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The New York State Poison Centers

TOXICOLOGY LETTER

COMPRISING THE LONG ISLAND, NEW YORK CITY, RUTH LAWRENCE, UPSTATE NEW YORK, AND WESTERN NEW YORK POISON CENTERS

Questions from the Drug Information Center

Contributed by: Jennifer Beaver, Pharm.D. Candidate St John Fisher School of Pharmacy
Sharon Ternullo, Pharm.D, DABAT. Ruth A. Lawrence Poison and Drug Information Center

Question:

An emergency medicine physician called the Drug Information Center after reading in an emergency medicine journal about the use of intravenous lipid emulsion for the treatment of calcium channel blocker toxicity. The physician is inquiring whether this is a viable treatment alternative he should consider for calcium channel overdoses.

Answer:

Intravenous lipid emulsions typically contain triglycerides and a phospholipid emulsifier. They are currently approved for use in total parenteral nutrition to provide calories and essential fatty acids, as well as for the prevention and treatment of essential fatty acid deficiency.

Considerable research has been done in recent years on the use of intravenous lipid emulsion as an antidote for local anesthetic toxicity. Although not approved for this indication, several promising animal studies have been performed 1-4 and several case reports have described successful resuscitation of patients who had already failed conventional treatments for anesthetic toxicity.[5-10] Due to the demonstrated success with local anesthetics, research has begun to emerge on the use of fat emulsion for other lipophilic drugs such as cyclic antidepressants, beta blockers, and calcium channel blockers[11-22].

There are several possible mechanisms by which intravenous fat emulsion could act as an antidote for lipophilic drug toxicity. Intravenous lipid emulsion might create a separate intravascular compartment which would act as a sink for lipophilic drugs and therefore reduce free drug availability. It is also possible that intravenous lipid emulsion could overcome inhibition of carnitine acyltransferase. Carnitine acyltransferase is essential for the transport of fatty acids across the inner mitochondrial membrane and mitochondrial lipid metabolism. The local anesthetic bupivacaine is a known inhibitor of carnitine acyltransferase. The third possibility is that the intravenous lipid emulsion could have a direct inotropic effect by increasing cardiac myocyte calcium[16, 17]

There have been two recent animal studies as well as two human case reports on the use of intravenous lipid emulsion for calcium channel blocker toxicity. Tebbutt et al published a study in 2006 that was the first one to use intravenous lipid emulsion for calcium channel blocker toxicity[17]. The study was a blinded randomized placebo-controlled study in 30 Wistar female rats. The rats were given verapamil at a constant rate of 37.5mg/kg/hr until death occurred. Five minutes into the infusion, half of the rats were given 12.4mL/kg (2.48g/kg) of

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Program Announcements ••

Ruth A. Lawrence: Monthly conference: every 4 weeks on Thursdays (11am to noon), and every 4 weeks on Tuesdays (10am-11am).

UNY: The 2010 Toxicology Teaching Day is Scheduled for 11/3/10. Please mark your calendars!!

NYC: Consultants Case Conference • The first Thursday of the Month from 2-4pm

Long Island Regional Poison and Drug Information Center: Please look for our spring programs

Please call administrative telephone numbers for more information.

Toxicology Advice Centers ••

Administrative Phone Numbers - To obtain a consult in your area, call 1.800.222.1222.

Western New York Poison Center (WNY) ..... 716.878.7871 • http://wnypoison.org
Ruth A. Lawrence NY Poison Center (FL) ..... 585.273.4155 • www.FingerLakesPoison.org
Upstate New York Poison Center (UNY) ..... 315.464.7078 • www.upstatepoison.org
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INH-Associated Hepatotoxicity

David Story, M.D., Lewis S. Nelson, M.D.

Case Summary

A 13 year-old boy presents to the emergency department with four days of jaundice, upper abdominal pain, nausea, vomiting, and headache. He had a positive tuberculin skin test two months prior, and had been taking INH (isonicotinylhydrazine, isoniazid). The patient has no other pertinent past medical history and uses no other medications. He had visited his primary care physician four days prior for nausea and vomiting. Although the INH was discontinued at that time, he developed progressive jaundice and abdominal pain.

