Treatment of urinary tract infection in persons with spinal cord injury: guidelines, evidence, and clinical practice

A questionnaire-based survey and review of the literature

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Objectives: To investigate current clinical practice in the treatment of urinary tract infections (UTIs) in persons with spinal cord injury (SCI) in SCI centers where German is spoken and to compare it with current guidelines and evidence-based standards evaluated by a literature review.

Methods: A standardized questionnaire was mailed to 16 SCI rehabilitation centers. The results were compared with a literature review

Results: Of the 16 centers, 13 responded. Indications for UTI treatment, medications, and treatment duration differed substantially among the individual centers and from the existing guidelines. Antibiotic treatment is regarded as the method of choice. Compared with the existing literature, patients in two center were undertreated, whereas they were overtreated in seven centers.

Conclusion: Even in specialized centers, treatment of UTI in patients with SCI is based more on personal experience of the treating physicians than on published evidence. This may at least partly be due to the paucity of evidence-based data. The observed tendency toward overtreatment with antibiotics carries substantial future risks, as this strategy may well lead to the induction of multiresistant bacterial strains. Therefore, developing guidelines would be an important step toward a unification of the different treatment strategies, thus reducing unnecessary antibiotic treatment. Furthermore, evidence-based studies evaluating the success of antibiotic treatment as well as the usefulness of alternative strategies are urgently needed.

Keywords: Urinary tract infection, Spinal cord injuries, Evidence-based medicine, Clinical guidelines, Antibiotic therapy, Neurogenic bladder, Cephalosporins, Fluoroquinolones, Cotrimoxazole, Homeopathy

Introduction

Virtually all patients with spinal cord injuries (SCIs) suffer from neurogenic lower urinary tract dysfunction. As a result of impaired storage and voiding function, urinary tract infections (UTIs) occur frequently in this group of patients. UTI is the leading cause for septicemia in patients with spinal cord lesions, which is associated with a significantly increased mortality.¹ Furthermore, symptomatic UTIs are often bothersome for the patients and are therefore related to a decreased health-related quality of life. As UTIs are often recurrent and the bacterial strains are increasingly resistant to antibiotic treatment,² UTIs are a clinical challenge for both patients and caregivers. Thus, one would anticipate a significant body of well-designed studies analyzing the treatment

options for UTI in individuals with SCI, leading to clear-cut recommendations in the existing guidelines. However, this is not the case.

UTIs are not mentioned in the guidelines of the European Urological Association (EAU) on neurogenic lower urinary tract dysfunction.³ The EAU guidelines on urological infections state that screening for and treatment of asymptomatic UTI in patients with SCI is not recommended.⁴ A guideline of an expert panel of German-speaking urologists recommends treatment of relevant UTI, defined as 10^5 bacteria/ml combined with >100 leukocytes/mm³. Antibiotic treatment should be initiated according to the results of microbiologic sensitivity testing.⁵ Due to the paucity of recommendations in the specific guidelines, we undertook a questionnaire-based survey evaluating the current clinical practice of UTI treatment in German-speaking centers specializing in the urological treatment of patients with SCI in

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Germany, Switzerland, and Austria and compared the results with the guidelines recommendations and to the existing evidence based on a literature review.

Methods

A standardized, self-developed questionnaire, evaluating the individual modalities for diagnosis and treatment of UTI in SCI, was mailed to 16 centers in Germany, Switzerland, and Austria. The questionnaire was written in German and only German-speaking centers were contacted. Centers qualified if urologists were included in the rehabilitation team and if the center had at least 30 inpatients. In all, 16 centers met these criteria.

The questionnaire consisted of nine multiple-choice questions concerning definition of 'UTI' and 'symptomatic UTI', use of diagnostic procedures, indications for UTI treatment, therapeutic substances/drugs used, and dosage/duration of treatment. At the end of each question, participants were asked to add any comments or details not covered by the multiple-choice answers.

