



Analysis of the factors influencing development of urinary tract infections in patients with spinal cord injuries

Analiza faktora razvoja infekcije urinarnog trakta kod bolesnika sa povredom kičmene moždine

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Abstract

Background/Aim. Urinary tract infections are still the most frequent complications in patients with spinal cord injury (SCI). The aim of this study was to analyze the factors influencing development of urinary tract infections during rehabilitation in patients with SCI. **Methods.** This retrospective case/control study including 540 patients with SCI which were rehabilitated in the Clinic for Rehabilitation “Dr Miroslav Zotović” between January 2000 and December 2009. We used patient files and other available medical documentation for obtaining information contained in this study, such as the manner of bladder emptying, the type of neurological disorder of the bladder, the neurological level and completeness of a lesion, the injury etiology, treatment method, secondary complications and associated injuries, kidney and bladder calculosis, age and sex. **Results.** Out of the total number of patients included in the study, 152 (28.1%) were without urinary tract infections, whereas 388

(71.9%) had urinary tract infections. There were 389 (72%) male and 151 (28%) female patients. The average age of patients without urinary tract infections was 51.0 ± 15.4 years, whereas the mean age of patients with urinary tract infections was 44.3 ± 16.9 years. The results of our study showed that the occurrence of urinary tract infections during rehabilitation in patients with SCIs was associated with the following factors: combined injuries (OR = 3.5), anemia (OR = 5.67), type of the bladder functional disorder (OR = 40–60) and crystals in urine (OR = 7.54). **Conclusion.** The physicians should take precautions and try to make the early diagnosis and rapid appropriate treatment of urinary tract infections in patients with SCI who also have functional bladder disorder, combined spinal injuries, anemia or urine crystals.

Key words: spinal cord injuries; urinary tract infections; risk factors; urinary catheterization; multiple trauma; anemia; rehabilitation.

Apstrakt

Uvod/Cilj. Infekcije urinarnog trakta još uvek su najčešće komplikacije kod bolesnika sa povredom kičmene moždine. Cilj rada bio je da se ispituju faktori koji mogu uticati na razvoj urinarnih infekcija u toku rehabilitacije bolesnika sa povredom kičmene moždine. **Metode.** Ova retrospektivna studija slučaja obuhvatila je 540 ispitanika sa povredom kičmene moždine koji su rehabilitovani u Klinici za rehabilitaciju „Dr Miroslav Zotović“ u periodu od januara 2000. do decembra 2009. godine. Za dobijanje podataka koji su korišćeni u ovoj studiji kao što su način pražnjenja

mokraćne bešike, vrsta neurološkog poremećaja mokraćne bešike, neurološki nivo i kompletnost lezije, etiologija povrede, način lečenja, sekundarne komplikacije, udružene povrede, kalkuloze bubrega i bešike, starost i pol, korišćene su istorije bolesti i ostala medicinska dokumentacija. **Rezultati.** Od ukupnog broja ispitanika koji su bili uključeni u ovu studiju 152 (28,1%) je bilo bez urinarnih infekcija, dok je 388 (71,9%) imalo urinarne infekcije. Bilo je 389 (72%) muškaraca i 151 (28%) žena. Prosečna starost ispitanika bez urinarnih infekcija bila je $51,0 \pm 15,4$, a bolesnika sa urinarnim infekcijama $44,3 \pm 16,9$ godina. Rezultati naše studije ukazuju na to da su faktori koji naj-

više doprinose razvoju urinarnih infekcija tokom rehabilitacije bolesnika sa povredom kičmene moždine udružene povrede (OR = 3,5), anemija (OR = 5,67), način pražnjenja mokraćne bešike (OR = 40–60) i kristali u urinu (OR = 7,54). **Zaključak.** Kliničari bi trebalo da sprovedu ranu dijagnostiku i adekvatno terapijsko lečenje infekcija urinarnog trakta kod osoba sa povredom kičmene moždine i

poremećajem pražnjenja mokraćne bešike, kombinovanim povredama, anemijom i kristalima u urinu.