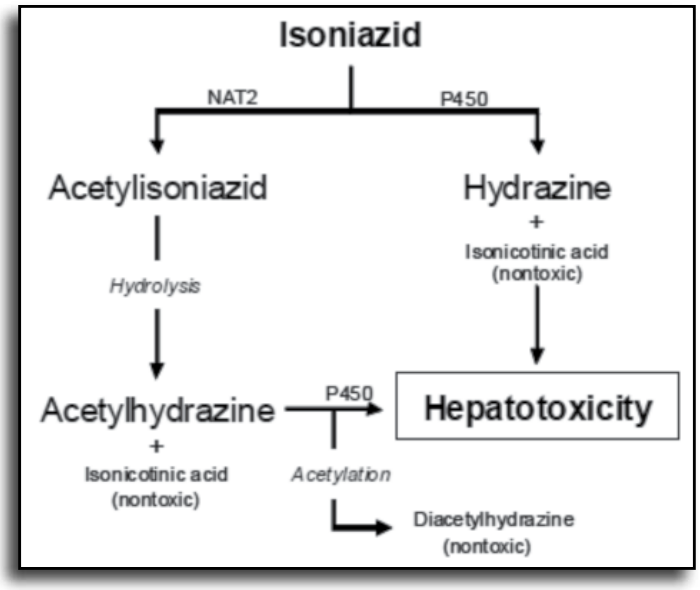
On physical examination, he is alert and oriented with the following vital signs: blood pressure, 113/62 mmHg; heart rate 88 beats/minute; respiratory rate 14 breaths/minute; pulse oximetry 100% on room air; temperature 37.1°C. His skin is jaundiced, but without ecchymoses or petechiae. Eye examination reveals scleral icterus. Cardiovascular and pulmonary findings are unremarkable. His abdomen is soft, but diffusely tender to palpation without any organomegaly, rebound, guarding, or rigidity. Initial pertinent laboratory results include: AST >2600 IU/L; ALT >2600 IU/L; total bilirubin >20 mg/dL; INR 3.7; acetaminophen concentration < 10 mcg/mL.

What is the mechanism by which INH treats tuberculosis?

INH interferes with synthesis of mycolic acids, which are 70 to 90 carbon fatty acids that are a key component of the mycobacterial cell wall. INH, a prodrug that enters mycobacterium by passive diffusion, where it is metabolized by intracellular catalasereductase, katG, to its active form (INH-NAD). This active form irreversibly inhibits InhA, an enzyme required for the synthesis of mycolic acids that requires NADH as a cofactor. Without mycolic acids the cell wall cannot be properly developed and the mycobacterium dies. *(Vilcheze 2007)*

How does INH cause hepatotoxicity?

The primary means for INH metabolism in humans is through acetylation by Nacetyltransferase (NAT-2) in the liver generating acetylisoniazid. Acetylisoniazid can undergo hydrolysis to form acetylhydrazine (and nontoxic isonicotinic acid). Polymorphisms of NAT-2 have been identified in the population that relegate humans to be either "rapid" or "slow" acetylators. *[see figure]* Slow acetylators shunt some INH to a secondary metabolic pathway of oxidation via Cytochrome P450, producing hydrazine (and nontoxic isonicotinic acid also). It appears that both acetylhydrazine and hydrazine, generated by the rapid and slow acetylators respectively, are capable of participating in reactions that generate oxidative stress (e.g., free radicals). Hydrazine may induce Cytochrome P 450 (specifically CYP2E1), increasing production of additional toxic metabolite. Thus, hepatotoxicity may occur in both rapid and slow acetylators, though for slightly different reasons. *(Gurumurthy 1984)*



What is the frequency of hepatotoxicity in patients taking isoniazid?

It was previously suggested that approximately 10% of all patients treated with INH will have 2-3 fold increase in baseline alanine aminotransferase (ALT), and that 10% of those patients (1% overall) develop clinical hepatitis (nausea, vomiting, jaundice, or abdominal pain). (Kopanoff, et al) Furthermore, 10% of this latter group (0.1% overall) developed fulminant hepatic failure and required liver transplantation or died. However, this pessimistic data was subsequently refuted based on the exclusion of high risk patients (e.g., those over 35 year of age with unknown PPD converter status) and a more aggressive approach to surveillance for early signs of hepatotoxicity. A prospective 7 year long study in a public health clinic followed a population of over 11,000 patients for the duration of treatment for latent tuberculosis with INH. (Nolan, et al) Eleven patients were identified as having clinical hepatitis, all of whom improved when the drug was discontinued. Not only did the investigators demonstrate a reduced incidence of hepatotoxicity in therapeutic INH use (0.1% vs 1%), they also identified that increasing age is a risk factor for developing hepatotoxicity. Another study reported the incidence of hepatotoxicity (defined as aspartate aminotransferase (AST) > 5x the ULN) as 0.6% (19/3377 patients), although only 1 of the 19 had clinical symptoms. The higher frequency may be due to an older patient population, as 55% of the study cohort was over the age of 35. Indeed, the subgroup data analysis showed that risk factors for developing hepatotoxicity were age >50 years old and a baseline AST concentration greater than the ULN. *(Fountain 2005)*

