Acute Digitalis Delirium Associated with Intravenous Digoxin Administration

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Abstract

A 77-year-old woman with a reduced ejection fraction was admitted to the hospital for atrial fibrillation with a rapid ventricular rate. Intravenous digoxin was used to slow her ventricular rate. On multiple occasions in the absence of elevated serum digoxin concentrations, she demonstrated multiple episodes of acute delirium associated with the acute intravenous administration of digoxin.

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Key Words

Digoxin • Toxicity • Atrial fibrillation

Introduction

Due to its narrow therapeutic range, digoxin toxicity is not uncommon. Compared to the classically reported adverse effects of gastrointestinal disturbances, cardiac dysrhythmias, and visual alterations, altered mental status and delirium are reported less frequently and are not always recognized as manifestations of digoxin toxicity. Delirium tends to occur most commonly in elderly patients with chronically increased serum digoxin concentrations [1]. We describe a case of repeated episodes of acute delirium occurring in response to administering intravenous digoxin in the absence of elevated serum digoxin concentrations.

Case Report

A 77-year-old white woman (84.8 kg) presented with complaints of shortness of breath and an increase in weight of approximately 20 pounds over the past month. Upon presentation, she was noted to be in new onset atrial fibrillation with a ventricular rate of 153 beats per minute. She was subsequently admitted to the hospital. The physical exam and laboratory investigation were both consistent with decompensated congestive heart failure. After initial aggressive diuresis, attempts at heart rate control, and anticoagulation therapy, a transesophageal echocardiogram revealed severely reduced left ventricular systolic function with an estimated left ventricular ejection fraction of 15%.

Two attempts of DC cardioversion failed to maintain the patient in sinus rhythm. The first attempt maintained sinus rhythm for only a few seconds. The second attempt was performed after 72 hours of an amiodarone intravenous infusion. The patient was maintained in sinus rhythm for only 12 hours. Therefore, pharmacotherapeutic management of the atrial fibrillation focused only on rate control.

Due to the relative contraindication of using a beta blocker or calcium channel blocker in a patient with acute decompensated heart failure, digoxin 0.25 mg was given intravenously for ventricular rate control. Immediately following administration, the patient demonstrated new onset transient confusion and

impaired short-term memory (she had no previous history of neuropsychiatric problems). Additional digoxin was not given until hospital day 5 when digoxin was again given for ventricular rate control. A dose of 0.25 mg were given intravenously at 1:28 p.m. and 6:45 p.m. Following the administration of each of these doses, the patient reported a feeling of malaise and both family and staff observed an alteration in the patient's mental status with delirium and agitation which occurred within minutes after each of these doses. The following day, the patient received an additional 0.125 mg dose of digoxin intravenously at 12:18 a.m. Once again, immediately after administration the patient was noted to be agitated and disoriented. She paced around her room until 5:00 a.m. at which time she sat in a chair and stared into space and was non-communicative. At this time, digoxin-induced toxicity was suspected; however, a serum digoxin concentration obtained at 2:43 a.m. was 1.0 ng/mL. To further test if patient's mental status changes were related to digoxin, a decision was made to closely monitor the patient when the next digoxin dose was administered later in the day. About 10 minutes after intravenous digoxin 0.25 mg was administered at 1:41 p.m., the patient once again became acutely confused, agitated, and delirious. She exhibited paranoid thoughts as well as a "flight of ideas" (making reference to airplanes on the roof and dogs barking in the room next door). This behavior continued for nearly an hour. A serum determination of all electrolytes obtained during this time period was normal. Seven hours after this digoxin dose, the patient's serum digoxin level was 1.5 ng/mL. Her mental status improved throughout the night and she was functioning normally the next day. No further digoxin was administered to the patient during her hospital stay. The patient did not demonstrate any further neuropsychiatric symptoms for the remainder of her hospitalization.

No signs of dysrhythmias associated with digoxin toxicity were seen upon a review of telemetry records during the hour that followed each of the digoxin doses. The patient only displayed continuous atrial fibrillation with occasional premature ventricular contractions.

Discussion

Although digoxin toxicity generally results from elevated serum digoxin concentrations, it can occur within concentrations considered "therapeutic," [2] especially in the presence of electrolyte abnormalities (hypokalemia, hypomagnesemia, hypercalcemia), hypothyroidism, hypoxia, or amyloidosis [2,3].