Ključne reči:

kičmena moždina, povrede; urinarni trakt, infekcije; faktori rizika; kateterizacija urinarnog trakta; povrede, multiple; anemija; rehabilitacija.

Introduction

A spinal cord injury (SCI) is characterized by the loss of motor function and sensibility below the injury level and the loss of reflex activity¹.

The causes of SCIs include trauma, vascular disorders, tumors both of malignant and benign etiology, infections, development disorders, etc². The patients with SCIs may suffer from many secondary complications, like urinary tract infections, decubital ulcers, cardiovascular and respiratory tract diseases, etc³. Urinary tract infections are the most frequent complications occurring after SCI and use to be the main cause of death in the past⁴. In addition, the risk of nosocomial infections is greater in patients with SCI than in patients without SCI. A patient is suffering from urinary tract infection if, apart from confirmed bacteriuria, has one of the following clinical symptoms: increased body temperature (> 38°C), stomach pain, urinary incontinence, increased spasticity, suprapubic pain, frequent urination, dysuria, unpleasant urine odor, etc⁵. If these symptoms are missing, a patient has asymptomatic bacteriuria. The asymptomatic bacteriuria should not be treated with antibiotics⁶.

The loss of reflex activity after SCI is characterized by partial or complete loss of sphincter control (urination and defecation). Incontinence, vesicoureteral reflux, permanent catheter use, performance of intermittent catheterization or self-catheterization are only some of the factors which may influence the development of urinary tract infections⁷. Additionally, these factors may also influence the reoccurrence of urinary tract infections both during rehabilitation and in the post-rehabilitation period⁸. Some studies say that urinary tract infections are the most frequent cause for rehospitalization after SCIs⁹. Knowing the factors which may influence the development of urinary tract infections, we can create a prediction model and thus decrease the frequency and adverse influence of urinary tract infections on the duration of rehabilitation and quality of life¹⁰.

The aim of this study was to determine factors influencing the development of urinary tract infections in patients with SCIs during rehabilitation.

Method

This retrospective case/control study enrolled 592 patients with SCIs hospitalized at the Clinic for Rehabilitation "Dr Miroslav Zotović" in Belgrade, Serbia between January 2000 and December 2009. The cases were the patients with developed urinary tract infections, and the controls were the patients in which urinary tract infections did not develop.

The cases and controls were matched according to the age and sex.

The patients meeting the following criteria were included in the study: diagnosed with SCIs and hospitalized at the Clinic for Rehabilitation "Dr Miroslav Zotović" in Belgrade, suffering from bladder emptying disorder caused by SCIs, and hospitalized longer than 30 days.

The criteria for exclusion from the study were: any kind of deterioration of the basic disease causing termination of the rehabilitation process, the patients younger than 18 years.

Based on the exclusion criteria, 52 patients were excluded from the study, and the remaining 540 were taken into account for statistics and drawing conclusions.

The presence of urinary tract infection was confirmed by urine culture with antibiogram. The following laboratory analyses were done in patients diagnosed with urinary tract infection: complete blood count with erythrocyte sedimentation rate, leukocyte formula, blood biochemistry, urine biochemistry and urine sediment analysis. Blood biochemistry included: the level of urea, creatinine, uric acid, serum albumins and proteins, alkaline phosphatase, and serum iron level.

The following potential risk factors for urinary tract infections in patients with SCIs were noted if present: method of bladder emptying, type of neurological disorder of the bladder, neurological level and completeness of the lesion, injury etiology, treatment method, secondary complications and combined injuries, bladder and/or kidney calculi, age and sex. The information was obtained from the patient's files and other available medical documentation of the patients.

The subjects were duly informed about the methodology of this study and voluntarily signed a consent form. The study was approved by local Ethics Committee (Clinic for Rehabilitation "Dr Miroslav Zotović") under the registration number 03-1882/2013.

