

TOXALERT



MARYLAND POISON CENTER

January, 2000

Volume 17, Issue 1

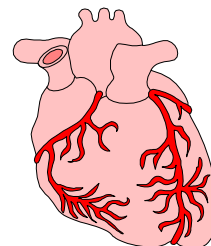
Calcium Channel Blocker Overdose

Suzanne Doyon, MD, ACMT

An 80 year old woman presented to the emergency department (ED) 3 hours after ingesting 20 verapamil-SR 240 mg. She was slightly lethargic with a pulse of 43/minute and blood pressure of 50 mm Hg systolic. She received one dose of activated charcoal in the ED. Two liters of NS were administered without an improvement in the blood pressure. Dopamine was started and she was given 10 cc of calcium gluconate IV. Her vital signs remained unchanged. The Maryland Poison Center was consulted at this time.

Calcium Channel Blocker (CCB) overdoses are one of the leading causes of death from poisoning. In 1998 there were 8600 potentially toxic exposures with 48 deaths attributable to CCBs reported to the American Association of Poison Control Centers. The incidence of death is 56 per 1000 cases. There are 3 general types of CCBs: dihydropyridines which include nifedipine; phenylalkylamines which include diltiazem; and benzothiazepines which include verapamil. The majority of deaths are due to exposures to verapamil and diltiazem which exert profound myocardial depression and severe peripheral dilatation. Fatalities are least common with nifedipine-like drugs because they are associated with peripheral vasodilation but less myocardial suppression than verapamil and diltiazem. The sustained release preparations (such as Calan-SR[®] and Cardizem-CD[®]) are particularly difficult to manage because peak effects are not reached until approximately 24 hours post-ingestion. Children are especially susceptible to the toxic effects of CCBs, exhibiting severe symptoms with as little as one tablet. CCB overdoses may present with altered mental status, bradycardia and hypotension. Hyperglycemia and lactic acidosis occasionally occur. A newly documented complication of CCB overdose is ischemic colitis occurring more than 24 hours post ingestion. It carries a poor prognosis if recognition is delayed.

The Maryland Poison Center can provide invaluable help and expertise in the management of these poisonings as will be illustrated in this case. The initial approach to treatment of these poisonings is to place the patient on a cardiac monitor, establish oxygenation, and administer intravenous fluid boluses to correct the hypotension. Symptomatic bradycardia secondary to CCB overdose should be treated with atropine. A total of 3 mg of atropine is administered intravenously.



Calcium administration is indicated for hypotension and cardiac conduction defects. However, meta analyses of severe CCB overdoses have shown calcium to be effective in about 50% of cases. Calcium chloride, which provides 13.6 mEq calcium/10 cc, is preferred over calcium gluconate. This is approximately 3 times more available calcium than in 10 cc of calcium gluconate. There is no consensus on the proper administration of parenteral calcium. Multiple IV boluses of 10 cc of 10% calcium chloride every 15-30 minutes to keep the serum calcium between 10 –15 mEq/L is reasonable. The same can be achieved with a bolus followed by an infusion of calcium chloride. Caution is advised to not overshoot since serum calcium above 15 mEq/L has been associated with multiple complications including CNS depression, arrhythmias and death.

The preferred second line agent is intravenous glucagon. Radio-labeled glucagon has been documented to bind to the myocardium and, therefore, is believed to have its own receptor on the heart muscle. The inotropic action of glucagon seems to be related to an increase of cAMP

Atropine, calcium and glucagon are the preferred agents used to reverse the hypotension and bradycardia seen in CCB overdoses.

Calcium Channel Blockers (continued)

levels in the myocardium. Glucagon increases the heart rate, cardiac index, blood pressure and stroke volume. The initial dose of glucagon is 3 mg IV over 1 minute. If ineffective, it should be followed by a 7 mg dose over 1 minute. The onset of action of glucagon is within 5 minutes and the duration of action is 15 minutes. Therefore, the bolus must be followed with an infusion of 3-5 mg or more per hour in order to support the heart rate and blood pressure. Hyperglycemia and vomiting are the adverse events most often associated with glucagon administration. It is, therefore, recommended that the patient have an NG tube placed followed by low wall suction, and that blood glucose be closely monitored with the administration of insulin to treat hyperglycemia (when blood sugars reach double the baseline). Glucagon is supplied in vials containing 1 mg/vial and a diluent containing phenol. Sterile water should be used as the diluent rather than the phenol since phenol given intravenously can cause hypotension and renal disturbances.

The choice of sympathomimetic agent is based upon numerous factors including pharmacologic profile of each drug, the patient's underlying physiologic condition and the physician's familiarity and comfort level with the agent. Direct acting agents like norepinephrine and epinephrine are preferred because of direct alpha and beta effects. If the sympathomimetic agent is unsuccessful at supporting the blood pressure and heart rate, a Swan Ganz catheter insertion may be helpful in determining whether myocardial suppressant or peripheral vasodilatory effects are responsible for the hypotension.

