Chronic digoxin toxicity in elderly British Columbians

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A 76-year-old, 120 kg diabetic male presented to the emergency department with confusion and dizziness. His family reported that he had the "flu" for the last week with poor appetite and weakness. For the past 3 years he had been receiving digoxin 0.25 mg daily for heart failure. Other medications included furosemide, metoprolol, ramipril, clopidogrel, ASA, and insulin. His labwork showed a post-distributional serum digoxin level of 6.1 nmol/L (normal: 0.5 to 2.5), serum creatinine of 385 µmol/L (estimated GFR 26 mL/min; normal: 75-125), blood urea nitrogen of 26 mmol/L (normal: 2.5-8.0) and a serum potassium of 7.4 mmol/L (normal: 3.5-5.0). The patient appeared dehydrated with a heart rate of 30 beats per minute and an ECG showing third degree heart block. The patient was treated with intravenous fluids and 6 vials of Digibind® antidote. He recovered uneventfully.

Digoxin is commonly prescribed in the elderly for management of atrial fibrillation and heart failure at doses between 0.0625 mg and 0.25 mg once daily.(1) After absorption digoxin is widely distributed in tissues with a distribution phase of approximately 6 to 8 hours.(2) Digoxin has a narrow therapeutic window with post distributional therapeutic serum concentrations ranging from 0.5 to 2.5 nmol/L. Serum levels of approximately 1.3 nmol/L are recommended for optimal benefit in heart failure.(3)

Digoxin is eliminated by the kidneys and chronic toxicity typically occurs in elderly patients who develop an acute decline in renal function while taking prescribed doses. The cause of acute kidney injury in this population is usually multifactoral and the onset is unpredictable. Older patients have decreased renal reserve and often take medications such as ACE inhibitors, NSAIDS, or diuretics which may adversely alter renal function. In addition, older people have a decreased thirst drive which may lead to dehydration and pre-renal azotemia that is further exacerbated by any intercurrent illness associated with reduced oral intake. Elderly patients with acute kidney injury often experience a combination of these factors.

Symptoms of digoxin toxicity include visual disturbances, gastrointestinal symptoms, ataxia, weakness, hyperkalemia, bradycardia, and atrial or ventricular dysrhythmias.(4) Chronic digoxin toxicity can be insidious and life threatening.

Digoxin immune Fab (Digibind®) is an effective antidote for digoxin toxicity. It is prepared by immunizing sheep with a digoxin analogue coupled to an immunogenic protein. The resulting immune response produces digoxin-specific antigen binding fragments (Fabs), which are isolated and formulated into a sterile powder for injection. Following intravenous administration, the Fabs rapidly form stable complexes with unbound digoxin in blood and interstitial fluid, essentially inactivating the drug. The digoxin-Fab complexes are then excreted by the kidneys over a period of days. Doses are typically calculated using a post-distributional serum digoxin level and the patient's weight. The average dose for most patients presenting with chronic digoxin toxicity is 2 to 3 vials at a cost of $460.84 per vial.

Since the early 1990's the BC Drug & Poison Information Centre (DPIC) has offered an antidote replacement program for Digbind®. Physicians call DPIC for a consultation with a medical toxicologist and, if Digibind® is required, an appropriate dose is released via the hospital pharmacy. DPIC then couriers replacement Digibind® to the treating hospital. This program standardizes treatment for digoxin poisoned patients across the province, resulting in optimal care and reduced costs. It also allows for collection of epidemiological data on digoxin toxicity, which is unique in North America.

Approximately 23,000 British Columbians receive regular prescriptions for digoxin. In 2010 DPIC was consulted on 55 cases of chronic digoxin toxicity, 51 involving patients over the age of 65 years. Of these elderly patients, 47 required Digibind® and subsequently recovered uneventfully. Four patients were treated conservatively without Digibind®.

In summary, digoxin toxicity in British Columbia occurs primarily in the elderly causing morbidity to the patient and a significant cost to the healthcare system. Decreased renal reserve, susceptibility to dehydration, and adverse renal effects from other typically prescribed medications make this population vulnerable to acute kidney injury and subsequent digoxin toxicity. In patients for whom digoxin therapy is efficacious, using the lowest therapeutic dose along with monitoring of serum digoxin levels and renal function every several months may help to optimize therapy and reduce toxic events. Patients reporting symptoms consistent with

digoxin toxicity should be referred to a hospital emergency for assessment. Hospital administered digoxin-specific antigen binding fragments are effective antidotes for patients with significant digoxin toxicity.

Note: *GlaxoSmithKline Inc. recently announced the discontinuation of Digibind® injection as of November 14, 2011. DigiFab®, another digoxin immune fab product manufactured by BTG in the United States, will replace Digibind® in the marketplace. DigiFab® is distributed in Canada by Paladin Labs Inc. DPIC will continue with the antidote replacement program using DigiFab®.*

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We are grateful to all the First Nations who have cared for and nurtured the lands and waters around us for all time, including the x?m??k??y??m (Musqueam), Sk?wx?wu?7mesh U?xwumixw (Squamish Nation), and s?l?ílw?ta? (Tsleil-Waututh Nation) on whose unceded and ancestral territory our centre is located.