

Original Article

Results of medications and bladder managements of vesicoureteral reflux in patients with a spinal cord lesion

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Abstract

The purpose of the present study was to study the outcome of medical treatments and methods used to treat vesicoureteral reflux (VUR) in patients with spinal cord lesions. We retrospectively collected data from the outpatient records of 73 spinal cord lesion patients with VUR. The treatments for VUR were anticholinergics (89%) and antibiotics (41%). The methods of bladder management undertaken were indwelling urethral catheterization (67%), intermittent catheterization (30%), and use of a urinary condom (3%). After VUR treatment, 58.9% of the patients showed VUR improvement. Patients with unilateral VUR responded to treatment better than patient with bilateral VUR. However, no significant evidence of certain medications or bladder management was more effective than others at treating VUR in patients with spinal cord injuries.

Keywords: spinal cord injury, neurogenic bladder, vesicoureteral reflux, bladder management, anticholinergic

1. Introduction

Spinal cord injury (SCI) patients often have neurogenic voiding dysfunction which requires bladder management for urinary drainage using methods such as indwelling urethral catheterization, clean intermittent catheterization, and the application of a urinary condom (Cameron *et al.*, 2010). Moreover, the neurourological problems that result in SCI can also result in complications such as vesicoureteral reflux (VUR), hydronephrosis, urinary tract infection (UTI), and sepsis (Cardenas & Hooton, 1995).

Despite advances in medical treatments and interventions, 11–30% of SCI patients continue to experience VUR (Ogawa, 1991; Thongchim, Tamnanthong, & Arayawichanon, 2010). The risk factors for VUR in SCI patients are low compliance of the bladder, high urethral pressure, increased detrusor pressure, recurrent UTI, and SCI between the 10th thoracic and 2nd lumbar levels (Gabrielle, 2008; Suzuki & Ushiyama, 2001). VUR is an important cause of

morbidity and mortality in SCI patients. If not properly managed, the condition can lead to hydronephrosis, renal failure, and death (Ku, 2005; Siroky, 2002; Taweel & Seyam, 2015).

Treatment options for VUR depend on the severity of the condition. The goal is to reduce or halt reflux, and prevent additional permanent kidney damage (Fuente *et al.*, 2014). Oral anticholinergic medications are usually prescribed to decrease detrusor pressure, as high detrusor pressure carries a high risk for renal dysfunction and VUR (Consortium for Spinal Cord Medicine, 2006; Morton *et al.*, 2002; Ponce Díaz-Reixa *et al.*, 2007). In addition, anticholinergic therapy to improve autonomic dysreflexia and bladder storage is the mainstay treatment for neurogenic bladder (Cameron, 2016). The use of alpha blockers is also recommended in cases of closed bladder neck in order to relax the internal urethral sphincter (Cameron, 2016; Ponce Díaz-Reixa *et al.*, 2007). A combination of alpha blocker with anticholinergic medication is recommended for neurogenic bladder patients with elevated residual urine or obstructive symptoms (Cameron, 2016). In terms of bladder management, indwelling urethral catheterization, clean intermittent catheterization, and the use of urinary condom are frequently advised.

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To the best of our knowledge, no previously published studies have compared the various medications and methods of bladder management used to treat VUR in SCI patients. The lack of research studies is one of the obstacles for better treatment of VUR in SCI patients. The purpose of the present study was to study the outcome of medical treatments and methods that are currently used to treat VUR in patients with spinal cord lesions.

2. Materials and Methods

2.1 Participants

This study examined SCI patients with VUR who presented at the Rehabilitation Medicine Clinic of Srinagarind Hospital from 1 January 2012 to 31 December 2016. The inclusion criteria were age over 18 years old, history of neurogenic bladder, and no history of congenital anomalies in the kidney-ureter-bladder system. The exclusion criteria were history of urological stones, pregnancy, and multiple sclerosis.

