on the premise that patients who are depressed exhibit the "cognitive triad" of depression, which includes a negative view of themselves, the world, and the future. Patients with depression also exhibit cognitive distortions that help to maintain their negative beliefs. CBT for depression typically includes behavioral strategies (i.e., activity scheduling), as well as cognitive restructuring to change negative automatic thoughts and addressing maladaptive schemas.[33]

There is evidence supporting the use of CBT with individuals of all ages. It is also considered being efficacious for the prevention of relapse. It is particularly valuable for elderly patients, who may be more prone to problems or side effects with medications.

Mindfulness-based cognitive therapy (MBCT) was designed to reduce relapse among individuals who have been successfully treated for an episode of recurrent major depressive disorder. The primary treatment component is mindfulness training. MBCT specifically focuses on ruminative thought processes as being a risk factor for relapse. Research indicates that MBCT is effective in reducing the risk of relapse in patients with recurrent depression, especially in those with the most severe residual symptoms.[34-35]

Interpersonal Therapy (IPT)

Interpersonal therapy (IPT) is a time-limited (typically 16 sessions) treatment for major depressive disorder. IPT draws from attachment theory and emphasize the role of interpersonal relationships, focusing on current interpersonal difficulties. Specific areas of emphasis include grief, interpersonal disputes, role transitions, and interpersonal deficits.[36]

Differential Diagnosis

- Adjustment disorders
- Anaemia
- Chronic Fatigue syndrome
- Dissociative disorders
- Illness anxiety disorders
- Hypoglycemia
- Hypopituitarism
- Schizoaffective disorders
- Schizophrenia
- Somatic symptom disorders

Prognosis

The very high morbidity and mortality rates associated with major depression contribute to the high suicide rates. Although there are excellent medication treatments available, approximately 50% of patients may not respond right away. Although complete remission is uncommon, at least 40% of patients experience partial remission within a year.[37-38]

Relapses are typical, though, and many patients need a range of therapies to manage their symptoms. Most patients with depression have low quality of life.

In the US, depression is a factor in close to 40,000 suicide cases annually. Older guys had the greatest suicide rate.[39-40]

Antidepressants (ADs):

ADs are drugs that are prescribed to help people who are suffering from clinical depression. Also be used to treat diseases including GAD (generalized anxiety disorder), OCD (obsessive- compulsive disorder), and PTSD (post-traumatic stress disorder). ADs are sometimes prescribed to persons who suffer from longterm (chronic) pain.[41]

Table1. Antidepressant drug classes and mode of action ADRs reported [42]

Classification	Mode of action	Drugs Examples	Reported ADRs
SSRIs	At the presynaptic neuronal membrane, selectively inhibit serotonin (5-HT) reuptake.	Citalopram, fluoxetine, paroxetine,escitalopram, and sertraline	i. sexual dysfunction, weight gain, and sleep disturbance. ii. In pregnancy (neonatal seizures, premature birth, fetal and infant death)
SNRIs	Both serotonin and norepinephrine reuptake inhibition; dopamine reuptake is mildly inhibited.	Duloxetine and venlafaxine	Blood pressure rises, tachycardia, anxiety, diaphoresis, and tremors
MAOIs	Competitively inhibit monoamine oxidase; The reversibility and activity against MAOa and MAOb of the medicines in this class varies	Tranylcypromine and phenelzine	Hypertensive crisis, persistent hypotension, insomnia, increased anxiety, agitation, and dry mouth
SM	Serotonin reuptake inhibitor that also serves as a 5HT2 antagonist	trazodone	Somnolence and fatigue.
NDRIS	Dopamine reuptake inhibition with some norepinephrine effects	bupropion	Headache, insomnia, nausea, and dry mouth
NASSADs	Inhibition of the adrenergic alpha2-autoreceptors and alpha2- heteroreceptors additionally by inhibiting 5- HT2 and 5-HT3 receptors.	mirtazapine	Drowsiness, sedation, malaise, orlassitude.

TCAs	Norepinephrine and serotonin reuptake into presynaptic terminals inhibition.	Amitriptyline, imipramine, nortriptyline, desipramine	Constipation, dizziness, and xerostomia

1. SSRIs (selective serotonin reuptake inhibitors)

The most commonly used antidepressant is SSRIs, which have minimal adverse effects on other classes. The most well-known SSRI is fluoxetine. Citalopram, escitalopram, paroxetine, and sertraline are some of the other SSRIs.

2. SNRIs (Serotonin-noradrenaline reuptake inhibitors)

SNRIs are ADs that are comparable to SSRIs but are intended to be more effective. However, there is no conclusive evidence that SNRIs are more successful in the treatment of depression. Duloxetine and venlafaxine are examples of SNRIs.

3. NASSADs (Noradrenaline and specific serotonergic ADs)

NASSADs may help some patients who simply cannot take SSRIs. NASSADs have similar ADRs to SSRIs but are less likely to cause sexual problems. Nevertheless, initially produce an increase in drowsiness.

4. TCAs (Tricyclic antidepressants)

TCAs are an older type of antidepressant that, due to the higher risk of overdose, is no longer proposed as the first line of therapy for depression. TCAs are used to treat several mental illnesses, including OCD and bipolar disorder. TCAs include clomipramine, amitriptyline, dosulepin, lofepramine, and nortriptyline. Chronic nerve pain can be treated with TCAs such as amitriptyline.

5. SARIs (Serotonin antagonists and reuptake inhibitors)

SARIs are not typically recommended as a first-line antidepressant, although they may be takenif other ADs have failed or caused negative effects.

6. MAOIs (Monoamine oxidase inhibitors)

MAOIs are an antidepressant that is no longer commonly prescribed. They should only be given by a specialist because they have the potential to cause serious side effects. MAOIs include tranylcypromine, phenelzine, and isocarboxazid.

7. Other antidepressant treatments

Talking therapies, such as cognitive-behavior therapy (CBT), are another option for treating depression. ADs and CBT are commonly used to treat people with moderate to severe depression. ADs work fast to relieve symptoms, while CBT takes longer to address the causes of depression. Exercise has also been shown to help people who are suffering from mild depression.[43-48]

Conclusion

Depression occurs commonly, causing suffering, functional impairment, increased risk of suicide, added health care costs, and productivity losses. Effective treatments are available both when depression occurs alone and when it co-occurs with general medical illnesses.

Depression is a very common disorder encountered by the nurse practitioner, primary care provider, psychiatrist, and mental health worker, coordinating as an inter professional healthcare team. The disorder has extremely high

morbidity including the risk of suicide. All healthcare workers should be knowledgeable about this disorder and refer the patient to a psychiatrist if there is a risk of self-harm.

Education plays an important role in the successful treatment of major depressive disorder. This would include the education of the family and the patient. Lack of accurate information and misperceptions of the illness as a personal weakness or failing leads to painful stigmatization and avoidance of the diagnosis by many of those affected. Patients should know the rationale behind the choice of treatment, potential adverse effects, and expected results.

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