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Case Report

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Sudden Blindness in a Hemodialysis Patient on Digoxin

Lawrence McMahon[a, b], Sara Safari[a], Edward Smith[a], Wilma Tesoriero[b], Robert MacGinley[a, b, c], Stephen Holt[a, b]

Abstract

A hemodialysis patient with atrial fibrillation and ischemic heart disease, already taking amiodarone and diltiazem, presented with complete blindness after commencing digoxin. A highly elevated serum digoxin concentration was discovered and treated with Digibind®, with gradual but complete return of his vision. This case highlights a rare complication of digoxin potentiated by renal failure, medication interactions and poor communication.

Keywords: Dialysis; Digoxin; Blindness; Toxicity

Introduction

The concurrence of ischemic heart disease and atrial fibrillation is relatively common in dialysis patients. Digoxin remains a staple resource for rate control, but ventricular dysfunction, fluid and electrolyte imbalance, especially during dialysis, and the potential for toxicity can complicate management. The balance between rate control and toxicity is a particular concern in this group because of the relatively small therapeutic window and the associated difficulty in achieving and maintaining therapeutic concentrations. This is because drug clearance during dialysis is unpredictable and often compounded by lack of patient awareness, dose confusion or poor communication between medical staff. Other medications can also alter absorption and metabolism. We present a rare case of bilateral blindness due to digoxin toxicity which highlights these concerns.

Case Report

A 69-year-old chronic hemodialysis patient presented to the emergency department following progressive visual loss following his last hemodialysis session 3 days previously. At presentation, the patient described deterioration of his vision for the past 2 days, initially as bilateral "black and white spots" on a background of clear vision but progressing to the merest perception of movement from 1 m. He also complained of dizziness, bi-temporal headache and generalized weakness. He had end-stage kidney disease secondary to insulin-requiring diabetes and had received hemodialysis thrice weekly for 1 year, with ongoing management issues of intra-dialytic weight gain. Other co-morbidities included ischemic heart disease with multiple revascularization procedures (including seven coronary artery stents) and systemic hypertension. Relevant drug history included amiodarone (200 mg daily for 9 months) and diltiazem (180 mg modified release daily for 6 months). Digoxin (125 µg daily) had been added for better control of his atrial fibrillation (AF) 3 weeks prior to presentation, information which only became apparent to the dialysis team when he complained of visual loss.

On examination, he did not appear unwell but was bradycardic (about 40 bpm). His blood pressure was maintained at 119/51 mm Hg. Neurological examination confirmed very poor visual acuity and reduced limb power bilaterally. An ECG confirmed sinus bradycardia with first-degree atrioventricular heart block (PR 140 ms). He was admitted to the cardiac high-dependency area. Serum digoxin concentration was found to be 7.1 nmol/L (reference therapeutic interval: 0.6 - 1.0 nmol/L) and he was treated with digoxin immune FAB (Digibind®).

Ophthalmological review considered his fundoscopy findings normal and the patient was diagnosed with optic neuropathy secondary to digoxin toxicity. By day 3, he was able to discern the color green, followed (day 5) by red, blue and yellow. By day 6, he reported his vision as normal. Digoxin was considered to be the cause of the patient's visual

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[a]Department of Renal Medicine, Eastern Health, Monash University, Melbourne, Australia
[b]Eastern Health Integrated Renal Service, Eastern Health, Melbourne, Australia
[c]Corresponding author: Robert MacGinley, Department of Renal Medicine, Level 2, 5 Arnold Street, Box Hill, Victoria 3128, Australia. Email: rob.macginley@deakin.edu.au

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loss due to its recent commencement at an inappropriate dose, compounded by concurrent treatment with amiodarone and other medications, and subsequent toxic serum levels. The response to treatment within 3 days confirmed the diagnosis.

