



A Systematic Review of Depression and Its Treatment

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Abstract

Now a day's depression is a very common disorder, results in a loss of social function, reduced the quality of life etc. The antidepressants are treating the depression. The aim is to prevent depression. Antidepressant is used for antidepressant. It has dual effect on nor epinephrine (NE) and dopamine (DA) neuro-transmitter system. The dosage form taken three times in a day, it is taken two times in a day and it is taken one time in a day.

Keywords

Depression, diagnosis, treatment.

INTRODUCTION

Mood disorders are mental disorders characterized by periods of depression sometimes alternating with periods of elevated mood. Major depression may represent a spectrum of disorders, varying in severity from mild and self-limited conditions to extraordinarily severe, psychotic, incapacitating, and deadly diseases. Physiological and pharmacological modifications of these brain regions may have important behavioral consequences and useful clinical effects regardless of the underlying cause of any mental disorder. Clinical depression must be distinguished from normal grief, sadness, disappointment and the dysphoria or demoralization often associated with medical illness.^[1]

Depression, with a lifetime prevalence of around 17% in the USA and a point prevalence of 5%, is associated with substantial morbidity and mortality. MDD represents one of the most common causes of disability in the developed world like chronic pain to

coronary artery disease. When depression coexists with other medical conditions, the patient's disease burden increases, and the quality of life. [13]

Pathogenesis of depression:

Depression is associated with change in substance in the brain that help nerve cells communicate, such as serotonin, dopamine and norepinephrine. According to the permissive hypothesis, depression arises when low serotonin levels promote low levels of norepinephrine, another monoamine neurotransmitter. [2]

The monoamine hypothesis postulates that a deficiency of certain neurotransmitters is responsible for the corresponding features of depression. Norepinephrine may be related to alertness and energy as well as anxiety, attention, and interest in life. Serotonin to anxiety, obsessions, and compulsions. Dopamine to attention, motivation, pleasure and reward, as well as interest in life. The proponents of this theory recommend the

choice of an antidepressant with mechanism of action that impacts the most prominent symptoms.^[2]

The tendency to develop depression may be inherited, there is some evidence that this disorder may run in families, through biological and environmental factors may also be responsible. The increase in depression in industrialised societies has

been linked to diet, particularly to reduced levels of omega-3 fatty acids in intensively farmed food and processed foods. Alcohol can have a negative effect on mood, and misuse of alcohol, benzodiazepine based tranquilizers, and sleeping medication can all play a major role in the length and severity of depression. Poor sleep quality co-occurs with major depression.^[3]

MECHANISM OF DEPRESSION:

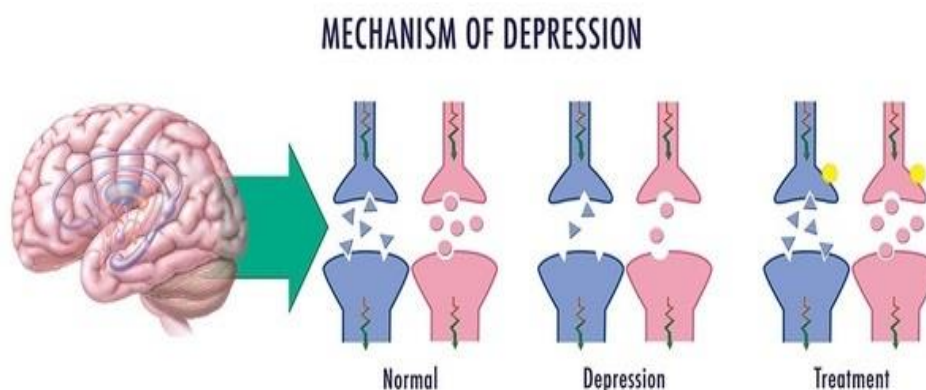


Figure 1: Mechanism of Depression

Types of Depression:^[5]

People experience this mood disorder in different ways. There are also different types of depression. Symptoms can range from relatively minor through to very severe, so it is helpful to be aware of the range of conditions and their specific symptoms. The type of depression you have helps determine the kind of medical treatment you should receive.^[14]

Major Depressive Disorder (MDD):

Major depression is sometimes called major depressive disorder, clinical depression, unipolar depression or simply 'depression'. It involves low mood and/or loss of interest and pleasure in usual activities, as well as other symptoms. The symptoms are experienced most days and last for at least two weeks.^[14]

