Unexplained Hypotension and Exertional Dyspnea in a Night-Cycled Peritoneal Dialysis Patient—A Rare Form of Icodextrin Hypersensitivity

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In recent years, icodextrin 7.5% has been used in PD as an alternative to glucose to achieve sustained reliable ultrafiltration (UF) and clearance without adversely increasing glucose absorption. Icodextrin is generally well tolerated. The most commonly reported adverse events are cutaneous reactions. We report a rare form of hypersensitivity to icodextrin 7.5% that was accompanied by dyspnea and symptomatic hypotension, without increased UF to account for the observed hypotension.

Icodextrin produces symptomatic hypotension in up to 40% of patients by a known mechanism of increased UF and corresponding weight loss. However, it can also produce symptomatic hypotension accompanied by several other systemic symptoms in a hypersensitivity reaction. Discontinuation of the icodextrin results in prompt resolution of those symptoms. Treating nephrologists must be aware of this rare form of icodextrin hypersensitivity.

Key words
Hypersensitivity, icodextrin

Background
In recent years, icodextrin 7.5% has increasingly been used in peritoneal dialysis (PD) patients as an alternative to glucose for simultaneously achieving sustained, reliable ultrafiltration (UF) and enhanced clearance, while not adversely increasing glucose absorption and therefore exacerbating diabetic control problems in susceptible patients (1–3). Icodextrin is generally well tolerated, with few side effects (1–3). The most commonly reported adverse effects of icodextrin are cutaneous hypersensitivity reactions (4–11). Even though icodextrin is known to produce symptomatic hypotension in up to 40% of patients, necessitating a reduction in the use of antihypertensive medications, that hypotension is usually correlated with weight loss and concurrent higher achieved UF in PD patients (12).

Recently, we used icodextrin to manage a 76-year-old obese white woman with diabetic end-stage renal disease on night-cycled PD (IPD). She subsequently presented with severe symptomatic hypotension (systolic blood pressure: 60 – 70 mmHg) absent significant UF or weight loss. The hypotension was also associated with other systemic symptoms such as early-morning upper-respiratory flu-like symptoms, dysgeusia, fatigue, and dyspnea. An extensive workup (cardiopulmonary, endocrine, and other) was negative. As a last resort, icodextrin hypersensitivity was suspected, and icodextrin was withdrawn from the patient’s IPD prescription. All her symptoms resolved promptly and dramatically within 36 hours of icodextrin discontinuation.

Our patient demonstrates an unusual and rare form of icodextrin hypersensitivity reaction, producing a syndrome of multiple symptoms (dyspnea; symptomatic hypotension with orthostatism, lightheadedness, fatigue, and malaise; and dysgeusia) in the absence of any cutaneous reaction and without increased UF or weight loss. The symptoms promptly resolved after discontinuation of icodextrin and continuation of IPD with dextrose-containing solution only.

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Case description

Our patient had a prior history of a coronary artery bypass graft procedure in 2005 and a subsequent aortic valve replacement for severe aortic stenosis in 2011. She had done well for more than a year (2012–2013) on a 9-hour, night-cycled, 5-exchange IPD prescription (2.3 L of dextrose solution per exchange), without any daytime dwell. She met monitored weekly Kt/V targets. At the time, she had also maintained significant residual renal function.

Peritonitis was treated in August 2013. With observation of failing residual renal function after the peritonitis episode, delivered weekly Kt/V declined. As a result, an additional icodextrin day dwell (morning fill volume) was added to the IPD prescription in early September 2013.

