

Adverse Effects of Antipsychotic Drugs - A Review

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ABSTRACT

Antipsychotic drugs which are also known as Neuroleptics are group of psychotropic drugs or psychopharmacological agents¹ that are primarily used to manage psychoses including delusions, hallucinations, paranoia, or disordered thought. Besides their antipsychotic action, they had been reported to have some adverse effects which can be seen in Cardiovascular system, Metabolic system, Skeletal and Muscular system, Cognitive and Emotional side effects, and Sexual dysfunction. These adverse effects were mainly observed when they used for longer duration or taken in larger doses or with sudden change in their dose.

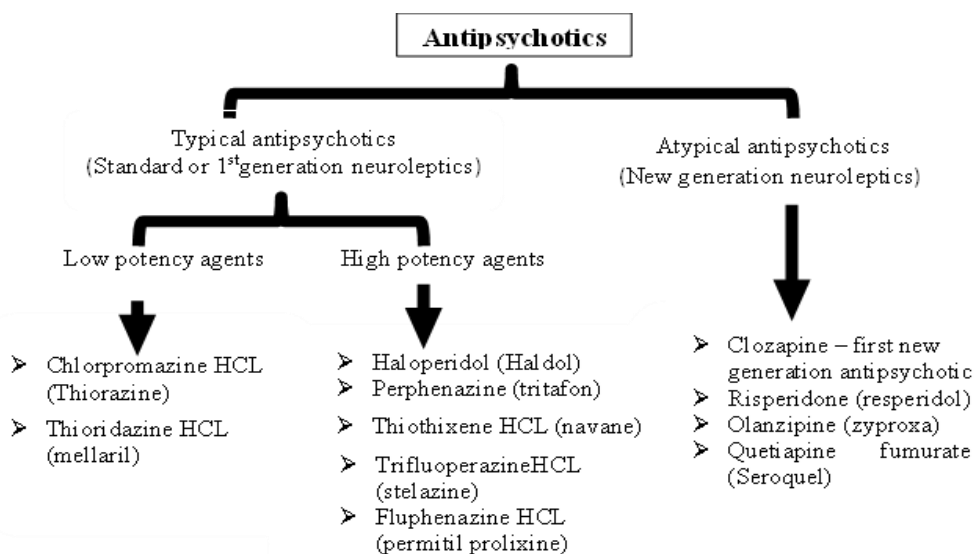
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INTRODUCTION

Antipsychotic drugs are psychotropic drugs which are used primarily for the treatment of number of mental diseases. Besides their antipsychotic action, there are many side effects observed. Now-a-days there is increased concern on the adverse effects of antipsychotic drugs.

Antipsychotic drugs can be classified into two categories.

1. Typical or first-generation antipsychotic drugs.
2. Atypical or second-generation antipsychotic drugs.



ADVERSE EFFECTS OF ANTIPSYCHOTIC DRUGS:

Antipsychotic drugs are safe when used in single or infrequent doses. Adverse effects range from minimal symptoms like nausea and headache to severe symptoms like tardive dyskinesia which may increase the life mortality rate.

CENTRAL NERVOUS SYSTEM: EXTRAPYRAMIDAL SIDE EFFECTS

Extrapyramidal side effects include acute dystonia, acute akathisia, parkinsonism, chronic EPS, tardive EPS (tardive dyskinesia, tardive akathisia).

ACUTE DYSTONIA: Dystonia occurs more often in younger, male individuals. Incidence ranges from 10.1% to 51.2%. Treatment includes anti-parkinsonian drugs.

ACUTE AKATHISIA: "Means inability to sit". Antipsychotic drugs induced akathisia worsens the psychotic symptoms. Incidence ranges from 20 % to 75%.

PARKINSONISM: Perioral tremor "rabbits' syndrome" is an uncommon type of extrapyramidal side effect that often appears after a few years of medication. It responds to anti-cholinergic drugs.

MALIGNANT NEUROLEPTIC SYNDROME: This dangerous drug withdrawal syndrome may last 5-10 days. Treatment includes IV dantrolene and bromocriptine.

TARDIVE DYSKINESIA (TD): TD occurs late in therapy, sometimes even after withdrawal of anti-psychotic drugs. TD is more common in elderly women and its incidence ranges from 10 to 20%. It is seen as a common problem in individuals receiving long term anti-psychotic drug treatment.

NEURO PSYCHIATRIC EFFECTS COGNITION AND BEHAVIOURAL EFFECTS:

A report by de Alarcon and Carney in 1969 highlighted that anti-psychotic drug causes depression in patients receiving flupentixol and decanoate, which may sometime lead to suicide. By 1980 more than 30 published

papers had drawn attention to the relationship between anti-psychotic drugs and depression. Neuroleptics when used in higher doses are associated with violent, disturbed behavior and a deterioration in mental state which in came to know by a report, by Barner and Bridge in 1980; Bardessarimet in 1988; Van Putten in 1990.

