High-dose Insulin Euglycemic Therapy (HIET) is an advanced first-line treatment for life-threatening Calcium Channel Blocker (CCB) overdose. Its use has also proven efficacious in severe Beta Blocker (BB) poisoning, as well as combined exposure to both agents. HIET restores cardiac output and ameliorates associated symptoms while conventional therapies such as atropine, glucagon, calcium boluses, and high-dose vasopressors often fail to improve hemodynamic stability in severely poisoned patients.

Serious CCB poisonings impair impulse generation and conduction and directly depress myocardial contraction, often with concomitant peripheral vascular relaxation. Initial bradycardia and hypotension may spiral down into asystole and cardiogenic shock. Hyperglycemia occurs because they also inhibit pancreatic release of insulin and induce peripheral insulin resistance, which impairs use of glucose as fuel. A mediator of the rapid clinical decline is thought to be faulty cellular-energy platform which renders the patient resistant to therapy.

So why use Insulin?

High-dose insulin appears to improve hemodynamic function and increase response to previously failed therapies in life-threatening CCB overdose. HIET is considered first line therapy — start it EARLY and start it FIRST in the course of treatment when blood pressure begins to fall. Introducing this treatment too late in the clinical course may preclude its success in restoring cardiac output.

Under normal conditions myocardial cells preferentially oxidize fatty acids for energy. In poor hemodynamic conditions as in CCB overdose, they switch to glucose utilization as the main fuel source. CCB-induced low insulin and insulin resistance deny uptake of glucose, preventing its use as the main energy substrate. HIET overcomes hypoinsulinemia and insulin resistance to break the vicious cycle of hemodynamic deterioration leading to cardiogenic shock and death. HIET restores the impaired cellular-energy platform which allows other conventional therapies to work more effectively.

Early evidence from a retrospective study of 40 verapamil or diltiazem overdose patients at five university teaching hospitals suggests that serum glucose correlates directly with the severity of CCB toxicity. The percentage of increase and the degree of hyperglycemia stratify the severity of CCB poisoning. (Levine 2007)

(Figure 1) Adapted from Levine et al 2007

The median peak glucose was only 145 mg/dL if overdose was not severe, compared to 364 mg/dL if the overdose was severe. The percentage rise of blood glucose from admission was 0% if not severe vs. 71% higher from admission if severe CCB overdose. In effect, the percentage of increase in serum glucose is a better predictor of severe toxicity than hemodynamic derangements. (Levine 2007).
Start HIET EARLY and start it FIRST!

Draw blood for baseline labs, then administer 1-2 amps \( D_{50} \) if needed, and a high dose insulin bolus (≥ 1 unit/kg) to rapidly saturate insulin receptors. Immediately start a continuous infusion of insulin at the same dose per hour as was just given in the bolus.

A significant inotropic response should commence in 15 to 30 minutes if the bolus dose of insulin was high enough. If blood pressure does not improve, re-bolus insulin at a higher dose and raise the insulin infusion rate to match the re-bolus dose. Give a sufficient volume of 5-10% dextrose in water to maintain blood glucose in a high-normal range (100-200 mg/dL) with frequent bedside glucose monitoring every 30 minutes at the beginning of therapy, and hourly thereafter. The optimal dose of insulin in humans for both the bolus and infusion has yet to be determined. Bolus doses up to 10 units/kg and continuous infusions up to 22 units/kg/hour have been administered with positive outcomes and minimal adverse effects (Engebretsen 2011.)

Severely CCB-poisoned patients may present with, or quickly develop a blood glucose >300 mg/dL. Since the intent of HIET is to maintain euglycemia while boosting circulating insulin levels, it is not necessary to give a glucose bolus first to a patient who is already hyperglycemic to begin with (i.e., blood glucose initially >200 mg/dL.) However, after the administration of insulin bolus(es) and during insulin infusion, the patient still requires frequent bedside glucose monitoring and supplemental glucose to maintain euglycemia. Supplemental glucose infusion may be required for up to 24 hours in some instances after discontinuation of high-dose insulin (Engebretsen 2011.)

Are there special considerations for diabetic patients when HIET is instituted?

