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Research Article

DEPRESSION: A REVIEW AND ITS MANAGEMENT

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ABSTRACT

Depression disability disorder is a major contributor to the global burden of disease. Today, around 350 million people are estimated to be affected worldwide with this disorder. Depression is different from usual short-lived mood fluctuations. It is a long-lasting mood disorder with moderate to severe intensity and sometimes leads to suicidal incidents. Medically depression is a common but treatable disorder which is difficult to diagnose in the primary stages. A barrier to the effective treatment includes scarcity of appropriate resources, deficit of psychiatrists, misdiagnosis and societal infrastructure. Therefore pertinent resources and trained sensitised physicians are required for proper diagnosis and treatment of depressive disorders. The article reviews the clinical updates for the treatment of depression.

INTRODUCTION

Depression is a serious mood disorder causing a persistent feeling of sadness and loss of interest. It is very different from the common experience of unhappiness and tension for a short duration time duration. Sometimes situation is so serious that patient tries suicide attempts. The seriousness of the disease can be measured as it is described as "living in a black hole" where one has an intense feeling of loneliness. In terms of public health significance, depression is reported as the third leading cause of global disease burden as it accounts for 4.3% of total disability during life span. If the existing trends prolong, it will become the leading cause of disease burden by the year 2030 [1,2].

Unlike other diseases or disorders, there is no one simple explanation for depression. Two main factors responsible for depression are biological and social. Causing factors are depicted in Fig. 1.

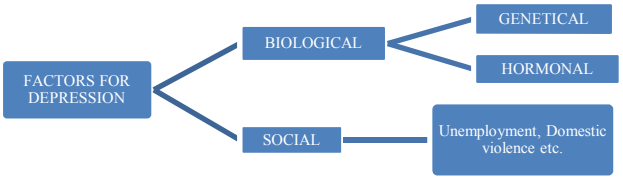

Fig 1 Factors causing depression

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Researchers on data accumulation implicate genetic risk as an important factor for depression [3,4,5]. But the prevalence of depression in women provoked the scientists to search the role of sex hormone in initiating certain forms of depression [6]. The obvious difference in male and female sex hormones and the link between increased rates of depression in women, as well as the link between mood and menstrual cycle indicates the major contribution of gonadal or sex hormone in causing depression. Besides biological factors various social factors are also equivalently responsible for the cause of depression. Whatever the cause on occurrence the range of depression varies from mild to severe. Diagnostic and Statistical Manual of Mental Disorders classified depression as 9 types on the basis of severity: Major depression, Dysthymia, Postpartum depression, Seasonal affective disorder (SAD), Atypical depression, Psychotic depression, Bipolar disorders, Pre-menstrual dysphoric disorder, Situational depression.

Epidemiology

Epidemiological studies shows that average age of onset of depression is 24 years but it occurs anytime throughout the lifespan [7] and is directly associated with gender, age and marital status [8]. Demographic studies indicates that occurrence of depression is more pronounced among people who are single, divorced or widowed. Nuclear families and elderly age also contributes depression to a higher risk [9]. Strong epidemiological evidence supports the genetic contribution for depression upto 80% [10]. However, heritability in women is significantly higher in comparison to men [11]. A finding of many well-designed epidemiological studies conducted in United States [12] and worldwide [13]

has been consistently replicated and confirms the prevalence of depression in women. According to WHO (2008) report women are afflicted twice to depression in comparison to their male counterpart thus also considered as feminized issue [14,15]. Research conducted in developing countries reveals the fact that maternal depression may be a risk factor for poor growth in young children [16]. WHO globally ranked depression as 4th leading cause of disability and predicted it as 2nd leading cause by 2020 [17,18]. Approximately about 9.5% of the US population above 18 years have a depressive disorder [19]. Absolute rate of depression vary during adulthood and are highest in midlife.

In Indian context, recent studies with accurate methodology reported an overall prevalence of 15.9% for depression [20]. A study conducted by the Government of India indicates that one out of every five Indians is suffering from depression as there is an alarming increase in rates of suicides. The National Crime Record Bureau statistics reveal that a total 1,35,445 people committed suicide in 2012, which accounts to 371 suicides /day.

