Treatment for digoxin overdose

- B. Trimble

Digoxin Overdose

Digoxin is derived from the leaves of a digitalis plant (foxglove). Some plants have chemicals that can cause symptoms similar to digoxin if eaten, such as lily of the valley and oleander. Digoxin is a substrate of P-glycoprotein. Drugs that induce or inhibit P-glycoprotein in the intestines or the kidneys have the potential to alter digoxin pharmacokinetics (Katzung, Mastes, & Trevor, 2012).

Digoxin increases the strength of heart contractions by inhibiting the activity of the enzyme ATPase. ATPase controls the movement of calcium, sodium, and potassium into the heart muscle. ATPase increases the amount of calcium in heart muscle, which increases the force of contractions. Digoxin slows the electrical conduction between the atrium and ventricles of the heart and slows ventricular contractions. Digoxin is eliminated through the kidneys and should be reduced in dosage in patients with kidney dysfunction (Katzung, Mastes, & Trevor, 2012).

Medications such as verapamil, quinidine, Amiodarone, indomethacin, spironolactone,

Alprazolam and itraconazole can increase drug levels and the risk of toxicity of digoxin. Furosemide and other diuretics that reduce blood potassium or magnesium levels may predispose patients to drug induced abnormal heart rhythms. Saquinvard and ritonavir increase the amount of digoxin in the body and may cause toxicity (PubMed, 2013).

Assessment of the severity of toxicity and etiology (accidental, unintentional, or deliberate overdose) altered drug metabolism due to decreased renal function or interaction with other drugs is necessary. Consideration of factors that influence treatment include age, medical history, chronicity of digoxin intoxication, severity of heart disease, and/or renal insufficiency and ECG changes (Katzung, Mastes, & Trevor, 2012). Symptoms of digoxin toxicity include anorexia, nausea, vomiting, diarrhea, visual changes, cardiac arrhythmias (1st degree, 2 nd degree " Wenckebach", or 3 rd degree heart block), atrial tachycardia with AV block, AV dissociation, accelerated junctional, unifocal or multifocal premature ventricular contractions, ventricular tachycardia, and ventricular fibrillation (Patel, 2011). Toxicity is usually associated with levels greater than 2 mg/ml. Low body weight, advanced age, impaired renal function, hyperkalemia, hyper-calcemia, or hypo-magnesium may cause digoxin toxicity. Other symptoms may include decreased consciousness, decreased urine output, difficulty breathing, and overall swelling (Brunton, Chabner, & Knollman, 2011).

Treatment will consist of emergency protocol if outside the hospital; this includes calling emergency medical services and CPR. Once the patient is in medical care, the treatment will depend upon the severity of symptoms and levels of digoxin in the body. Laboratory testing will include serum electrolytes, digoxin levels, and thyroid function tests. The patient will be placed on continuous cardiac monitoring with a 12 lead ECG obtained (Brunton, Chabner, & Knollman, 2011). The primary focus is to correct electrolyte levels; if hypokalemic administer potassium to reach a level of 4. 0 to 5. 5 mmol/L. Activated charcoal will be administered either orally or per

nasogastric tube in order to bind undigested digoxin. If bradycardic and symptomatic, atropine may be given intravenously. Peak cardiac effects of digoxin occur 3 to 6 hours after ingestion. Gastrointestinal symptoms precede cardiac manifestation. Neurological symptoms like fatigue and malaise are common. Visual disturbances occur with aberration in color vision, mostly yellow-green. Activated charcoal binds to the digoxin and prevents recirculation to the enterohepatic circulation. Cholestyramine may be used for chronic toxicity in patients with renal insufficiency. Continuous hemodynamic monitoring includes the ECG and 12 lead EKG (Brunton, Chabner, & Knollman, 2011). Prompt measurement of electrolyte levels (potassium, calcium, digoxin, BUN, creatinine, and CMP). Sodium bicarbonate may be administered to correct metabolic acidosis along with glucose and insulin to enhance potassium uptake by the cells (Brunton, Chabner, & Knollman, 2011). Magnesium may serve as a temporary antiarrthymic until digifab is available. Hypomagnesium increases myocardial digoxin uptake and decreases cellular sodium/potassium ATPase activity. Digibind (digifab or digoxin immune Fab) is an immunoglobulin fragment that binds with digoxin. In acute intentional overdose digibind (40 mg reconstituted with 4 ml sterile water) is administered 4 to 6 vials as a loading dose over 30 minutes as an emergent IV bolus. The bolus is followed by 0. 5 mg/minute for 8 hours and then 0. 1 mg/ minute for 6 hours (Patel, 2011).

