Intermittent catheterization and urinary tract infection in multiple sclerosis patients

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Introduction: We sought to investigate whether starting clean intermittent catheterization (CIC) for multiple sclerosis (MS) patients with lower urinary tract symptoms (LUTS) and elevated post-void residual (PVR) would improve urinary quality of life (QoL) and decrease risk of urinary tract infection (UTI).

Materials and methods: We retrospectively reviewed an institutional data base for MS patients with PVR > 100 mL and obstructive LUTS. Patients were categorized by subsequent choice of treatment: CIC versus medical treatment. Outcomes compared over 1-year follow up included incidence of UTI, urinary QoL, emergency room visits, and adherence to therapy. **Results:** Between 2014 and 2017, 37 patients met inclusion criteria. Nineteen patients started daily CIC, while 18 patients had pharmacologic therapy. At 1-year follow up, the CIC group had less improvement in urinary symptoms (26% improvement from baseline versus 72%, p = 0.02) and 7 times greater odds of having minimum one UTI within 1 year (OR 6.8, p = 0.01). The CIC group was also more likely to start an additional treatment for LUTS, and to visit the ED (all p < 0.05).

Conclusions: In this group of MS patients with LUTS and elevated PVR, initiation of CIC was associated with increased incidence of UTI and less improvement in urinary symptoms over the subsequent year compared to pharmacologic treatment.

Key Words: urinary tract infection, urinary quality of life, multiple sclerosis, intermittent catheterization, urinary retention

Introduction

Multiple sclerosis (MS) affects approximately 100 per 100,000 people with an incidence that is continuing to rise.¹ Urinary symptoms including urinary retention are common among patients with MS, and it has been shown that approximately 1 in 4 MS patients

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Address correspondence to Dr. Lauren E Corona, Department of Urology, The University of Michigan, A. Alfred Taubman Center, 1500 E Medical Center Dr, SPC 5330, Ann Arbor, MI 48109 USA performs some type of catheterization.² In addition to urinary symptoms, cognitive dysfunction affects up to 40%-60% of MS patients and, together with physical disabilities, leads to a constellation of factors that can significantly impact functional status and ability to learn and perform clean intermittent catheterization (CIC).³ Indeed, Mahajan et al showed that MS patients that catheterized consistently reported lower quality of life (QoL) scores across multiple domains.²

Despite multiple advances in bladder management in MS patients in recent years, there is little consensus on what defines pathological urinary retention and when CIC should be initiated in this population. In their consensus document on bladder management in people with MS, a panel in the United Kingdom places great importance on CIC for managing bladder symptoms and recommends its initiation with post-void residual (PVR) greater than 100 cc.⁴ The French propose a definition of MS related urinary retention as greater than 300 cc, which is similar to the current American Urological Association (AUA) recommendations for urinary retention in non-neurologic patients.^{5,6}

In addition, little is known on how urinary retention affects QoL and rate of urinary tract infection (UTI) in this patient population. In a recent study, Dray et al showed no relationship between elevated PVR on worsening lower urinary tract symptoms (LUTS), QoL scores, incontinence, or risk of recurrent UTI.7 Furthermore, well-designed studies that show the long term effects of catheterization in this population are lacking.8 Considering the potential significant impact of intermittent catheterization on QoL, more information is needed on its efficacy and morbidity to guide decision making in the MS patient population with urinary retention, ensuring that the benefits of CIC outweigh the risks. To this end, we investigated whether the initiation of CIC in MS patients with LUTS and elevated PVR would improve urinary QoL and incidence of UTI compared to medical treatment for their LUTS despite the elevated residual urine.

Materials and methods

Following Institutional Review Board approval, we retrospectively abstracted data from adult MS patients referred to an institutional neuro-urology clinic for evaluation between January 2014 and June 2017. We included patients with a PVR > 100 mL via ultrasound or catheterization who started new urologic treatment for urinary symptoms for an elevated PVR and obstructive LUTS. Patients were followed for 1 year, with scheduled visits every 3-4 months with additional visits as needed basis depending on efficacy of treatment. Abstracted data included patient demographics, MS duration, previous documentation of UTI, medications, and treatment choices.

All patients were assessed for LUTS with the AUA Symptom Index (AUA SI)⁹ and for incontinence severity with the Michigan Incontinence Symptom Index (M-ISI).¹⁰ These questionnaire scores were obtained at the initial visit prior to initiating treatment. If repeated at the follow up visit, the scores were also abstracted. All patients started on CIC were taught per standardized protocol with recommend catheterization every 3 to 6 hours.