Melancholia: A less common and more severe form of depression which causes slowed movements and a complete loss of pleasure in everything.^[15]

Psychotic depression: Sometimes people with a depressive disorder can lose touch with reality and experience psychosis. This can involve hallucinations or delusions or Paranoia.^[16]

Atypical depression: It is a misunderstood form of depression. A common sign of atypical depression is a sense of heaviness in the arms and legs like a form of paralysis. However, a study published in the Archives of General psychiatry found that oversleeping and overeating are the two most

important symptoms for diagnosing atypical depression.^[16]

Antenatal and postnatal depression: It is triggered by pregnancy or child birth. It is characterized by feelings of extreme sadness, fatigue, loneliness, hopelessness, suicidal thoughts, fears about hurting the baby and feelings of disconnect from the child. Up to 10% of pregnant women and 16% in the 3 months after birth will suffer from depression.^[17]

Bipolar disorder: Bipolar disorder used to be known as 'manic depression' because the person experiences periods of depression and periods of mania, with periods of normal mood in between. This disorder affects about 2 to 3 percent of the population and has one of the highest risks for suicide.^[18]

Seasonal affective disorder (SAD): The periods of depression that occur in particular seasons, particularly winter, and related to low levels of sunlight. It's characterized by mood disturbances that begin and end in a particular season. People with SAD depression are more likely to experience a lack of energy, sleep too much, overeat, gain weight and crave for carbohydrates **Premenstrual Dysphoric Disorder:** Women with PMDD have depression and other symptoms at the start of their period. Symptoms include depression, anxiety and mood swings. Unlike premenstrual syndrome (PMS), which affects up to 85 percent of women and has milder

symptoms, PMDD affects about 5 percent of women and is much more severe .^[18]

Situational Depression: Also called adjustment disorder, situational depression is triggered by a stressful or life-changing event, such as job loss, the death of a loved one, trauma. Symptoms of situational depression may include excessive sadness, worry or nervousness, and if they don't go away, they may become warning signs of major depression.^[19]

Cyclothymic disorder: Cyclothymic disorder is often described as a milder form of bipolar disorder. The person experiences chronic fluctuating moods over at least two years, involving periods of hypomania and periods of depressive symptoms, with very short of normality between. The duration of the symptoms is shorter, less severe and not as regular, and therefore don't fit the criteria of bipolar disorder or major depression.^[19]

Dysthymic disorder: The symptoms of dysthymia are similar to those of major depression but are less severe. However, in the case of dysthymia, symptoms last longer. A person has to have this milder depression for more than two years to be diagnosed with dysthymia.^[20]

Symptoms of Depression:^[6]

Symptoms of depression interfere with all areas of a person's life, including work and social relationships.

- Intense feeling of sadness and despair.
- Loss of interest and pleasure in usual activities.
- Low energy, fatigue or feeling "slowed down".
- Feeling of worthlessness and guilt.
- Psychomotor retardation or variable agitation.
- Suicidal thoughts or actual suicide attempts.
- Feeling of hopelessness, difficulties in thinking, mental slowing.
- Loss of concentration, remembering, making decisions.
- Pessimistic worry, self-deprecation, hostility.
- Loss of libido.
- Disturbances in sleep patterns like insomnia or hypersomnia.
- Altered eating pattern with anorexia and weight loss or sometime overeating.
- Disruption of normal circadian and ultradian rhythms of activity, body temperature and many endocrine functions.

Diagnosis:^[7]

Major depressive episodes are diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR) criteria. To meet the criteria for a major depressive episode, patients should experience at least five or more persistent

symptoms for at least 2 weeks. These symptoms include depressed mood, loss of interest or pleasure in activities, change in appetite, unintentional weight gain or loss, insomnia or excess sedation, psychomotor agitation or retardation, decreased energy or fatigue, feelings of worthlessness or inappropriate guilt, decreased ability to concentrate, and recurrent thoughts of suicide, death or suicide attempt. The lack of diagnostic or even syndromal specificity of most psychotropic drugs tends to reduce the chances of finding a discrete mechanistic correlate for a specific disease based simply on the actions of therapeutic agents.

