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Urinary tract infection in patients with spinal cord injury after urodynamics under fosfomycin prophylaxis: a retrospective analysis

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Abstract

Background: Urinary tract infection (UTI) is a common complication of spinal cord injury (SCI). Urodynamic testing is widely used for characterization of vesico-sphincteric dysfunction and for therapeutic orientation. As an invasive procedure, the risk of UTI is increased so, in some medical centers, antibiotic prophylaxis is instituted. Fosfomycin is one of the antibiotics used.

Objective: The aim of this study was to evaluate the incidence of UTI after urodynamics in patients with SCI, under fosfomycin prophylaxis.

Methods: Retrospective analysis was performed on patients with SCI, admitted to a rehabilitation center between January 2016 and June 2017, who underwent urodynamics studies under fosfomycin prophylaxis. Demographic data, risk factors for UTI—bacteriuria before urodynamics, high residual volume (>100 mL), bladder emptying method, vesico-sphincteric dyssynergia, and detrusor hyperactivity were analyzed. The incidence of UTI after urodynamics was evaluated.

Results: The study included 84 patients, predominantly men 55 (65.5%). The mean age of the patients was 55.6 (18.9). Eleven (22.5%) had vesico-sphincteric dyssynergia, 32 (65.3%) detrusor hyperactivity and 22 (44.9%) had a high residual volume. Thirty-seven (44.1%) had asymptomatic bacteriuria before the urodynamics. Urinary complaints suggestive of UTI after urodynamics were observed in 2(2.4%) of patients, without significant bacteriuria and identification of bacterial agent.

Conclusions: The incidence of UTI after invasive procedures is reported between 3% and 20% in the literature, so antibiotic prophylaxis has been instituted, although controversial. In the study, in none of the patients the diagnosis of UTI was confirmed. Fosfomycin prophylaxis may have been important in reducing the incidence of UTI.

Keywords: antibiotic prophylaxis, urinary tract infection, urodynamic study

Introduction

The spinal cord injury (SCI) is a clinical condition with great organic, psychosocial, and functional impact, which leads to multiple clinical complications, of which the neurogenic bladder is the most common.[1,2]

Depending of the type and neurological level of the lesion, patients may require continuous or intermittent catheterizations (IC) to achieve complete bladder emptying, which increases the risk of urinary tract infections (UTIs), a major factor for morbidity and mortality in patients with SCI.[1,2]

On the contrary, factors such as vesico-sphincteric dyssynergia, detrusor muscle hyperactivity, and high post-micturition residual volumes (RVs) are also described as factors that increase the risk of UTI in these patients.[3,4] Consequently, the presence of a neurogenic bladder in patients with SCI requires periodic monitoring, usually performed through cytochemical and microbiological study of urine, kidney, and bladder ultrasounds and urodynamic study (UDS) for the avoidance/prevention of complications that can be fatal in these patients.

Currently, UDS is widely used to characterize vesico-sphincteric dysfunction and for therapeutic orientation. As an invasive procedure, resulting from lower urinary tract instrumentation, the risk of UTI increases. In this context, the American Urological Association and European Association of Urology recommend the institution of antibiotic prophylaxis in patients with SCI at the time of UDS, namely, in the presence of risk factors such as advanced age (older than 70 years), smoking, diabetes *mellitus*, immunosuppression, anatomical alterations of the urinary tract, bladder catheterization, bacterial colonization, recurrent UTIs, and prolonged hospitalization.[5–7] In some medical centers, antibiotic prophylaxis before UDS is instituted for all patients with SCI.

In the literature, the most commonly described antibiotics are amoxicillin/clavulanic acid, trimethoprim/sulfamethoxazole, nitrofurantoin, and quinolones.[5] Worldwide, antibiotic resistance rates among gram-negative bacilli are rising rapidly, namely with quinolones.[8] Thus, some study groups recommend that alternative antimicrobial agents, as fosfomycin, should be

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evaluated. Treatment with this antibiotic has been demonstrated as effective as the standard course of treatment of UTI and may be preferable due to its simpler administration.[9,10] As that, in recent years, fosfomycin has been used in the prophylaxis of patients undergoing UDS, despite its use being scarcely investigated and described in the literature.

