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Depression and its Management-An Overview

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ABSTRACT

Depression, a common and disabling condition, is often misunderstood by patients, family members. Major depression is a mood disorder characterized by a sense of inadequacy, decreased activity, pessimisms and sadness where these symptoms severely disrupt and adversely affect the person's life, sometimes to such an extent that suicide is attempted or results. Depressive disorders often start at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is the leading cause of disability worldwide in terms of total years lost due to disability. Criteria for major depressive disorders are listed in the dsm-v, but even less severe depression may merit intervention-especially if chronic. Depression may not be caused by the simple deficiency of serotonin in brain, but rather, it is a complex interplay of various neurotransmitters including serotonin, norepinephrine, dopamine and histamine in certain brain areas. A variety of pharmacologic, psychosocial and alternative treatments like herbal medications are available for treating depression.

Keywords: Depression, bipolar disorder, antidepressants, selective serotonin reuptake inhibitor, psychotherapy

Introduction

Depression comes from the late Latin word " depressare" and the classical Latin word "deprimere'' . Deprimere,literally means' press down', de translates into 'down' and premere translates into 'to press'. Depression also refers to a depressed topography or the fact of being pressed down[1] Depression is a common mental disorder that presents with depressed moods, loss of interest or pleasure, decreased energy, feeling of guilt or self worth, disturbed sleep or appetite and poor concentration.[2]Depression is a state of mental illness. It is characterized by deep long lasting feeling of sadness or despair. It can affect people of any age group including young children and teens.[3] Depression is largely seen by the general public and mainstream media as a neuropsychiatric illness [4] As estimated by WHO, depression shall become the second largest illness in terms of morbidity by another decade in the world. Already one out of every five women and twelve men have depression. [5] Depression affective disorders is one of the common psychiatric disorders. 5-6% of population is depressed and an estimated 15% of people may become depressed during their life time. [6] The primary mood disorders include major depression, dysthymia, bipolar disorder and cyclothymia. [7] Major depression and Mania are two extremes of affective disorders which refer to a pathological change in mood state.[8] Depression represents a spectrum from dysthymia to major depression.[9] Anxiety and depression are the leading psychiatric disorders now. It is the 4th cause of disability around the world and is estimated to be the 2nd leading cause of disability by 2020. [10]

Epidemiology:

The median age of onset of major depression is in early 30's. At any one time 2.3%- 4.9 % of individuals have this disorder. The condition is more common in setting of physical illness, reaching level of 15% - 20% in nursing home residents and 22% - 33% in individuals with chronic medical condition. [9]The prevalence of major depressive disorder in USA is 5.4% - 8.9%. [11] and of bipolar disorder 1.7% - 3.7%. Major depression affects 5 to 13% of medical outpatients[5], yet is often undiagnosed and untreated.[12] Depression is the leading cause of disability and premature death among people aged 18 to 44 years and is expected to be the second leading cause of disability for the people of these ages by 2020.[13,14] Depressive illness has also been shown to be associated with increase rate of death and disability from cardiovascular diseases.[15,16]

Types of Depression:

- **Major depressive disorder:** Major depressive disorder includes patients who have experienced one episode of depression and those who have recurrent depressive episodes. This disorder is commonly referred to as Unipolar.[7] The classic depression type, Major Depression is a state where a dark mood is all-consuming and one loses interest in activities, even ones that are usually pleasurable. Thought of death or suicide may occur. [17]
- **Mania:** If the mood becomes elated or irritable this may be a symptom of Mania. The term 'mania' is used to describe severe cases, frequently associated with psychotic symptoms. Hypomania describes a less severe form of disorder.[18] Mania often affects thinking, judgement, and social behaviour in ways that may cause serious problems and embarrassment. [19,20]
- **Bipolar and Unipolar disorders*:*** If a patient develops one or more severe episodes of a mood disorder which includes a manic episode, the condition may be termed as bipolar disorder .[18] Two types of Bipolar disorder have been described which depends on the severity of manic episodes.
- **Bipolar 1** disorder characterized by full manic episodes and major depressive episodes, whereas
- **Bipolar 2** disorder has hypomanic and major depressive episodes.[7]
- **Unipolar mood disorder** is used to describe single episodes of depression.[18]
- **Dysthymia**: Dysthymia is characterized by chronic depressive symptoms rather than episodes of mood disturbance. Dysthymia is most commonly encountered in primary care settings, is less often diagnosed and treated, yet causes significant social and occupational dysfunction.[7] Dysthymia is also called Persistent Depressive Disorder.[17]
- **Cyclothymia:** Cyclothymia is a milder form of bipolar illness. It is a chronic mood disturbance of greater than 2 years characterized by numerous episodes of hypomania and depression that are not severe enough to meet criteria for major depression. Cyclothymia patients may require mood stabilizers if their mood instability causes significant distress in their social and occupational functioning.[7]

