

Anti-Depressant Drugs: A Brief Review

Vandana Sharma

Department of Psychology, I.N.P.G. College, Meerut-U.P.(India)

ABSTRACT

Depression is a serious problem of modern fast and busy life. It is affecting more than 50% of world population. Sometimes depression and anxiety affect a person simultaneously and some drugs are common to both the illness. A number of safe anti-depressant drugs are available which act upon neurotransmitters including nor-epinephrine, serotonin and glutamate etc. Herbal drugs are also available as an alternative therapy. This paper reviews both alleopathic as well as herbal anti-depressant drugs for the purpose of dissemination of information.

Keywords- anti-depressant drugs, nor-epinephrine, serotonin, glutamate, mechanism of action.

I. INTRODUCTION

Depression disorder is one of the main diseases of modern world which is consequence of worries generated under work pressure in this busy life style. This is of two types: (i) major depression i.e. unipolar depression and (ii) persistent depressive disorder or bipolar I and II disorder (also known as manic depressive illness). Risk of unipolar disorder to get converted into life time disorder is approximately 15% more in female in comparison to male¹. Furthermore, in unipolar depression mood swing is in same direction but in bipolar depression it alternates with mania². Sometimes depression remains undiagnosed and people underestimate it, this situation may sometime culminate in suicide³. Depression in few cases complicates treatment of other diseases⁴. To treat depression anti-depressants are used. Anti-depressants increase alertness, therefore, bring behavioral changes towards characteristics like sadness, change in appetite, sleep disorder, loss of interest in pleasure, psychomotor disturbances, suicidal thoughts and feeling of unworthiness etc.⁵. Use of psychoactive drugs like anti-depressants is continuously increasing throughout world now-a-days⁶⁻⁷

II. ANTIDEPRESSANT DRUGS

In ancient literature depression was described as melancholia by Hippocrates in 4th century B.C⁸. Depression is characterized by sleep disorders, feeling of sadness, change in appetite, loss of interest in pleasure, psychomotor disturbances, feeling of inferiority and suicidal thoughts. Helplessness, hopelessness, despair and guilt feeling are also associated with depressed mood. Variable characteristics of depression are lowness, loss of drive, sleep and ambition, agitation, hypochondriases. Its somatic symptoms include weight loss/gain, constipation, headache etc. sometimes delusion, depersonalization and hallucination also occur with it⁹. Depression affects public health through distress, ill health and financial burden¹⁰. Approximately 50% of the depression patients commit suicide¹¹. Anti-depressants are normally taken for 4 to 6 months and they are taken for moderate to severe depression, obsessive compulsive disorders, eating disorder, chronic pain, post traumatic stress disorder (PTSD), panic attack and severe anxiety⁵.

III.CLASSIFICATION OF ANTI-DEPRESSANTS

Anti-depressant drugs can be categorized in following classes:

A. *Monoamine oxidase inhibitors (MAOIs): e.g.*

- 1) Isocarboxazide
- 2) Pargyline
- 3) Tranylcypromine
- 4) Phenazine
- 5) Nialamide
- 6) Iproniazide;

Monoamine oxidase is complex enzyme system present in almost every organ and catalyses deamination i.e. inactivation of natural biogenic amines particularly adrenalin (epinephrine), noradrenalin (norepinephrine) and 5HT (serotonin). MAOs have efficacy equivalent to tricyclic anti-depressants (TCAs) but are rarely used on account of their toxicity¹².

B. *Tricyclic anti-depressants(TCAs) : e.g.*

- 1) *Dibenzazepines: disipramine, imipramine, trimipramine, cloimipramine etc.*
- 2) *Dibenzoxepines: Doxepine*
- 3) *Dibenzoxazepines: Loxapine, amoxapine*
- 4) *Dibenzocycloheptanes: Protriptyline, amitriptyline and nortriptyline.*

Most widely used drugs for depression are TCAs in which two benzene rings are joined to central six membered ring. They are further divided into : tertiary amines and secondary amines. TCAs elevate mood, increase physical activity, change sleep pattern, normalize appetite and reduce morbidity in 60-70% patients who suffer from major depression. Because of role of norepinephrine in nociception tricyclic anti-depressants are used in variety of pains¹³.

C. *Noradrenaline-serotonin reuptake inhibitors (NSRIs):e.g.*

- 1) *Clomipramie*
- 2) *Doxepine*
- 3) *Amitriptyline*
- 4) *Imipramine*
- 5) *Dothepin*
- 6) *Trimipramine*

These drugs cause enhanced serotonergic or noradrenergic neurotransmission. Initial inhibition of serotonin i.e. 5HT transporter (SERT) leads to activation of 5HT_{1A} and 5HT_{1D} autoreceptors result in serotonergic neurotransmission by negative feedback mechanism till serotonergic autoreceptors are desensitized (Goodman Gilman, 2018).

D. *Selective serotonin reuptake inhibitors (SSRIs): e.g.*

- 1) *Citalopram*

- 2) *Paroxetine*
- 3) *Fluoxetine*
- 4) *Fluvoxamine*
- 5) *Sertraline*

SSRTs are used to treat major depression and are also anti-anxiety agents for generalized anxiety, social anxiety, obsessive compulsive disorder and panic¹⁴. SSRTs: paroxetine and sertraline are used as a treatment of post-traumatic stress disorder (PTSD).