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The Red Seed: *Abrus precatorius*

David H. Jang, M.D., Lewis S. Nelson, M.D.

A 20 year-old man presented to the emergency department (ED) complaining of nausea, vomiting, and watery diarrhea for approximately 6-8 hours prior to arrival. He denied any drug or medication use, recent illness or antibiotic use, travel, or changes in his diet. He was alert and in no apparent distress. His vital signs included: blood pressure, 119/55 mmHg; heart rate 92 beats/minute; respiratory rate 18 breaths/minute; and temperature 99.8° F. His heart and lung examinations were unremarkable. The abdomen was soft, and bowel sounds were hyperactive, and a stool sample was negative for occult blood. The general neurologic examination was normal with intact strength, sensation, cranial nerves, gait, and reflexes. Initial pertinent laboratory results included: white blood cell count 12,300 cells/mm^3; hemoglobin 11 g/dL; platelets 390x10^3/ μL; normal serum chemistry including anion gap, renal function, and hepatic studies. An acetaminophen concentration was <10 ug/mL.

The patient was initially diagnosed as having viral gastroenteritis. Several additional episodes of diarrhea and emesis are partially relieved with the combination of ondansetron and metoclopramide, and intravenous normal saline was administered to correct presumed intravascular volume depletion. The patient subsequently admitted to feeling depressed but denied any pill ingestion. While awaiting psychiatry evaluation the patient's father arrived with a box of small hard red and black seeds and thinks that his son ingested them in a suicide attempt *[figure 1]*

What seeds could this patient have ingested?

Many seeds and berries can induce gastroenteritis when ingested, either through irritation of the gastrointestinal tract (such as *Dieffenbachia*) or due to their content of pharmacologically active xenobiotics. Pokeweed (*Phytolacca americana*) berries, which are green (not red) when unripe, induce severe gastrointestinal effects, though these berries are less toxin when mature and purple-colored. The presence of a mitogen in pokeweed results in a marked lymphocytosis that lasts several days. The small, firm, red (tomato-like) berries of American bittersweet or woody nightshade (*Solanum dulcamara*) contain solanine and related solanaceous alkaloids, which are also found in green potatoes and unripe tomatoes. Solanaceous alkaloids may also produce central nervous system effects including delirium and coma. The common or European Yew (*Taxus baccata*) is an evergreen shrub with nontoxic, soft, red, fleshy berries with a hard green core that contains cardiotoxic taxine alkaloids. The nicotine-like component found in *Wisteria* vine results in nicotinic cholinergic effects including vomiting and diarrhea, as well as hypertension, diaphoresis, and muscle weakness. Golden Chain (*Laburnum*) seeds contain cytisine another nicotinic agonist, and Betel nut (*Arecu catechu*) contains arecholine.

Case Continuation:

Upon the discovery of ingestion of these seeds, the Poison Control Center was contacted. The seeds were described as approximately 1 cm in size with a red shiny coat and a black band at one end A picture of the seeds was transmitted to the NYCPCC through electronic mail, allowing their identification as *Abrus precatorius*. The patient was re-interviewed and admitted to chewing 10 seeds and swallowing them 4-6 hours prior to the development of his symptoms.

What is *Abrus* seed and why are they available?

Abrus precatorius is a plant that originates from southeast Asia and now can be found in subtropical areas of the world. The name *Abrus*, meaning beautiful or graceful, is used to describe the appearance of the seed. The seed is found in a variety of colors such as black, orange, and most commonly, red with a glossy appearance with the black band at the end that attaches to the plant. The seeds are used in a variety of jewelry, trinkets, and ornaments; the *Abrus* seed itself is known by a variety of names that include rosary pea, prayer bead, and jequirity bean. Precare (from which the species name is derived), meaning to pray, references its common use in rosaries.

