

Solifenacin-Induced Small Bowel Pseudo-Obstruction

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An 89-year-old woman was admitted to Johns Hopkins Hospital with a small bowel obstruction and symptoms of urinary retention. She had been started on solifenacin for bladder overactivity 10 days prior to her presentation. Withdrawal of the solifenacin resulted in a full recovery, which has persisted for greater than 6 months without surgical intervention. This is the first reported case report of small bowel pseudo-obstruction due to solifenacin. *Journal of Hospital Medicine* 2008;3:176–178. © 2008 Society of Hospital Medicine.

KEYWORDS: solifenacin, Vesicare, small bowel obstruction, urinary retention, intestinal pseudo-obstruction.

Solifenacin succinate, an antimuscarinic agent, is approved for the treatment of overactive bladder and described as “well tolerated” in the elderly.¹ We present the case of solifenacin-induced small bowel pseudo-obstruction in an 89-year-old woman.

FINDINGS

An 89-year-old woman with untreated stage 0 chronic lymphocytic leukemia and a history of stage III colorectal cancer treated with hemicolectomy and adjuvant capecitabine in 2003 was admitted to Johns Hopkins Hospital in 2006. She reported feeling “dehydrated,” nauseated, and constipated, with decreased output from her colostomy. She also noted no urine output for 4 days and felt that she had to urinate, “but I can’t.” This coincided with a decrease in fluid intake. She denied fevers, chills, abdominal pain, or loss of appetite. While waiting to be seen in the emergency department, the patient was finally able to urinate.

She had no evidence of colon cancer recurrence, with a normal postoperative positron-emission tomography (PET) scan in 2003, colonoscopy in 2005, and screening computerized tomography (CT) scan in 2005. She also had a history of well-controlled hypertension and hypothyroidism, hyperlipidemia, chemotherapy-induced neuropathy, and anxiety.

Her home medication regimen included solifenacin 5 mg once daily (started 10 days prior to her admission) for bladder overactivity, buspirone 5 mg 3 times a day, metoprolol 25 mg twice a day, pantoprazole 40 mg once daily, levothyroxine 100 μ g once daily, lisinopril/hydrochlorothiazide 20 mg/25 mg twice daily, gabapentin 300 mg twice a day, and fenofibrate 145 mg nightly.

The patient appeared nontoxic. Her exam was remarkable only for hypoactive bowel sounds and mild diffuse abdominal tenderness without distension or peritoneal signs. A Foley catheter

TABLE 1
Randomized Placebo-Controlled Double-Blind Studies of Solifenacin

	Patients in safety analysis (n)			Constipation, n (%)			Micturition/24 hours	Mean decrease from baseline		
	Placebo	5 mg	10 mg	Placebo	5 mg	10 mg		Baseline	Placebo	5 mg
	Chapple et al. ^{6*†‡}	267	279	268	5 (1.9)	20 (7.2)	21 (7.8)	12.08-12.32	1.2	2.19
Cardozo et al. ^{4*†‡}	301	299	307	6 (2.0)	11 (3.7)	28 (9.1)	12.05-12.31	1.59	2.37	2.81
Wagg ^{3†}	422	192	431	18 (4.3)	18 (9.4)	78 (18.1)	11.6-11.7	1.1	2.0	2.5

*Trials lasted 12 weeks and did not utilize an intention-to-treat analysis.

†Inclusion criteria: men and women at least 18 years old, symptoms of overactive bladder syndrome for at least 3 months, average frequency of at least 8 voids/24 hours.

‡Exclusion criteria included significant bladder outlet obstruction, postvoid residual > 200 mL, presence of a neurological cause for detrusor muscle overactivity, any medical condition contraindicating the use of antimuscarinic medication, diabetic neuropathy, and use of any drugs with cholinergic or anticholinergic side effects.

§Pooled analysis of patients at least 65 years old in Chapple et al.,⁶ Cardozo et al.,⁴ and 2 unpublished studies.¹



FIGURE 1. Long arrow: dilated loop of small bowel with air fluid levels. Short arrow: decompressed loop of small bowel distal to the obstruction.

ter was placed, and her postvoid residual was only 50 cc of urine. Her admission serum blood urea nitrogen and creatinine were 90 and 3.4 mg/dL, respectively, as compared with 18 and 0.8 mg/dL 2 months prior to presentation. A CT scan of the abdomen (Figure 1) revealed multiple dilated loops of small bowel with a transition point at the left lower quadrant ostomy site, consistent with a small bowel obstruction. A PET scan revealed no evidence of malignancy. A renal ultrasound showed no evidence of obstruction.

With cessation of solifenacin and lisinopril/hydrochlorothiazide and hydration with normal saline, her constipation resolved, as did her acute renal failure and perception of urinary retention. She began to tolerate a regular diet after 4 days of hospitalization, and her colostomy output normal-

ized. At follow-up 8 months after admission, her creatinine was 0.8 mg/dL, and a screening abdominal CT showed complete resolution of the small bowel obstruction.

DISCUSSION

We believe that this patient developed small bowel pseudo-obstruction as well the feeling of urinary retention because of treatment with solifenacin, an antimuscarinic agent approved for the treatment of bladder overactivity. Her acute renal failure was a result of prerenal azotemia. This particular patient was at increased risk for developing antimuscarinic-induced bowel obstruction because of her previous surgery and exposure to chemotherapy.

In the 4 randomized trials cited in the prescribing information for solifenacin,² only 189 patients of the 1811 who received the active drug were greater than 75 years old. Healthy elderly patients ranging from 64 to 78 years of age (mean 68.0 years) who received 2 weeks of treatment with solifenacin 5 and 10 mg had a mean AUC₀₋₂₄ that was “approximately 20%” higher than that of younger subjects.³ In the 4 12-week double-blind clinical trials in which 1158 patients were treated with solifenacin 10 mg, there were 3 serious intestinal adverse events: 1 patient had a fecal impaction, 1 patient had a colonic obstruction, and 1 patient had an intestinal obstruction.² Patients receiving solifenacin 5 and 10 mg were more likely to experience constipation than those receiving placebo (5.4%, 13.4%, and 2.9%, respectively).² Given the dearth of clinical data on patients greater than 75 years old, the effects of age on the pharmacokinetics, the higher likelihood of

bowel pathology in the elderly, the increased risk of solifenacin-induced side effects in the elderly as reported in the pooled analysis of patients at least 65 years old,⁴ and the small clinical benefit of solifenacin,⁴⁻⁶ physicians should seriously consider whether the benefits of solifenacin outweigh both the known and the possible risks.

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