

## Antipsychotic drugs

Also called Narcoleptic drugs or major tranquilizers .

### Classification:

- Typical
- Atypical or
- First generation as chlorpromazine.  
Second generation as olanzapin .  
Third generation as aripiprazole.

#### i. Typical antipsychotics (1<sup>st</sup> generation ) :

##### 1. Phenothiazine group :

They are the major & oldest group of antipsychotics ,has three types :

a. **Aliphatic** : as **chlorpromazine (largactil)** doses are : **25 ,50,100 mg**

They antipsychotic effect is reached with the dose of(100 mg-1g )

b. **Piprazine** : as **Trifluoperazine (stelazine)** doses are : **1,2,5mg**  
They antipsychotic effect is reached with the dose of (5-30mg). other drug is fluphenazine .

c. **Piperidine** : as **Thioridazine (Mellaril )**,the antipsychotic dose is reached within (100-80)mg .

2. **Butryophenone** : as **Haloperidol**, the effective doses is (5-60) mg

3. **Dibenzoxapine** : as **loxapine** .

4. **Thioxanthine** : as **flupenthixol**.

5. **Diphenylbutyl piperidine** : as **pimozide** , the dose is (4-12) mg.

6. **Benzamide** : as **sulupride** .

#### ii. Atypical drugs (second generation ) :

1.**olanzapin** : 10-20mg /day (olan , zeprax -5or 10mg ) .

2. **Risperidone** : 2-12 mg /day (Risperdal )-1,2or 4mg ) .

3. **clozapine** : 25-800 mg/day (leponex -25,50or 100mg ) .

4. **quetiapine** : 50-750 mg/day (seroquel 100 or 200mg).

iii. **Third generation antipsychotic** : aripiprazole

**Long acting (Depot injections ):**

1. **Fluphenazine deaconate** (Modecate )25 mg deep IM injection every 2-4 weeks .
2. **Haloperidol decanted** (Haldol ) 50 or 100 mg deep IM injection every 2-4weeks .
3. **Flupenthixol deaconate** (flunaxol, Depexol )20,40 or 100 mg deep IM injection every 2-4weeks .
4. **Risperdal consta** 25,37 mg deep IM injection every 2-4 weeks .- Atypical antipsychotic .
5. **Aripiprazole** (Aripiprex ) 300 or 400 mg deep IM INJECTION EVERY 2-4WEEKS .-Third generation antipsychotic .

**Q /how would choose antipsychotic drugs for a psychotic patient ?**

**A /** we have to groups .

Chlorpromazine Olanzapine Thioridazine	Haloperidol Moderate Risperidone Trifluoperazine
<ol style="list-style-type: none"> <li>1. More sedation .</li> <li>2. Less extra pyramidal symptoms .</li> <li>3. More ant cholinergic Sid effects .</li> <li>4. More epilepsy .</li> <li>5. More hypertensive</li> </ol>	<ol style="list-style-type: none"> <li>1. Less sedation .</li> <li>2. More extra pyramidal symptoms.</li> <li>3. Less ant cholinergic Sid effects –preferred in elderly .</li> <li>4. Less epilepsy – pereferrred with epilepsy .</li> <li>5. Less hypotensive .</li> </ol>

Q / How to describe Modecate ?

A / It is the brand name of the fluphenazine decanoate ,It is antipsychotic drug belong to the piprazine group which is a type of phenothiazine .

**Side effects of Antipsychotics:**

**1. Central nervous system** : (Extra pyramidal symptoms )

**A –Acute dystonia:**

Sudden contractions of muscles especially in the eyes  
**(oculogyric crises )**neck (torticollis)& protrusion of the tongue .

It occurs after hours of few days from taking the drug.

Treated by

- Anticholinergics (procyclidine I.V) .
- Antihistamine (Diphenhydramine ) .
- Valium
- Discontinue the drug &change it to another.

For prophylaxis give :

- Oral procyclidine
- Benzhexol HCl .

### **B –Akathisia :**

Unpleasant motor restlessness after 1-2 weeks .

Treated by :- Stop the drug &change it to another.

- Beta blockers (propranolol
- Anti-cholinergic are not useful .

### **C - pseudo- parkinsonism :-**

- Tremor , Rigidity &Hypokinesia (involves shuffling gait, loss of blinking ,loss of swinging of hand ,mask face &micrographia ) .