The seeds of *Abrus precatorius* have been used through history in a variety of roles. Due to their uniform size and weight, they were once known as rati, and used as weights for weighing gold and silver. The *Abrus* seeds have also been used for medicinal purposes, including the treatment of chronic eye disease. Arabic culture has purportedly used the seed as an aphrodisiac known as coq's eye. The toxicity of the *Abrus* seed was associated with its use as a fish poison as well as a homicidal agent.

What is the mechanism of toxicity of abrin?

While all parts of the plants are considered toxic, the seeds, which contains abrin, are the most toxic portion of the plant. Abrin (similar in mechanism to ricin) is considered one of the most toxic plant substances. Abrin consists of two dissimilar, disulfide-linked polypeptide chains known as the A-chain and B-chain. The A-chain is a glycosidase that removes an adenine residue from an exposed loop of 28 S ribosomal RNA, which stops protein synthesis. The B-chain is the portion that binds β-D-galactopyranoside moieties on the cell membrane, allowing the complex to undergo endocytosis, bringing the A-chain internally to exert its toxic effect.

How dangerous is the *Abrus* seed?

Abrin has an estimated human fatal dose of 0.1-1 μg/kg, and there are reported deaths after both accidental and intentional poisoning. Most cases of *Abrus* seed ingestions

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Clinical Pearls: Drug Induced Movement Disorders

Jamie Nelsen, Pharm.D. Upstate NY Poison Center

Illustrative Case: A 30 YOF was administered promethazine prior to a procedure to manage anticipated nausea. Approximately one hour late she was transferred to the ED due to a presumed adverse drug reaction. The patient is restless, nervous, rocking back and forth. She is described as AAO x 3, but "not quite right". The patient has been given diphenhydramine 25 mg IV x 1 and lorazepam 2 mg x 2 without observed response. The patients vital signs include: BP 189/98 mmHg; HR 117 bpm; RR 22 bpm; afebrile.

By the end of this review the reader should be able to:

1. *Identify various types of dyskinesias based on presenting symptoms*
2. *Provide optimal management strategies based on clinical symptoms*
3. *Provide education regarding the etiology and care of patients with drug induced movement disorders (DIMDs)*

Defining Dyskinesias: Dyskinesias broadly refer to abnormalities in motor tone and difficulty or distortion in performing voluntary movements. There are several types of movement disorders, but this review will focus primarily on the acute DIMDs.

a. **Dystonia:** A sustained, involuntary muscle contraction or spasms resulting in abnormal postures or twisting repetitive movements. Affected body parts typically include: jaw, back, neck, eyes. Depending on the affected muscle group, difficulty with walking, breathing, speech, and swallowing may occur.

b. **Choreoathetoid:** Abnormal, irregular involuntary movements often described as writhing or twisting. Symptoms are not painful but may result in embarrassment in social settings. The orofacial region, tongue, upper and lower extremities are often involved. Lip smacking, chewing movements, and tongue protrusion are common. *(A chronic disorder tartive dyskinesia can also result in some of these findings, although it is unlikely to present in the ED and is therefore not discussed.)*

c. **Akathisia:** A subjective feeling of restlessness and need to move. It is clinically described as difficulty sitting still, repetitive leg movements, restlessness, and a subjective feeling of inner agitation.

Pharmacology and Management: It is important to be able to recognize and identify a particular subset of movement disorder. In doing so, you will have greater insight into the pharmacology of such DIMDs and therefore be better able to select the most appropriate management. Please note lists of associated drugs are NOT complete.

a. **Dystonia:** Dopamine withdrawal or antagonism **(not enough dopamine)** causes a release of acetylcholine (Ach) in the basal ganglia, resulting in increased motor tone. The optimal treatment therefore aims to block Ach binding using an anticholinergic drug, such as diphenhydramine (25-50 mg IV).
   - Associated drugs include: antipsychotics, antiemetics

b. **Choreoathetoid:** Drugs that **increase dopamine** in the basal ganglia ultimately results in decreased inhibitory tone (GABA) which manifests as choreoathetoid movements. Notably, this etiology is the opposite of the cause of dystonia. Consequently optimal management is obtained via removal of the offending agent and a benzodiazepine (preferably diazepam for rapid onset) as clinically indicated.
   - Associated drugs include: stimulants, estrogen/progestins

c. **Akathisia:** Is thought to be the result of **acute dopamine antagonism** and resultant increased norepinephrine in the basal ganglia. Treatment, therefore would consist of reducing the dose (or removing) the offending agent, and using a lipophillic beta-antagonist (such as propranolol) to reduce the central hyperactivity. Management may also be augmented by a benzodiazepine.
   - Associated drugs include: antipsychotics, antiemetics, lithium, SSRIs

