Penile Gangrene following Use of Midodrine Hydrochloride for Hypotension in a Male Diabetic Patient Undergoing CAPD

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Abstract: A 74 year old diabetic nephropathy patient had symptomatic postural hypotension with normal left ventricular function. As there was no significant response to discontinuation of antihypertensives, he was started on midodrine hydrochloride, which led to a significant symptomatic improvement. After 3 weeks, he developed a gangrenous patch over his glans penis. A Doppler ultrasound showed deceased blood flow in the penile artery. The penile artery which was probably already undergoing arteriosclerotic changes, deteriorated further due to vasoconstriction. Midodrine hydrochloride has to be cautiously used in dialysis patients.

Keywords: Diabetic nephropathy, midodrine hydrochloride, penile gangrene, peritoneal dialysis, postural hypotension

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is given as a renal replacement therapy (RRT) for patients who prefer to have a home dialysis in India. The most common complications seen are catheter related infections and cardiovascular events. Challenges faced with volume management and dry weight adjustment can be very tricky in patients on home peritoneal dialysis using different concentrations of glucose in the dialysis fluid to achieve ultrafiltration. Lately, multifrequency bioimpedence spectroscopy (MFBS) is used as a useful tool in volume management preventing the development of hypervolemia or hypovolemia.

There is a subset of CAPD patients who develop significant postural hypotension related to diabetic autonomic insufficiency in spite of having good left ventricular function (1). Volume depletion from excessive ultrafiltration, heart failure and antihypertensive medications include other causes of hypotension in CAPD patients(1). The recommendations for management of hypotension are reduction in concentration of hypertonic dialysate, discontinuation of antihypertensives and diuretics, and treatment of autonomic insufficiency with drugs such as midodrine hydrochloride (1,2). Midodrine hydrochloride is a vasoressor agent which acts on α1 adrenergic receptors in blood vessels, producing an increase in vascular tone, and hence is being used widely as an oral molecule for treatment of postural hypotension with variable success (2).
Here we describe a type 2 diabetic nephropathy patient on CAPD who had profound hypotension with normal left ventricular function (LVF). He was treated with midodrine hydrochloride and he developed, within 3 weeks, a penile gangrene due to ischemia to the penile artery.

Case Report

A 74 year old male patient weighing 155 pounds, with type 2 diabetic nephropathy, who was undergoing continuous ambulatory peritoneal dialysis (CAPD) since 2013, relocated to our unit for continuing care. He was doing 3 two liter exchanges of Dianeal®, with 1.5 % X two exchanges and 2.5 % X one exchange. He complained of poor appetite with generalized pruritis. His blood pressure was 70/50 mm Hg in sitting position and 60/40 mm Hg in standing position with a pulse rate of 74 beats per minute. He was doing exchanges only during the day with 8 hours night dry. He was on carvedilol 3.125 mg and furosemide 100 mg a day. His echocardiogram showed concentric left ventricular hypertrophy with ejection fraction 65 %, annular calcification of the posterior mitral leaflet and sclerosed aortic valve. Hemoglobin was 9.9 g/dL, WBC count 14,600 cells / cu mm, platelet count 241,000 / cu mm, creatinine 4.7 mg/dL, blood urea 136 mg/dL, total protein 6.5 g/dL, albumin 2.6 g/dL with normal serum electrolytes. His blood sugar was not optimally controlled with insulin injection. Serum calcium was 7.7 mg/dL, phosphorous was 7 mg/dL and iPTH was 270.7 pg/L. He had a urine output of 500 to 600 mL/day and an ultrafiltration of 800 to 1000 ml by CAPD. He was on sevalamer carbonate 800 mg three times a day. His oxygen saturation (SpO2) was 97% at room air. As he had significant symptomatic hypotension with inability to sit or stand, carvedilol and furosemide were discontinued. However his systolic blood pressure continued to be less than 80 mm of Hg. He was initiated on Midodrine hydrochloride 5 mg 3 times a day for symptomatic hypotension, the dose was later stepped up to 10, 5 and 10 mg per day. His blood pressure improved to 100/40 mm Hg in sitting position. He had clinical evidence of balanitis and erectile dysfunction. After 10 days of initiation of midodrine hydrochloride, he complained of discomfort in the penis, and denied any history of trauma. The glans penis was found to be gangrenous for approximately 2 cm length, as shown in figure 1. He also developed an erythematous maculopapular skin rash in the extremities, thorax and anterior abdominal wall, which was not pruritic. Hence a biopsy of the skin was done which did not show...
evidence of vasculitis, and had histological features suggestive of acquired perforating dermatosis, which has been reported in patients with chronic kidney disease. A Doppler ultrasound study showed decreased blood flow in the penile artery, as shown in figure 2. He is being conservatively treated with regular follow up and midodrine was temporarily discontinued. However, he was advised nocturnal supine dialysis, 3 exchanges spanning 12 hours at night which he refused. He continues on CAPD and restarted midodrine at 10, 5 and 10 mg per day as he felt better with a blood pressure of 110/60 mm of Hg, and he is able to ambulate. His blood sugar is currently controlled with injection human mixtard. Two months later, the gangrenous portion of the glans penis is undergoing auto amputation. A body composition monitoring was done after initiating him on midodrine, and the values showed decreased volume status and increased fat content.

**Discussion**

Postural hypotension which is symptomatic, is a challenging task in diabetic patients on CAPD. The use of body composition monitoring for volume status guides in adjusting the concentration of dialysis fluid, to avoid hypervolemia and hypovolemia. CAPD which provides 24 hour ultrafiltration, produced profound hypotension in our patient along with variable volume of daily urine output, furosemide and carvedilol therapy, hypoalbuminemia and autonomic insufficiency. In spite of discontinuing furosemide and carvedilol, the patient remained hypotensive and hence midodrine was added as a rescue therapy to prevent hypotension, and was beneficial. Although, we have used midodrine in many patients who have hypotension, this is the first instance where a penile gangrene developed following therapy. Penile gangrene has also been reported in ESRD patients due to circulatory insufficiency caused by severe arteriosclerosis(3-5). Midodrine acts on alpha-1 adrenergic receptors and produces vasoconstriction. We postulate that the already ischemic penis due to arteriosclerosis deteriorated, leading to gangrene, with the use of midodrine hydrochloride. To our knowledge, this is the first case report of penile gangrene in a CAPD patient, following the use of midodrine hydrochloride.

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**References**


