

CORRELATION AMONG BACTERIOLOGICAL, LABORATORY AND CLINICAL CHARACTERISTICS OF NOSOCOMIALLY ACQUIRED URINARY TRACT INFECTIONS (NAUTI)

Milan Potic

Urinary tract infections occurring at least 48 hours upon admission into hospital can be considered nosocomially acquired. Microorganisms which cause them are various and show a high degree of resistance to antibiotics. Clinical characteristics of NAUTI can vary from slightly elevated values of C-reactive protein (CRP) to sepsis with lethal outcome. The aim of the paper was to evaluate bacteriological, laboratory and clinical parameters of NAUTI as well as their correlation.

The study comprised seventy-five patients from the Urology Clinic during the period of four months. Three samples of urine were taken to determine NAUTI and multiple antibiotic resistance index (MAR). The samples were taken upon the admission, on the fifth day in hospital and on the fifth postoperative day. Blood samples were taken at the same time to determine laboratory characteristics. Clinical parameters were also noted. Bacteriological, laboratory and clinical characteristics were analyzed using the Pearson's correlation test.

The most frequently isolated microorganism was *E. Coli* (28%). In 48 urine samples (62%), the number of isolated bacteria was under 10⁵ /ml of urine. In 61 isolates (74, 4%), MAR index values were higher than 0,5. Forty-two patients (56%) had fever. Shiver was noted in 22 (29, 3%) patients. Nine patients (12%) had sepsis. CRP values were elevated in 66 (88%) patients, while values of serum leukocytes were over 10x10⁹/l in 21 patients (28%).

The most common pathogens of NAUTI are *E. Coli*, *Klebsiella* and *Pseudomonas*. There is a high level of antibiotic resistance among pathogens causing NAUTI. CRP is the most sensitive routine parameter for NAUTI. The rise in the number of isolated bacteria in patients with NAUTI is followed by elevation of CRP. Leukocytosis is not a parameter sensitive enough for determining and following NAUTI. NAUTIs are followed in more than half of cases by fever, while shiver is not very common. The incidence of sepsis in NAUTI is 12 %. *Acta Medica Medianae* 2007;46(2):5-8.

Key words: correlation, nosocomial infection, laboratory parameters, clinical parameters

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Microorganisms which cause them are various and show a high degree of resistance to antibiotics. Clinical characteristics of NAUTI can vary from asymptomatic bacteriuria, symptomatic bacteriuria, cystitis, pyelonephritis, systemic inflammatory response (SIRS) to urosepsis with lethal results (5).

Introduction

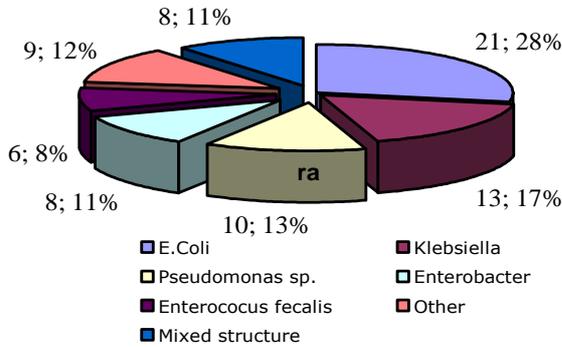
Urinary tract infections occurring at least 48 hours upon admission into hospital can be considered nosocomially acquired. Nosocomial infections in urology account for 40-50% of all nosocomial infections (1). In 66-68% they are the result of instrumentation (1). Among catheterized patients, the rate of nosocomial infections is 65-76% (2). There are three main routes of infection: ascending rout through urethra when placing catheter, trough the mucus layer between catheter and urethra and through catheter tube (3). Inadequate hospital care, broad antibiotic usage, high risk patients, invasive diagnostics as well as methods of urine drainage can be considered as predisposing factors for NAUTI (4).

Material and methods

Seventy-five patients from the Urology Clinic were followed up during the period of four months. Three samples of urine were taken to determine NAUTI, identify the microorganisms and multiple antibiotic resistance index (MAR). The samples were taken on the admission day, on the fifth day in hospital and on the fifth postoperative day. The method for determining the values of MAR index was described by Krumpalman 1983. Blood samples were taken at the same time to determine CRP values and serum leukocytes. Clinical parameters included body temperature, shiver and sepsis. Bacteriological, laboratory and clinical characteristics were analyzed using the Pearson's correlation test.

