INTRODUCTION

Background: Calcium channel blockers (CCBs) were initially introduced for use in the US in 1981. Sustained-release formulations were available 10 years later. Indications for use of these drugs are angina, hypertension, arrhythmias, and migraine prophylaxis.

Calcium channel blocker overdose is rapidly emerging as the most lethal prescription drug ingestion. Overdose by short-acting agents is characterized by rapid progression to cardiac arrest. Overdose by extended-relief formulations result in delayed onset of arrhythmias, shock, sudden cardiac collapse, and bowel ischemia.

Pathophysiology: Calcium channel blockers have the following 4 cardiovascular effects:

1. Peripheral vasodilatation
2. Negative chronotropy (decreased heart rate)
3. Negative inotropy (decreased cardiac contractility)
4. Negative dromotropy (decreased cardiac conduction)

Other physiologic responses to CCB overdose include suppression of insulin release from the pancreas and decreased free fatty acid utilization by the myocardium. These factors produce hyperglycemia, lactic acidosis, and depressed cardiac contractility.

Frequency:

- In the US: In 1996, the American Association of Poison Control Centers (AAPCC) reported 8555 exposures to calcium channel blockers resulting in 58 fatalities and 225 major outcomes.
In 1997, the AAPCC reported 9077 exposures to calcium channel blockers, resulting in 44 fatalities and 232 major outcomes.

In 1998, the AAPCC reported 8666 exposures to calcium channel blockers, resulting in 61 fatalities and 277 major outcomes.

In 1999, the AAPCC reported 8844 exposures to calcium channel blockers, resulting in 61 fatalities and 243 major outcomes.

Mortality/Morbidity: Premature discharge of patients with calcium channel blocker overdose, especially extended-release formulations, may result in severe morbidity or mortality.

- In 1996, the AAPCC reported 58 fatalities and 225 major outcomes.
- In 1997, the AAPCC reported 44 fatalities and 232 major outcomes.
- In 1998, the AAPCC reported 61 fatalities and 277 major outcomes.
- In 1999, the AAPCC reported 61 fatalities and 243 major outcomes.

Age:

- In 1996, with 8555 total exposures reported, 2299 exposures occurred in children younger than 6 years (27% of reported cases).
- In 1997, with 9077 total exposures reported, 2560 exposures occurred in children younger than 6 years (28% of reported cases).
- In 1998, with 8666 total exposures reported, 2197 exposures occurred in children younger than 6 years (25% of reported cases).
- In 1999, with 8844 total exposures reported, 2304 exposures occurred in children younger than 6 years (26% of reported cases).

History: Generally, patients with calcium channel blocker overdose present with empty pill bottles or a witnessed ingestion. When a history is unavailable, patients present with a cardiodepressive toxidrome and decreased heart rate and blood pressure.

- Children can become symptomatic with as little as one tablet. In young children, calcium channel blockers have the potential to be fatal with single tablet ingestions. Delayed onset of hypotension has been reported in children with extended-release tablet ingestion. All children with suspected calcium channel blocker ingestions of any amount should be evaluated in a health care facility and monitored in an ICU setting for signs of delayed toxicity.
- Carefully question the caretakers of children who present with depressed blood pressure or heart rate to see if anyone in the household is taking blood pressure or heart medicine.
- In adults, deliberate overdoses are more likely to involve multiple medications, and alcohol is frequently a co-ingestant.
- Establishing the complete list of medications that the patient may have had access to is important.

Physical: Focus the physical examination on mental status and cardiovascular assessment.