### **D – tardive dyskinesia :**

- Buccolingual masticatory movement &can manifest in the limbs .
- Occur in chronic schizophrenia ,female ,obese & above 50 years old .
- There is a controversy whether this symptom is a complication of schizophrenia itself or the antipsychotics, because some schizophrenic patients didn't take the drug & still developed this symptom, but 10% --20%of patients on antipsychotics develops this complication .
- It is not an early sign & usually develops after 5 years from taking the drug, it never occur before six months duration of treatment .
- Sulupride is the most antipsychotic that develops it & the second most common is the Malarial.
- Treatment :

There must be a balance between psychotic symptoms & side effect and this is achieved by adjusting the dose .

The tardive dyskinesia doesn't mean to stop the antipsychotic but can change to another drug with less effect on aggravating tardive dyskinesia .

We can use Tegretol ,Valium & vitamin E .

### **E – neuroleptic malignant syndrome :**

It is an allergy to the drug, catatonic like stage , it is due to dopamine depletion from dopaminergic receptors . it is not dose related .

#### **The main symptoms are :**

1. Fever .
2. Rigidity .
3. Disturbed level of consciousness.
4. Autonomic disturbance .

#### **The causative drugs :**

1. 50%haloperidol .
2. 25% modicate
3. 25% other drugs .

#### **Associated diseases :**

- 1.50% in schizophrenia .
2. 25% in mood disorders .

#### **The important investigations that must be done :**

1. Increased CPK .
2. Increased ESR .
3. Leukocytosis .
4. Impaired liver function test .

#### **Treatment :**

Resuscitation (IV fluids ) &prevent Renal failure .

Dantrolene (muscle relaxant ) IV2-3mg/kg –side effect hepatotoxicity .

Bromocriptine (Dopamine agonist ) 2.5 -10 mg /day &max dose is 60 mg.

Sinemet (carbidopa & levodopa ) .

Amantadine ( anti-viral)

ECT is the last choice of treatment for this

F- Epilepsy

Antipsychotic don not cause epilepsy but they reduce the threshold of epilepsy .

2- Cardiovascular system:

Hypotention, ischemia ,arrhymias.

ECG changes :

- Tachycardia.
- Low voltage.
- Wide QRS .
- Prolong PR interval .
- Flat P wave.
- Notching of Q wave .

3- Hematological side effect:

Clozapine causes agranulocytosis ( Lukopenia) so there must be a blood test for WBC every 1 week for the first 3 months .

& then every 2 weeks for the second 3 months .

& then every month for the next 6 months.

Antipsychotic mainly clozapine , olanzapine causes hypercholesterolemia & hyperinsulinemia increase weight.

4- Eye:

Thioridazine causes retinitis pigmentosa , blurred vision.

5- Skin:

Urticarial , allergy, edema mainly by chlorpromazine & olanzapine.

6- Endocrine:

Hyperprolactinemia leading to reduced LH FSH leading to :

- Decreased sexual desire.
- Decreased pontecy.
- Amenorrhea or dysmenorrheal.
- Erectile dysfunction .
- Infertility.

7- Anticholinergic side effects:

- Pereipheral: urin retention, constipation . blurred vision & dry mouth .

- Central:Delirium.
- More in chlorpromazine.
- 8- Gastrointestinal side effect :  
Nausea, vomiting, diarrhea, constipation, obstructive jaundice (orthostatic) & increased level of uric acid. Jaundice by chlorpromazine while uric acid increased level is by Risperidone.
- Notes:
  - Food & antacids decrease the absorption of haloperidol, half –life is 10hours & the highest peak of effect is reached after:
    - 2-4 hours with oral drugs
    - 30-60 minutes with IM
    - 15-30 minutes with IV
  - Excreted mainly through portal system & to a lower extent through kidney .
- **Non –psychotic benefits of antipsychotics :**
  - i –increase appetite ,can be used for anorexia nervosa
  - ii –anxiolytics.
  - iii- used for neurobehavioral disorders which are marked by multiple motor tics with one or more vocal tic as in Gilles de la Tourette syndrome , haloperidol is used in low doses .
  - iv –Huntington chorea .
  - v –Anti pruritic agent (for severe pruritus ) .
  - vi –for nausea & vomiting .
  - vii –intractable hiccups.