

Antipsychotic drugs or Neuroleptic drugs

called ant schizophrenic or Major tranquilizers

Learning objectives

Definition of psychosis and dopamine hypothesis of schizophrenia ,classification of antipsychotic drugs ,pharmacological action of antipsychotic ,therapeutic indications and side effects .

Antipsychotic drugs or Neuroleptic drugs called ant schizophrenic or Major tranquilizers

The term anti-psychotic and neuroleptic are used to denote a group of drugs that is used mainly for the treatment of (schizophrenia); and they are effective in some other psychotic state e.g. mania and delirium.

Chemical classification of antipsychotic drugs into:-

- 1) **Phenothiazine derivative**; which subdivided into-
 - a) Aliphatic derivatives :- Chlorpromazine (largactil)^R .
 - b) Piperidine derivatives :- Thioridazine .
 - c) Piperazine derivatives: - Fluphenazine and Trifluoperazine.
- 2) **Thioxanthine derivative** e,g.:- Thiothixene .
- 3) **Butyrophenone derivatives** e.g. Haloperidol.
- 4) **Miscellaneous structures** e.g. Clozapine , Olanzapine and Risperidone .

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Pharmacokinetic of neuroleptic drugs

- They are incompletely absorbed from intestine ;they undergo significant first pass metabolism in liver ;they are highly binding to plasma protein with large volume of distribution ;they are lipid soluble compound can reach to brain .
- Dopamine hypothesis of schizophrenia :-
- It proposes that this disorder is caused by relative excess of functional activity of the neurotransmitter dopamine in specific neuronal tracts in the brain ; particularly in the mesolimbic system .

Mechanism of action :-

- **1) Dopamine receptors –blocking activity in the brain .**
- All the neuroleptic drugs block dopamine receptors in the brain and the periphery ;they are five different dopamine receptors consisting 2 families D1-like receptors include D1and D5
- D2-like receptors include D2;D3and D4 .
- The clinical efficacy of neuroleptic drugs is correlates closely with their ability to block D2 receptors in the mesolimbic system of the brain .
- **2) Serotonin receptor –blocking activity in the brain .**
The newer drugs Clozapine ,Olanzapine and Risperidone appear to act through inhibition of serotonin receptors (5-HT) .

The pharmacological action of neuroleptic drugs

- **1) Anti psychotic actions :-**
- All the neuroleptic drugs reduce the hallucination and delusion associated with schizophrenia by blocking dopamine receptors in the mesolimbic system of the brain .
- **2) Extapyramidal effects :-**
- these effects occur with chronic treatment with neuroleptic drugs due to block dopamine receptors in the nigrostriatal pathway lead to Parkinson like symptoms (dystonia ;akathisia and tardive dyskinesia) .
- **3) Antiemetic effect :-**
- most of the neuroleptic drugs have antiemetic effect that are mediated by blocking D2 –dopaminergic receptors of the chemoreceptor trigger zone of the medulla (CTZ) ; except Thioridazine is not effective antiemetic .

The pharmacological action of neuroleptic drugs

4) Antimuscarinic effect :-

some of the neuroleptic particularly Thioridazine ; Chlorproazine ; Clozapine and Olanzapine ; causes antimuscarinic effects include blurred vision ; confusion ; dry mouth ; constipation ;etc .

5) other effects :-

- a-** Blocking of alpha adrenergic receptors causes orthostatic hypotension
- b –** Blocking D2 receptor in pituitary gland lead to an increase in the prolactin release .
- c-** Blocking of histaminic receptors lead to sedation like with Chlorpromazine and Clozapine .

Therapeutic uses of neuroleptic drugs :-

- 1:- Schizophrenia the primary indication of neuroleptic drugs**
- 2:- manic episode in patients with bipolar effective disorder ;used in combined with antidepressant drugs or Lithium .**
- 3:- Neuroleptic used in combined with narcotic analgesia for treatment of chronic pain and anxiety in cancer cases .**

- 4:- Chlorpromazine is used to treat •
intractable hiccup . •**
- 5:- Prochlorperazine is useful in the
treatment of disease or drugs induced
nausea ; but not due motion sickness .**
- 6:- Senile dementia of Alzheimer disease .**
- 7:- H1-receptor blocking action by
Phenothiazine are used for the relief purities
(itching) .**

Contraindications and cautions:-

- **1:-** Acute agitation due to alcohol or other drugs withdrawal may be aggravated by the neuroleptic (it is treated by simple sedation like diazepam) .
- **2:-** In epileptic patients; because the neuroleptic drugs can lower seizer threshold .
- **3:-** Development agranulocytosis from using of neuroleptic drugs .

Side effects :-

- **1) Extrapyramidal side effects :-**
it is time dependent with dystonia occur within a few days of treatment followed by akathisia ; Parkinson symptoms of bradykinesia ; rigidity and tremor occur later on ; tardive dyskinesia occur after months or year of treatment .
- **2) Antimuscarinic side effects :-** Thioridazine is show strong antimuscarinic activity with few extra pyramidal disturbances ; in contrast with Haloperidol and Fluphenazine which have low Anticholinergic activity and produce extra pyramidal effects .
- **3) Neuroleptic malignant syndrome :-** fatal reaction to neuroleptic drugs characterized by muscle rigidity ; fever ; unstable blood pressure .

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4) Neuroleptic drugs depress the hypothalamus

causing amenorrhea and galactorrhea in female ;decrease libido with gynecomastia in male .

5) block alpha receptors resulting in lowered blood pressure and orthostatic hypotension .

6) Significant weight gain commonly occur with a typical neuroleptic drugs (Clozapine,Olanzapine ; and Risperidone .)