Pathophysiology of Depression

Nerves communicate with one another via chemical transmission. Chemical transmission requires several steps including synthesis of neurotransmitters, their storage and regulated release. Neurotransmitters are synthesised from amino acid in the brain via enzymatic reactions, then stored in synaptic vesicles and finally released into the synaptic cleft by a Ca^{2+} dependent process. Neurotransmitter molecule gets coupled with guanine nucleotide binding protein, which is the initial regulatory component in transmission signalling [21]. Signal transduction initiate a pathway via phosphorylation of protein kinases and control brain functions by regulation of receptor modulation, neurotransmitters release etc [22]. Disrupted function of the chemical transmission results into depression. These well established mechanisms are now the target of antidepressant pharmaceutics.

The first major hypothesis of depression proposed that functional deficiency of monoaminergic transmitters are one of the cause of depression [23,24,25].

Clinical observations and animal experimental data strengthen the evidence for this hypothesis. Depressive state arises due to altered synthesis, storage or release of transmitters [26]. But the pathophysiology of depression cannot be explained by a single monoamine related mechanism [27,28,29,30]. Some in-vivo studies investigate the effect of transport proteins in different states of depression because it plays a crucial role in monoaminergic transmission, as they reduces the availability of neurotransmitters [31]. Abnormality in transmission can also arises due to change in receptor function that is either changes in coupling between transmitters and receptors or changes in the signal transduction [32,33]. On the basis of these findings hypothesis of depression illustrates that signal transduction pathways affect the functional balance between neurotransmitter systems and physiological processes.

Depression Management

Methods adopted for depression management vary on the basis of its severity and cause. Specific screening is an urgent requirement for accurate diagnosis and treatment at onset of the disorder. Treatment options for depression outlined by the W.H.O. mhGAP Intervention Guide consist of psychosocial support combined with psychotherapeutic and pharmacological treatment according to the severity of the problem [34]. Patients suffering from the below threshold depression level can be treated with psychosocial interventions and counselling by experienced psychotherapists. But for moderate to severe depression level pharmacological treatment with antidepressant drugs is the core pathway of treatment.

Pharmacological Treatment of Depression

Antidepressants are effective alternative for depression management. They are prescribed as first-line treatment options in moderate and severe depressive disorder. But they are not recommended for short duration mood disorders and depression in children and adolescents [35,36].

Existing antidepressants

Kuhn introduced imipramine in 1950s, for the treatment of depression. Since then large number of antidepressants have captured the market.

Table 1 Adverse effects and over-dose toxicity of existing antidepressants

Groups of Antidepressants	Marketed Antidepressants	Adverse Effects			Over-dose toxicity
		Sedation	Anti-Cholinergic	Nausea	
Monoamine oxidase inhibitors (MAOIs) (Fig 2)	Isocarboxazid	+	++	+	High
	Phenelzine	+	+	+	High
	Tranylcypromine	-	+	+	High
	Moclobemide	-	-	+	Low
Noradrenaline and specific serotoninergic antidepressants (NASSAs) (Fig 3)	Mirtazapine	+++	-	-	Low
	Mianserin	++	+	-	Low
	Trazodone	+++	-	+	Low
Serotonin and noradrenaline reuptake inhibitors ((SNRIs) (Fig 4)	Duloxetine	-	-	++	Moderate
	Venlafaxine	-	-	++	Moderate
	Citaloparm	-	-	++	Moderate
Selective serotonin reuptake inhibitors (SSRIs) (Fig 5)	Escitaloparm	-	-	++	Low
	Fluvoxamine	+	-	++	Low
	Paroxetine	+	-	++	Low
	Sertraline	-	-	++	Low
	Fluoxetine	-	-	++	Low
Tricyclics (Fig 6)	Amitriptyline	+++	+++	-	High
	Clomipramine	++	+++	+	Moderate
	Dosulepin	+++	++	-	High
	Lofepramin	+	++	-	Low
	Imipramine	++	+++	-	High
	Nortriptyline	+	++	-	High
	Trimipramine	++	+++	-	High