For the literature review, a database research (MEDLINE, Current Contents) was performed, using the search terms 'urinary tract infection', 'bladder infection', 'neurogenic bladder', 'neurogenic bladder dysfunction', 'neurogenic lower urinary tract dysfunction', 'spinal cord lesion', and 'spinal cord injury'.

The indications for UTI treatment in the individual centers were compared with the recommendations and guidelines and meta-analyses. When patients who should have received treatment according to the reviewed literature (i.e., symptomatic UTI irrespective of leukocyte or bacteria counts in urine) did not qualify for therapy in an individual center, this was rated as 'undertreatment', whereas treatment of patients who did not require therapy according to the literature was termed 'undertreatment'.

Results

Of the 16 centers that were sent questionnaires, 13 returned the completed questionnaire.

Diagnosis of UTI

In all centers, dipstick testing was performed as a screening test, but definitive urinalyses were performed by microscopy. Five centers initiated a urine culture if any bacteriuria was present, whereas eight centers required a combination of bacteriuria and a certain quantity of leukocytes in urine (median 90 leukocytes/mm³, range 40–100 leukocytes/mm³).

Treatment indication

Whereas in 11 centers, every symptomatic UTI was treated irrespective of the urinary leukocyte count, two

centers based their decision not merely on symptoms, but also on 'significant leukocyturia' (>100/ml). In seven centers, asymptomatic bacteriuria was treated when the amount of bacteria and leukocytes was regarded as significant. The definition of 'significant', however, varied from 40 to 500 leukocytes/mm³ and from 10 000 to 1 million bacteria/ml, respectively.

Most frequently listed symptoms leading to the diagnosis of a symptomatic UTI were fever (if other reasons were excluded), dysuria, new onset of incontinence, impaired general well-being, decreased bladder capacity, and increased general spasticity (Table 1).

Two centers did not rely solely on symptoms as an indication for treatment, but required a certain number of bacteria and leukocytes in urine ('undertreatment'); in seven centers, both symptomatic UTI and asymptomatic bacteriuria were treated (overtreatment).

Treatment strategy

All centers agreed that treatment should only be started after a urine specimen has been obtained for microbiologic testing. Twelve centers initiated empiric treatment prior to the results if severe symptoms and/or fever were present. Antibiotic treatment was used as first-line therapy in 11 centers, whereas 2 centers relied on phytotherapy (cranberries, bearberry leaf tea). For UTI in patients with indwelling catheters, five centers recommended increased fluid intake (>1.5 l) or bladder irrigation with sterile saline solution prior to antibiotic treatment. Antibiotics most frequently used for empiric treatment were fluoroquinolones ($n = 7$) and cotrimoxazole ($n = 2$).

Regarding the duration of treatment, mean treatment interval for symptomatic UTI without fever was 7.8 days (range 3–10 days), whereas this time span was extended to 10.2 days (range 7–14 days) if fever was present.

Discussion

This survey was initiated to determine to what extent treatment of UTI in persons with SCI is based on

Table 1 Symptoms leading to the diagnosis of 'symptomatic UTI': frequency of mention

Symptom	Times mentioned (#)
Fever without other causes	13
Dysuria	11
New onset incontinence	10
Suprapubic pain	9
Impaired general well-being	9
Decreased bladder capacity	9
Increased general spasticity	9
Hematuria without other causes	9
New onset voiding problems	7

current guidelines and evidence-based medicine. Thus, we exclusively included centers that specialized in rehabilitation and treatment of persons with SCI. As the questionnaire was designed in German, only German-speaking centers were included.