2.2 Methodology

The outpatient records were retrospectively reviewed and data were collected regarding each patient. The data included age, sex, cause of SCI, neurological level, American Spinal Injury Association classification, underlying disease, duration of VUR, medications, methods of bladder management, and preliminary and secondary voiding cystourethrography (VCUG) results. VUR grading was interpreted by radiologists who did not know the baseline characteristics of the participants. Regarding the operational definition of response to VUR treatment in the unilateral VUR group, improvement in VUR grading by at least one level (e.g., VUR grade 3 regressing to grade 2) whereas non-response to VUR treatment was defined as lack of improvement in terms of VUR grading (Kirsch *et al.*, 2014). In cases of bilateral VUR, the results from each site were considered.

The definition of response to VUR treatment in bilateral VUR group was improvement in VUR grading by at least one level on both sides and non-response was defined as lack of improvement on one or both sides. This study was approved by the Khon Kaen University Ethics Committee in Human Research (HE591532).

2.3 Statistical analysis

The available data from all participants were analyzed and no imputations were performed in cases of missing data. All statistical tests were two-sided with a significance level of 0.05. All statistical analyses used SPSS version 17.0. All baseline characteristics are presented as percentage, mean, and standard deviation. Associations between medications or methods of bladder management and the results of VUR treatment were analyzed using the chi-square and Fisher’s exact tests with significance set at $P < 0.05$.

3. Results

From a total of 648 SCI patients who presented at the rehabilitation medicine clinic, only 73 patients met the eligibility criteria with complete data from 1 January 2012 to 31 December 2016. Of the 73 patients, 22 had quadriplegia, 46 had paraplegia, and five had cauda equina syndrome. Most of the patients were male and the average age was 45 years. Most of the participants had unilateral VUR and indwelling catheterization was the most common method of bladder management. The other baseline characteristics of these participants are summarized in Table 1.

All 73 participants received medications and underwent bladder management. The most common medication administered was oxybutynin, an anticholinergic drug, (mean dose: 14 mg/day) in 78% of the participants. Ofloxacin was the most commonly used antibiotic in 27.4% of the patients. Nine of the participants received alpha blockers (prazosin or

Table 1. Baseline characteristics of 73 patients in this study and their types of spinal defects.

Data	Quadriplegia	Paraplegia	Cauda equina syndrome	All (73 cases)
Number	22	46	5	73
Gender				
Male/female	18/4	31/15	5/0	54/19
Age (years)				
Mean±SD	45.77±11.41	43.31±12.18	48.20±11.30	45.76±11.63
Complete lesion	7	24	0	31
Incomplete lesion	15	22	5	42
Duration of injury (years)	10.90±5.6	11.74±6.2	9.0±3.8	10.55±5.2
Cause				
Trauma	16	26	2	44
Non-trauma	6	20	3	29
VUR				
Unilateral	21	34	4	59
Bilateral	1	12	1	14
Methods of bladder management				
Indwelling catheterization	18	29	2	49
Clean intermittent catheterization	4	15	3	22
Urinary condom	0	2	0	2

VUR=vesicoureteric reflux

doxazosin), and most received a combination of anticholinergic and antibiotic prophylaxis (31%) (Table 2). The types of bladder management used were indwelling urethral catheterization (67%), clean intermittent catheterization (30%), and urinary condom (3%) (Table 3).

Forty-three (58.9%) of the participants were responsive to these treatments, whereas 30 (41.1%) of the participants were non-responsive. In the responsive VUR group, the patients with unilateral VUR responded to their treatment better than patients with bilateral VUR (Table 4). Most of both unilateral and bilateral VUR responsive groups had VUR grading from grade 3 to grade 0 (Table 5).

The only baseline factor associated with response to VUR treatment was trauma (Table 6). However, there were no statistically significant associations between the type of medication or the method of bladder management and VUR treatment results (Table 7).

4. Discussion

Most of the patients in this study experienced improvement with regard to their VUR. Moreover, patients with unilateral VUR showed more improvement than those

Table 3. Bladder management.

Method of bladder management	n (%)	Duration (months)		
		MIN	MAX	MEAN
Indwelling catheterization	49 (67)	3	36	8
Clean intermittent catheterization	22 (30)	3	12	6
Urinary condom	2 (3)	5	6	5.5

Table 2. Medications.

