Digoxin toxicity in renal failure: role of the electrocardiogram

Introduction

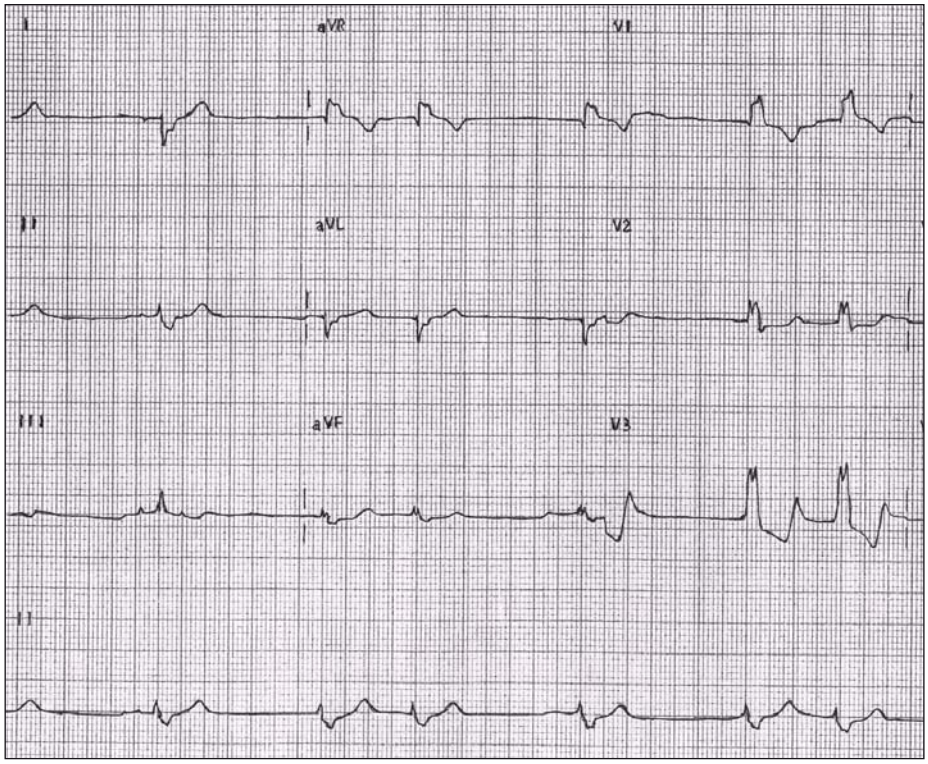
Digoxin toxicity can be a life-threatening emergency. This article describes a case highlighting the use of the 12-lead electrocardiogram in renal failure patients who are taking digoxin to diagnose and manage digoxin toxicity.

Case Report

A 66-year-old man with a past history of chronic persistent atrial fibrillation, chronic renal insufficiency and prior myocardial infarction presented to the emergency room with weakness and dizziness of 3 days' duration. On further questioning, the patient admitted to having some visual disturbances but denied any nausea, vomiting, chest pain, palpitations or syncope. The patient's medications on admission included digoxin, warfarin, carvedilol, pravastatin, erythropoietin, calcitriol and pantoprazole. Physical examination on admission revealed a regularly irregular pulse at 50/min and blood pressure of 100/60 mmHg with normal systemic examination.

The initial set of laboratory tests which had been done in the emergency room showed that he was anaemic (haematocrit 10 g/dl), potassium of 6.1 mg/dl and creatinine of 7.1 mg/dl. The admission 12-lead electrocardiogram is shown in *Figure 1*. The plasma digoxin level was 2.62 ng/ml in this patient. This patient was given Digibind (Fab antibody directed against digoxin) and haemodialysed. The patient's symptoms improved consequently with disappearance of atrioventricular block.

Figure 1. The rhythm strip shows evidence of high degree atrioventricular block with junctional escape rhythm, and an additional focus of origin of impulses (close to the first focus) in the atrioventricular junction showing the highly irritable nature of the myocardium.



Discussion

Digoxin has been used extensively in patients with atrial fibrillation and systolic heart failure over the last two centuries. Digoxin is cleared from the body predominantly by the kidneys, with insignificant contribution from hepatic metabolism in subjects with good renal function. Hence, it is not uncommon to find high levels of plasma digoxin in patients with renal insufficiency. Digoxin toxicity can result in cardiac as well as extra-cardiac symptoms. A significant proportion of such patients present with nausea, vomiting or visual disturbances (Kastor and Yurchak, 1967). Physical examination can often be misleading as seen in this case. Patients may present with a regular pulse giving a false impression of sinus rhythm.