Etiology:

The etiology of depressive disorder is too complex to be totally explained by a single social, developmental or biologic theory. Several factors appear to work together to cause or precipitate depressive disorder.[21] In depression the genetic, hormonal, biochemical , environmental and social factors all have some role in determining an individual's susceptibility to developing the disorder, with major life events sometimes, but not always, acting as a precipitant for a particular episode.[18] Depression is thought to be caused by an imbalance of certain brain chemicals called" Neurotransmitter" that carry signals in brain which the body uses to control mood. Some of common factors that may cause depression are genetic trauma and high level of stress, mental illness such as schizophrenia and substance abuse, postpartum depression (women may develop depression after birth of baby), serious medical condition such as heart disease, cancer and HIV, use of certain medications, alcohol and drug abuse,

individuals with low self –esteem, trauma and high level of stress due to financial problems, breakup of relationship or loss of a loved one. [3]

1) Genetic causes: To some extent depressive illness can be inherited. What appears to be inherited is a vulnerability to depression. This means that if we have close relatives who have clinical depression , we may inherit a tendency to develop illness . It does not mean that we are destined to become depressed. [22,23] When a mother or father has a bipolar disorder, their child will have a 25% chance of developing some type of clinical depression. If both parents have bipolar disorder, the chance of their child also developing bipolar disorder is between 50% and 75%.[24] Studies on twins reveal that, when one of the identical twin becomes depressed the other will also develop clinical depression approximately 76% of the times.[25] Research has also been done with fraternal twins and have shown that when one fraternal twin becomes depressed, the other also develops depression about 19% of times.[26,27]

2) Environmental causes: Environmental causes of depression include events such as stress, traumatic events and childhood difficulties.[28]

(a) Stress: There appears to be a very complex relationship between stressful situation and the development of clinical depression. Negative stresses are loss of loved one, loss of job, loss of relationship and divorce. Positive stresses are planning for a wedding, preparing for a new job, moving to a new city etc. Both negative and positive stresses from environmental events can precede the development of depression.[28]

(b)Traumatic events: It is a fact that many people have experienced a traumatic event prior to developing depression. Traumatic events in the lives of people include loss of a loved one, a serious medical illness, the end of a marriage or significant financial loss. These types of events can destroy the sense of control and stability in a person's life, often leading to emotional distress. [28]

(c) Childhood difficulties: It has long been known that people with severe difficulties in childhood have higher rates of clinical depression. The most common childhood difficulties include sexual, emotional or physical abuse, dysfunctional upbringing, parental separation, and mental illness in one or both of the parents. [28]

SIGNS & SYMPTOMS: [7]

- ★ Depressed mood, loss of enjoyment
- ★ Disturbed sleep
- ★ Insomnia or Hypersomnia
- ★ Reduced interest or pleasure
- ★ Loss or increase of either appetite or weight
- ★ Thought of suicide or death or suicidal behaviour
- ★ Aches, pains, headaches, or cramps that won't go away
- ★ Digestive problems that don't get better, even with treatment
- ★ Irritability
- ★ Low self-esteem
- ★ More talkative than usual; pressure to keep talking etc.

Pathophysiology:[21]

It is the depletion of the neurotransmitters Serotonin, Nor-epinephrine and Dopamine in the central nervous system which causes clinically significant depression.

Diagnostic Criteria for Mood Disorders:

1) Biologic markers of depression: Investigators continue to search for biologic or pharmacodynamic markers to assist in the diagnosis and treatment of depressed patients. Although no biologic marker has been discovered, several biologic abnormalities are present in many depressed patients. Approximately 45% to 60% of patients with major depression have a neuro-endocrine abnormality, including hypersecretion of cortisol, lack of cortisol suppression after dexamethasone administration (i.e, a positive dexamethasone suppression test), or an abnormal or diminished thyroid-stimulating

hormone response to the administration of thyrotropin-releasing hormone.[29]

2) Diagnostic and Statistical Manual of Mental Disorder (DSM-5)[30]

Five (or more) of the following symptoms should be present nearly every day during the same 2-week period:

★ Depressed mood
★ Markedly diminished interest or pleasure in (almost) all activities
★ Significant weight loss or decrease or increase in appetite
★ Insomnia or hypersomnia
★ Psychomotor agitation or retardation
★ Fatigue or loss of energy
★ Feelings of worthlessness or excessive or inappropriate guilt
★ Diminished ability to think or concentrate or indecisiveness
★ Recurrent thoughts of death, suicidal ideation or a suicide attempt or a specific plan for committing suicide.

Rating Scales:[31]

Various rating scales can be used to assist with the assessment of the severity of the disorder. Two of the more commonly used rating scales are the **Beck Depression Inventory** and the **Hamilton Depression Rating Scale.**

Beck Depression inventory- This is a self – reporting scale looking at 21 depressive symptoms. The subject is asked to read a series of statements and mark on a scale of 1-4 how severe their symptoms are. The higher the score, the more severely depressed a person may be.