To be able to compare the current state of care to evidence-based treatment recommendations or guidelines, we undertook a literature survey. Unfortunately, only few published evidence-based guidelines focus on this topic. Moreover, the majority of studies evaluating treatment options for UTI included patients with different underlying disorders; only a small number of studies exclusively dealt with SCI. Recently, a meta-analysis analyzed the current literature related to treatment of UTIs in patients with SCI. It came to the conclusion that antibiotic therapy should only be established in symptomatic UTI. As bacteria seem to be more resistant during the acute phase of SCI, the authors recommend treatment with fluoroquinolones or cefuroxime, whereas in patients with chronic SCI, nitrofurantoin or trimethoprim are first-choice agents, and fluoroquinolones are regarded as second choice.⁶ On the other hand, Waites *et al.*⁷ pointed out that treatment of symptomatic UTI with ciprofloxacin led to the development of ciprofloxacin-resistant strains in more than 50% of the patients at follow-up. As a consequence, they opted for the use of ciprofloxacin only in symptomatic persons not responding to other oral agents. In our survey, ciprofloxacin was the most frequently used substance despite Waites *et al.*'s findings.

Although some authors indicate that in the case of a 'relevant' bacteriuria, with varying definitions of this term, treatment is indicated irrespective of symptoms, there is a broad consensus in the recent literature that only symptomatic UTI^{1,4,6} should be treated. Treatment of asymptomatic bacteriuria may well increase the risk of inducing multidrug resistance and is therefore not advised. Despite this clear statement, more than 50% of the centers included in this survey initiated antibiotic treatment in the case of asymptomatic bacteriuria if the amount of bacteria was regarded as 'relevant'.

The term 'symptomatic UTI' is not well defined. Whereas most authors agree on fever as a symptom,^{1,4,5} other symptoms are less well established. Our survey reflects this situation, as the symptoms utilized by the different centers varied considerably. This uncertainty led to the situation that the care rendered in two centers constituted 'undertreatment' with regard to guidelines, whereas in seven centers, the care was considered as 'overtreatment'.

In our survey, all participants agreed that treatment should be started only after having taken a urine

specimen for microbiologic testing. If possible, treatment should be initiated according to the test results. This is in accordance with several studies,^{1,5} as merely microbiologic testing enables the treating physicians to detect hygienic problems, and most important, to establish adequate effective treatment. Moreover, only statistical evaluation of the centers' individual epidemiology enables empiric treatment, as UTIs in patients with SCI are caused by a wide variety of organisms and are frequently polymicrobial.¹ Therefore, general recommendations for empiric treatment are not possible, but it must be based on the statistics of the respective center.

Deciding which antibiotic drug to use cannot merely be based on the results of microbiologic testing; several other factors must be taken into account. Nitrofurantoin, e.g. achieves only poor parenchymal concentrations and should not be used in patients with pyelonephritis, prostatitis, or epididymitis. Other drugs, such as cotrimoxazole, third-generation cephalosporins, and fluoroquinolones, cover a broad spectrum of bacteria, reach adequate parenchymal and urine concentrations, and can be administered orally. Consequently, these drugs were among the most frequently used medications in the survey.

Regarding the duration of UTI treatment, no consensus in the literature could be found.⁶ In a randomized, double-blind, placebo-controlled trial, comparing the effectiveness of a 3-day versus a 14-day treatment course of ciprofloxacin 250 mg twice a day in 60 patients with acute symptomatic UTI, Dow *et al.* observed microbiological relapse in 11 patients and a symptomatic relapse in 7 patients taking a 3-day course, whereas a relapse was found in 2 and 0 patients, respectively, after a 14-day treatment. Their findings indicate that treatment for 14 days leads to improved clinical and microbiological outcomes.⁸

Based on the results of their meta-analysis, the authors recommend a 7- or 5-day course for UTI without fever in patients with acute or chronic SCI, respectively. UTI with fever should be always treated for 14 days.⁶ In our survey, the mean treatment duration for symptomatic UTI without fever corresponded to these recommendations, whereas UTI with fever were treated for a lesser time span than recommended. Noticeably, the range of the treatment intervals was wide, depicting the variety of different opinions concerning the length of treatment even in specialized centers.

In an era of growing resistance of bacteria to antibiotics, treatment of UTI is not without risks. Hinkel *et al.*² demonstrated that over a 5-year period, the resistance of bacterial strains isolated in persons with SCI against commonly used antibiotics increased significantly.

To avoid the problems related to antibiotic treatment of symptomatic UTI, several other treatment strategies

have been utilized. Unfortunately, for all other treatment options, there is little literature available.

