

ANTIPSYCHOTICS

MBChB Year 4, UoN

Dr Judy Kamau

INDICATIONS

- Acute psychotic episodes in schizophrenia and schizoaffective disorder
- Maintenance treatment in schizophrenia and schizoaffective disorders
- Mania
- Depression with psychotic symptoms
- Delusional disorders
- Substance induced psychotic disorders

INDICATIONS

- Severe agitation and violent behaviour
- Tourette syndrome
- Childhood schizophrenia
- Other disorders depending on presentation:
 - Mental disorders caused by a medical conditions
 - Delirium and dementia
 - Autism spectrum disorders

ANTIPSYCHOTICS

- Introduced in the 1950s
- Two groups:
 - Dopamine receptor antagonists (First generation antipsychotic/ atypical antipsychotics)
 - Serotonin-dopamine antagonists (second generation/atypical antipsychotics)

First generation antipsychotics

Groups include:

- Phenothiazines
- Butyrophenones
- Thiothanzines
- Dibenzoxapines
- Dihydroindoles
- Diphenyl-butylpiperidines

First generation antipsychotics

- All associated with extrapyramidal side effects at their clinically effective doses

Second generation antipsychotics

- Some can be used as monotherapy for bipolar mood disorder
- Include:
 - Risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone, lurasidone, clozapine
- Mechanism of action:
- Higher ratio of serotonin to dopamine blockade than the typical antipsychotics

Second generation antipsychotics

- Are more specific to the mesolimbic than the striatal dopamine system
- Lower risk of extrapyramidal side effects
- Some can be used as adjunct treatment for treatment resistant depression; PTSD and Anxiety

Factors influencing the pharmacokinetics of antipsychotics

- Age: elderly patients may demonstrate reduced clearance rates
- Medical conditions: hepatic disease can reduce clearance
- Enzyme inducers: carbamazepine, phenytoin, ethambutol, barbiturates
- Clearance inhibitors: SSRIs, TCAs, cimetidine, beta blockers, erythromycin, ciprofloxacin, ketoconazole

long acting depot preparations

- Useful in overcoming problems with compliance
- Typically given once every one to four weeks
- Include:
 - Haloperidol decanoate
 - Fluphenazine decanoate
 - Flupenthixol decanoate
 - Zuclopenthixol decanoate
 - Paliperidone palmitate
 - Risperidone microspheres
 - Olanzapine pamoate

ADVERSE EFFECTS

- Extrapiramidal side effects
 - Dystonia: uncontrolled muscle spasm e.g. oculogyric crises, torticollis
 - Pseudo-parkinsonism: tremor, rigidity, bradykinesia, bradyphrenia
 - Akathisia: subjective unpleasant state of inner restlessness
 - Tardive dyskinesia: lip smacking, tongue protrusion, choreiform hand movements

ADVERSE EFFECTS

- Neuroleptic malignant syndrome
 - Hyperthermia, muscular rigidity, dystonia, akinesia, mutism, confusion, agitation, raised blood pressure and pulse. Raised wbc, CPK, liver enzymes and plasma myoglobin
 - Higher mortality with depot preparations
- Lowered seizure threshold
- Sedation
- Central anticholinergic effects
 - Agitation, disorientation, hallucinations, seizures, high fever, dilated pupils

ADVERSE EFFECTS

- Cardiac effects (prolonged QT intervals; torsade pointes) : phenothiazines, haloperidol, sertindole, quetiapine
- Sedation: chlorpromazine
- Orthostatic hypotension through adrenergic blockade: chlorpromazine, thioridazine,
- Hyperprolactinaemia
- Weight gain: clozapine, olanzapine, chlorpromazine, quetiapine, risperidone

ADVERSE EFFECTS

- Diabetes and impaired glucose tolerance: phenothiazines, clozapine, olanzapine, risperidone, quetiapine
- Sexual dysfunction: through dopamine blockade; increase prolactin levels or anticholinergic effects

Questions?