During hospitalization the patients underwent the series of tests for evaluating the type of neurogenic injury of the bladder after SCI and the presence of neurological consequences: full urodynamic testing¹¹ for evaluating the bladder functional condition, to diagnose of bladder and kidney calculi were diagnosed with radiographic and ultrasound examination, American Association Impairment Scale (AAIS) test for evaluating the neurological level and completeness of lesion^{12,13}, Modified Ashworth Score (MAS) test for evaluating the degree of spasticity¹⁴, Manual Muscle Test (MMT) for evaluating the muscle strength¹⁵.

For the primary data analysis, we used descriptive statistical methods, statistical hypothesis testing and the methods for analyzing the relationship between the outcome and potential predictors. We used the following descriptive statistical met-

hods: the measures of central tendency (arithmetic mean), variability measures (standard deviation) and relative numbers. For testing the hypotheses on the difference between frequencies, we used the following: χ^2 -square test, Fisher's test of exact probability and McNemar's test; *t*-test and Mann-Whitney test were used for testing the hypotheses on the arithmetic mean differences. Logistic regression was used as the method for analyzing binary outcome and potential predictors.

Statistical hypotheses were analyzed at the level of significance of 0.05.

Results

Out of the total number of the patients included in the study, 152 (28.1%) were without urinary tract infections, whereas 388 (71.9%) had urinary tract infections.

There were 389 (72%) male and 151 (28%) female patients. Exactly 73.2% of the male patients and 26.8% of the female patients had urinary tract infection. The difference in the prevalence of sexes between the studied groups was not statistically significant ($p = 0.338$).

The mean age was found to be 46.2 ± 16.7 years. The average age of patients without urinary tract infections was 51.0 ± 15.4 years, whereas the mean age of patients with urinary tract infections was 44.3 ± 16.9 years. There was a significant age difference between the studied groups ($p < 0.001$): urinary tract infections occurred more frequently in younger patients. These and other characteristics of the patients with SCI are shown in Table 1.

ficant ($p < 0.001$). Urinary tract infections occurred more frequently in patients with traumatic SCI.

Out of the total number of patients, 195 (36.1%) had a complete and 345 (63.9%) had an incomplete SCI. Urinary tract infections were present in 61.4% of the patients with incomplete SCI and in 90.3% of the patients with complete SCI.

Urinary tract infections occurred more frequently in the patients with complete SCI ($p < 0.001$).

In all the patients with SCI, the most common was complete lesion American Spinal Injury Association (ASIA) A (195 patients, or 36.1%), followed by the ASIA C (201 patients, or 37.2%), ASIA B (94 patients, or 17.4%) and ASIA D type (50 patients, 9.3%). The patients without urinary tract infections most frequently had ASIA C level on admission (92 patients, 60.5%), whereas the patients with urinary tract infections most frequently had ASIA A level on admission (176 patients, 45.4%). There was a significant difference in the frequency of ASIA levels on admission between the studied groups ($p < 0.001$).

In the patients with SCI, the most common were thoracic injuries (42.8%), followed by cervical (35.0%) and lumbar ones (22.2%). Urinary tract infections were present in 68.3% of the patients with cervical injuries, in 79.7% of the patients with thoracic injuries, and in 62.5% of the patients with lumbar injuries. There was significant difference in the frequency of certain neurological level of injury on admittance between the studied groups ($p < 0.001$). Urinary tract infections were more frequent in patients with thoracic spine injuries.