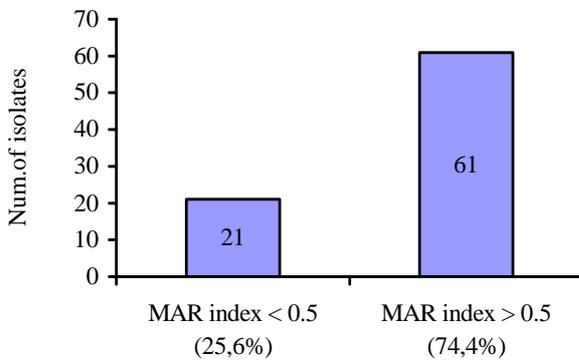
Results

The structure of microorganisms responsible for NAUTI is shown in Graph 1. The most frequently isolated microorganisms are *E. Coli* 21/75 (28%), *Klebsiella* 13/75 (17%) and *Pseudomonas* 10/75 (13%) followed by *Enterobacter* 8/75 (11%) and *Enterococcus fecalis* 6/75 (8%), while 8/75 (11%) of patients have isolates with two microorganisms.

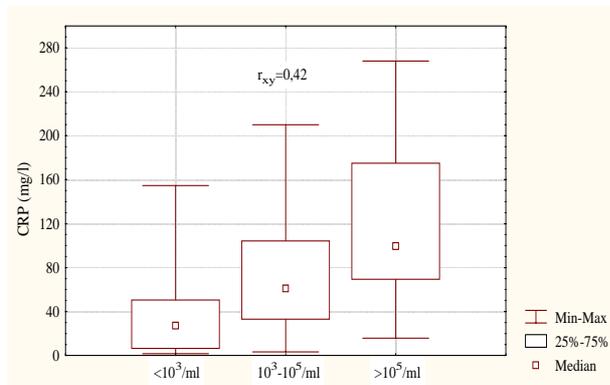


Graph 1. Structure of NAUTI pathogens

Graph 2 shows resistance of bacteria responsible for NAUTI by MAR index. In 61/82 (74,4%) isolates, the value of MAR index was higher than 0,5. In 21/82 (25,6%), the value of MAR index was lower than 0,5. Mean value of MAR index was 0,65 with standard deviation 0,18.



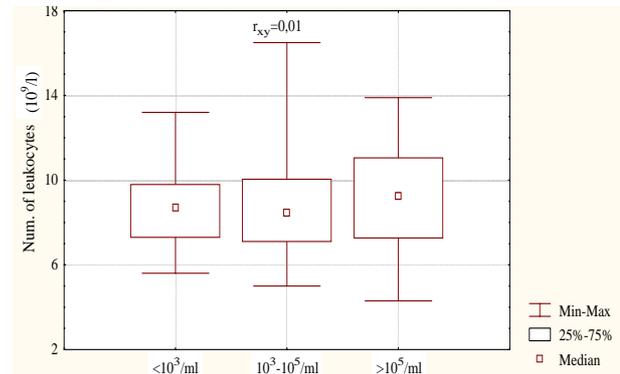
Graph 2. Resistance of NAUTI pathogens (MAR index)



Graph 3. Changes of CRP values with regard to the number of isolated bacteria

In 12/75 (16%) of patients the number of isolated microorganisms was less than 10^3 /ml of urine. In 27/75 (36%) of patients, the number of isolated microorganisms was higher than 10^5 /ml of urine. The most frequently isolated number of microorganisms (48%) was in range 10^3 - 10^5 /ml of urine.

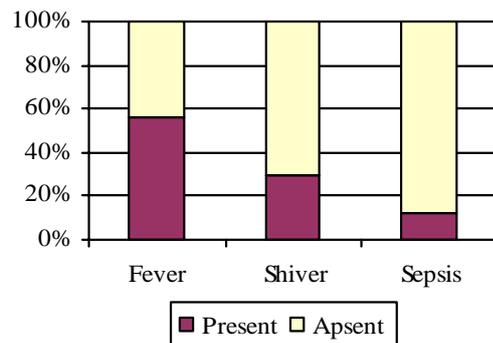
Graph 3 represents the change in CRP levels in regard to the number of isolated germs. CRP levels were elevated in 66/75 of patients. Mean CRP level in group with up to 10^3 /ml of urine was 27mg/l. In group with 10^3 - 10^5 /ml of urine, CRP mean value was 61,2mg/l. Mean CRP level in group with more than 10^5 bacteria/ml of urine was 99,65mg/l. There is a statistically significant positive correlation between the number of isolated bacteria and CRP levels ($p=0.001$).