Hamilton Depression Rating Scale: This rating scale is used by a healthcare professional at the end of an interview to rate the severity of the depression .[18] The Hamilton depression rating scale is clinician-rated scale that is intended to provide an analysis of the severity of anxiety in adults, adolescents, and children.[32]

The score level of depression :

- 10-13 mild,
- 14-17 mild to moderate;
- 17 moderate to severe

Treatment:

A) Non Pharmacologic:

1) Lifestyle changes (healthy eating and exercise)

2) Sleep hygiene. [33]

3)Psychotherapy*:* Depression – specific psychotherapy is recommended as an initial treatment of choice for patients with mild to moderate depression.[34] Most patients with depression prefer non-pharmacological means of treatment instead of antidepressants, due to stigma, cost and the perceived risk of addiction and dependence.[35] Psychotherapy has been proven to be as effective as antidepressants for patient with mild to moderate major depression.[36] however, many primary care physicians have minimal training in psychotherapy.[37]

There are two main types of psychotherapy commonly used to treat depression.

★ **Cognitive – Behavioural Therapy (CBT)** helps change negative ways of thinking and behaving. CBT works by identifying any dysfunctional thoughts and replacing them with more helpful ones, with the intent of modifying negative behaviours and emotions that perpetuate the depression. [38] CBT is the best studied psychotherapeutic intervention .[39,40] **Interpersonal Therapy (IPT)** helps people understand and work through troubled personal relationship that may cause depression.[3]
★ **Electroconvulsive Therapy** is the most effective treatment for older patients with major depression, with efficacy ranging from 60% to 80%. [41,42,43] Electroconvulsive therapy is also indicated for patients with severe or psychotic depression and patients with severe malnutrition or a medical condition that worsens because they have refused to take their medication.[42,43,44] ECT has been and continues to be the most effective treatment for major depression. [45,46]

B) Pharmacologic treatment:

Therapy with an antidepressants agent is the preferred treatment in cases of moderate to severe major depression. Antidepressants should be prescribed if there is no improvement following psychotherapy, the patient is unsuitable for psychotherapy, or the patient meets the criteria for moderate to severe depression. [47] Antidepressants can be classified in several ways , including by chemical structure and presumed mechanism of antidepressant activity.[29] 50-65% of patients respond to the first antidepressant. Choice can be guided by matching patient's symptoms to side effects profile, presence of medical and psychiatric co-morbidity and prior response. [28]

Table 1: Classification of Antidepressants by Receptor selectivity and site of action [48]

Class of antidepressants	Drugs in class	Receptors mediated pharmacological action	Other receptor site affected	Receptor mediated side effects
Tricyclic antidepressants	Amitriptyline, Clomipramine Doxepin,Imipraminr, Trimipramine, Desipramine, Nortriptyline, Protriptyline	Inhibit reuptake of serotonin, norepinephrine and dopamine, depending on the compound	Adrenergic, cholinergic, histaminergic	Dry mouth, dizziness, blurred vision, constipation, sedation, orthostatic hypotension, tachycardia.
Triazolopyridines	Trazodone, Nefazodone	Mixed seratonergic and noradrenergic effects	α1 adrenergic, histaminergic	Priapism (trazodone), sedation.
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram, Fluoxetine Fluvoxamine, Paroxetine, Sertraline.	Selectively inhibit reuptake of serotonin	Minor,but clinically significant, depending on the compound	Nausea, sleep disturbances, sexual dysfunction, appetite changes, headache, dry mouth.
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	Venlafaxine, Duloxetine	Inhibit reuptake of both serotonin and norepinephrine	Dopaminergic (low affinity)	All of the side effects of SSRIs, hypertension, tachycardia.
Multiple receptor antidepressants	Mirtazapine	Combined effects on noradrenergic (presynaptic α2) and serotonergic (5-HT1 and 5-HT3) receptors.	Histaminic(H1), low affinity for dopaminergic, cholinergic, muscarinic receptors.	Drowsiness, hypercholesterolemia,weigh t gain.
Monoamine oxidase inhibitors	Moclobemide, phenelzine, isocarboxazid	Inhibit activity of MAO-A,MAO-B	α1 adrenergic	Orthostatic hypertension
Miscellaneous	Bupropion	Mixed effects on norepinephrine and dopamine	Negligible	

St.John's Wort: St. John's Wort (hypericin) is a popular alternative treatment for depression. Despite European studies demonstrating the efficacy of St.John's Wwort. [49]. Increasingly, consumers are choosing alternative form of therapy, such as herbal medication including St.John's Wort . Some evaluations have found that the active ingredient in St.John's Wort, hypericum is a safe and effective treatment for mild to moderate depression when compared with placebo, TCAs, and fluoxetine. [29]

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