Kidney Medicine

Dobutamine-Induced Myoclonus in a Peritoneal Dialysis Patient: Case Report

Edva Noel, Bolajoko Fayoda, Rizwan Rabbani, Yves-Smith Benjamin, Jean Lee, and Avrum Gillespie

Dobutamine is a weak beta-1 and a potent beta-2 adrenergic agonist commonly used to treat patients in cardiogenic shock. It enhances myocardial contractibility, increasing cardiac output. Myoclonus in patients receiving an infusion of dobutamine is rare and, although not fully understood, seems more common in patients with severe kidney failure. To our knowledge, this is the first reported case of dobutamine-induced myoclonus in a patient with kidney failure receiving peritoneal dialysis. Only 7% of the 518,749 patients of the United States requiring kidney replacement therapy receive peritoneal dialysis, with only a small unknown number of those with advanced heart failure manage with an infusion of inotropic medication. The low prevalence of combined advanced heart failure and kidney failure could partly explain this condition's rarity. In this study, we report the case of a 64-year-old woman with kidney failure receiving peritoneal dialysis in whom myoclonus developed 3 weeks after starting a dobutamine infusion for advanced refractory heart failure. Infectious and other pharmacologic causes of myoclonus were ruled out. Initially, uremia was suspected; however, despite increasing her peritoneal dialysis dose, it was only after discontinuing the dobutamine infusion that her myoclonus resolved.

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INTRODUCTION

Dobutamine is a weak beta-1 and a potent beta-2 adrenergic agonist used in critical care settings to manage cardiogenic shock and as a home inotrope for people with advanced heart failure. It enhances myocardial contractibility, increasing cardiac output. Commonly reported dobutamine side effects include cardiac dysrhythmias, angina, and eosinophilic myocarditis. Myoclonus is a rare but underrecognized adverse effect of dobutamine infusion.[1] Most reports of dobutamine-associated myoclonus are in patients with severe kidney failure (KF). We report the case of a 64-year-old woman with KF receiving peritoneal dialysis (PD) who presented with a concern of myoclonus 3 weeks after starting a home dobutamine infusion for advanced refractory heart failure.

CASE PRESENTATION

The patient was a 64-year-old woman who presented to this hospital with a concern of abnormal movements that she noticed since waking up on the day of the presentation. She denied experiencing fever, chills, headache, visual changes, mental status changes, or focalized weakness. She had a past medical history of hypothyroidism, pulmonary sarcoidosis, sleep apnea, secondary pulmonary hypertension, paroxysmal atrial fibrillation, dilated nonischemic cardiomyopathy with automated implantable cardioverter-defibrillator placement, and KF secondary to cardiorenal syndrome on receiving PD. She was on a home dobutamine infusion at 5 mcg/kg/min for her stage D systolic heart failure because she was not a candidate for other advanced therapies. Two weeks before this presentation, she was admitted to this hospital for *Staphylococcus epidermidis* bacteremia and worsening heart failure owing to an infected tunneled catheter used for milrinone infusion. Despite resolution of the infection, her blood pressure remained persistently low, with a systolic blood pressure of 60-70 mm Hg associated with dizziness. Thus, her milrinone infusion was switched to dobutamine infusion, which was started at 2.5 mcg/kg/min and then increased to 5 mcg/kg/min, which improved hypotension and its symptoms. She was discharged home on that dose. Her family history was notable for ischemic heart disease in her mother, nonspecific heart disease in her brother and father, and nonspecified heart failure in another brother; however, there was no family history of kidney disease or movement disorders. She had quit smoking cigarettes 16 years earlier. She did not drink alcohol or use illicit drugs—she was only allergic to codeine, which causes itchiness. Her home medication included the following: apixaban, 5 mg twice daily; fludrocortisone, 0.1 mg daily; atorvastatin, 20 mg nightly; calcium acetate, 667 mg 3 times daily with meals; and cinacalcet, 30 mg daily.

On physical examination, she was in no distress and was afebrile, with a blood pressure of 114/78 mm Hg, a respiratory rate of 18 breaths/min, and an oxygen saturation level of 99% on a 2-L/min nasal cannula. The heart was at a controlled rate, and the lungs were clear on auscultation. The abdomen was soft, and the PD catheter exit site was clean and nontender. The legs were with trace edema.

Neurological examination was remarkable for a patient alert and oriented in time and space. There was no asterixis; however, she exhibited an abnormal movement best described as myoclonus with a brief, lightning-like jerking affecting the neck and upper extremities, sparing the lower

extremities and the trunk. Intentional movements of the affected body parts exacerbated the jerking. The cranial nerves were intact, and there was no focal neurological deficit. A head computed tomographic scan without contrast showed mild-to-moderate chronic white matter disease. A complete blood count was remarkable for mild leukocytosis (11,400 cells/uL), anemia with a hemoglobin concentration of 9.9 g/dL, a serum urea nitrogen concentration of 54 mg/dL, a serum creatinine concentration of 16.3 g/dL, a potassium concentration of 3.7 mEq/L, and a serum sodium concentration of 134 mEq/L corrected with a calcium concentration of 9.4 mg/dL. The peritoneal fluid cell count was 22 WBC/μL. Other potential causes of myoclonus were ruled out, including drugs—gabapentin was discontinued during the previous admission—and infectious causes—negative microbiology data and the jerks were not consistent with chorea. Despite the abnormal movements being atypical for uremia, this was ruled out by increasing her PD dose from her home dose of 11,000 mL/d (KpT/V 2.33) to 12,000 mL/d (KpT/V 2.2). On day 2, the serum creatinine concentration was at her baseline, 13.4 mg/dL; however, her myoclonus persisted. We suspected dobutamine as the cause of the myoclonus; hence, it was discontinued, milrinone was restarted, and her dialysis dose was decreased to 5 exchanges/d (~10,000 mL/d). Her symptoms resolved by hospital day 4. The patient was discharged home and has had no recurrence of myoclonus.