Discussion

Sudden loss of vision demands urgent investigation and treatment. Common causes include bilateral cavernous sinus thrombosis; copper deficiency; iatrogenic causes, for example digoxin or lignocaine; migraine, occipital stroke and posterior circulation TIA; tobacco amblyopia; and methanol intoxication. In this case, intracranial pathology was excluded by normal brain imaging. Causes of unilateral blindness, such as idiopathic optic neuropathy, central retinal artery or vein occlusion, and vitreous hemorrhage from diabetic retinopathy, rarely occur simultaneously bilaterally and were excluded by normal fundoscopy. Amiodarone has been reported to cause visual loss, but changes are usually slowly progressive and often permanent due to optic neuritis and atrophy [1].

Digoxin is a cardiac glycoside frequently used as a rate-control agent in AF and in heart failure. The narrow therapeutic index means that toxicity is common and gastrointestinal, neuropsychological and cardiac rhythm disturbances are early signs of toxicity. It is also known to cause visual disturbances, including dyschromatopsia and visual-field defects. Orally administered, it is highly bioavailable and has a very high volume of distribution V_d. It is renally excreted (up to 80%) as the intact molecule, but has a half-life ($t_{1/2}$) up to 44 h, even in patients with normal renal function largely due to the large V_d. The $t_{1/2}$ lengthens progressively as GFR falls and can be prolonged up to three-fold in end-stage kidney disease. Elimination is highly variable due to genetic polymorphisms for both renal and non-renal excretion pathways. Serum concentrations > 1.2 nmol/L have been associated with worse survival in patients with heart failure [2]. For urgent treatment of toxicity, the use of a digoxin binding antibody fragments (Digibind®) is useful, but it is important to note that hemodialysis is inefficient at removing both free digoxin and immune FAB fragments. Once Digibind® has been administered, measuring serum total digoxin concentrations is also unhelpful as levels remain high due to assay interference. Although measurement of serum free digoxin may be useful in such cases, it is rarely available.

Digoxin toxicity may be affected by changes in drug levels or in distribution. Some of the mechanisms are exemplified in the presentation of this patient.

Drug interactions by medications such as amiodarone and non-dihydropyridine calcium antagonists act through inhibition of the cellular efflux pump, P-glycoprotein (P-gp), for which digoxin is a substrate. Azoles and macrolide antibiotics exert similar inhibitory effects, resulting in both increased intracellular concentrations and reduced excretion. The rate-slowing effect of other cardiac drugs (such as beta blockers, calcium channel blockers and amiodarone) can potentiate the negative chronotropic effects of digoxin.

Second, the $t_{1/2}$ can be increased by drugs which reduce the GFR, such as angiotensin blockers, non-steroidal anti-inflammatory drugs and calcineurin inhibitors. Regular assessment of renal function should be performed on all patients taking digoxin.

Third, reduced muscle mass reduces the volume of distribution; hence, appropriate dosing should be based on lean body weight and adjusted if weight loss is noted. Loss of muscle mass in dialysis patients is common, but reduction in lean weight can be missed because target weights may not have been reset and all dialysis patients require repeated and regular reassessment of their fluid status.

Finally, drugs inducing electrolyte changes (for example, hypercalcemia or hypomagnesemia) can potentiate the adverse cardiac effects of digoxin by increasing myocardial uptake without changing the plasma concentration [3]. Electrolyte disturbance is common in renal impairment or dialysis patients.

The retinal abnormalities associated with digoxin toxicity are associated with reversible rod and cone dysfunction. Symptoms usually consist of halos around lights and defects in color perception (dyschromatopsia), although our patient seemed to describe visual scotomata initially. When tested specifically in one study of elderly hospitalized patients, red-green abnormalities were detected in a high proportion of elderly patients taking digoxin, even when levels were within the therapeutic range [4]. Digoxin-related blindness has been reported only rarely [5].

In practice, digoxin remains a valuable drug but both the patients and their caregivers should be aware that it can cause severe adverse effects. Consideration should be given to the use of a prescribing algorithm [6] and digoxin levels need to be checked regularly in high risk patients. Toxicity is often potentiated by concurrent drug use, particularly when multiple points of care are involved, and good communication is essential between all care-givers, especially in high-risk situations.

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