Considerations: Based on the noted pharmacology and management strategies discussed above, it would be wise to remember a few caveats:

1. Remember to consider the half-life of the inciting drug. It is often longer than the half-life of the treating agent (diphenhydramine, propranolol) and repeat doses may be needed. The clinician should be made aware of the need for continued therapy and the patient counseled appropriately. Ultimately duration of therapy will be determined based on reappearance of symptoms once therapy is stopped.
   - Ex: risperidone (t/2 ~24h) induced dystonia would warrant 48-72 h of diphenhydramine q 6-8 hours.
   - Ex: fluphenazine (t/2 12-20 h) induced akathesia would warrant 24-72 h of propranolol q 6 hours.
2. Although patients with akathisia may have accompanying anxiety, these patients should not receive dopamine antagonists such as haldol or atypical antipsychotics, as this may contribute to their etiology (make symptoms worse).
3. It is important to distinguish choreoathetoid movements from dystonias in order to avoid inadvertently making the patient anticholinergic with a therapy (such as benadryl) that is not expected to work considering the etiology (too much dopamine).

Case Continuation:

This patient has clinical manifestations of toxicity most closely associated with akathesia. The MD has already

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Clinical Pearls: Drug Induced Movement Disorders

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given 10 mg ativan without response. The following was advised: 1) propranolol 60 mg oral, or can try 1 mg IV if can't take oral, 2) switch to diazepam for quicker onset, 3) avoid haldol. The MD called approximately an hour later to say that the patient had an excellent response to propranolol and diazepam. Follow up the following day reveled that the patient was AAO x 3 and did not need additional therapy.

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The Red Seed: *Abrus precatorius*

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are unintentional and occur in children. Ingesting the intact seeds typically results in no clinical findings, as they pass through the gastrointestinal tract without incident due to the hard shell. Abrin released during chewing is poorly absorbed systemically from the gastrointestinal tract, though the gastrointestinal mucosal cells themselves are affected. This manifests as significant vomiting and diarrhea with resultant hypovolemia and electrolyte disturbances, which can be severe and life threatening, particularly in areas with less advanced healthcare systems. Parenteral administration of abrin or ricin is considerably more concerning and has been associated with a high fatality rate in reported cases. Death in this situation is due to multisystem organ failure as cellular protein synthesis is disrupted throughout the body. There are a few reported cases of abrin causing acute demyelinating encephalitis.

What is the treatment for patients with abrin poisoning?

Patients with concerning (e.g., numerous or chewed) ingestions of chewed or otherwise damaged (e.g., strung as rosaries) *Abrus* seeds should be admitted and observed since the onset of clinical toxicity may be delayed for many hours. While there are no antidotes for poisoning by abrin, management consists primarily of supportive care. Attention to intravascular volume status as well as electrolyte replacement should be sufficient. Differentiating systemic toxicity from sepsis or systemic inflammatory response syndrome can be difficult, and they may be coexistent. The few reported cases of acute demyelinating encephalitis suggest success with the use corticosteroids, though this is not adequately studied.

Case Conclusion:

The patient was admitted to the intensive care unit (ICU) for observation and management of his fluid and electrolyte status. He continued to have frequent episodes of emesis as well as diarrhea that were ameliorated with antiemetics. The patient was observed for two days during which time he gradually improved. The patient admitted to ordering a box of Abrus seeds online from Asia after reading on the Internet about the use of this seed in suicide. He was evaluated by psychiatry and was eventually discharged with no permanent sequelae for outpatient follow-up.

