



> THE PATIENT

90-year-old man

> SIGNS & SYMPTOMS

- Dyspnea
- Lower extremity edema
- Limitations in daily activities

CASE REPORT

Ryan Paulus, DO (PGY2);

Brian Schmidt, DO

Department of Family
Medicine, University
of North Carolina,
Chapel Hill (Dr. Paulus);
OhioHealth, Columbus
(Dr. Schmidt)

 ryan_paulus@med.unc.edu

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> THE CASE

An obese 90-year-old White man presented for a 1-month follow-up with his family physician after being hospitalized for an acute exacerbation of heart failure (HF). In addition to New York Heart Association (NYHA) Class III heart failure with reduced ejection fraction (HFrEF), he had a history of tobacco abuse, hyperlipidemia, atrial fibrillation, coronary artery disease, stage 3 chronic kidney disease, and benign prostatic hyperplasia. The patient's family accompanied him during the visit to discuss hospice care.

The patient complained of persistent shortness of breath that limited his activities of daily living (ADLs) and lower extremity and scrotal edema. He denied chest pain, orthopnea, paroxysmal nocturnal dyspnea, ascites, nocturia, and nocturnal cough.

The patient had undergone a coronary artery bypass graft 23 years earlier. His HF was being managed with metoprolol tartrate 25 mg bid, spironolactone 25 mg/d, and furosemide 80 mg/d.

Examination revealed bilateral 3+ pitting edema in the lower extremities midway up the shin, crackles to the inferior scapula bilaterally, and a 3/6 systolic murmur with regular rate and rhythm. The remainder of the physical exam was normal. The patient's vitals were within normal limits, with an oxygen saturation of 90%.

The patient's most recent chest x-ray demonstrated mild cardiomegaly. An echocardiogram showed an ejection fraction of 44% with severe bi-atrial enlargement, moderate-to-severe mitral regurgitation, and mild-to-moderate aortic insufficiency. His brain natriuretic peptide (BNP) was 915 pg/mL (normal range for patients ages 75-99 years, < 450 pg/mL).

THE DIAGNOSIS

The differential diagnosis for the patient's shortness of breath included chronic obstructive pulmonary disease secondary to his smoking history, pulmonary embolus, respiratory infection, anemia, and medication-related adverse effects. The patient's history of renal disease merited consideration of a nephrotic syndrome causing low albumin, which could explain his edema. Another possible cause of the edema was venous insufficiency. However, given the patient's extensive cardiac history, the most likely explanation for his shortness of breath and edema was congestive HF that was unresponsive to the current diuretic regimen.

Several changes to the patient's medications were made. Lisinopril 2.5 mg/d was started due to the mortality benefit of angiotensin-converting enzyme inhibitors in the treatment of HFrEF.¹ Metoprolol tartrate 25 mg/d was transitioned to metoprolol succinate 50 mg/d, as only the longer-acting succinate version has shown mortality benefit in HFrEF.¹ (Other beta-blockers with mortality benefit include carvedilol and bisoprolol.¹) The furosemide 80 mg/d was replaced with torsemide 100 mg/d to provide an enhanced diuretic effect for symptomatic relief. The spironolactone dose was not increased due to concerns about

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the patient's renal function. Of note, spironolactone was included in the patient's regimen based on his NYHA classification, as well as the potential mortality benefits and improvement in edema seen in HFrEF patients.¹ Spironolactone can be used with loop and/or thiazide diuretics in the treatment of HF.

Within 5 days, the patient had lost 6 lb and his oxygen saturation had improved from 90% to 95%. He reported improvements in his breathing and was able to move around more easily.

DISCUSSION

There are several possible explanations for torsemide's superior diuretic effect in this patient. Unlike furosemide, torsemide absorption is not influenced by intestinal edema, which is commonly seen in patients with HF. It has a longer half-life and improved bioavailability that is not altered by food intake. Torsemide also inhibits the actions of aldosterone through its interaction with the renin-angiotensin-aldosterone system and aldosterone receptor, leading to further diuresis and reduced cardiac remodeling.²

■ **What the evidence shows.** The TORIC trial was an open-label, nonrandomized, post-marketing surveillance study of 1377 patients with NYHA Class II–III HF who received diuretic therapy with torsemide 10 mg/d, furosemide 40 mg/d, or another diuretic for 12 months.³ Significantly lower total mortality and cardiac mortality was found in the torsemide group; in addition, a significantly greater proportion of patients in the torsemide group showed improvement in NYHA classification.³ Murray et al reported a reduction in hospitalization rates with torsemide therapy vs furosemide therapy in a randomized trial of 234 HF patients (32% vs 17%, $P = 0.01$).⁴ The ASCEND-HF trial, a large international acute HF trial comparing torsemide with furosemide, demonstrated a nonsignificant reduction in 30-day and 180-day events (all-cause mortality or HF hospitalization) in those receiving torsemide, after risk adjustment.⁵ Torsemide has also been shown to improve quality of life compared to furosemide.⁶

Preliminary results from the TORNADO

trial,⁷ a multicenter randomized controlled trial, demonstrated superior symptom improvement in HF patients taking torsemide compared to those taking furosemide.⁸ The preliminary endpoint—a composite of improvement in NYHA class, improvement in distance of at least 50 m during a 6-minute walk test, and a decrease in fluid retention of at least 0.5 ohms at 3-month follow-up—was achieved by 94% and 58% of patients on torsemide and furosemide, respectively ($P = 0.03$).⁸ A total of 7 patients (3 in the torsemide and 4 in the furosemide group) were hospitalized for worsening HF during the follow-up period.⁸

A 2020 meta-analysis of more than 19,000 patients compared furosemide to torsemide and found a number needed to treat (NNT) of 23 to prevent a hospitalization due to HF; an NNT of 5 for improvement in NYHA functional status; and an NNT of 40 for reduction in cardiac mortality.⁹

■ **Our patient** reported feeling “great” at the 6-week follow-up appointment, with significant improvement in breathing and ability to perform his ADLs. His NYHA classification improved to Class II. He had lost 26 pounds (back to his weight 9 months prior), and his oxygen saturation was 97%.

On exam, the bilateral peripheral edema in his lower extremities had improved from 3+ to 1+, with the edema extending just distal to the mid-shin. Only mild crackles were present at the lung bases. The remainder of his physical examination was unchanged. His vital signs were within normal limits with no signs of hypotension. A basic metabolic panel was obtained to confirm his electrolytes were still within normal limits. His BNP had decreased to 230 pg/mL.

The patient declined the referral for hospice evaluation due to the significant improvement in his symptoms.

THE TAKEAWAY

A significant clinical improvement and improved quality of life were achieved with the transition from furosemide to torsemide. It is apparent that the patient's furosemide had an inferior diuretic effect compared to torse-

mid, whether that be secondary to his dose or due to the unpredictable nature of furosemide's bioavailability, especially in the setting of intestinal edema.

A growing body of literature⁹⁻¹¹ suggests torsemide's superiority over furosemide with no signs of increased adverse effects. Although additional prospective, head-to-head trials are needed, at this point in time it is appropriate to consider the use of torsemide in a patient with HF who does not seem to be fully responding to furosemide. **JFP**

CORRESPONDENCE

Ryan Paulus, DO, 590 Manning Drive, Chapel Hill, NC 27599; ryan_paulus@med.unc.edu

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