Graph 4. Changes of serum leukocyte values in regard to the number of isolated bacteria

Graph 4 shows changes in serum leukocyte values in regard to the number of isolated bacteria. Serum leukocytes values higher than 10×10^9 /l are noted in 21/75 (28%) of patients. Mean serum leukocyte value in the group with up to 10^3 bacteria/ml of urine was $8,7 \times 10^9$ /l. In the group with the number of isolated bacteria ranging from 10^3 to 10^5 /ml, the mean value was $8,45 \times 10^9$ /l, while in group with more than 10^5 /ml of isolated bacteria the mean value was $9,25 \times 10^9$ /l. Correlation between number of bacteria and serum leukocyte values was statistically insignificant ($p=0,97$).

Graph 5 shows changes of clinical parameters in NAUTI. High temperature was present in 42/75 (56%) of patients, while shiver was present in 22/75 (29,3%) of patients. The incidence of sepsis was (9/75) 12%.



Graph 5 Clinical parameters in NAUTI

Discussion

The most frequently isolated microorganism is *E. Coli* 21/75 (28%). Large studies are naming *Pseudomonas* to be the most common with 25%, while *E. Coli* is on the third place with incidence of 13%. We must mention that that was the study comprising the period from 1994 to 1999, including 10 000 analyzed patients (6). In the results of epidemiological studies, Consensus conference on NAUTI 2003 emphasizes that *E. Coli* can be the predominant cause of NAUTI, but not as predominant as in community-acquired urinary tract infections. This comes as a result of incidence rise of enteral flora and *Pseudomonas* in NAUTI, which contributes to our results. European study group on nosocomial infections (ESGNI) also lists *E. Coli* as predominant microorganism in NAUTI with 37,4% in European countries, while in non-European countries, the incidence is lower - 30,6% on account of *Pseudomonas aeruginosa* rise (7). In our study, the incidence of *Klebsiella* was (13/75) 17% and *Pseudomonas* (10/75) 13%. In 8/75 of patients (11%), the isolates had two microorganisms. In European countries, mixed samples have the incidence of 7,5%, while in non-European countries, the incidence is 6,8% (8).

Analyzing the resistance of bacteria to antibiotics using the MAR index, we came to the result that 61/75 (74,4%) of patients show high degree of resistance, MAR index higher than 0,5. High level of resistance is mainly the cause of broad antibiotic usage (9). Trend of rise in resistance to antibiotics dates from the time when beta lactam antibiotics were used as empiric therapy in the treatment of NAUTI, continuing in the era of trimethoprim sulfametoksazol. In the twentieth century, the need for overcoming the problem of resistance for treatment of NAUTI resulted in new type of antibiotics called fluoroquinolones, which became the empiric standard throughout the twentieth century (Nickel 2005). There are not many papers analyzing resistance regardless of the type of bacteria. ESGNI gives the results of resistance of gram negative bacteria to Ampicillin (66%), Ciprofloxacin (16,7%) and Gentamycin (17,8%). The same authors evaluate resistance of *Pseudomonas* slightly higher to Ciprofloxacin (42,9%), 46% to Gentamicin, and 19,4% to Amikacin (7). In the same study, the resistance to Imipenem is reported to be 2,8% in total and 13,5% for *Pseudomonas aeruginosa*, while in our study there was no resistance to carbapenems.

In 48% of the patients, the number of isolated bacteria in urine sample was ranging from 10^3 /ml to 10^5 /ml. Over 10^5 /ml was registered in 36% of samples, while in 16% of the patients, the number of isolated bacteria per ml of urine was less than 10^3 /ml. Approximately the same results are reported by other authors (8), pre-

senting the following: 10^3 - 10^5 /ml in 48,6%, over 10^5 /ml in 32,4% and less than 10^3 /ml in 19%.

CRP is taken into consideration as an acute inflammation protein. Elevated values were noted in 66/75 (88%) patients. Studies linking CRP and NAUTI are not available. Serum leukocytes are commonly used. In our study, a positive correlation between the number of bacteria and CRP level was determined with high statistical significance ($p=0,001$). Median value of CRP in the group with less than 10^3 bacteria/ml of urine was 27mg/l. In the group with 10^3 - 10^5 bacteria /ml of urine, the median value was 61,2mg/l, while in the group with more than 10^5 bacteria /ml of urine, the median value was 99,65mg/l.