Digoxin toxicity can have a highly variable clinical presentation but is commonly manifested by gastrointestinal, cardiac, and/or visual symptoms [3]. Altered mental status, sometimes presenting as delirium, is a known but less commonly encountered problem which frequently is not recognized by health professionals as a manifestation of digoxin toxicity.

Cases of delirium associated with digoxin use have been well-documented [4-6], beginning with the initial description by Duroziez in 1874 [7]. The majority of these reported cases were associated with either elevated serum concentrations or supratherapeutic doses of digitalis preparations. One case reported by Grubb [4] described a 68-year-old woman with no history of mental illness who was admitted to the hospital with severe agitation after being started on oral digoxin 0.25 mg daily 6 months prior for her heart failure. The evaluation demonstrated elevated serum digoxin concentration of 3.5 ng/mL. The patient's mental status improved markedly after the digoxin was discontinued with a full recovery of mental status in 11 days. Shear and Sacks [5] described a 73-year-old woman on digoxin 0.25 mg daily demonstrated disorientation, agitation, and poor memory. A measured digoxin concentration in this patient was also elevated at 3.7 ng/mL.

Our patient demonstrated changes in mental status similar to the cases described above but the symptoms occurred in the absence of an elevated digoxin concentration. Eisendrath and Sweeney [6] described two elderly male patients exhibiting signs of delirium in conjunction with therapeutic serum digoxin concentrations. Both patients exhibited confusion, disorientation, significantly altered affect, and impaired short-term memory days to weeks after digoxin initiation. After the digoxin was discontinued, both patients were improved within 3 days with a complete recovery in 1 to 2 weeks. A possible explanation given for the neurologic events in the face of therapeutic

digoxin concentrations provided by Eisendrath and Sweeney [6] was the modestly low albumin concentration in these two patients. In contrast, the patient we describe above had a normal albumin concentration (3.8 mg/dL) and the confusion occurred within minutes of receiving single intravenous bolus doses of digoxin. Our patient's mental status returned to her baseline state within 24 hours after the last digoxin dose was administered and sooner after earlier doses.

Our case differs from those previously published in the literature in that the abnormal behavior occurred within minutes of administering intravenous digoxin on more than one occasion and not during any other time. These episodes also occurred in the face of two therapeutic serum digoxin concentrations, suggesting our patient's behavior was directly related to the intravenous digoxin administration as opposed to persistently elevated serum concentrations. Amiodarone has been implicated in causing altered mental status [8]. However, our patient did not demonstrate any altered mental status while on amiodarone alone, only shortly after being administered digoxin.

Amiodarone also has been implicated in reducing the tissue protein binding of digoxin, thereby reducing the volume of distribution of digoxin and causing an increase in digoxin serum concentrations and the risk for toxicity [9]. However, measured digoxin serum concentrations were not present in our patient and the patient was not on amiodarone the first time she demonstrated altered mental status after receiving digoxin.

A search of the literature did not demonstrate similar cases associated with the acute intravenous administration of digoxin. Due to its relatively rare incidence, the mechanism of acute digoxin induced

delirium is not well studied. Martin and Shad [10] did describe a patient who experienced a hypersensitivity reaction to an intravenous bolus dose of digoxin but their patient's mental status was not altered during the event.

When administered intravenously, digoxin has an approximate 6-hour distribution phase where its serum concentrations are elevated [11]. Toxicity is generally not seen at this time because digoxin is mostly in the systemic circulation rather than within tissues. Our patient appeared to be hypersensitive to the central nervous system effects of the higher digoxin serum concentrations that are present acutely following intravenous administration. A few hours later, once serum concentrations lowered to therapeutic concentrations as digoxin distributed into tissues, the patient consistently became asymptomatic.

In summary, we report a case of acute delirium directly associated with the intravenous use of digoxin on multiple occasions in an elderly woman, which were unrelated to elevated serum digoxin concentrations. Not only do health professionals need to be aware of the potential for digoxin to induce delirium when serum concentrations are elevated but also during acute intravenous administration. Early recognition and avoiding further digoxin administration in such instances is critical for the patient safety and the avoidance of potential adverse clinical outcomes.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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