Management of digoxin toxicity poses a difficult challenge in the setting of advanced renal disease. Contrary to popular belief, free digoxin is dialyzable. However, digoxin is highly bound to proteins, and has a large volume of distribution (5.6 litres/kg). Hence, dialysis is able to remove only a small proportion of ingested digoxin. The rate at which digoxin returns to plasma from body tissues is the rate-limiting factor in its clearance in patients with end-stage renal disease. Digibind (Glaxo Wellcome, Research Triangle Park, NC) (Fab directed against digoxin) antibody is especially useful in symptomatic patients with life-threatening arrhythmia and hyperkalaemia. The number of Digibind vials needed can be calculated as: vials of digoxin-specific Fab fragments = [digoxin level (ng/ml) x mass (kg)] ÷ 100

Digibind has a small volume of distribution (0.4 cc/kg), and is distributed primarily in extracellular space. Since it has 10^9–10^{10} times higher digoxin affinity compared to sodium pump receptors, it binds to free plasma digoxin and

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sequesters tissue-bound and albumin-bound digoxin. Decrease in plasma levels of free digoxin results in intravascular sequestration of tissue-bound digoxin leading to much higher concentration of plasma digoxin levels (Kramer, 1977; Rabetoy et al, 1990; Ujhelyi and Robert, 1995).

Digoxin measurement after administration of Digibind is of little value as the plasma digoxin is predominantly bound and inactive. In such patients, clinical improvement with electrocardiographic changes should be used as markers of improvement rather than plasma digoxin levels. Digibind–digoxin complex can be cleared from the blood through glomerular filtration or through hepatic metabolism.

Digibind has a relatively shorter half-life compared to digoxin leading to rebound increase in free plasma digoxin in 12–24 hours in patients with normal renal function. However, its elimination half-life is significantly prolonged in renal failure, and this delays the rebound by 12–130 hours in patients with renal insufficiency. This allows more time for renal as well as hepatic elimination of the complex. The free digoxin resulting from this dissociation can bind to circulating albumin, Digibind or diffuse into tissues. Hence, the rebound increase in plasma digoxin can have unpredictable effects (Valdes and Jortani, 1998).

The fear of delayed rebound in patients with end-stage renal disease necessitates longer periods of monitoring in these patients, and removal of the complex through plasma filtration if large amounts of digoxin are ingested (Peterson and Peterson, 1986). This patient was taking digoxin 0.125 mg daily. He required Digibind administration to sequester intracellular digoxin. This was followed by haemodialysis to remove excessive potassium. He was observed in the hospital for a few days. By the end of first week, his electrocardiogram returned to baseline and plasma digoxin returned to normal level.

Conclusions

Digoxin toxicity is not uncommon in patients with renal failure. Standard 12-lead electrocardiogram helps detect cases of digoxin toxicity early, and helps guide subsequent management. BJHM

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Computed tomography visualization of intracerebral haematoma 'pouring' directly into ventricular system

An 83-year-old woman was admitted to a university teaching hospital following an episode of collapse. She had a background history of atrial fibrillation, hypertension and ischaemic heart disease. She was on aspirin but no other anticoagulation medication. On admission, her Glasgow Coma Scale was 15/15 initially and when this deteriorated to 8/15, 1 day after admission, a computed tomography (CT) scan of the brain was done. The CT showed a 2 cm intraparenchymal haemorrhage within the right parietal lobe. Blood was seen to extend out of the haematoma and was seen to directly 'pour' into the adjacent lateral ventricle (*Figure 1*). Blood was also seen to lie dependently in the occipital horns of both lateral ventricles. The patient was treated conservatively and unfortunately deteriorated further and died the following day. BJHM

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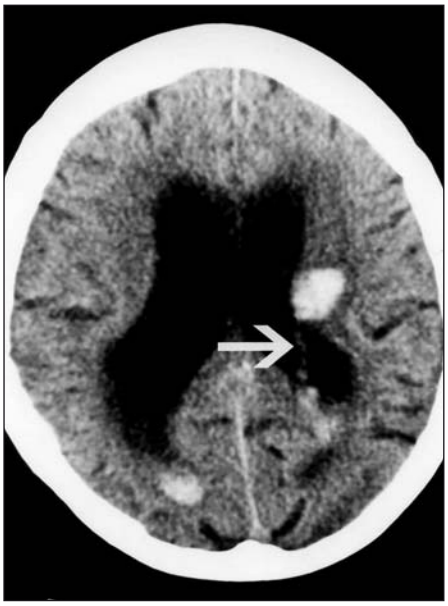

Figure 1. Axial non-contrast enhanced computed tomography scan of the brain demonstrates right parietal intracranial haemorrhage with direct extension into the adjacent lateral ventricle resulting in a 'pouring' effect.