After the addition of icodextrin, the patient’s Kt/V quickly improved to 1.9 from 1.57, but without any observed additional UF or weight loss. However, from mid-September 2013, our patient started to experience increasing lightheadedness; fatigue; dyspnea that was worse with exertion, including mere conversation; early-morning flu-like symptoms of the upper respiratory tract; dysgeusia; and low at-home blood pressure (BP) measurements. On admission to the critical care unit during the first week of October 2013, she was lightheaded and somnolent, and she complained of increasing fatigue and exertional dyspnea. She was otherwise alert, oriented in all three relevant dimensions, nonfocal, and not depressed. Blood pressure was 64/44 mmHg, and pulse was 84 bpm with a regular heart rhythm. Orthostatism was not attempted.

Chest and cardiac examinations were unremarkable. The patient was not pale and had no evident peripheral edema. Her weight, at 98 kg, was unchanged from baseline. Hemoglobin was 11.4 g/dL, basic metabolic profile was otherwise unremarkable, and liver profile tests were normal. Thyroid function tests—including thyroid-stimulating hormone, free T3, free T4, and morning cortisone levels—all fell within normal limits. Chest radiography was stable, electrocardiography measures were unchanged, and acute myocardial infarction was ruled out by serial electrocardiography and troponin I tests. Left ventricular ejection fraction was stable at 60% on echocardiography, without any wall-motion abnormalities, and the stented tissue aortic valve prosthesis appeared normal.

After this extensive, albeit negative, workup of our patient’s symptoms, the possibility of icodextrin hypersensitivity was entertained (13–15). Icodextrin was discontinued from the IPD prescription. Within 24 hours, the patient was already feeling better. At 36 hours, she was asymptomatic. Blood pressure on day 2 of her hospitalization was 150/70 mmHg, and pulse was 88 bpm. On orthostatic testing, systolic BP was 146 mmHg sitting and unchanged at 147 mmHg standing.

The patient has since remained asymptomatic (through March 2014), while continuing on night-cycled IPD using only dextrose-based solutions (2.5% and 4.25%) during an extended exchange period (6 exchanges over 11 hours). On her current modified icodextrin-free IPD prescription, she has continued to maintain adequate weekly Kt/V. As a consequence of the increased glucose exposure since icodextrin discontinuation, she has had to increase her insulin dose to achieve the desired HbA1c goal (1–3,14).

Conclusions

Symptomatic hypotension has been reported in up to 40% of PD patients. Typically, observed changes in systolic BP are significantly correlated with weight loss because of a higher achieved UF volume with icodextrin than with glucose—2.27% solution, for instance (12). Indeed, many patients require a reduction in their antihypertensive medications to manage the resultant hypotension (12).

The hypersensitivity reactions most commonly reported with icodextrin use are cutaneous adverse effects, and those cutaneous reactions to icodextrin are estimated to occur in up to 15% of patients (4–11,16). Other rare icodextrin hypersensitivity reactions that have been reported include cases of allergic sterile peritonitis (13,15,17–20). Even more rarely associated with the use of icodextrin is a hypersensitivity-type reaction that includes dyspnea, symptomatic hypotension, flu-like symptoms, fatigue, generalized weakness, and an abnormal sense of taste (13–15). Most pertinently, and as was evident in our case report, the symptomatic hypotension in that hypersensitivity setting is a component of a set of other apparently unrelated, albeit systemic, symptoms (13–15). Most importantly, for the purposes of differential diagnosis, the hypotension is dissociated from any weight loss or increased UF volume (14).

We posit that physicians must be aware of this rare form of icodextrin-induced hypersensitivity reaction, because prompt discontinuation of icodextrin while continuing PD with only dextrose-based solutions results in rapid resolution of the symptoms. Prompt
discontinuation of icodextrin can prevent further unnecessary and potentially hazardous and invasive diagnostic procedures during a workup for symptomatic hypotension in such patients.

The exact mechanisms of this hypersensitivity reaction remain speculative at this point. Some studies have suggested that dextran antibodies are potentially the culprits in some icodextrin reactions in PD patients (10).

Acknowledgments
This case report is dedicated to all our patients, past, present, and future, without whom there would be no case reports.

Disclosures
No conflicts of interest declared.

References

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