Treatment:^[7]

The decision to treat with an antidepressant is guided by the presenting clinical syndrome, its severity, and by the patient's personal and family history. Three treatment options exist for the treatment of depression: pharmacotherapy, psychotherapy, and electroconvulsive therapy (ECT). Complementary or alternative treatments used in major depression include St. John's wort, S-adenosyl methionine, omega-3 fatty acids, and folate.^[14]

Pharmacotherapy:^[7]

Pharmacotherapy option includes treatment by antidepressant drugs. Pharmacotherapy can be used for mild to severe major depression and produces a response in 50 % to 75 % of patients. Antidepressants have similar efficacy, either directly or indirectly, the actions of nor epinephrine and / or serotonin in the brain, however, they differ in adverse effects, mechanism of action, drug-drug interactions, and cost. According to a 2007 report by the Centers for Disease Control and Prevention, antidepressant drugs were the most commonly prescribed medications in the USA at the time of the survey.^[8]

The antidepressant use may be related to the broad application of these agents for conditions other than major depression. For example, antidepressants have received Food and Drug Administration (FDA) approvals for the treatment of panic disorder, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD), treat pain disorders such as neuropathic pain and the pain associated with fibromyalgia, premenstrual dysphoric disorder (PMDD), mitigating the vasomotor symptoms of menopause, and treating stress urinary incontinence.^[9]

Monoamine oxidase inhibitors (MAOIs):

MAOIs inhibit monoamine oxidase, which is responsible for the breakdown of neurotransmitters such as dopamine (DA), serotonin (5-HT) and norepinephrine (NE). Current MAOIs include the

hydrazine derivatives phenelzine and isocarboxazid and the non-hydrazines tranylcypromine, selegiline and moclobemide. The MAO inhibitors are indicated for depressed patients who are unresponsive or allergic to TCAs or who experience strong anxiety or low psychomotor activity or phobic states. A special subcategory of depression, called atypical depression, may respond to MAO inhibitors. Severe and often unpredictable side effects due to drug-food and drug-drug interactions limit the widespread use of MAO inhibitors.^[10]

Tricyclic Antidepressants (TCA's): Tricyclic amines (TCAs) can be classified as tertiary and secondary amines. The actions of tricyclic antidepressants include a range of complex, secondary adaptations to their initial and sustained actions as inhibitors of NE neuronal transport and variable blockade of 5-HT transport. Tricyclic antidepressants with secondary-amine side chains or the *N*-demethylated metabolites of agents with tertiaryamine moieties are relatively selective inhibitors of NE transport. The TCAs tend to be well absorbed and have long half-lives. The tertiary amine TCAs, including imipramine, amitriptyline, trimipramine, doxepin, dothiepin, clomipramine. The secondary amine TCA's, including desipramine and nortriptyline, lack active metabolites and have fairly linear kinetics. TCAs produce their antidepressant effect by inhibiting the reuptake of 5-HT and NE. Tertiary and secondary amines have equal potency in blocking NE reuptake. Tertiary amines possess greater potency for blocking 5-HT reuptake and greater affinity for these other receptors. Uses include major depressions, phobic and panic anxiety states, neuropathic pain, enuresis and obsessive-compulsive disorder (OCD).^[10]

Selective Serotonin Reuptake Inhibitors (SSRIs):

SSRIs are considered to be first-line antidepressants for the treatment of depression. SSRIs exert their antidepressant effect by blocking the reuptake of serotonin. These drugs are safer in overdose than the tricyclic group. Selective serotonin reuptake inhibitors (SSRIs) do not stimulate appetite and have much fewer antimuscarinic side effects than the tricyclics and other catecholamine-uptake inhibitors. Examples include fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram and escitalopram. Clinical uses include major depressions, anxiety states, PMS, bulimia, OCD and alcoholism.

Atypical Antidepressants:

The atypical antidepressants are a mixed group of agents that have actions at several different sites. This group includes bupropion, mirtazapine, nefazodone and trazodone. The actions of the drugs remain poorly understood. This drug acts as a weak

dopamine and norepinephrine reuptake inhibitor to alleviate the symptoms of depression. It is unique in that it assists in decreasing the craving and attenuating the withdrawal symptoms for nicotine in tobacco users trying to quit smoking. Mirtazapine blocks presynaptic α_2 receptors, preventing feedback inhibition of transmitter release.^[11]

CONCLUSION

It is an aminoketone class of anti-depressant drug. The basic goal is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage form is an important element to accomplish this goal.^[12]

It is one of the most important antidepressant drugs used in the treatment of major depressive disorders, with a half-life of 8-24 hours. When it is given as immediate release dosage form, several toxic side effects like seizures are observed. So we are going for any formulation so that we can maintain the dose within the therapeutic window range.^[12]

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