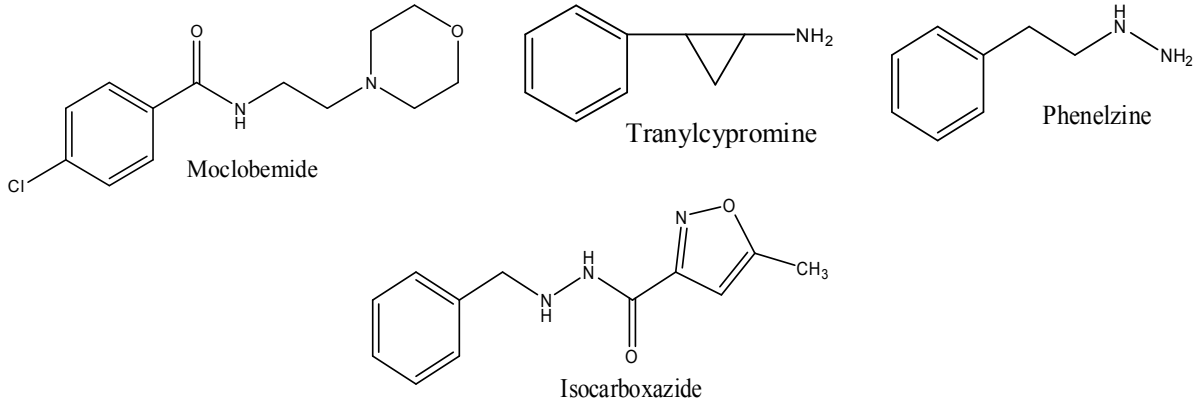

Fig 2 Monoamine oxidase inhibitors (MAOIs)

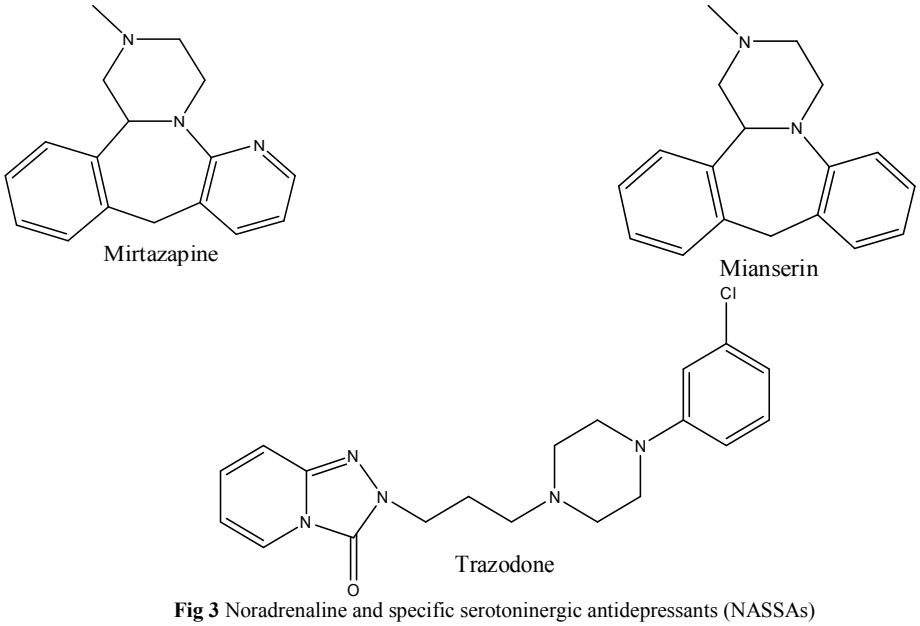

Fig 3 Noradrenaline and specific serotoninergic antidepressants (NASSAs)

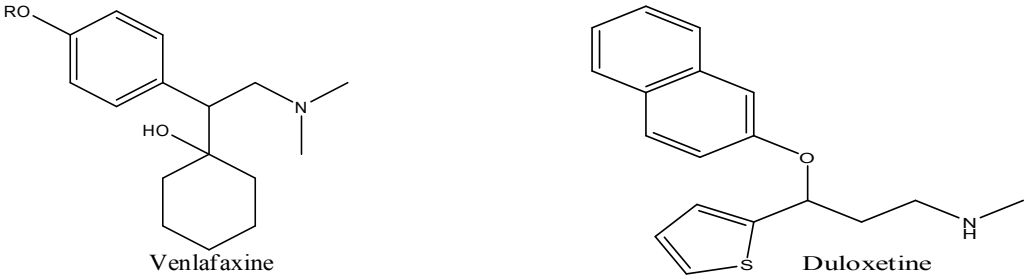

Fig 4 Serotonin and noradrenaline reuptake inhibitors (SNRIs)