- Hypotension
- Bradycardia, with variable degrees of heart block
- Altered mental status or seizures secondary to hypotension
- Occasional cases of bowel infarction caused by mesenteric underperfusion

Causes:

- Verapamil (eg, Calan, Isoptin), a phenylalkylamine, produces hypotension and heart block.
  - Several extended-release formulations are available (eg, Isoptin SR, Calan SR, Verelan, Covera-HS).
  - All extended-release formulations require longer observation periods to ensure that no delayed onset of toxicity occurs.
- Nifedipine (eg, Procardia, Procardia XL, Adalat, Adalat CC) is representative of the dihydropyridine class, which produces profound hypotension with less heart block.
  - Overdoses with CCBs in this class may present with reflex tachycardia.
  - Other drugs in the dihydropyridine class of calcium channel blockers act similarly; they include nicardipine (eg,
Cardene, Carden SR), nimodipine (Nimotop), nitrendipine, isradipine (DynaCirc, DynaCirc SR), amlodipine (Norvasc), felodipine (Plendil), and nisoldipine (Sular).

- Amlodipine has a particularly long half-life of 45 hours.
- All dihydropyridines exert their greatest effect on vascular smooth muscle, producing vasodilatation.
- The sustained-release or controlled-release preparations also need prolonged observation for the same reasons prolonged observation is required for extended-release formulations.

- Diltiazem (Cardizem), the only CCB in the benzodiazepine class, produces significant antidromotropic effects.
  - Patients ingesting diltiazem typically present with heart block and lesser degrees of hypotension.
  - Delayed-release formulations include Cardizem CD, Cardizem SR, Dilacor XR, Tiamate, Teczem, and Tiazac. These require longer observation periods to insure no delayed onset of toxicity.

- Bepridil (Vascor), used for refractory angina, is a unique calcium channel blocker with some sodium channel blocking activity.
  - Bepridil has been shown to prolong the QTc interval through its potassium channel blocking effect; therefore, it may cause torsade de pointes.
  - About 1% of patients treated with this drug experienced ventricular arrhythmias.

- Mibefradil (Posicor), a new selective T-channel calcium channel blocker, was alleged to have less negative inotropy at therapeutic concentrations; however, it has been removed from the worldwide market after multiple adverse drug interactions were reported.
  - Mibefradil is proarrhythmic and may increase levels of tricyclic antidepressants and many other medications through competitive inhibition of cytochrome P450 C4A.
  - When patients are taking mibefradil, drugs that prolong the QTc interval (eg, terfenadine) should be used cautiously or not at all.
  - Soon after mibefradil's release, a box warning was added to the package insert; it warned that AV block and bradycardia has occurred with standard use, especially if the drug is taken in conjunction with beta-blockers or other calcium channel blockers.
  - On June 8, 1998, the drug was withdrawn from the US market because of adverse drug interactions with 26 other medications. A report by Mullins et al detailed 4 life-threatening cases of cardiogenic shock when mibefradil was used at recommended doses with calcium channel blockers and beta-blockers.

**DIFFERENTIALS**

- Lactic Acidosis
- Myocardial Infarction
- Plant Poisoning, Glycosides - Coumarin
- Shock, Cardiogenic
- Toxicity, Antidepressant
- Toxicity, Antidysrhythmic
- Toxicity, Beta-blocker
- Toxicity, Calcium Channel Blocker
- Toxicity, Clonidine
- Toxicity, Digitalis

**Other Problems to be Considered:**

The most likely differential diagnostic problems for a cardiodepressive toxic syndrome are as follows:

- Calcium channel blocker overdose
- Beta-blocker overdose
- Digitalis overdose
- Clonidine overdose
- Acute myocardial infarction with cardiogenic shock
Lab Studies:
- Hyperglycemia may occur as calcium channel blockade inhibits insulin release.
- Lactic acidosis may occur and an arterial blood gas (ABG) may suggest acidemia.
- Blood levels are generally not available with any reasonable turn around time. Treatment must be instituted based on symptoms. Blood levels are available to confirm elevated levels if the diagnosis is in doubt.

Imaging Studies:
- A chest x-ray may be helpful to determine heart size and presence or absence of congestive heart failure. In patients with CHF, aggressive fluid boluses to treat hypotension may exacerbate heart failure or cause acute pulmonary edema.
- If bowel obstruction or perforation is suspected, 3-dimensional abdominal x-rays are recommended.