Out of the total number of patients, 132 (24.4%) had

Table 1
Characteristics of the patients with spinal cord injuries

| Parameter | Patients | | <i>p</i> |
|---|-----------------------|--------------------------|----------|
| | with UTI (n = 388) | without UTI (n = 152) | |
| Age (years), $\bar{x} \pm SD$ | 44.3 \pm 16.9 | 51.0 \pm 15.4 | < 0.001 |
| Sex, n (%) | | | |
| male | 284 (73.2) | 105 (69.1) | 0.338 |
| female | 104 (26.8) | 47 (30.9) | |
| Etiology of injury, n (%) | | | |
| traumatic | 264 (68) | 57 (37.5) | < 0.001 |
| non-traumatic | 124 (32) | 95 (62.5) | |
| Completeness of injury, n (%) | | | |
| complete | 176 (45.4) | 19 (12.5) | < 0.001 |
| incomplete | 212 (56.4) | 133 (87.5) | |
| Level of injury, n (%) | | | |
| cervical | 129 (68.3) | 60 (31.7) | < 0.001 |
| thoracic | 184 (79.7) | 47 (20.3) | |
| lumbar | 75 (62.5) | 45 (37.5) | |
| Length of stay (days), $\bar{x} \pm SD$ | 166.7 \pm 89.5 | 96.4 \pm 66.6 | < 0.001 |

UTI – urinary tract infections.

Out of the total number of patients 321 (59.4%) had traumatic SCI, and 219 (40.6%) non-traumatic injuries. Urinary tract infections were present in 68.0% of the patients with traumatic injuries and in 32.0% of the patients with non-traumatic injuries. The difference in the frequency of urinary tract infections between the studied groups was signi-

ficant ($p < 0.001$). Urinary tract infections occurred more frequently in patients with traumatic SCI. Out of the total number of patients, 195 (36.1%) had a complete and 345 (63.9%) had an incomplete SCI. Urinary tract infections were present in 61.4% of the patients with incomplete SCI and in 90.3% of the patients with complete SCI. Urinary tract infections occurred more frequently in the patients with complete SCI ($p < 0.001$). In all the patients with SCI, the most common was complete lesion American Spinal Injury Association (ASIA) A (195 patients, or 36.1%), followed by the ASIA C (201 patients, or 37.2%), ASIA B (94 patients, or 17.4%) and ASIA D type (50 patients, 9.3%). The patients without urinary tract infections most frequently had ASIA C level on admission (92 patients, 60.5%), whereas the patients with urinary tract infections most frequently had ASIA A level on admission (176 patients, 45.4%). There was a significant difference in the frequency of ASIA levels on admission between the studied groups ($p < 0.001$). In the patients with SCI, the most common were thoracic injuries (42.8%), followed by cervical (35.0%) and lumbar ones (22.2%). Urinary tract infections were present in 68.3% of the patients with cervical injuries, in 79.7% of the patients with thoracic injuries, and in 62.5% of the patients with lumbar injuries. There was significant difference in the frequency of certain neurological level of injury on admittance between the studied groups ($p < 0.001$). Urinary tract infections were more frequent in patients with thoracic spine injuries. Out of the total number of patients, 132 (24.4%) had

ference in the frequency of bladder functional disorders between the studied groups ($p < 0.001$).

Various methods of bladder emptying were used: intermittent self-catheterization in 278 (51.5%) of the patients, intermittent catheterization in 69 (12.8%) of the patients, tapping in 28 (5.2%) patients, permanent catheter in 31 (5.7%) of the patients and spontaneous emptying (urgent urination) in 134 (24.8%) of the patients. In patients without urinary tract infections, the most common method of bladder emptying was spontaneous one (urgent urination) (72.4%), whereas in those with urinary tract infections, the most frequent method was intermittent self-catheterization (62.9%). There was a significant difference in the methods of bladder emptying between the studied groups ($p < 0.001$).

There were 127 (23.5%) patients with combined SCIs, and 413 (76.5%) without combined injuries. Exactly 13.8% of the patients without urinary tract infections had combined injuries, whereas the number of patients with urinary tract infections and combined injuries was 27.3%. There was a significant difference in frequency of combined injuries between the studied groups ($p = 0.001$).

Out of the total number of patients, 291 (53.9%) were not anemic, whereas 249 (46.1%) of them were. Exactly 10.5% of the patients without urinary tract infections had anemia, whereas the number of patients with urinary tract infections and anemia was 60.2%. There was a significant difference in the rate of anemia between the studied groups ($p < 0.001$).