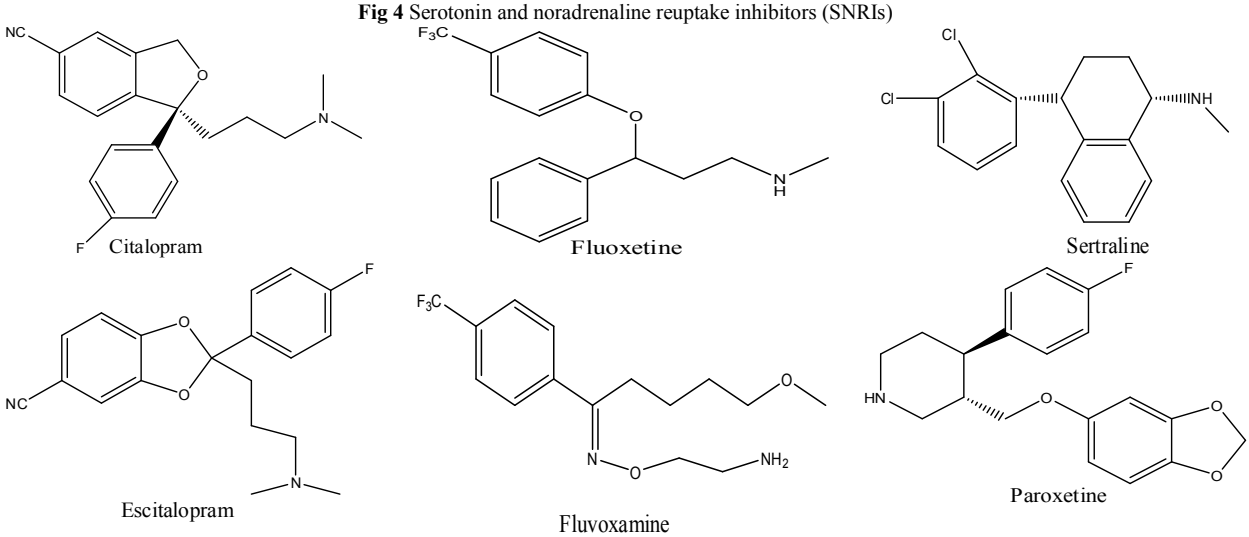

Fig 5 Selective serotonin reuptake inhibitors (SSRIs)

Royal College of Psychiatrists, England, has classified current antidepressant drugs into 5 groups [37]. Existing antidepressants their adverse effects and over-dose toxicity levels are listed in table 1 [38,39].

Choice of antidepressants

The choice of antidepressants is made on the basis of patients past experiences, previous response, adverse effect profile, cost, age, gender, genetic factors etc [40,41].