Outcomes

Patients were categorized into two groups by subsequent choice of treatment: CIC versus initiation or dose adjustment of a medical treatment (alpha blocker, antimuscarinic, ß-3 agonist). All options were

reviewed and treatment choice was per shared decision making between patient and urologist. Data were then reviewed for 1 year from the date of initiation. Within this year, multiple variables were abstracted including development of UTI (defined as a positive culture or subjective symptoms treated with antibiotics), adherence to CIC regimen and, if not, reason for discontinuation, initiation of a second treatment, type of treatment initiated, number of hospitalizations and ED visits, recorded falls, and record of any other urologic intervention. Our primary outcome was the incidence of UTI after starting any treatment. Urinary symptoms were reported as improved if a subsequent AUA-SI or M-ISI score was decreased at follow up or if the clinic note at follow up reported a subjective > 50% improvement in symptoms.

Statistical analysis

An intention to treat analysis was performed based on initial treatment assignment (CIC versus other). We compared demographics, UTI incidence, change in urinary symptoms, hospitalizations, ED visits, falls, and imaging or interventions between groups using student's t-test for continuous variables and chi-square or fisher exact test for categorical variables. Univariate analysis was also performed to identify predictors for UTI. All tests of significance were two-tailed and set at a p value of < 0.05. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).



Figure 1. Percentage of patients with urinary tract infection, second treatment initiation, no improvement in symptoms, and ≥ 1 visit emergency department visit within one year of initiation on CIC (black bars) versus medical treatment (gray bars). *p value < 0.05.

Results

We identified 37 patients with MS, LUTS, and PVR > 100 mL. Nineteen patients (51%) were started on CIC while 18 (49%) patients were prescribed medical treatment. Median age was 58 (range 28-82) years, the group was 70% female, and median duration of MS was 14 (range 1-47) years. This was not significantly different between groups. The majority (22/37) had

progressive MS. LUTS were high overall for the group with median AUA-SS of 20 and M-ISI of 15 at time of treatment discussion. The CIC group had a higher PVR (287 mL versus 176 mL, p < 0.01) at baseline. The groups were similar in urinary symptom scores, creatinine, medication use, and reported history of recurrent UTI, Table 1.

UTI within 1 year of treatment was significantly more common in those started on CIC (74% versus

TABLE 1. Demographics

	CIC	Medical treatment $n = 18$	p value	
Maan aga (waa)	n = 19	n = 10	0.8	
Mean age (yrs.)	39	56	0.8	
Gender	(22)	E (29)	1.0	
n, % female	6 (32) 13 (68)	3 (28) 13 (72)		
Race	10 (00)	10 (72)	0.54	
n, % white	15 (79)	11 (61)	0.01	
n, % black	3 (16)	6 (33)		
n, % unknown	1 (5)	1 (6)		
Mean MS duration (yrs.)	19	14	0.16	
Mean creatinine (mg/dL)	0.88	0.83	0.6	
Mean PVR (mL)	287	176	< 0.01	
Mean AUA SS total	19.5	20.3	0.71	
Mean AUA SS bother	3.7	4.1	0.47	
Mean M-ISI SS total	15.7	13.9	0.51	
Mean M-ISI SS bother	3.65	3.35	0.73	
On alpha blockers (n, % yes)	7 (37)	10 (56)	0.33	
On antimuscarinics (n, % yes)	10 (53)	6 (33)	0.32	
Mean # medications per patient	2.4	2.2	0.59	
Hx recurrent UTI (n, % yes)	6 (32)	3 (17)	0.45	
UTI within 1 yr. (n, % yes)	14 (74)	5 (28)	< 0.01	
Stay in Tx at 1 yr. (n, % yes)	10 (56)	13 (72)	0.49	
Second Tx within 1 yr. (n, % yes)	12 (67)	5 (28)	0.04	
Improved symptoms at follow up (n, % yes)	5 (26)	13 (72)	0.02	
Mean # hospitalizations within 1 yr.	0.84	0.56	0.41	
Hospitalization within 1 yr. (n, % yes)	9 (47)	6 (33)	0.51	
Mean # ED visits within 1 yr.	1	0.22	< 0.01	
ED visit within 1 yr. (n, % yes)	12 (63)	3 (17)	< 0.01	
Fall within 1 yr. (n, % yes)	11 (58)	8 (44)	0.52	
Imaging/cysto/OR/FUDS within 1 year (n, % yes)	3 (16)	2 (11)	1.0	
		1 1 1 1 1 1 0 1	0	

