ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY
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The Maryland Poison Center's Monthly Update: News, Advances, Information

One size may not fit all when treating calcium channel blockers

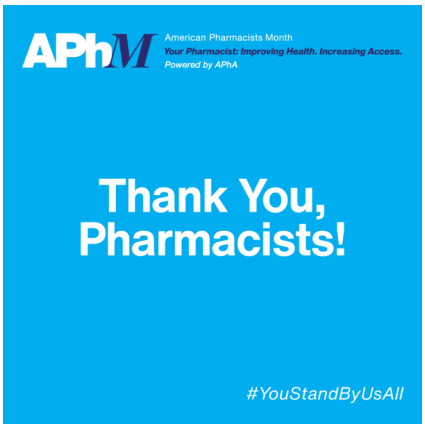
Calcium channel blockers (CCBs) are a commonly used class of medications that consist of nondihydropyridines (NDHPs), verapamil and diltiazem, and dihydropyridines (DHPs), such as amlodipine. Both subclasses block calcium channels to decrease contraction of smooth muscles. In therapeutic dosing, NDHPs have a greater affinity towards cardiac cells and decrease heart rate and strength of contractions. They are often used to treat arrhythmias and angina. DHPs act primarily in vascular smooth muscle cells with minimal influence on cardiac cells and are primarily used for hypertension. In overdose, this selectivity can be lost resulting in hypotension from vasodilation and bradycardia. Amlodipine also activates endothelial nitric oxide synthase (eNOS) resulting in nitric oxide-dependent vasodilation in peripheral and coronary arteries.

High dose insulin (HDI) has become a component of standard therapy in severe CCB poisoning. HDI acts as a dose-dependent inotrope through multiple mechanisms, as well as a vasodilator via an increase of eNOS. This ultimately leads to an increase in cardiac output, enhanced perfusion and improvement in cardiogenic shock. HDI's supporting literature is largely based on verapamil poisoning, but it is frequently given for all types of CCB overdoses.

Recent data suggest that over the last few years there has been an increase in fatalities related to amlodipine overdoses, possibly due to increased use for hypertension (*Clin Toxicol (Phila) 2022 Sep; 60(S2):3*). Amlodipine is cardiotoxic in overdose and HDI has been used for treatment. The unique activity on eNOS may produce synergistic vasodilation with HDI and worsen vasoplegic shock. A small, retrospective study from one poison center was done to determine if amlodipine-poisoned patients experienced more vasodilation compared to NDHP-poisoned patients when treated with HDI (*Clin Toxicol (Phila) 2022 Oct 25*). The amlodipine group was found to have a higher number of concomitant vasopressors and higher epinephrine doses. These findings suggest that amlodipine-poisoned patients treated with HDI had more vasodilatory effects compared to patients with NDHP toxicity and are consistent with proposed mechanisms.

HDI therapy should be initiated in combination with traditional vasopressors. Doses of both vasopressors and HDI should be titrated to effect based on the individual patient's response. Evaluation of perfusion using more tools than just the blood pressure should help guide dose adjustments. Some experts recommend a more moderate dose of HDI to achieve a "happy medium," balancing inotropic support without exacerbating vasodilation.

Contact your local poison center at 1-800-222-1222 for patient-specific treatment recommendations for calcium channel blocker poisoning.



October is National Pharmacist's Month. The MPC currently employs 16 pharmacists full time.

Did you know?

Amlodipine has the longest half-life of the dihydropyridine calcium channel blockers.

The half-life with therapeutic use is about 30 to 50 hours which makes amlodipine an effective once daily treatment option. A delay in more serious clinical effects may also occur with patients going into shock a few hours after ingestion. This is why most poison centers and toxicologists recommend a long duration of observation and warn about a prolonged duration of critical illness in amlodipine overdose.

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