E. Serotonin receptor antagonists :

A number of antagonists of this class are anti-depressants . e.g. nefazodone and trazodone, mianserin and mirtazapine. Mianserin and mirtazapine are sedating and are used as drugs of choice for depression patients with insomnia.

F. Atypical anti-depressants: e.g.

- 1) *Trazodone*
- 2) *Bupropione*

These are anti-depressants for bipolar disorder or manic depression. Atypical anti-depressants are chemically different from other anti-depressant drugs and relatively safer, have lesser side effects like cardiac and anticholinergic. These are new generation anti-depressants. Trazodone acts by blocking reuptake of serotonin at pre-synaptic neuronal membrane. It has no effect on reuptake of dopamine or noradrenalin. It's sedative effect is produced by blocking action of alpha adrenalin and modest histamine blockade. Bupropione is for attention deficit disorder too. It is used to help people stop smoking⁵. Atypical antipsychotics are in use for major depression without psychotic features¹⁵.

G. Newer anti-depressants: Newer anti-depressant drugs in use are:

1. *Vilazodone ;*
2. *Vortioxetine ;*
3. *Agomelatine ;*

Vilazodone was approved by Food and Drug Administration (FDA) in 2011 as anti-depressant and is selective serotonin reuptake inhibitor. SSRIs increase serotonin level through inhibition of reuptake of serotonin transporter (SERT)¹⁶. The side effects due to inhibition of serotonin reuptake inhibitor are reduced by it and improvements in the state of anxiety are observed¹⁷. Use of new drug Vortioxetine started in 2013. This drug in addition to inhibit serotonin uptake also causes different effects on serotonin receptor subtypes 5HT7- 5HT3 antagonist receptor, 5HT1B and 5HT1A agonist¹⁸. Agomelatine is another drug in the category "Drug Innovation". It promotes resynchronization of circadian rhythms altered in depression patients¹⁹.

H. Herbal anti-depressant drugs_: Jatamasi (*Nordostachys jatamansi*) is effective in treating depression²⁰. *Withania somnifera* (Ashwagandha) too helps in fighting depression²¹. Nirgundi (*Vitex nergundo*) is also anti-depressant. Kapikacehu (*Mucuna pruriens*)²² and *Tinospora cordifolia* (Giloy)²³ are other anti-depressant herbs used in various Ayurveda formulations.

IV.MECHANISM OF ACTION OF ANTI-DEPRESSANT DRUGS

During depression some of neurotransmitters like serotonin (5-hydroxytryptamine or 5HT) and noradrenalin do not work properly. Anti-depressants regulate their functioning.

Monoamino oxidase (MAO) inhibitors act by catalysing deamination or deactivation of natural biogenic amines like noradrenalin, adrenalin and serotonin which are neurotransmitters. Inhibition of MAOs increase these biogenic amines at nerve endings as well as intercellular concentration of endogenous amines by inhibiting deamination which is probably cause of anti-depressant activity. These drugs may form complexes with MAOs and inhibit their action i.e. why they are called MAO inhibitors. MAOs may also form covalent bonds with **enzymes** to inactivate them⁵.

Tricyclic anti-depressants (TCAs) inhibit reuptake of neurotransmitters 5HT and noradrenalin in their respective nerve terminals. Reuptake is responsible for deactivation of neurotransmitters in brain. After the release of neurotransmitters from neurones they are removed from extracellular space through transporters (i.e. reuptake sites) present on cell membrane. TCAs block transporters. Inhibition of uptake by anti-depressants allow neurotransmitters to remain active in synapse for longer time and there by cures depression.

Anti-depressants evoke regulation and are responsible for effectiveness of therapy. These responses are altered G-protein coupling and cyclic nucleotide signalling, increased neurogenesis in hippocampus and induction of neurotropic factors etc.²⁴.

A new target of depression is N-methyl-D-aspartate (NDMA) which is known for involvement in memory and learning. Fast acting antidepressants interact with neurotransmitter glutamate, level of which gets altered during depression. Studies have revealed that glutamate may be better target for the treatment of depression than serotonin as its latency period is longer¹⁶.

V.SIDE EFFECTS OF ANTI-DEPRESSANTS

Side effects associated with anti-depressants are constipation, drying of mouth, sweating, urinary retention, tachycardia, decreased visual accommodation, arrhythmias and hypotension etc. MAOs cause hypertension and headache, nausea, palpitation and vomiting may also occur. TCAs may be associated with sweating, constipation, drying of mouth, blurred vision, drowsiness, weight gain and hypotension etc. They may also lead to convulsions and seizure, transient insomnia, disturbed motor function, tremors and schizophrenic symptoms. Use of anti-depressants may also cause mania. Few other side effects of anti-depressants are jaundice, allergy, photosensitivity and dyscrasias of blood like agranulocytosis. Few other symptoms have been reported in several cases. Few to mention are: dizziness, headache, cold sweats, cramps, anxiety, restlessness.

CONCLUSION

Anti-depressants though cure depression but have a number of serious side effects. However, herbal drugs as in Ayurveda with lesser side effects are better; although their action is not very fast.

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