In 209 (38.7%) patients urine crystals were not found, whereas in 331 (61.3%) of them were. In 16.4% of the patients without urinary tract infections urine crystals were fo-

und, whereas the number of patients with urinary tract infections and urine crystals was 78.9%. There was a significant difference in the frequency of urine crystals between the studied groups ($p < 0.001$).

The average duration of rehabilitation for all the patients was 147.0 ± 89.4 days. The minimal duration of rehabilitation was 28 and the maximal was 533 days. The average duration of rehabilitation in the patients with urinary tract infections was 166.7 ± 89.5 days, and in patients without urinary tract infections the average duration was 96.4 ± 66.6 days, which made significant difference ($p < 0.001$). The rehabilitation lasted much longer in the patients with urinary tract infections.

The model of multiple logistic regression included those predictors which had statistical significance at the level of 0.05 within the model of simple logistic regression, as well as those predictors which were considered, based on the previous research, as potentially significant for the development of urinary tract infections during rehabilitation. The model contained 13 predictors which were compared in 540 patients, and 387 of them had the result which was of interest to the study. The entire model (with all the predictors) was statistically significant ($p < 0.001$) (Table 2).

Logistic regression was used for analyzing the relationship between binary results and potential predictors.

In the model of multiple logistic regression, the statistically significant predictors for the development of urinary tract infections during rehabilitation were the following: combined injuries ($B = 1.259$; $p = 0.009$), type of bladder functional disorder [hyper-reflexic bladder ($B =$

Table 2

| Independent variable | B | p | OR | 95% confidence interval | |
|--|--------|---------|--------------------|-------------------------|-------------|
| | | | | lower limit | upper limit |
| Age | -0.005 | 0.638 | 1.00 | 0.97 | 1.02 |
| Gender | 0.566 | 0.128 | 1.76 | 0.85 | 3.65 |
| Etiology of injury | -0.132 | 0.739 | 0.88 | 0.40 | 1.90 |
| Combined spinal cord injury | 1.259 | 0.009 | 3.52 | 1.37 | 9.08 |
| Urinary infections before rehabilitation | 1.275 | 0.221 | 3.58 | 0.46 | 27.62 |
| Type of lesion | 0.120 | 0.790 | 1.13 | 0.47 | 2.74 |
| Pressure ulcers during rehabilitation | 1.014 | 0.171 | 2.76 | 0.65 | 11.78 |
| Spasticity during rehabilitation | 0.682 | 0.134 | 1.98 | 0.81 | 4.83 |
| Neurological level of injury | | | | | |
| cervical | | | reference category | | |
| thoracic | 0.730 | 0.141 | 2.08 | 0.79 | 5.49 |
| lumbar | 0.033 | 0.955 | 1.03 | 0.33 | 3.21 |
| Type of bladder emptying | | | | | |
| spontaneous | | | reference category | | |
| intermittent self-catheterization | -1.057 | 0.440 | 0.35 | 0.02 | 5.07 |
| intermittent catheterization | -0.137 | 0.925 | 0.87 | 0.05 | 15.05 |
| tapping/Crede maneuver | -1.619 | 0.283 | 0.20 | 0.01 | 3.81 |
| permanent catheter | 0.167 | 0.917 | 1.18 | 0.05 | 27.67 |
| Type of functional bladder disorder | | | | | |
| none | | | reference category | | |
| hyper-reflexic bladder | 4.078 | 0.002 | 59.01 | 4.47 | 779.85 |
| hypotonic bladder | 3.603 | 0.011 | 39.69 | 2.29 | 586.92 |
| Anemia | 1.739 | < 0.001 | 5.69 | 2.64 | 12.26 |
| Urine crystals | 2.020 | < 0.001 | 7.54 | 3.84 | 14.80 |

4.078; $p = 0.002$) and hypotonic bladder ($B = 3.603$; $p = 0.011$) in relation to bladder injury with urgent urination as a reference category], anemia ($B = 1.739$; $p < 0.001$) and urine crystals ($B = 2.020$; $p < 0.001$)

Discussion

Urinary tract infections frequently follow SCI, but chances for their development were 3.5 times higher in our patients with combined SCIs. This is not surprising, since severity of SCI was already linked to increased complication rate, including the urinary tract infection¹⁶. More severe SCIs, more difficult to treat and the patients with such injuries are longer hospitalized, which increases risk of all kinds of nosocomial infections including urinary tract ones¹⁷.

