toxtidbits
the maryland poison center's monthly update. news. advances. information.

1-800-222-1222

October 2011

Acute Metformin Overdose

Metformin is a biguanide used as a first-line oral hypoglycemic medication in the treatment of type 2 diabetes. Product formulations include immediate release (e.g. Glucophage®), extended-release (e.g. Glucophage® XR), and in combination with sulfonylureas. Metformin decreases hepatic glucose production and increases peripheral insulin sensitivity with minor effect in decreasing intestinal glucose absorption.

The minimum toxic dose of metformin is not well defined. There are case reports in which severe toxicity developed after ingestion of 25 to 35 grams of metformin by adults. Children have tolerated ingestions up to 1700 mg. At therapeutic doses and with mild to moderate toxicity, nausea, vomiting, and abdominal pain can develop. With severe toxicity, metabolic acidosis with hyperlactatemia (lactic acidosis) can occur. Although this rare and potentially fatal complication mainly occurs in patients with renal insufficiency, hepatic disease, alcoholism, and advanced age, it has been reported in patients without risk factors following acute metformin overdoses. Lactic acidosis occurs through the inhibition of both lactate uptake and conversion of lactate to glucose by metformin. Signs and symptoms may be nonspecific and can include lethargy, confusion, hypotension, hypothermia, decreased cardiac output and tachypnea. Because metformin does not increase insulin secretion, hypoglycemia has rarely been reported with therapeutic use or acute overdose.

In an overdose with an immediate release product, a 4 to 6 hour observation period is recommended in asymptomatic patients; longer with sustained release products or unknown formulations. Activated charcoal should be considered if the patient presents soon after an acute ingestion. Patients with large ingestions should have serial (every 2 hours) monitoring of serum electrolytes and lactate levels. Dextrose IV is given if symptomatic hypoglycemia occurs or blood glucose is < 60 mg/dL. Intravenous sodium bicarbonate (1 to 2 mEq/kg IV bolus as a starting dose) should be given to patients who develop severe lactic acidosis, while monitoring for sodium overload. Hemodialysis is effective in improving acid-base status and clinical outcome in patients with severe lactic acidosis, but does not adequately remove the accumulated drug.

Bik-Wai Bilvick Tai
PharmD Candidate, Class of 2012
University of Maryland School of Pharmacy

DID YOU KNOW THAT… *there are reports of serotonin syndrome when linezolid or methylene blue are given to patients taking certain psychiatric drugs?*

The FDA recently released safety alerts about this potentially life-threatening drug interaction. Linezolid (Zyvox®, an antibiotic) and methylene blue (used to treat methemoglobinemia) inhibit monoamine oxidase A, an enzyme that breaks down serotonin. High levels of serotonin result when these drugs are given to patients who are taking a selective serotonin reuptake inhibitor (SSRI) or a serotonin norepinephrine reuptake inhibitor (SNRI), drugs commonly used for depression and anxiety disorders. Read more about serotonin syndrome in our September 2010 ToxTidbits at www.mdpoison.com .

Maryland Poison Center
University of Maryland School of Pharmacy

Subscribe to ToxTidbits *and read past issues at* www.mdpoison.com .