MS = multiple sclerosis; PVR = post void residual; AUA SS = American Urological Association Symptom Score; M-ISI = Michigan Incontinence Symptom Index; Hx = history; UTI = urinary tract infection; Tx = treatment; ED = emergency department; cysto = cystoscopy; OR = operating room; FUDS = fluorourodynamics 28%, p < 0.01). The CIC group was also more likely over the following year to start an additional treatment for LUTS (67% versus 28%, p = 0.04) and to visit the ED (63% versus 17%, p < 0.01), Table 1, Figure 1. Symptoms could be reassessed in 26 of the 37 patients based on repeat AUA-SS, M-ISI, or documentation in the clinic note. Of those, the CIC group had less improvement in urinary symptoms (26% of patients reported any improvement from baseline versus 72% in the medical treatment group, p = 0.02). There were no differences in hospitalization rates, incidence of falls, or number of imaging/interventions performed within 1 year between groups. After 1 year, 56% of patients started on CIC and 72% of patients placed on medical treatment continued this initial treatment.

Univariate logistic regression revealed that patients who reported a history of previous UTI's were at greatest risk for subsequent UTI after initiating treatment (OR 34, p = 0.03). However, it was noted that those started on CIC also had 7 times greater odds of UTI within 1 year versus those started on medical treatment (OR 6.8, p = 0.01). Those with a longer duration of MS (OR 1.1, p = 0.04), those initiated on a second treatment (OR 4.7, p = 0.03), and those not on alpha blockers (OR 9.4, p < 0.01) were also more likely to have UTI within 1 year on univariate analysis, Table 2.

Variable	Odds ratio	95% CI	p value	
Started on CIC	6.8	1.5-30.8	0.01	
Increasing PVR	1.000	0.994-1.007	0.98	
Improved symptoms	2.37	0.09-6.76	0.31	
No second Tx within 1 yr.	0.28	0.07-1.12	0.07	
Increasing age	1.035	0.975-1.099	0.26	
Sex female	2.96	0.62-14.06	0.17	
Longer MS duration	1.09	1.002-1.18	0.04	
Higher AUA SS total	0.96	0.87-1.06	0.44	
Higher AUA SS bother	1.00	0.6-1.67	0.99	
Higher M-ISI total	1.02	0.93-1.13	0.63	
Higher M-ISI bother	1.0	0.74-1.35	1.0	
Not on alpha blocker	9.4	1.93-45.93	< 0.01	
Not on anticholinergic	0.8	0.2-3.1	0.74	
Did not stay in Tx at 1 yr.	1.6	0.4-6.7	0.5	
Started second Tx within 1 yr.	4.7	1.15-19.3	0.03	
Greater # of medications	0.72	0.38-1.36	0.31	
Hx of recurrent UTI	33.5	1.52-739	0.03	
Greater # of hospitalizations	1.48	0.74-2.94	0.27	
No hospitalizations within 1 yr.	0.51	0.13-2.0	0.33	
Greater # of ED visits	1.82	0.79-4.22	0.16	
No ED visit within 1 yr.	0.39	0.096-1.61	0.19	
No falls within 1 yr.	0.25	0.06-1.04	0.06	
No imaging/cysto/OR/FUDS within 1 yr.	0.67	0.1-4.56	0.68	

TABLE 2. Predictors of urinary tract infection

Univariate logistic regression to identify predictors of UTI within 1 year of treatment initiation of entire population CIC = clean intermittent catheterization; PVR = post void residual; Tx = treatment;

MS = multiple sclerosis; AUA SS = American Urological Association Symptom Score;

M-ISI = Michigan Incontinence Symptom Index; Hx = history;

ED = emergency department; cysto = cystoscopy; OR = operating room; FUDS = fluorourodynamics

Discussion

Our study showed that initiation of CIC in MS patients with LUTS and elevated PVR was associated with a greater incidence of urinary tract infections in the subsequent year compared to those started on medical treatments. Likewise, there was less improvement in urinary symptoms with CIC initiation compared to medical therapy. Those started on CIC were also more likely over the following year to start an additional treatment for LUTS and visit the ED, while there was no difference in hospitalization rate, incidence of falls, or number of imaging/interventions performed within 1 year. Collectively, these findings suggest that CIC initiation is not without risk in this MS patient population with a PVR > 100 mL and goals for its initiation should be carefully considered in the context of its morbidity.