Type of medications	n (%)	Dosage (mg/day)			Duration (months)		
		MIN	MAX	MEAN	MIN	MAX	MEAN
Anticholinergic							
Oxybutynin	57 (78)	5	30	14	1	12	6.6
Trospium HCl	7 (9.5)	20	80	48	3	12	8
Oxyphencyclimine	1 (1.3)	15	15	15	3	3	3
Antibiotics							
Ofloxacin and ciprofloxacin	20 (27.4)	400	400	400	1	9	4
Sulfamethoxazole and trimethoprim	2 (2.7)	1000	1000	1000	3	3	3
Amoxicillin/clavulanate potassium	7 (9.6)	160	320	228	3	3	3
Amoxicillin/clavulanate potassium	1(1.3)	2000	2000	2000	3	3	3
Alpha blocker							
Prazosin	7 (9.6)	1	5	2.2	3	7	4.7
Doxazosin	2 (2.7)	2	2	2	3	6	4.5
Combined medications							
Antibiotic & anticholinergic	23 (31)				3	36	7
Anticholinergic & alpha blocker	2 (2.7)				5	6	5.5
Anticholinergic, antibiotic & alpha blocker	5 (6.8)				3	31	9.4

Table 4. Outcome of VUR treatment.

	At baseline (first time VCUG) (Number)	After treatment (follow-up VCUG) (Number)
Responsive VUR (n=43, 58.9%)	Unilateral VUR (35)	No VUR (31) Unilateral VUR (4)
	Bilateral VUR (8)	No VUR (6) Unilateral VUR (1) Bilateral VUR (1)
Non-responsive VUR (n=30, 41.1%)	Unilateral VUR (24)	Unilateral VUR (22) Bilateral VUR (2)
	Bilateral VUR (6)	Bilateral VUR (6)

VUR=vesicoureteric reflux, VCUG=voiding cystourethrography

Table 5. VUR grading change in 43 responsive VUR patients.

VUR grading	Follow-up	Unilateral VUR (N=35 sides, 35 participants)		Bilateral VUR (N=16 sides, 8 participants)	
		Right	Left	Right	Left
Preliminary 5	0	-	2	-	-
4	1	2	-	-	-
	0	2	1	-	-
3	2	-	1	1	-
	1	-	1	-	1
2	0	7	6	5	5
	1	-	-	-	1
1	0	1	-	1	-
	0	4	8	1	1

VUR=vesicoureteric reflux

Table 6. Association between baseline factors and VUR treatment results.

Factors	Result of treatment		P-value
	Responsive n (%)	Non-responsive n (%)	
Age (years)			
21-40	12 (16.4)	9 (12.3)	0.615
41-60	33 (45.2)	19 (26.0)	
Gender			
Female	10 (13.7)	9 (12.3)	0.348
Male	35 (47.9)	19 (26.0)	
Spinal cord injury type			
Tetraplegia	14 (19.2)	8 (11.0)	0.632
Paraplegia	27 (37)	19 (26.0)	
Cauda equina syndrome	4 (5.5)	1 (1.4)	
Cause			
Trauma	32 (43.8)	12 (16.4)	0.016*
Non-trauma	13 (17.8)	16 (21.9)	
AIS			
Complete	20 (27.4)	11 (15.1)	0.660
Incomplete	25 (34.2)	17 (23.3)	
VUR			
Unilateral	28 (38.4)	33 (45.2)	0.188
Bilateral	8 (10.9)	4 (5.5)	

* P<0.05 AIS=American Spinal Injury Association Impairment Scale, VUR=vesicoureteric reflux

with bilateral VUR. These findings were similar to those of a study by Ponce Diaz-Reixa J, *et al.* which found a 23.7% reduction in VUR after conservative treatment by indwelling catheter and anticholinergics, especially in unilateral reflux patients (Ponce Díaz-Reixa *et al.*, 2007). In addition, one study found that ipsilateral renal function was more likely to be preserved in unilateral VUR (Donnelly, Gylys-Morin, Wacksman & Gelfand, 1997). These results indicated that the prognosis in terms of VUR improvement was better in unilateral VUR patients.