Other Tests:
- Obtain a 12-lead electrocardiogram (ECG) for all cases and perform continuous cardiac monitoring until stable.

Procedures:
- Transcutaneous or transvenous pacing may be required if hemodynamically unstable heart block fails to respond to medical therapy.

Prehospital Care: Rapid transport before the patient deteriorates is crucial. Empiric use of glucagon (5-15 mg IV) may be warranted for patients with an unknown overdose presenting with bradycardia or hypotension. Consider using calcium only if a witness confirms a calcium channel blocker overdose; calcium may induce fatal arrhythmias in digoxin overdose, which can present with similar findings. Treat hypotension with fluid boluses. If profound hypotension fails to respond to fluid resuscitation, administer a dopamine or norepinephrine drip, if permitted by local protocol. If the patient deteriorates to cardiac arrest from a calcium channel blocker overdose, perform prolonged cardiopulmonary resuscitation (CPR) in the field because patients have survived neurologically intact after an hour of CPR.
- Establish ABCs, obtain IV access, provide oxygen, and monitor closely.
- Avoid ipecac syrup.
- Administer IV glucagon if hypotension is present. Administer fluid bolus of normal saline if no evidence of decompensated congestive heart failure exists.
- Atropine may be tried if hemodynamically significant bradycardia occurs; however, heart block is usually resistant to atropine in calcium channel blocker toxicity. Mid-dose dopamine (5-10 mcg/kg/min) may improve heart rate and contractility.
- Administer IV calcium chloride (up to 4 g) and/or glucagon (up to 15 mg) if hypotension persists.
- Consider dopamine or norepinephrine infusion if a long transport time is likely, as permitted by local prehospital care protocols.

Emergency Department Care: Aggressive cardiovascular support is necessary for managing the massive calcium channel blocker overdose. While calcium chloride in high doses (4-6 g) may overcome some of the adverse effects of CCBs, it rarely restores normal cardiovascular status. According to many case reports, glucagon and inamrinone (formerly amrinone) have been used with good results. However, vasopressors are frequently necessary for adequate resuscitation and should be started early if hypotension occurs (see Medication). Additional basic overdose management includes airway protection, gastric lavage, and activated charcoal.
- Gastric decontamination
  - Gastric lavage may be useful in early presentations (<1-2 h postingestion), especially in cases of extended- or delayed-release tablet ingestion.
  - Activated charcoal (50-100 g PO) should be administered after gastric lavage.
  - Completely asymptomatic patients may be treated with activated charcoal and close observation.
  - Whole bowel irrigation with percutaneous endoscopic gastrostomy (PEG) solution (eg, GoLYTELY, NuLytely, Colyte) may be useful in extended-release preparations. However, be sure that ileus, bowel obstruction, or bowel ischemia have not occurred; case reports of bowel ischemia and infarction have appeared with calcium channel blocker overdose.
- Medications
Administer glucagon (5-15 mg IV bolus) followed by an infusion after fluid resuscitation is performed for persistent hypotension.

- Calcium chloride (1-4 g IV, slowly) can be administered for hypotension or heart block.
- Vasopressor support to maintain blood pressure and cardiac output is critical. In the hypotensive patient, administer dopamine at medium-to-high doses early for cardiac contractility for heart rate support and norepinephrine for blood pressure support. Inamrinone may be of additional benefit in profound cardiac contractile failure (see Medication).

- In a series of case reports, high dose insulin infusion (0.1-1 U/kg/h) with dextrose infusion (usually D10W-D25W) to maintain normal serum glucose levels have been successful for stabilizing cardiac output.

- Anecdotal efficacy of cardiopulmonary bypass exists in cases of severe poisoning resistant to aggressive medical treatments, such as patients failing glucagon and norepinephrine infusions.