Serum leukocytes do not show significant correlation with the number of bacteria in our study ($p=0,97$). The significance of monitoring the values of leukocytes is in categorization of SIRS and sepsis (8). Only 21/75 (28,0%) of patients had serum leukocytes over 10×10^9 /l. Median serum leukocyte value in group with up to 10^3 bacteria/ml of urine was $8,7 \times 10^9$ /l. In the group with number of isolated bacteria ranging from 10^3 to 10^5 /ml the median value was $8,45 \times 10^9$ /l, while in the group with more than 10^5 /ml of isolated bacteria the median was $9,25 \times 10^9$ /l.

Fever was noted in 42/75 (56%) of patients. Other studies give reports of 51,1%, with differences between European countries (44,7%) and non-European countries (59%). Difference is also reported between catheterized (57,0%) and non-catheterized (42,3%) patients (8). In our study, these differences between catheterized and non-catheterized patients were not analyzed.

Shiver was present in 22/75 (29,3%) of patients and, as a rule, is always associated with fever. The incidence of 29,3% can not be considered relevant in diagnosis and following NAUTI. The incidence of sepsis is 12%. Other Euro-Asian studies report the incidence of sepsis as high as 12%, with differences among geographical regions and types of institutions (1). Unlike this study, ESGNI reports up to 31,9% of sepsis (8).

Conclusion

The most common pathogens of NAUTI are *E. Coli*, *Klebsiella* and *Pseudomonas*. There is a high level of antibiotic resistance among pathogens causing NAUTI. CRP is the most sensitive routine parameter for NAUTI. The rise in the number of isolated bacteria in patients with NAUTI is followed by elevation of CRP. Leukocytosis is not a parameter sensitive enough for determining and following NAUTI. NAUTI are followed in more than half of cases by fever, while shiver is not very common. The incidence of sepsis in NAUTI is 12 percent.

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KORELACIJA IZMEĐU BAKTERIOLOŠKIH, LABORATORIJSKIH I KLINIČKIH PARAMETARA NOZOKOMIJALNIH INFEKCIJA URINARNOG TRAKTA

Milan Potić

Nozokomijalnim infekcijama urinarnog trakta (NIUT) smatraju se infekcije koje nastaju najmanje 48 sati po prijemu na bolničko lečenje. Mikroorganizmi koji se javljaju kao uzročnici raznovrsni su i pokazuju visok stepen rezistencije na antibiotike. Kliničke karakteristike NIUT mogu varirati od neznatnih povećanja vrednosti C-reaktivnog proteina (CRP) pa do razvoja urosepse sa letalnim ishodom. Cilj rada bio je proceniti pojavu i korelaciju između bakterioloških, laboratorijskih i kliničkih indikatora NIUT.

U periodu od 4 meseca analizirano je sedamdeset pet bolesnika Urološke klinike u Nišu. Tri uzorka urina uzimana su sa ciljem da se utvrdi NIUT i da se odredi index multipne antibiotske rezistencije (MAR). Uzorci su uzimani na prijemu, petog hospitalnog dana i petog postoperativnog dana. Uzorci krvi su uzimani u isto vreme da bi se odredili laboratorijski parametri infekcije. Klinički parametri su evidentirani. Bakteriološke, laboratorijske i kliničke karakteristike analizirane su primenom Pearson korelacionog testa.

Najčešće izolovani uzročnik NIUT je *E. Coli* (28%). U 48 uzoraka urina (62%) broj bakterija je bio ispod 105 po ml urina. MAR indeks je u 61 izolatu (74,4%) pokazao vrednost iznad 0,5. Povišenu telesnu temperaturu razvilo je 42 bolesnika (56%). Drhtavicu je imalo 22 (29,3%). Sepsu je dobilo 9 bolesnika (12%). CRP je bio povišen kod 66 bolesnika (88%), dok su vrednosti leukocita preko 10x10⁹/L zabeležene kod 21 bolesnika (28%).

Najčešći uzročnici NIUT su *E.Coli*, *Klebsiella* i *Pseudomonas*. Kod NIUT postoji visok procenat multipne antibiotske rezistencije. CRP je najsenzitivniji rutinski parametar kod NIUT. Porastom broja klica kod bolesnika sa NIUT rastu vrednosti CRP. Serumaska leukocitoza je nedovoljno senzitivna parametar za otkrivanje i praćenje NIUT.

NIUT su u više od polovine slučajeva praćene povišenom telesnom temperaturom, dok se drhtavica ne javlja tako često. Učestalost sepsa kod NIUT je 12%. *Acta Medica Medianae* 2007;46(2):5-8.

Ključne reči: korelacija, nozokomijalna infekcija, laboratorijski parametri, klinički parametri