There was no significant association between regular use of antibiotic prophylaxis and VUR improvement. This was consistent with the results of previous studies which found that antimicrobial prophylaxis did not have a statistically significant association with VUR improvement in neurogenic bladder patients caused by spinal cord dysfunction (Morton *et al.*, 2002). In addition, a study showed that antibiotic prophylaxis was not significantly associated with VUR reduction (Robinson, 2013). According to the 2015 guidelines on urological conditions, continuous or post-coital antibiotic prophylaxis for prevention of recurrent UTI should be considered only after counseling and behavioral modification has been attempted, and when non-antimicrobial treatments have been unsuccessful (Grabe, Bartoletti &, Johansen, 2015). Moreover, there were no statistically significant associations between anticholinergic medications, alpha blockers, or combinations of the two and VUR improvement which were results that were similar to the findings in a previous study (Thongchim, Tamnanthong & Arayawichanont, 2010). In this study, there was a chance of VUR reduction in SCI patients who received medication, but the connection was not statistically significant. In clinical practice, the prescription of a

Table 7. Association between type treatment and VUR treatment results.

Factors	Result of treatment		P-value
	Responsive (n)	Non- responsive (n)	
Anticholinergic drugs			
Usage	39	26	0.410
Non-usage	6	2	
Antibiotic drugs			
Usage	17	13	0.465
Non-usage	28	15	
Combined medications (antibiotic & anticholinergic)			
Usage	40	27	0.390
Non-usage	5	1	
Alpha blocker			
Usage	5	4	0.730
Non-usage	40	24	
Drainage procedure			
Indwelling catheterization	29	20	0.730
Clean intermittent catheter	15	7	
Urinary condom	1	1	
Medication + bladder management			
Anticholinergic + indwelling catheterization	24	19	0.280
Anticholinergic + clean intermittent catheterization	14	6	
Combined medications + bladder management			
Anticholinergic + antibiotic + indwelling catheterization	10	7	1.000
Anticholinergic + antibiotic + clean intermittent catheterization	7	4	

medication by the physician for the patient should be based on the clinical symptoms and urological investigations of the patient.

In the current study, none of the methods of bladder management were significantly associated with VUR improvement to a greater degree than any other management. This finding differs from those of a previous study which recommended the use of indwelling catheterization during the early phase of VUR treatment (Consortium for Spinal Cord Medicine, 2006). However, bladder management strategies used in the treatment of VUR in SCI patients depend on many factors such as physical deficit, severity of VUR, patient caregivers, and socioeconomic environment. The risks and benefits of various methods of bladder management must be weighed with consideration for each individual case (Wu & Franco, 2017).

In this study, SCI due to trauma was associated with VUR improvement as it entails a single injury to the spinal cord, as opposed to non-traumatic SCI which is caused by

chronic damage to the spinal cord. Thus, traumatic SCI may result in better VUR treatment outcomes.

The main limitation of our study was that video urodynamic studies, which are considered the gold standard for evaluation of neurogenic bladder patients, were not available in our setting. Therefore, bladder management in our setting was performed based on the VCUG findings. Future studies in other settings should use video urodynamic studies to assess the urological function in neurogenic bladder. In addition, our study lacked information on the UTI rate which may reflect on the results of antibiotic prophylaxis because most of the patients with UTI are usually treated in local health care settings. Moreover, the design in this study was retrospective which could not control any randomization and this study was confined to a single hospital where treatments depended on the preferences of the attending staff physicians. In addition, some subgroups had few participants and any desired differences could not be demonstrated. Furthermore, the results can not be generalized to other hospitals or medical clinic settings. However, it is hoped that the results reported here provide useful information to other hospitals where they attempt to manage VUR in SCI patients. The results of this study provide the basis for further studies and may guide the development of VUR treatment concepts. Future prospective studies should aim at reducing VUR through optimization of therapeutic methods as well as monitoring renal function and the UTI rate in order to confirm that the interventions improve renal function.

5. Conclusions

There was no statistically significant evidence regarding which medical treatment or method of bladder management was best to improve VUR in SCI patients. Therefore, the treatments and methods in bladder management should be considered on a case-by-case basis.

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