- A patient developing acute respiratory distress syndrome (ARDS) has been successfully treated with partial liquid ventilation.

Consultations:
- Consult an AAPCC certified regional poison control center or a medical toxicologist in all cases to assist in management because several options for treatment exist and each case is unique.

### MEDICATION

Aggressive cardiovascular support is necessary for management of massive calcium channel blocker overdose. While calcium may overcome some adverse effects of CCBs, it rarely restores normal cardiovascular status. According to many case reports, glucagon and inamrinone (formerly inamrinone) have been used with good results. However, vasopressors are frequently necessary for adequate resuscitation and should be started early if hypotension occurs. Recent case reports suggest that use of high dose insulin, with maintenance of euglycemia by dextrose infusion, may be efficacious.

**Drug Category: GI decontaminants** - Used to minimize systemic absorption of ingested calcium channel blockers.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Activated charcoal (Liqui-Char)- Most useful within 4 h of ingestion, repeated doses may be used, especially with ingestions of sustained-released agents.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>1 g/kg PO (first dose usually with cathartic), up to 50-100 g; may repeat dose q4h at 0.5 g/kg (alternate with cathartic, monitor for active bowel sounds)</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>1 g/kg PO (&lt;2 y: omit cathartic), up to 15-30 g; may repeat dose q4h at 0.5 g/kg (alternate with cathartic, monitor for active bowel sounds)</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; poisoning or overdose of mineral acids and alkalies; unprotected airway with absent gag reflex</td>
</tr>
<tr>
<td>Interactions</td>
<td>May inactivate ipecac syrup if used concomitantly; effectiveness of other medications decreases with coadministration; do not mix with sherbert, milk, or ice cream (decreases adsorptive properties)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Monitor for active bowel sounds before readministration to minimize risk of charcoal ileus; not very effective in poisonings of ethanol, methanol, and iron salts; induce emesis before administering; after emesis with ipecac syrup, patient may not tolerate activated charcoal for 1-2 h; can administer in early stages of gastric lavage; without sorbitol, gastric lavage returns are black</td>
</tr>
</tbody>
</table>
**Drug Category: Antidotes** - Used to reverse calcium channel blockade or counteract the effects of reduced intracellular calcium.

Some animal models and human case reports suggest a significant response in cardiac output with hyperinsulinemic therapy with concomitant maintenance of euglycemia with supplemental dextrose. No prospective human trials exist to verify this result.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Calcium chloride- Moderates nerve and muscle-performance by regulating action potential excitation threshold. Used to overcome calcium channel blockade.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>1000-4000 mg (1-4 g) slow IV push of 10% solution</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>20-25 mg/kg IV push (0.2 mL/kg of 10% solution, repeat if response occurs)</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Ventricular fibrillation not associated with hyperkalemia; digitalis toxicity; hypercalcemia; renal insufficiency; cardiac disease</td>
</tr>
<tr>
<td>Interactions</td>
<td>Coadministration with digoxin may cause arrhythmias; coadministration with thiazides may induce hypercalcemia; may antagonize effects of calcium channel blockers, atenolol, and sodium polystyrene sulfonate; precipitates with sodium bicarbonate and may be sclerosing to peripheral veins</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Administer slowly (not to exceed 0.5-1 mL/min) to avoid extravasation; hypercalcemia may occur in renal failure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Glucagon- Acts via cAMP to increase cardiac contractility and also may decrease heart block. One study suggests that glucagon has maximal effect in normocalcemic environment. Hypocalcemia and hypercalcemia decrease efficacy; therefore, consider IV glucagon before calcium. Mix in a Mini-Bag (50-100mL) of NS and infuse over several minutes. Do not use diluent (eg, propylene glycol) supplied with single use kits.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>5-15 mg IV</td>
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<tr>
<td>Pediatric Dose</td>
<td>150 mcg/kg IV over 1 min followed by 2-5 mg/h infusion</td>
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<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; pheochromocytoma</td>
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<tr>
<td>Interactions</td>
<td>May enhance effects of anticoagulants (although onset may be delayed); monitor prothrombin activity and for signs of bleeding in patients receiving anticoagulants; adjust dose accordingly; do not use diluent when administering high doses of glucagon</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>B - Usually safe but benefits must outweigh the risks.</td>
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</tbody>
</table>
### Precautions