DISCUSSION

Dobutamine-induced myoclonus is a rare or perhaps underrecognized condition. A review of the literature yielded only 3 previous reports on this disorder.[1-3] It is not on the list of the adverse effects of this drug by Micromedex.[4] The low prevalence of combined advanced heart failure and KF could partly explain this condition's uncommonness. Milrinone infusion is the most common inotropic medication used in this patient population; however, in some refractory cases, especially those with persistent hypotension, dobutamine is used. Advanced therapies for this subset of patients include mechanical circulatory support as destination therapy or as a bridge to heart transplants. Our patient was deemed to not be a candidate for advanced therapies owing to her multiple other medical comorbid conditions.

We found no data on the exact number of patients with advanced heart failure who were receiving inotropes and dialysis or with advanced KF; however, as of 2020, 270 patients were on the waitlist for a combined heart and kidney transplant.[5] Hence, we assume that only a tiny fraction of this already low number of patients with combined advanced heart and KF are simultaneously receiving inotropes and dialysis.

The mechanism by which dobutamine induces myoclonus is not well understood. Myoclonus is particularly interesting to nephrologists because it can be seen in acute kidney injury and chronic KF either as a manifestation of accumulation of medications or as uremic toxins.[6,7] Etiologically, Marsden et al[8] classified myoclonus as physiologic, essential, epileptic, and symptomatic. Metabolic and toxic myoclonus are 2 subclasses of symptomatic myoclonus and comprise KF and drug-induced myoclonus, respectively.[8] Uremic myoclonus is a well-known manifestation of end-stage KF and is characterized by involuntary jerks of the extremities and, often, the trunk. It is usually associated with a flapping tremor and resolves with dialysis.[7] Several drugs have been linked with myoclonus, including antiepileptic medications, such as phenytoin and lamotrigine; antibiotics, such as levofloxacin and cefepime; and selective serotonin reuptake inhibitors.[9]

Dobutamine is a cardioselective synthetic sympathomimetic amine with a structure similar to that of isoproterenol and dopamine. Dobutamine is metabolized by catechol-O-methyl in the liver and eliminated through urine as conjugates of dobutamine and 3-O-methyl dobutamine. The latter is an inactive metabolite of dobutamine; however, the effect of its accumulation is unknown. One observation is that all previously reported cases occurred in patients with kidney disease.[1-3] Wierre et al[1] first reported a series of 6 patients, in which he observed myoclonus 2-3 days after starting on a continuous dobutamine infusion to treat their cardiogenic shock. The patients were 2 men and 4 women with a mean age of 68.6 ± 6.35 years. They had acute kidney injury from acute decompensated heart failure, with a creatinine clearance of 15.5 ± 2.5 mL/min/1.73 m^2—none of the 6 patients required dialysis. In a proposed explanation of the condition, Wierre et al[1] hypothesized an increased uptake of dobutamine by the central nervous system owing to a cumulation of 2 mechanisms facilitated by KF: (1) a decrease in dobutamine biotransformation and (2) an increased blood-brain barrier permeability caused by P-glycoprotein (Pgp) inhibition 1. In the case reported by Boord et al,[3] a drug-drug interaction leading to inhibition of Pgp1 was emphasized. In their patient, amiodarone, simvastatin, and carvedilol were identified as potential inhibitors of Pgp1. Our patient was receiving atorvastatin and cinacalcet, 2 potential inhibitors of Pgp1. The neurotoxicity is proposed to be from a direct effect of the beta-adrenergic agonist properties of dobutamine on the central nervous system owing to its excessive concentration in the central nervous system. Similarly, there have been reports of myoclonus caused by a high cumulative dose of beta-adrenergic agonists used to treat acute exacerbation of chronic obstructive lung disease.[10,11] In all cases, myoclonus resolved after discontinuing dobutamine or the beta-adrenergic agonists. An exciting aspect of our case is that it is, to our knowledge, the first report of dobutamine-associated myoclonus in a patient with KF receiving PD.

This case adds to the growing evidence-based research of dobutamine-induced myoclonus. It seems to be a rare side effect in a small but comorbid group of patients with both advanced heart failure and KF, and nephrologists, cardiologists, and intensivists need to be aware of this side effect especially because this is not listed as a side effect by the maker of this drug. The exact pathophysiology is not well understood; however, an estimated glomerular filtration rate of <15-20 mL/min/1.73 m^2 potentiated by drugs that inhibit Pgp1 seems essential. Our case is unique because it is, to our knowledge, the first to report dobutamine-induced myoclonus in a patient with KF receiving PD. Although we are convinced that stopping dobutamine was key to the resolution of myoclonus, we cannot exclude the probability that the 24-hour increase in dialysis dose might have accelerated her recovery. As more and more cases are reported, further analysis will undoubtedly shed light on the unknown aspects of this condition.

ARTICLE INFORMATION

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