The fourth line agent is amrinone, which is a non-catecholamine inotropic agent that increases cAMP intracellularly. There are several animal studies and a few human case reports where it was used successfully in the treatment of CCB over-

doses. However, amrinone has the potential to cause peripheral vasodilation and should be used with extreme caution and never without the concomitant use of another vasopressor agent.

Intra-aortic balloon counterpulsation is another possible invasive therapeutic modality. A large balloon is inserted in the femoral artery and inflated and deflated in cycle to simulate systole and diastole. There are case reports of its successful use in isolated severe CCB cases. Simultaneous cardiac pacing is usually required.

After consultation with the Maryland Poison Center and their medical toxicologist on-call, the patient received glucagon 3 mg followed by glucagon 7 mg. She responded to the second glucagon dose and an infusion of glucagon at 7 mg/hr was started. Norepinephrine 4 ug/min had already been administered and continued to be administered for approximately 20 hours. She received over 175 mg of glucagon IV over a 28 hour period. The Maryland Poison Center was able to communicate to the hospital pharmacy the 24-hour glucagon needs of this patient. Since an insufficient amount of glucagon was in stock at the hospital, the MPC assisted in obtaining the required amount from other sources. The patient was extubated on hospital day 3 and did not develop any additional complications from this overdose.

This case illustrates how deficient our hospitals are in glucagon. The Maryland Poison Center suggests that every hospital maintain a 100-150 mg supply of glucagon.

Many hospitals do not stock enough glucagon to treat a severe CCB overdose.

Every hospital pharmacy should keep 100-150 mg of glucagon in stock.



National Poison Prevention Week

March 19-25, 2000

Call the
Maryland
Poison
Center for
all poison-
ings:

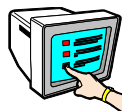
410-
706-7701

Or

1-800-
492-2414

House-
hold
bleach
+
ammonia
=
chloramin
e gas

We're on the Web!



The Maryland Poison Center (MPC) was among the first regional poison centers to be on the world wide web. Since 1994, we have continually worked to improve our website, offering information for health professionals and the general public. There you will find Clin Tox FAQ's, Toxalert on-line, poison prevention education and general information about the MPC.

Come visit the MPC at:

www.pharmacy.umaryland.edu/~mpc

**If you have visited our website in the past, please note that our address has recently changed.*

New Health Educator

The Maryland Poison Center is pleased to announce that Melissa Melum, R.N. has joined our team as Health Educator. Melissa comes to us with experience in a variety of public and professional education settings. Melissa will be developing and distributing poison prevention education materials, coordinating poison prevention programs for the public and implementing activities for National Poison Prevention Week. For information on available materials and programs, call Melissa Melum at 410-706-7604.

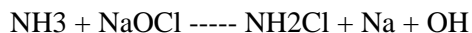
The MPC also provides speakers on a variety of topics for hospital in-services, grand rounds, paramedic classes, pharmacy meetings and other health professional education programs. For more information, call Lisa Booze at 410-706-7604.



TOXNOTES: Chloramine Gas

"I just mixed bleach and ammonia together to clean my sink and now I can't stop coughing!"

Household laundry bleaches are predominantly 3-6% solutions of sodium hypochlorite and are mildly alkaline. When mixed with an ammonia solution, chloramine gas is formed:



Chloramine is a respiratory irritant. Inhalation results in immediate mucous membrane irritation. Symptoms may include rhinorrhea, eye irritation, throat irritation, vomiting, coughing, chest pain and shortness of breath. Chemical pneumonitis, pulmonary edema and respiratory failure can occur following severe gas exposure, however, the majority of household exposures result in mild and transient symptoms that usually last for 6 hours or less.

Moving to fresh air may be all the treatment that is required. If respiratory distress occurs, administer 100 percent humidified supplemental oxygen with assisted ventilation as required to patients with persistent symptoms. Inhaled sympathomimetic bronchodilators may be beneficial if bronchospasm or wheezing are present. Patients with significant respiratory distress should be admitted to the hospital for observation for at least 24 hours.

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School of Pharmacy
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Baltimore, MD 21201

Bulk Rate
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Baltimore, MD



410-706-7701 or 1-800-492-2414

TOXALERT

Preventing Poisonings Through Community Education

Thursday, March 23, 2000
1 p.m. – 5 p.m.

Pharmacy Learning Center
University Of Maryland, Baltimore

A workshop for health professionals, educators and others who want to help keep patients, children and communities safe from poisons.

You will learn:

- *Why poisonings occur*
- *How to prevent poisonings*
- *How to teach children and adults about poisons*

Registration fee is \$30 and includes materials and parking.



For a
registration
form,
call 410-
706-7604.