Monitor blood glucose levels in hypoglycemic patients until asymptomatic; effective in treating hypoglycemia only if sufficient liver glycogen is present; because liver glycogen availability is necessary to treat hypoglycemic patients, has virtually no effects on patients with starvation, adrenal insufficiency, or chronic hypoglycemia; protect the airway or pretreat with antiemetics because vomiting frequently occurs.

### Drug Name

Inamrinone - formerly amrinone (Inocor)- Phosphodiesterase inhibitor that acts by inhibiting breakdown of cAMP, thus prolonging effect on the release of calcium into the cytosol. Increases cardiac contractility outside the alpha- and beta-adrenergic system through nonspecific stimulation of cAMP. Although milrinone and inamrinone are available, experience in treating CCB overdoses is limited to inamrinone. Use with severely depressed cardiac output.

### Adult Dose

0.75 mg/kg IV initial, followed by 5-10 mcg/kg/min maintenance infusion; additionally, 0.75 mg/kg may be administered 30 min after therapy begins; not to exceed 10 mg/kg/d

### Pediatric Dose

Not established

Suggested dosing: Administer as in adults; infants may require larger doses

### Contraindications

Documented hypersensitivity; uncorrected hypovolemia

### Interactions

Coadministration with diuretics may result in hypovolemia and decrease in filling pressure; cardiac glycosides have additive effects on inamrinone; admixing with furosemide or dextrose may cause precipitation

### Pregnancy

C - Safety for use during pregnancy has not been established.

### Precautions

Discontinue therapy if symptoms of liver toxicity develop; correct hypokalemic states before therapy; hypotension may occur during bolus

### Drug Name

Insulin (Novolin, Humulin)- CCBs may inhibit pancreatic insulin release and block free fatty acid uptake and utilization by the myocardium, which is needed for myocardial work and contractility. High dose insulin may change myocardial energy consumption from free fatty acids to carbohydrates. Administer dextrose through a central line as D25 or D50, with mean doses of 20 g/h reported with frequent (at least hourly) monitoring of serum glucose.

### Adult Dose

0.1-1 U/kg/h, with mean doses of 0.5 U/kg/h

### Pediatric Dose

Not established

### Contraindications

Documented hypersensitivity; hypoglycemia
Interactions

Medications that may decrease hypoglycemic effects include acetazolamide, AIDS antivirals, asparaginase, phenytoin, nicotine isoniazid, diltiazem, diuretics, corticosteroids, thiazide diuretics, thyroid estrogens, ethacrynic acid, calcitonin, oral contraceptives, diazoxide, dobutamine phenothiazines, cyclophosphamide, dextrothyroxine, lithium carbonate, epinephrine, morphine sulfate, and niacin; medications that may increase hypoglycemic effects include calcium, ACE inhibitors, alcohol, tetracyclines, beta blockers, lithium carbonate, anabolic steroids, pyridoxine, salicylates, MAOIs, mebendazole, sulfonamides, phenylbutazone, chloroquine, clofibrate, fenfluramine, guanethidine, octreotide, pentamidine, and sulfinpyrazone.

Pregnancy

B - Usually safe but benefits must outweigh the risks.

Precautions

Hyperthyroidism may increase renal clearance, and more may be required to treat hyperkalemia; hypothyroidism may delay turnover, and less may be required to treat hyperkalemia; monitor glucose carefully; dose adjustments of insulin may be necessary in patients with renal and hepatic dysfunction.