For patients with chronic toxicity that are dependent on digoxin, the initial dose is twice the bolus. This avoids complete reversal of clinical effects of digoxin. Response is typically within 20 to 30 minutes after infusion, elimination half- life is around 16 hours. Digoxin levels are unreliable for one

to two weeks after therapy. Complications in long-term digoxin users, who receive digibind treatment administration are that it may precipitate worsening of heart failure as reversing the beneficial inotropic agent of digoxin causes hypokalemia and atrial arrhythmias with rapid ventricular response (Katzung, Mastes, & Trevor, 2012). Hypokalemia has occurred in patients treated with standard therapy as well as with Fab fragments. Clinically adverse phenomena have occurs in patients with immunotherapy. Other untoward effects of Fab include anaphylaxis and serum sickness, this is because it is a sheep protein, but this is uncommon. Recrudescence of digoxin toxicity is possible within 7 to 14 days because Fab is eliminated more rapidly than digoxin released from tissue binary sites. Plasmapheresis may be performed or the agent reinstituted in such cases (Patel, 2011).

If hemodynamically stable, bradycardia and supraventricular arrhythmias may be treated with observation and supportive measures. Ensuring hydration to optimize renal clearance, administering gastrointestinal binding agents may be used. For patients with rate related ischemia or neurological unstable digiFab is the treatment of choice (PubMed, 2013). In unstable premature ventricular contractions, lidocaine may be effective. In ventricular tachycardia the best response is to digiFab, but phenytoin and lidocaine are useful if Fab is ineffective or unavailable (Brunton, Chabner, & Knollman, 2011). They depress the enhanced ventricular automaticity without significant slowing of AV conduction. Phenytoin may reverse digoxin induced prolongation of AV nodal conduction. Phenytoin has been shown to dissociate the inotropic and dysrhythmia actions of digoxin, suppressing digoxin tachycardia without diminishing the contractile affect and can terminate SVT

induced by digoxin. Doses for lidocaine are 100 mg bolus with an infusion of 1 to 4 mg/minute. Phenytoin dosage is 100 mg every 5 to 10 minutes up to a loading dose of 15 mg/kg. Magnesium sulfate dosage is 2 gram over 5 minutes followed by an infusion of 1 to 2 g/hour, with magnesium levels drawn every one to two hours. Atropine may be given for bradycardia to improve sinus and AV node conduction by inhibiting vagal activity (Brunton, Chabner, & Knollman, 2011). Phenytoin may reverse digoxin induced prolongation of the action potential in myocardial cells and may suspend tachycardia, prolongs effective refractory period, and depresses spontaneous depolarization in ventricular tissue. Lidocaine is a class IB antiarrthymic that increases the electrical stimulation threshold of the ventricles, suppressing the automaticity of conduction through the tissue. It combines with sodium channels and inhibits recovery after repolarization, resulting in decreased myocardial excitability and conduction velocity (Brunton, Chabner, & Knollman, 2011). Magnesium sulfate possesses properties that slow the rate of sinoatrial node impulse formation and prolong conduction times (Brunton, Chabner, & Knollman, 2011).

Prevention of unintentional overdose (accidental overdose, interaction with other medications, or the altered metabolism due to renal insufficiency) is mostly through patient education. Instructing the patient in the correct dosage of the medication; that blood tests will be necessary to ensure appropriate dosage; suggesting daily recording of heart rate and blood pressure. Advise the patient that many drugs interact with digoxin, and to inform the physician and pharmacist of all medications, including over the counter and herbal medications, and if started on a new prescription.

Advising the patient to report any sign/symptoms associated with digoxin toxicity. Review signs and symptoms of toxicity with the patient.

If the overdose were intentional, the patient would need the same consults as any other patient undergoing treatment (cardiologist, nephrologist, medical toxicologist, regional poison control center) as well as psychiatric consult. Follow up appointments with the patient to monitor drug and electrolyte levels.

Reference

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