

Perioperative Implications

Preoperative Concerns

- Obtain baseline ECG for all pts taking chronic phenothiazines to assess cardiac conduction and QT interval.
- Neuroleptic malignant syndrome may present in pts undergoing chronic treatment but may be precipitated by other antidopaminergic agents such as metoclopramide.

Induction/Maintenance

- Autonomic insufficiency from long-term use may contribute to profound intraop hypotension.

Adjuvants/Regional Anesthesia/Reversal

- Treat extrapyramidal side effects with diphenhydramine, benztropine, or benzodiazepines.
- Neuroleptic malignant syndrome is treated with bromocriptine, dantrolene, and aggressive hydration/monitoring.

Postoperative Concerns

- Clinically significant respiratory depression if given to pts <2 y old or those with pulm disease, especially if combined with opioids.
- Arrhythmias and prolonged QT.
- Increased risk of sedation and delirium, particularly in elderly pts.

Drug Interactions

- Increased risk of extrapyramidal symptoms if given with other antidopaminergic medications (typically metoclopramide).
- May increase concentration of other hepatically metabolized (CYP2D6) drugs (some beta-blockers and tricyclic antidepressants).

Anticipated Problems/Concerns

- Assess mental status, respiratory status, and CV function after administration, particularly in the early postop period.

Phenoxybenzamine

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Uses

- Incidence in USA: 3600 per y
- Rx for preop pheochromocytoma; occasionally for chronic Rx of pheochromocytoma and sympathetic hyperactivity states, carcinoid syndrome, BPH

Perioperative Risks

- Drug interactions: Sometimes requires very high doses of α -adrenergic agents to produce vasoconstriction.
- Vasodilation, orthostatic hypotension accentuated in hypovolemic pts.

Worry About

- Occasionally associated with confusional states.
- Associated with fatigue and prolonged sedation.

- Drop attacks on preop standing to urinate.
- Cost, which has increased since 1979 for this not-on-patent drug from \$0.10 a tablet to \$9.75 a tablet at the wholesale level (a 100-fold increase, as now there is apparently only one manufacturer).

Overview/Pharmacology

- α_1 blocker (relatively selective, α_1 being greater than α_2) by covalent (irreversible) binding to a receptor; compensatory response calls for production or availability of more (spare) receptors.
- Effect develops slowly; peak effect not attained for 2 h after IV or 4 h after oral administration.
- Absorption from GI tract incomplete.
- Renal excretion of 50% in 12 h, 80% in 24 h.

- Half-life of effect over 24 h; effects accumulate for at least 4–6 d.
- High lipid solubility at body pH.

Drug Class/Mechanism of Action

- α_1 blocker (a haloalkylamine).
- Chronically taken:
 - Decreases α_1 effects in pheochromocytoma.
 - High doses inhibit release of H₂ serotonin (occasionally used in carcinoid syndrome).
 - Ameliorates or prevents Raynaud phenomenon.
- Vasodilator for chronic treatment of CHF (occasionally), but worry about toxicity of promoting cancer when taken chronically.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vasodilation of mucous membranes of nasopharynx; miosis	Nasal congestion	Mouth breathing	
CV	Antihypertensive agent Postural hypotension, reflex tachycardia, increased CO	Orthostatic dizziness	Orthostatic vital signs	Hct ECG
GI	Increased intestinal motility, causes diarrhea	Orthostatic hypotension		
ENDO	Stimulates insulin release Increased presynaptic norepinephrine release (blockade of presynaptic α_2 receptors inhibiting release of norepinephrine)			
GU	Increased blood volume, Na ⁺ retention inhibits contraction of vas deferens	Impairs ejaculation		BUN, Cr, lytes
CNS	Depression, sedation, fatigue, extrapyramidal symptoms rarely, N/V, motor excitability rare		CNS exam	

Key References: Kinney MA, Narr BJ, Warner MA: Perioperative management of pheochromocytoma, *J Cardiothorac Vasc Anesth* 16(3):359–369, 2002; Wittles RM, Kaplan EL, Roizen MF: Safe and cost-effective preoperative preparation of patients with pheochromocytoma, *Anesth Analg* 91(2):302–304, 2000.

Perioperative Implications/Possible Drug Interactions

Preoperative Period

- Make sure pt is not hypovolemic.
- Interaction with methyldopa (Aldomet): Urinary incontinence
- Preop treatment: Major goal is to avoid pheochromocytoma crisis; preop and intraop goals are management of extra-adrenal surgery, same as for adrenal surgery. If is not on α -blocker before surgery, try to delay until appropriate degree of α -blockade is achieved. Increase dose of phenoxybenzamine by 10 mg bid to qid every third day until

appropriately blocked. Judge appropriate level of blockade by:

- No BP readings higher than 165/90 mm Hg (even during psychological stress) for 48 h before surgery.
- Orthostatic hypotension present, but BP on standing should not be lower than 80/45 mm Hg.
- ECG free of ST-T changes due to cardiomyopathy.
- Absence of other signs of catecholamine excess and presence of blockade effects such as nasal stuffiness.

Induction/Maintenance

- Can produce increased sedation; lower anesthetic requirements by one-third (not studied but anecdotally reported).

Muscle Relaxants

- No interactions known

Regional Anesthesia/Reversal

- No interactions known

Anticipated Problems/Concerns

- May need very high doses of vasopressors to increase vascular resistance, BP in pt taking large doses.
- CNS dysfunction by itself.