Our results show that patients with SCI and hyper-reflexic bladder have much more chances to develop urinary tract infection. Hyperreactivity of the bladder involves strong detrusor contractions uncoordinated with relaxation of the internal urethral sphincter, which create turbulent urethral urine flow with elements of retrograde urethrovaginal passage of urine. It was noted in a study on young girls with hyperreactivity of the bladder that urinary tract infection are much more frequent than in girls without the hyperreactivity¹⁸. On the other hand, as shown in our study, hypotonic bladder is also a risk factor for urinary tract infection, since delayed bladder emptying gives time to microorganisms to replicate and reach bladder mucosa. Urinary tract infections are more frequent in all patients with hypotonic bladder, regardless the cause¹⁹.

Anemia is a well-known risk factor for infections at multiplicity of sites in human organism. Decreased oxygenation of tissues disrupts natural barriers for infection, and the immune system is less efficient in such circumstances. Surgical patients with anemia more frequently develop postoperative infections than those with normal hemoglobin level²⁰. As shown in our study, the patients with SCI and anemia are much more likely to develop urinary tract infection than patients without anemia; this underlines necessity for early discovery and rapid treatment of iron-deficiency and other types of anemia in patients with SCI, in order to prevent emergence of urinary tract infections. Our results are similar to the results of previous studies on the relationship of anemia and SCIs. Grossman et al.²¹ in their study show that anemia is one of most frequent complications in acute SCI patients followed by pneumonia, pleural effusion, cardiac dysrhythmia, and severe bradycardia. In a study by Cuttitta et al.²² the risk factors of asymptomatic bacteriuria, and the association between different clinical and laboratory pa-

rameters and asymptomatic bacteriuria were examined. Their study showed that obesity and iron deficiency anemia were independent risk factors for asymptomatic bacteriuria.

The association between urine crystals and urinary tract infections observed in our patients with SCI could have been expected, since urine crystals are characteristics of concentrated and stagnant urine. Insufficient intake of water by patients with SCI and slowed bladder emptying create concentrated and stagnant urine, which is suitable medium for growth of microorganisms. The association of urine crystals and urinary tract infections has already been shown in many different patient groups^{23,24}. Torzewska et al.²⁵ in their *in vitro* study hypothesized that one of the reasons for recurrence of the disease may be the ability of bacteria to invade urothelial cells, persist in the host cells and serve as potential reservoirs for infection. An *in vitro* model was used in this study to analyze intracellular growth and crystallization in the presence of *Proteus mirabilis*, *Klebsiella pneumoniae* and *Escherichia coli*. Their results show that *Proteus mirabilis* has an ability to form crystals inside the host cells. Under these conditions bacteria are protected from antibiotic killing, which leads to persistent and recurrent infections. They also suspect that this phenomenon may play an important role in kidney stones formation.

There are certain limitations of our study, which may indirectly affect the obtained results. The study was conducted as a single-centre study, so local patterns of SCI patients care could mask some of the factors which could influence urinary tract infection rate. Besides, the study included both patients with traumatic and non-traumatic SCIs, which differ in many ways one from another. Future studies should concentrate on each of these two populations separately, in order to reveal some specific risk factors, but only after a sufficient number of patients is provided.

Conclusion

The patients with spinal cord injury and functional bladder disorder, combined spinal injuries, anemia or urine crystals are under increased risk for the development of urinary tract infections. When one or more of these factors are present in those with spinal cord injury, the physicians should take precautions and try to make the early diagnosis of urinary tract infections. This is the way to reduce the incidence of urinary tract infections and provide continuity in implementation of kinesitherapy which is often stopped due to these complication. It also will reduce the length of rehabilitation and increase quality of life of those with spinal cord injury.

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