However, currently, there are few studies evaluating the efficacy of antibiotic prophylaxis in patients with SCI undergoing UDS and the reported findings are controversial.

The aim of this study was to evaluate the incidence of UTI after UDS in patients with SCI, under antibiotic prophylaxis with fosfomycin.

Methods

Retrospective cohort study of patients with SCI, admitted to a Rehabilitation Center between January 2016 and June 2017, who underwent antibiotic prophylaxis with fosfomycin according to the following protocol: fosfomycin, 3000 mg, 1 time/day, in fasting, on UDS day and in the next day.

Several data were obtained through the clinical processes of patients, namely, age, sex, classification of SCI, risk factors for UTI, such as the presence of previous bacteriuria to the UDS, high RV (>100 mL), bladder emptying method [exclusive continuous catheterization (CC); IC during daytime and CC during nighttime; exclusive IC; micturation, with or without maneuvers (eg, Credé maneuver, suprapubic percussion and Valsalva maneuver) to external devices (diaper or urinary collector); voluntary micturation, with or without maneuver]. The presence of bladder dyssynergia and detrusor muscle hyperactivity as well as the presence of urethral trauma was also evaluated.

The incidence of UTI after UDS was determined, being the definition of UTI established according to the criteria of the National Institute on Disability and Rehabilitation Research (NIDRR) Consensus Statement, "Prevention and Management of Urinary Tract Infection among People with SCI"[11]: presence of significant bacteriuria ($>10^2$ Colony Forming Units (CFU)/mL in patients under IC, $>10^4$ CFU/mL in patients with urinary collector and any detectable concentration in patients with CC) plus the presence of at least one sign or symptom of UTI as presence of leukocyturia ($\geq$100 leukocytes/mm^3), discomfort or pain in the suprapubic or lumbar region or during micturition, urinary incontinence, fever, worsening of spasticity, autonomic dysreflexia, cloudy and fetid urine, lethargy, and malaise. Typical symptoms or signs of UTIs such as pollakiuria, dysuria, and urinary urgency may be absent in patients with SCI.[1]

All patients underwent a cytochemical and microbiological study of urine before the UDS.

Results

The study initially included 87 patients with SCI and neurogenic bladder. Of these, 3 were excluded due to lack of follow-up after the UDS (hospitalization discharge), resulting in a final sample of 84 patients, predominantly men 55(65.5%). The mean age of the patients observed was 55.6(18.9), of which 19(22.6%) patients were older than 70 years.

Regarding the classification of SCI, it was verified that the majority of the patients had incomplete lesions, mainly American Spinal Injury Association Impairment Scale D, that is, patients with motor function preserved below the neurologic level, and with most key muscles below the neurologic level having a muscle grade $\geq$3.

Table 1

Distribution of patients according to the type of lesion (American Spinal Injury Association Impairment Scale/spinal cord syndromes)

Type of spinal cord injury	N (%)
AIS A	14 (16.7%)
AIS B	7 (8.3%)
AIS C	12 (14.3%)
AIS D	38 (45.2%)
Spinal cord syndromes (cauda equina, central cord, conus medullaris)	13 (15.5%)

N = number of patients.

Thirteen (15.5%) patients had spinal cord syndromes, specifically, cauda equina, central cord, and conus medullaris syndromes (Table 1). Of these patients, 23(27.4%) had SCI with more than 2 years of evolution.

Regarding the bladder emptying method, it was verified that 60.8% of the patients presented some type of bladder catheterization. Most were under CC [34 (40.5%)] and, the remaining patients, 25(29.8%) had voluntary micturation, with or without maneuvers, 13(15.5%) were performing IC during daytime by schedule (usually 3/3 h) with CC during nighttime, 8 (9.5%) presented micturation to external devices (diaper or urinary collector) and 4(4.8%) presented exclusive IC.

Regarding the risk factors for UTI, it was observed that more than half of the patients had at least one risk factor [49(58.3%)]. Of these, 32(65.3%) patients had detrusor muscle hyperactivity, 22(44.9%) had a high RV, 11(22.5%) had vesico-sphincteric dyssynergia, and 4(8.2%) had urethral trauma, being that 36.7% of patients had more than 1 risk factor for UTI (Table 2).