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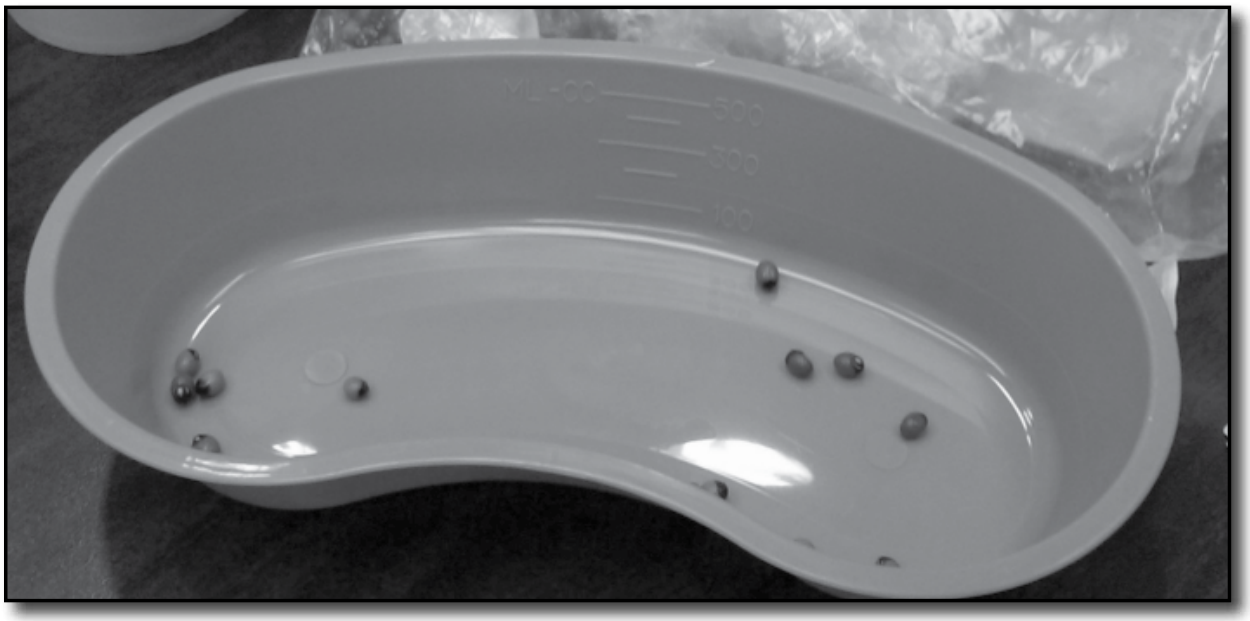

Figure 1: *The abrus seeds brought in by family members*

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What is the currently recommended regimen for the use of INH in patients with latent tuberculosis?

Recognizing the trade off between importance of treating latent tuberculosis and the slight increased risk of INH-induced hepatotoxicity in individuals older than 35 year of age, the current guidelines recommend treatment of all known PPD converters, regardless of age. (ATS 2000, Munsiff 2005) Pregnant woman, who have an increased risk of hepatotoxicity, should not be treated with INH prophylaxis unless the risk of developing tuberculosis is high. If possible, delaying therapy for 2-3 months after delivery is recommended, and breastfeeding is not a contraindication. INH is not teratogenic.

What are the current recommendations for INH hepatotoxicity surveillance?

The current recommendations for surveillance in patients using INH are complex and allow the physician discretion in choosing whom to monitor. The American Thoracic Society has the following recommendations *(Saukkonen 2005)*:

1. Baseline blood tests are generally not recommended for healthy patients treated with INH or rifampin
2. Baseline and follow up serum ALT and bilirubin are recommended for patients with a possible liver disorder: history of chronic liver disease (Hepatitis B or C, alcoholic cirrhosis), chronic alcohol use, HIV patients receiving HAART, pregnant women, and women up to 3 months post-partum
3. Baseline testing should be considered for those with chronic medical conditions
4. Baseline and follow up ALT concentrations for patients > 35 years old; can be monthly, bi-monthly, or at 1, 3, and 6 months, depending on perceived risk and ALT stability
5. ALT is the preferred lab test for detecting and tracking hepatotoxicity

What is the management of INH induced hepatotoxicity?

The mainstay of treatment for INH induced hepatotoxicity is discontinuation of the medication. In one study, seven out of eight patients receiving INH-related liver transplantations had continued to take INH following the development of clinical hepatotoxicity (Halpern 1993). The American Thoracic Society recommends the following interventions for hepatotoxicity (Saukkonen 2006):

1. INH should be withheld if ALT is at least three times the upper limit of normal (ULN) when jaundice and/or hepatitis symptoms are reported, or ALT is five times the ULN in the absence of symptoms
2. Rapid increases in ALT (even if below the ULN) may indicate need for more frequent monitoring
3. If baseline ALT is more than three times the ULN, an increase of two- to threefold is an indication to halt treatment, even in the absence of symptoms

Additionally, N-acetylcysteine prevents liver toxicity in rats receiving hepatotoxic doses of INH. (Attri 2000) Although there are no human studies regarding NAC treatment in this setting, the benign nature of this intervention and general utility in other hepatotoxic syndromes should prompt its use in most cases.