Though not discussed in the literature, it is possible that diabetics will be relatively resistant to HIET compared to non-diabetic patients and will require higher insulin bolus and infusion doses; though perhaps not. It is prudent to start with a moderate insulin dose and rapidly increase the dose if there is no improvement in the patient’s cardiovascular status within 20 minutes or so.

How safe is HIET?

Adverse effects associated with HIET are low glucose, low potassium and possibly low magnesium and phosphate. A prospective observational study indicated no episodes of hypoglycemia in the first 24 hours of treatment with HIET (Greene 2007.) The feared adverse effects are predictable, uncommon, and easily managed through bedside monitoring of glucose plus laboratory monitoring of potassium, magnesium and calcium. Potassium can be maintained at a low normal concentration as resultant hypokalemia is likely due to cellular shifts in contrast to depletion of total body stores.

Assistance with HIET is just a phone call away!

HIET can be lifesaving in the course of life threatening CCB and BB overdose if instituted EARLY and at adequate doses. For consultation with a specially trained Certified Specialist in Poison Information or our Medical Toxicologist; please contact the Missouri Poison Center at 1-800-222-1222. Healthcare professionals can also call 1-888-268-4195.

References:


Please Have Ready When You Call (if possible):

— Detail about the substance involved
— Estimated time of exposure
— Age and name of the patient
— Vital signs and symptoms
— A general idea of background or circumstances

The Missouri Poison Center is only as strong as our hospitals, so please let us hear from you and help us help our community. Why call us? Because we need you.
Got Mold?

The Missouri Poison Center (MPC) gets calls about mold every season of the year. Questions range from people who are concerned about getting sick after eating mold on food, to breathing mold while living in their homes.

The MPC wants to help you maintain a healthy perspective on the issues of mold because mold is all around us. Molds can be found almost anywhere; they can grow on virtually any substance provided moisture is present. There are molds that can grow on wood, paper, carpet, and foods.

People with allergies like hay fever and asthma may be hypersensitive to mold and may experience allergic reactions and breathing problems. A few molds, in the right conditions, produce “mycotoxins.” These are substances that can make a person sick; however, the available scientific literature concluded there was not enough evidence to determine a casual exposure can increase a person’s risk to become ill. Even if building a mold-free home were possible, maintaining it “mold-free” would be nearly impossible. Mold spores are commonly carried from outside and grow on the surfaces of humans, pets, potted plants, and on foods such as fresh fruit and cheeses. Mold spores also blow in through windows and doors. We routinely encounter mold spores as part of our everyday life indoors and outside.

Tips to control indoor mold growth:

- Control moisture and keep humidity low.
- Fix any water problems. These include dripping pipes, leaks, rainwater coming in through windows, etc.
- Don’t let wet clothing or laundry sit.
- Wet shoes and hats should be dried before they are put away.
- Use the bathroom ventilation system if you have one in your home. It is designed to take moisture out of the house and keep it out of other rooms.
- Cleanliness is vital in controlling mold.
- Keep dishcloths, towels, sponges, and mops clean and fresh. A musty smell means they are spreading mold. Discard items you can’t launder or clean.
- Clean the inside of the refrigerator and washer every few months. Scrub the visible mold on rubber casings.
- Don’t buy moldy foods. Examine food well before you buy it. Notify the store manager about mold on foods!

Poison centers give expert advice fast, over the phone. We can help you and your family with poison emergencies and with questions about poisoning. You can call day or night, 7 days a week, any day of the year.

No call is too big or too small...just call 1-800-222-1222 to speak with a poison expert.
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The Missouri Poison Center website can be found at: http://www.cardinalglennon.com. Click on Poison Center under the Support Services tab.

Public Education Materials
Missouri Poison Center is offering a variety of educational materials FREE of charge including magnets, stickers, and brochures. For a small fee, you can order the Toxic Plants Brochure for your garden club, the Bites and Stings Brochure for your scout troop, or the Poison Look-Alikes Brochure for your child care providers and parents. Please help us teach about poison prevention and spread the word that the Missouri Poison Center is open 24/7 and the call is free and confidential.