EPILEPTOGENIC EFFECTS

Anti -psychiatric drugs when given in higher dose or when indicated with other epileptic drugs or sudden change in their dose precipitate convulsive seizures. The main epileptogenic effect of anti-psychiatric drugs is due to their action on dopaminergic and cholinergic transmission. Other neuropsychiatric effects are cerebellar signs like ataxia, nystagmus, and dysarthria.

AUTONOMIC EFFECTS

Autonomic effects of anti-psychiatric drugs are due to cholinergic and alpha1 adrenergic blocking action.

SEDATION: Antipsychotic drugs have sedation effect with feeling of slowness, lethargy, and weakness. These may be due to their antihistaminergic action and alpha1 adrenergic blockage.

CARDIOVASCULAR SYSTEM EFFECTS:

Cardiovascular effects are due to anti alpha adrenergic blockade action. Side effects can be seen mainly by thioridazine and low potency phenothiazines. Common cardiovascular side effects include inhibition of ejaculation, palpitations, and postural hypotension. Hypotension is caused by depression of medullary vasopressor reflexes leading to decreased peripheral vascular resistance, and by alpha adrenoceptor blockage a report by alexander and Nino in 1969. ECG alterations like depressed ST segment, flattened T-waves, U-waves, and prolonged QT interval can be seen in patients particularly with low potency agents like thioridazine. Q-T prolongation and cardiac arrhythmias can be seen when

thioridazine, pimozide and ziprasidone are given in overdoses. Antipsychotic drug therapy is associated with increased cardiac associated mortality rate.

ANTICHOLINERGIC EFFECTS:

These effects can be due to peripheral cholinergic receptor blockage by neuroleptics and includes dizziness, light headedness. Most serious anticholinergic effects are precipitation of angle closure glaucoma, urinary retention, and paralytic ileus. Constipation due to reduced gastrointestinal motility.

DIABETES MELLITUS

Patients with schizophrenia are known to have diabetes more often than the general population. Both typical and atypical antipsychotics cause diabetes and diabetic ketoacidosis. An Italian study shown that the prevalence of diabetes in 95 schizophrenia patients to be 15.8% compared with a 3% prevalence in general Italian population. Insulin resistance may be an important factor in causing diabetes.

WEIGHT GAIN:

The patients taking antipsychotic medication have a higher rate of overweight and obesity than the general population. Many studies have shown that antipsychotic drugs have effect on weight gain. Weight gain may be due to increased appetite and increased leptin.

SEXUAL SIDE EFFECTS:

Sexual dysfunction is a common effect in individuals who are under antipsychotic medication for longer periods. When antipsychotic drugs are taken, they cause hyperprolactinemia (HPRL) by blocking D2 receptors which removes inhibitory effect of dopamine on prolactin secretion which results in increased secretion of prolactin that ultimately leads to HYPOGONADISM. Effects include Infertility, Gynecomastia or Galactorrhea. According to a study using PRSexDQ-SALSEX (a validated questionnaire to measure sexual dysfunction

in psychotic population) have shown that 50% men and 37% women have some degree of sexual dysfunction affecting arousal, libido, and orgasm. 50-70% of psychotropic-related sexual dysfunction is due to serotonergic compounds and hyperprolactinemic antipsychotics.

HEMATOLOGICAL EFFECTS:

Agranulocytosis is a major hematological side effect particularly with clozapine which leads to a variety of infections including upper respiratory tract.

OPHTHALMOLOGICAL EFFECTS: 25% of individuals who were taking chlorpromazine have chronic lenticular changes. Pigmentary retinopathy on the contrary, initially cause complaints of blurred vision, a brownish discoloration of vision or decreased nighttime visual acuity.

HYPERSENSITIVITY REACTIONS:

Cholestatic jaundice with portal infiltration occurs between 2-4 weeks of therapy and is more common with low potency phenothiazines.

Skin rashes, urticaria, contact dermatitis and photosensitivity. Agranulocytosis and myocarditis.

CONCLUSION

Antipsychotic medications are psychotropic substances with a beneficial therapeutic impact on psychoses. Antipsychotic drugs when indicated in infrequent doses are safer and improves the quality of the individual. But when they are indicated in overdoses or sudden change in their dose or sudden withdrawal from the medication leads to severe complications and adverse effects. Most side effects are mild and disappear with continued treatment. Others can be prevented or minimized by more thoughtful prescribing such as using the minimum dose required, avoiding unnecessary drug combinations and careful monitoring. Complications range from minimal symptoms to severe complications like tardive dyskinesia which is reported to

increase the mortality rate. Typical antipsychotic drugs are known to cause more extrapyramidal effects than atypical antipsychotic drugs. More effects are observed on weight gain, diabetes, sexual dysfunction, cardiovascular system, extrapyramidal system. Adverse effects depend on the dose and duration of the medication used.

Declaration by Authors

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