Case Conclusion

The patient was transferred for evaluation by a liver transplantation team. His vital signs remained stable throughout his admission. He received intravenous saline at a maintenance rate and oral vitamin K supplementation daily. N-acetylcysteine was recommended, but was not initiated by the healthcare team. He developed grade II encephalopathy, and his liver function abnormalities peaked shortly after transfer: AST 3490 IU/L; ALT 3366 IU/L; total bilirubin 30.5 mg/dL; and INR 5.0. Although his AST and ALT began to decline slowly, his bilirubin and coagulopathy persisted, suggesting liver failure. He subsequently underwent heterotopic liver transplantation on hospital day #10, after which his coagulopathy and hyperbilirubinemia corrected. He was stable for hospital discharge on day #16.

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Continued from page 1

20% intravenous lipid emulsion and the other half were given 12.4mL/kg of normal saline. The rats that received the study medication survived for significantly longer than the rats who received normal saline (44 ± 21 minutes vs. 24 ± 9 minutes, p=0.003), despite receiving nearly double the mean lethal dose (27.4mg/kg ± 13 vs. 14.7mg/kg ± 6, p=0.003) of verapamil.

The second study to use intravenous lipid emulsion for calcium channel blocker toxicity was performed by Bania et al and was published in 200718. This study was a blinded randomized placebo-controlled study which included 14 male mongrel dogs. Verapamil was first given at a constant rate of 6mg/kg/hr until the mean arterial pressure was reduced by 50%. The dose was then titrated to maintain this mean arterial pressure for 30 minutes. Next, verapamil was given intravenously at a constant rate of 2mg/kg/hr for an additional 90 minutes in an effort to simulate continued gastrointestinal absorption which would occur if orally ingested. The dogs were then given atropine (0.04mg/kg), calcium chloride (15mg/kg every 5 minutes x 3 doses) and saline (20mL/kg over 15 minutes). Finally, the dogs were either given 7mL/kg (1.4g/kg) 20% intravenous lipid emulsion or 7mL/kg saline over 30 minutes. Survival rates in the intravenous lipid emulsion group were 100% compared to 14% in the control group (p=0.01). Survival times were also significantly longer in the intravenous lipid emulsion group (120 minutes compared to 75 minutes, p=0.002).

The first case report to demonstrate the use of intravenous lipid emulsion in verapamil toxicity in humans was published as an abstract at the 2008 North American Congress of Clinical Toxicology Annual Meeting in Toronto, Canada[19]. This study, by Dulcourt and Aaron, involved a 52 year old male patient who presented with hypotensive shock following acute verapamil and atenolol ingestion. Following the failure of crystalloid, calcium, dopamine, norepinephrine, pacemaker placement, and high dose insulin; 20% intravenous lipid emulsion was given as a 1.5mL/kg (0.3g/kg) bolus followed by 0.25mL/kg/min (0.05g/kg/min) for 30 minutes. Within minutes, the patient's shock resolved and symptoms improved for several hours. Unfortunately 4 hours after discontinuing intravenous lipid emulsion the patient returned to a shock state and expired shortly after.

The second case report was published in May 2009 by Young et al [20]. This study described the use of intravenous lipid emulsion in a multi-drug overdose that included verapamil SR. The patient was a 32 year old male who was in cardiac shock and had failed all other treatment and resuscitation efforts (gastric lavage, activated charcoal, normal saline, norepinephrine, calcium gluconate, and intravenous glucagon). Intravenous lipid emulsion 100mL (20g) was given as a bolus over 20 minutes followed by an infusion of 0.5mL/kg/hr (0.1g/kg/hr) for 24 hours. The patient's symptoms began improving within one hour of the start of the fat emulsion infusion and the patient was eventually discharged on day [5].

In summary, based on the evidence available at this time, in patients with cardiac shock from calcium channel blocker ingestion, intravenous lipid emulsion could be considered a reasonable treatment alternative after other resuscitation efforts have been exhausted.

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UPSTATE
MEDICAL UNIVERSITY
Upstate NY Poison Center
750 East Adams Street
Syracuse, NY 13210