Drug Category: **Cardiovascular agents** - Vasopressors augment blood pressure by alpha stimulation induced vasoconstriction. Atropine rarely helps significant bradycardia or heart block; isoproterenol has an adverse cardiovascular hemodynamic profile greatly diminishing its potential for use in bradycardia. Use these agents only after considering the above factors.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Contraindications</th>
<th>Interactions</th>
<th>Pregnancy</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine (Levophed)</td>
<td>2 mcg/min IV; titrate to effect</td>
<td>0.1 mcg/kg/min IV; titrate to effect</td>
<td>Documented hypersensitivity; peripheral or mesenteric vascular thrombosis because ischemia may be increased and the area of the infarct extended</td>
<td>Enhance the pressor response by blocking the reflex bradycardia caused by norepinephrine</td>
<td>D - Unsafe in pregnancy</td>
<td>Correct blood-volume depletion, if possible, before therapy; administer into a large vein because extravasation may cause severe tissue necrosis; caution in occlusive vascular disease</td>
</tr>
<tr>
<td>Epinephrine (Adrenalin)</td>
<td>2 mcg/min IV; titrate to effect</td>
<td>0.1 mcg/min IV; titrate to effect</td>
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<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; cardiac arrhythmias; angle-closure glaucoma; local anesthesia in areas such as fingers or toes because vasoconstriction may produce sloughing of tissue; do not use during labor (may delay second stage)</td>
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<tr>
<td><strong>Interactions</strong></td>
<td>Increases toxicity of beta- and alpha-adrenergic blocking agents and that of halogenated inhalational anesthetics</td>
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<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Safety for use during pregnancy has not been established.</td>
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<tr>
<td><strong>Precautions</strong></td>
<td>Caution in elderly persons, prostatic hypertrophy, hypertension, cardiovascular disease, diabetes mellitus, hyperthyroidism, and cerebrovascular insufficiency; rapid IV infusions may cause fatality from cerebrovascular hemorrhage or cardiac arrhythmias; monitor IV site for signs of extravasation, which can cause local tissue necrosis (if extravasation occurs, local infiltration of phentolamine may prevent tissue necrosis)</td>
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<tr>
<td><strong>Drug Name</strong></td>
<td>Atropine (Atropair)- Used to increase heart rate through vagolytic effects, causing an increase in cardiac output. Seldom produces an adequate response.</td>
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<tr>
<td><strong>Adult Dose</strong></td>
<td>Hypotension: 0.5-1 mg IV with repeated doses at 5 min intervals until desired response Cardiac arrest: 1 mg IV repeated q3-5min Minimal dose: 0.5 mg IV Maximal dose: 0.04 mg/kg or 3 mg IV is fully vagolytic</td>
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<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Hypotension: 0.02 mg/kg IV; minimum dose: 0.1 mg IV Cardiac arrest: maximum single dose is 0.5 mg in children and 1 mg in adolescents; may repeat above dose once, not to exceed 1 mg in children and 2 mg in adolescents</td>
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<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; thyrotoxicosis; narrow-angle glaucoma; tachycardia</td>
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<tr>
<td><strong>Interactions</strong></td>
<td>Co-administration with other anticholinergics has additive effects; pharmacologic effects of atenolol and digoxin may increase; antipsychotic effects of phenothiazines may decrease; tricyclic antidepressants with anticholinergic activity may increase effects</td>
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<tr>
<td><strong>Precautions</strong></td>
<td>Avoid in Down syndrome and/or children with brain damage to prevent hyperreactive response; avoid in coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension; caution in peritonitis, ulcerative colitis, hepatic disease, and hiatal hernia with reflux esophagitis; in prostatic hypertrophy, prostatism can have dysuria and may require catheterization; administration in doses of &lt;0.5 mg can produce paradoxical bradycardia</td>
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</tbody>
</table>
**Drug Name**

Isoproterenol (Isuprel)- Has beta 1- and beta 2-adrenergic receptor activity. Binds beta-adrenergic receptors of heart, smooth muscle of bronchi, skeletal muscle, vasculature, and alimentary tract. Has positive inotropic and chronotropic actions. May be used if transvenous or transcutaneous pacemaker is unavailable or not capturing. Dopamine should be tried first for rate control because isoproterenol has several adverse cardiovascular effects. Can cause increased myocardial workload and precipitate ischemia. Vasodilatory properties may worsen hypotension. Avoid use unless all other options have failed.