Before conducting the UDS, the presence of bacteriuria was also evaluated with microbiological study of the urine, and was objectified in 37 (44.1%) patients, whose microorganism most frequently isolated was *Escherichia coli*. Of these, the majority presented as a risk factor the presence of bladder hyperactivity and high RV. They had asymptomatic bacteriuria, that is, without clinical repercussion (no urinary signs or symptoms) and, therefore, without the need of pharmacological intervention, according to NIDRR guidelines.[11]

After the UDS, 2 (2.4%) of the patients showed urinary symptoms, specifically, one patient with fetid urine and pollakiuria and the other with suprapubic discomfort. These patients with clinical manifestations underwent a cytochemical examination and a microbiological study of the urine and none of them demonstrated significant bacteriuria, as defined above, as well leukocyturia or identification of bacterial agent. Therefore, the incidence of UTI in the study, as defined by NIDRR,[11] was 0%.

Table 2

Risk factors for urinary tract infection in spinal cord injury patients

Risk factors for urinary tract infection	N (%)
Less than one risk factor	18 (36.7%)
Detrusor hyperactivity	32 (65.3%)
High residual volume	22 (44.9%)
Vesico-sphincteric dyssynergia	11 (22.5%)
Urethral trauma	4 (8.2%)

Discussion

UTI is the most common complication observed in patients with SCI[1] due to neurogenic bladder and its handling. In this context, bacteriuria is a recurrent problem in patients with vesico-sphincteric dysfunction, with a prevalence described in the literature of 50% to 90%,[12,13] and is often related to the use of catheterization for bladder emptying,[1,7] a factor found in 60.8% of the patients in the study. On the contrary, it is also associated with factors such as detrusor hyperactivity, vesico-sphincteric dyssynergia, and high RVs that lead to urinary stasis.[14,15] In the present study, bacteriuria was identified in 37 (44.1%) of the patients, lower than that described in the literature, and the majority of them had bladder hyperactivity and high RVs, risk factors associated with the onset of UTI, well established in the literature.

In terms of identified microorganisms, *E coli* was the most common, as demonstrated by Schaeffer and Chmiel[16], several decades ago, which report that this microbial agent is the most prevalent in the urethral meatus and that its colonization by potentially pathogenic bacteria increases the risk of bacteriuria associated with catheterization.[17]

The incidence of UTI following invasive procedures is reported to be between 3% and 20% in the literature.[5]

In the study, the incidence of UTI was 0%. According to the NIDRR,[11] the definition of UTI must meet the criteria: presence of significant bacteriuria ($>10^2$ CFU/mL in patients under IC, $>10^4$ CFU/mL in patients with urinary collector and any detectable concentration in patients with CC) plus the presence of at least one sign or symptom of UTI, as described above ("Methods"). Therefore, the incidence of UTI in the study, as defined by NIDRR,[11] was 0% because significant bacteriuria was absent.

As a high-risk group to develop postinterventional complications, antibiotic prophylaxis is recommended in SCI patients who perform UDS but there is still an ongoing discussion if antibiotic prophylaxis is necessary, being controversial among the literature.[18] However, in the reviews described in the literature, antibiotic prophylaxis appears to reduce the risk of significant bacteriuria and symptomatology in patients undergoing UDS compared to patients with nonprophylaxis.[5] In the present study, urinary complaints suggestive of UTI after UDS were observed in 2(2.4%) of the patients, one under CC and the other under IC during daytime by schedule (3/3 h) with CC during nighttime, but both without significant bacteriuria, leukocyturia, or identification of bacterial agent.

This study has some limitations, namely the fact of being a retrospective cohort study; having a small number of participants; the heterogeneity of the characteristics of the studied population regarding the age, type, and duration of SCI; and, finally, the variability of the period elapsed between the microbiological examination of the urine and the performance of the UDS. These limitations may have contributed to the absence of significant results in the evaluation of the effect of antibiotic prophylaxis on the prevention of UTI after UDS.

However, fosfomycin prophylaxis may have been important in limiting the occurrence of UTI in the population studied. Nevertheless, further studies, especially randomized controlled trials, would be necessary to attempt to define the onset, the length, and the type of antibiotic prophylaxis in patients with SCI undergoing UDS.

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Conflicts of interest

The authors declare no conflicts of interest.

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