Intermittent catheterization comes with a considerable number of hurdles. As reported by Panicker and Fowler, these are multiplied in the MS population and include physical (positional, dexterity, visual impairment, decreased cognition), social (anxiety, embarrassment, stigma, fear), and situational (inadequate facilitates, catheter availability, quality of teaching, access to help, and availability of nurse specialists) barriers unique to this population.¹¹ For these reasons amongst others, previous investigators have shown that MS patients that catheterize consistently report lower QoL scores.²

Given the above, it is vital to weigh the benefits against the added patient burden to catheterization. Prior studies have shown significant benefits of intermittent catheterization in the spinal cord injured and myelomeningocele populations including improvement in continence, improved renal function, and reduction in UTI, however there are limited data that strictly evaluate the MS population and, of those that do, results are mixed.¹²⁻¹⁴ Dray et al recently showed the absence of an association between urinary symptom severity and PVR volume in patients with MS, as well as no difference in historical report of recurrent UTI based on PVR volume.⁷ Similarly, while McClurg et al described reported improvement in leakage, nocturia, and frequency as reasons for continuation of CIC in patients with MS, those that discontinued CIC commonly listed increasing number of UTIs (as reported by the patient) and worse QoL as their reasons for doing so.¹⁵ In their 56 patient cohort, 25% of those initiated on CIC reported increase in number of UTIs at 8 months, while only 5% reported improvement in UTI frequency. In a separate online survey portion of their study, of the 455 respondents on CIC, 36% reported worsening of UTI after initiation

of CIC. Increased UTI was the commonest factor for discontinuation thereof.¹⁵ A 2018 systematic review from Tornic et al showed that catheterization (both CIC and indwelling) may improve bladder-specific QoL in MS patients, however recognized that disease specific and well-designed studies are lacking.⁸

This conversation regarding initiating CIC is critically important, given the lack of data for MS patients treated with alpha-blockers or neuromodulation for urinary retention. A few studies have described both clinical and urodynamic improvements in MS patients treated with PTNS, while another showed no benefit in the treatment of lower urinary tract dysfunction in eight patients with MS and neurogenic detrusor overactivity.¹⁶ The role of alpha-blockers in the treatment of MS patients with LUTS was last critically studied in 1995 where indoramin was compared to placebo in 18 men with MS and a PVR of > 50 mL. This study demonstrated no change in residual volume with treatment, but an improvement over placebo in maximum urinary flow rate.¹⁷ Our finding that alpha-blockers were protective against the development of UTI in this patient population is a finding worth further.

Our study has limitations. Our UTI definition was in part subjective in that it included patients with symptoms initiated on antibiotic therapy. However, subjective UTIs alone were the minority, comprising only 28% of patients that developed UTI within 1 year, while 73% had culture proven infections. Secondly, since these patients were followed from their initial visit after referral to our clinic, data on prior UTIs were limited and we were therefore unable to comment on change in UTI frequency before and after CIC initiation. It could be argued that UTI incidence might be highest in the initial CIC learning period, and thus the first year after initiation is not an accurate representation of the benefit that CIC might have on decreasing infection. However, our data show a high incidence of infection in this first year, and that is noteworthy. Finally, the retrospective nature and small sample size of our study introduces potential bias. A multivariable model was performed to identify predictors of UTI and CIC remained a predictor. However, given small sample size and the probability of collinear variables, we did not feel a multivariable analysis was appropriate.

These limitations notwithstanding, our findings help us understand the potential effect of CIC on the MS patient population with retention and LUTS. Incomplete bladder emptying is high in this population and CIC is often reflexively chosen when an elevated PVR is encountered. However, our study shows that decreasing PVR through catheterization could actually be associated with increased morbidity. These data, however, must be interpreted with caution. There are indeed patients that benefit from initiation of CIC and have improvement in their LUTS and a reduction in UTIs when their burdensome residual urine is evacuated. A cautious approach to the initiation of CIC must include an assessment of LUTS within a few weeks of initiation, as improvement should be rapid if overflow incontinence and urinary stasis were contributing to symptoms and infections. If improvement is equivocal or absent, then discussion of discontinuation of CIC should take place. Until further data are developed to better guide treatment, a shared decision model between the patient and a multidisciplinary team of physicians should be used for individualized treatment that highlights the potential risks and benefits of all available therapies.^{18,19}

Conclusions

In this group of MS patients with LUTS and elevated PVR, initiation of CIC was associated with increased risk of UTI and less improvement in urinary symptoms over the subsequent year compared to medical treatments. While these results need confirmation with a randomized controlled trial, they demonstrate that urologists might need to reevaluate the goals for catheterization and individualize therapy in this population.

Disclosures

Dr. Stoffel has grant funding from PCORI and Department of Defense and is the site PI for Uroplasty study. Dr. Cameron is an unpaid investigator for Medtronic and speaker for Wellspect. $\hfill \Box$

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