Bladder irrigation with sterile saline, acetic acid, and a neomycin-polymyxin solution had no effect on the degree of bacteriuria or pyuria in patients with indwelling catheters.⁹ Thus, bladder irrigation does not seem to be helpful.

In a randomized, double-blind, placebo-controlled study, cranberry, frequently used for the prevention of UTI, was not useful for the treatment of acute UTI in patients with SCI.¹⁰ Nasturtium herb and horseradish root provided a significant efficacy when tested in patients with recurrent symptomatic UTI, but no patient with SCI was included in that trial.¹¹

The initial results of case studies indicate that auto-vaccination may be clinically useful. This technique, which has been utilized in Eastern Europe for about 20 years, uses inactivated whole-cell vaccines manufactured from disease-causing microorganisms for modulation of the immune system of the individual patient.¹²

Limitations

Our survey has several shortcomings. First of all, the strategies of the individual centers could not be related to treatment results, as a detailed statistic about treatment success and failure in relation to the used treatment strategy was not available in any center. Furthermore, it is evident that treatment of UTI cannot be based on eradication of bacteria alone. If first-line treatment is not successful within 48 hours, not only resistant bacteria but also morphologic reasons for persistent infection, such as renal or prostatic abscess formation, stones, or obstruction, have to be ruled out by ultrasound, endoscopy, computerized tomography, or magnetic resonance imaging.

In summary, treatment of symptomatic UTI in patients with SCI remains a challenge. Although treatment is mandatory, antibiotic therapy alone has proven to be effective, but may well induce resistant strains. Our survey reflects this dilemma. Even in specialized centers, 'undertreatment' and 'overtreatment' were found when comparing the results of the survey to the published literature. As no evidence-based guideline is available, treatment of UTI in patients with SCI seems mainly to be based rather on the personal experience of the treating physicians rather than on published evidence. Although not an evidence-based guideline, a consensus statement of the National Institute on Disability and Rehabilitation Research provides an overview about definition, prevention, and management of UTI in SCI, based on a consensus validation conference. The definition of UTI as well as the proposed treatment regimens still reflect the dilemma of very few evidence-based

studies, but may be of practical help for anybody dealing with UTI in people with SCI.¹³

The observed tendency toward overtreatment with antibiotics carries substantial future risks, as this strategy may well lead to the induction of multiresistant bacterial strains. The tendency toward overtreatment may at least partly be due to the paucity of evidence-based data available. Clearly, evidence-based studies evaluating antibiotic treatment strategies in this cohort of patients are urgently needed.

The usefulness of alternative treatment options, however, should also be further evaluated. For example, the combination of nasturtium herb and horseradish root was successful in treating patients with UTI, but its usefulness in patients with SCI has not yet been assessed. In our personal experience, homeopathic treatment provided favorable results if initiated by experts. As this therapy is based on re-establishing equilibrium between the persons own driving force ('life force') and the opposing constitutional base ('miasm'), which determines the type and intensity of sickness, the treatment goal is to regain inner balance.¹⁴ Thus, this treatment is by its nature strictly individualized and therefore randomized studies are not feasible, but at least case studies should be performed in order to evaluate the extent to which homeopathy may add to the armamentarium of UTI treatment in persons with SCI.

Conclusion

Our evidence-based knowledge of UTI treatment in persons with SCI is scarce. According to evidence-based guidelines, merely symptomatic UTI should be treated with antibiotics. Treatment should be based on the results of microbiologic testing if possible, and taking a urine specimen is mandatory. For many details, however, like duration of treatment, substances to use, etc., sound medical evidence does not exist. The survey presented here clearly pointed out that treatment of UTI in patients with SCI is not well standardized even in expert centers. Thus, in addition to previous studies in this area, it was demonstrated that more education is needed on the current recommendations/consensus on the unique management of UTI in SCI individuals. Furthermore, as our evidence-based knowledge is limited, more well-designed studies are urgently needed.

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