**Adult Dose**

2-4 mcg/min IV; titrate cautiously

**Pediatric Dose**

0.1 mcg/kg/min IV; titrate cautiously

**Contraindications**

Documented hypersensitivity; tachyarrhythmias; tachycardia or heart block caused by digitalis intoxication; ventricular arrhythmias which require inotropic therapy; angina pectoris

**Interactions**

Bretylium increases action of vasopressors on adrenergic receptors, which may, in turn, result in arrhythmias; guanethidine may increase effect of direct-acting vasopressors, possibly resulting in severe hypertension; tricyclic antidepressants may potentiate pressor response of direct-acting vasopressors; slowly inactivated at alkaline pH

**Pregnancy**

C - Safety for use during pregnancy has not been established.

**Precautions**

By increasing myocardial oxygen requirements while decreasing effective coronary perfusion, may have a deleterious effect on the injured or failing heart; in some patients, presumably with organic disease of the AV node and its branches, may paradoxically worsen heart blocks or precipitate Adams-Stokes attacks; caution in coronary artery disease, coronary insufficiency, diabetes or hyperthyroidism and sensitivity to sympathomimetic amines; if heart rate exceeds 110 BPM, may be advisable to decrease infusion rate or temporarily discontinue infusion

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**FOLLOW-UP**

***Further Inpatient Care:***

- Admit all ingestions to ICU monitoring for 6-12 hours in standard-release preparation overdose and for 24-36 hours in extended-release or once-a-day preparation overdose.

***Further Outpatient Care:***

- If patient is hemodynamically stable, observation may occur in observation units if available to the ED.
  
  - Adequate ICU capabilities must be present in the observation unit because these patients may require intubation, pacemaker placement, or vasopressor support.
  
  - Only asymptomatic ingestions should be watched in an observation unit, and if cardiodepressive symptoms occur, transfer the patient to an ICU setting.

- After adequate observation time, the asymptomatic patient may be referred for psychiatric evaluation.

***Transfer:***

- Patients must be completely asymptomatic to be transferred and should only be transferred with units capable of advanced cardiac life support (ACLS), including intubation and pacing.
Complications:
- Anoxic encephalopathy from prolonged CNS hypoxia
- Bowel infarction from underperfusion of mesenteric circulation
- Adult respiratory distress syndrome

Prognosis:
- The patient has a reasonable prognosis if treated aggressively, as long as they do not deteriorate to cardiogenic shock.
  - However, even with deterioration, prolonged attempts at resuscitation of the toxin-induced cardiac arrest are warranted.
  - Anecdotal cases of prolonged CPR with aggressive vasopressor support have yielded neurologically intact survivors.

Patient Education:
- Advise older patients to keep all medications away from children and to use child-resistant caps if children live in or visit their home.
- Educate grandparents who keep pills in easy-to-open pill-tenders of the risks to their grandchildren, who can easily open these types of containers.
- Advise adults to keep the number of the nearest poison control center near the phone and to call them even for a single tablet ingestion by children.

Special Concerns:
- Bepridil is a unique calcium channel blocker with antiarrhythmic activity. It is also proarrhythmic, even at therapeutic doses, and may cause torsade de pointes.
- Mibefradil, which has been taken off the market, has been associated with profound cardiogenic shock and fatality when switching to another CCB after stopping mibefradil.

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