Antipsychotics

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Uses/Risk

- In a given year, 26.2% of Americans 18 y or older have some form of mental disorder.
- Schizophrenia has a community prevalence rate of 1%.
- Psychiatric disorders such as schizophrenia, bipolar disorder, major depression, and disorders with psychotic features are treated with this class of drugs.

Perioperative Risks

- Cardiovascular instability, including hypotension and arrhythmia
- Cardiomyopathy/myocarditis
- Extrapyramidal effects
- Drug-drug interaction
- Postop psychosis

Worry About

- Antipsychotics act as CNS depressants; thus anesthetic drugs need to be titrated carefully.
- Reports of hypotension and cardiopulmonary arrest with concomitant propranolol and haloperidol usage.
- Antipsychotics have selectivity for CYP2D6, which is metabolized by many beta blockers; thus coadministration may result in drug interactions.
- Clozapine, risperidone, chlorpromazine, haloperidol, olanzapine, thioridazine, and quetiapine linked with cardiomyopathy and myocarditis.
- Cardiovascular side effects: Hypotension, tachycardia, QT prolongation, and rarely VFIB.
- Extrapyramidal side effects: Dystonic reactions, tardive dyskinesia, and, importantly, laryngospasm, which is treated with anticholinergics.
- Most serious extrapyramidal reaction is neuroleptic malignant syndrome, which manifests as hyperthermia, muscle rigidity, autonomic instability, encephalopathy, and tachydysrhythmias.
  - Treat with dantrolene or bromocriptine.
  - Related to recent increased dose in antipsychotic or start of new medication.
- Hypothalamic dysfunction causing temperature dysregulation.
- Alters the endocrine system, including elevating prolactin and ADH and disrupting glucose regulation.

Overview/Pharmacology

- Schizophrenia is defined by disturbances in emotional, behavioral, and cognitive function.
- All antipsychotics block dopamine D2 receptors to some extent.
- Two classes of antipsychotics: Typical and atypical.
- Typical antipsychotics have predominantly antidopaminergic properties.
- Atypical antipsychotics have significantly greater 5-HT2A receptor than D2 receptor occupancy, as well as greater affinity for D1, D3, and D4 receptors than for D2 receptors.
- Atypical antipsychotics have less extrapyramidal adverse effects and little or no effect on prolactin levels.
- Atypical antipsychotics allow for fewer extrapyramidal side effects and have become the mainstays of treatment.
- Atypical antipsychotics appear to be more effective in treating negative symptoms of schizophrenia and treatment-resistant schizophrenia.
- Preop discontinuation of antipsychotics was common practice as it was thought to lower incidence of intraop hypotension; however, discontinuation causes periop psychosis.
- Recent studies have found that preop discontinuation did not significantly decrease the incidence of periop hypotension. Therefore the recommendation is to continue drug therapy throughout surgery.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension, tachycardia, QT interval prolongation, torsades de pointes, myocarditis, increased risk of MI	Palpitations, syncope	Heart sounds, BP, pulse	ECG, ECHO
ENDO	Amenorrhea, galactorrhea, abnormal temp regulation, increased prolactin, abnormal glucose Abnormal ADH and aldosterone	Cold intolerance		CMP, prolactin, LH, FSH, ADH, aldosterone
HEME	Agranulocytosis			CBC
GI	Paralytic ileus			Abdominal x-ray
NEURO	Psychosis Extrapyramidal side effects: 1. Tardive dyskinesia 2. Dystonic reactions 3. Akathisia 4. Parkinsonism		Choreoathetoid movements of head, limbs, trunk Slow sustained muscle contractions State of discomfort causing agitation and restlessness Tremor, bradykinesia, rigidity, postural instability	
GENERAL	Neuroleptic malignant syndrome	Increase of medication dosage or beginning new medication	Rigidity, autonomic instability, hyperthermia, arrhythmia	Increased WBC, Cr, and CK; myoglobinuria

Key References: Ellender R, Kaye AD, Kaye AM: Neuroleptic drugs. In Manchikanti L, Trescot A, Christo PJ, et al., editors: *Foundations of pain medicine and interventional pain management: A comprehensive review*, Paducah, KY, American Society of Interventional Pain Physicians, 2011, pp 553–558; Kaye AD, Liu H, Fox C, et al.: Psychiatric and behavioral disorders. In Fleisher LA, editor: *Anesthesia and uncommon diseases*, ed 6. Philadelphia, Elsevier, 2012, pp 444–461.

Perioperative Implications

Preoperative Preparation/Concerns

- History may be unreliable.
- Continue antipsychotic medications preop.
- Assess cardiac, hepatic enzymes, and WBC count.

Monitoring

- Routine
- Arrhythmia, hemodynamic changes
- Temperature

Airway

- Laryngospasm a possible side effect

Induction

- Hypotension after induction, particularly with chlorpromazine

Maintenance

- Drug-drug interactions, particularly with antihypertensive drugs.
- CV instability, arrhythmias.
- Thermoregulation; concern for hypothermia.
- Continue antipsychotics throughout surgery; total IV anesthesia with propofol, ketamine, and fentanyl can avoid many periop complications.

Extubation

- Usual criteria

Postoperative Period

- Postop confusion
- Postop ileus
- Decreased pain sensitivity

Anticipated Problems/Concerns

- Cardiovascular instability
- Cardiac arrhythmias
- Drug-drug interactions
- Hypothermia
- Neuroleptic malignant syndrome potential
- Drug side effects: Extrapyramidal, cardiac, and endocrine