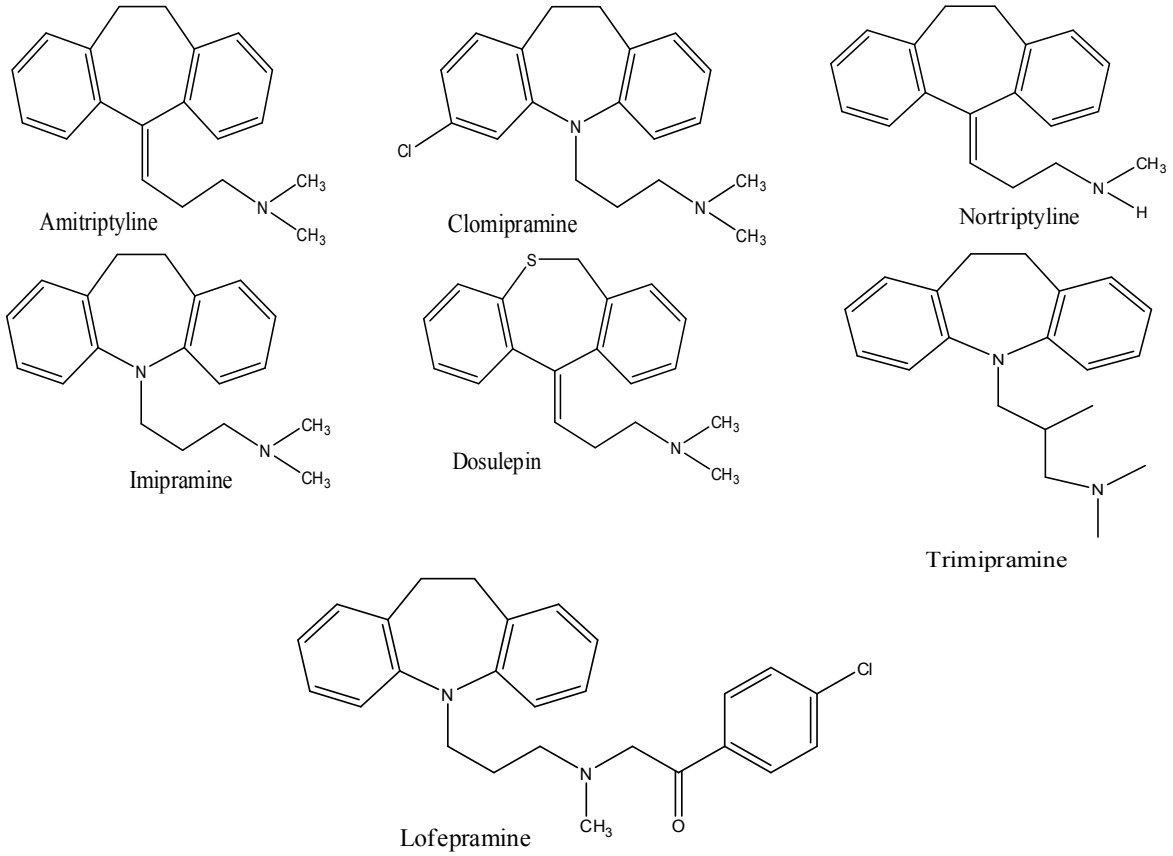

Fig 6 Tricyclic antidepressants

Mode of action of antidepressants

The basic principle involves in the pharmacology of antidepressants is to increase the transmission of monoamines as serotonin, noradrenaline or dopoamine. They achieve it by inhibiting the transporter responsible for the re-uptake of the monoamines.

Monoamine oxidase inhibitors ($MAOI_S$) block the mitochondrial enzyme monoamine oxidase, which breaks down neurotransmitters such as serotonin. If less serotonin is broken down, the patient experiences more stabilized moods and less anxiety.

Serotonin and noradrenaline reuptake inhibitors ((SNRIs) raise the levels of two neurotransmitters serotonin and norepinephrine in the brain, they play the key role in mood stabilization. SNRIs achieve this by blocking the 'reuptake' of serotonin and norepinephrine. Reuptake is the absorption process of neurotransmitters back into the part of the brain that released them. By blocking the reuptake process, SNRIs allow more serotonin and norepinephrine to be available in the brain. Action mode of Selective serotonin reuptake inhibitors (SSRIs) is similar to that of $SNRI_S$, but they are selective to serotonin.

Mirtazapine a Noradrenaline and specific serotoninergic antidepressant (NASSAs), increases noradrenaline and serotonin transmission by reducing the action of $alpha_2$-adrenoreceptor.

It can be concluded from table 1 that SSRIs are recommended as an initial choice to treat depression because of their lesser adverse effect and overall safety profile for toxicity [42]. Medication requires 4-6 weeks for improvement in depressive disorder symptoms. Physicians at starting prescribe lower dose and increase gradually after monitoring the degree of depressive symptoms and adverse effects of antidepressant on the patient.

Alternative Treatments for Depression

- Stress management, as meditation, relaxation and massage is the most common alternative treatment for people suffering with depression [43].
- Exercise is commonly viewed as an antidepressant an enhance feeling of well-being. Researchers have also strengthened the fact that exercise elevates mood and reduces depressive symptoms [44].
- Yoga is adopted as an antidepressant tool by our ancestors as it has a calming effect and helps to alleviate depression.
- In homeopathy, Kaliphos, a biochemic medicine is given for the treatment of mood disorders.
- Ayurveda classifies depression as vata related problem. Prescribed remedies are us of shirodhara oil, Brahmi tea etc.
- Herbal circulatory stimulants as panax, ginseng, rosemary and ginger may also prove beneficial in suppressing depression.
- Eating chocolates also lift mood temporarily.

- Protein and vitamin B enriched diet is helpful in providing cheerful disposition.
- Last but not least Vaastu shastra is also mentioned as a fruitful tool for treatment of depression by the vaastu experts.

Natural Alternatives for Depression Management

Some natural antidepressants are depicted in Fig. 7.

Fig 7 Natural antidepressants

CONCLUSION

Depression is a chronic psychiatric disorder and requires profound public health concern. The occurrence of depression results due to various biological and psychosocial factors, thus accurate diagnosis and treatment is essential for the well being of patient. The mode of treatment adopted may vary from psychotherapy to pharmacotherapy on the basis of the severity of the disorder. Besides, efficacy the treatment should also be cost effective. Pathophysiological studies has widens the scope of targeted antidepressants synthesis. Further researches are still required to increase the efficacy of antidepressants with minimal adverse effects.

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