

Güncel pratikte komplike olmamış idrar yolu enfeksiyonlarında sık karşılaşılan etken mikroorganizmalar ve antibiyotik duyarlılıklarının değerlendirilmesi

The evaluation of the common pathogenic microorganisms in uncomplicated urinary tract infections and the antibiotic susceptibilities in daily practice

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Özet

Amaç: Komplike olmamış üriner enfeksiyonlarda saptanan etken mikroorganizmaların sıklığını, antimikrobiyal ajanların enfeksiyon etkenlerine karşı etkinliğini ve sık rastlanan patojen mikroorganizmaların antibiyotik rezistanslarını değerlendirmek.

Gereç ve yöntem: Komplike olmamış idrar yolu enfeksiyonu şüphesi olan hastaların idrar kültürleri retrospektif olarak incelendi. Orta akım temiz yakalama tekniği kullanılarak üç idrar örneği rutin olarak toplandı. Alınan örnekler, standart mikrobiyolojik prosedürler kullanılarak test edildi. Antibiyotik duyarlılığı, Kirby-Bauer tekniği kullanılarak analiz edildi.

Bulgular: 2850 idrar kültürü değerlendirildi. En sık izole edilen etken patojen mikroorganizma *E. Coli* idi (%66.4). *E. Coli*'nin en sık direnç gösterdiği antibiyotikler ampicilin (63.2%) ve amoksisilin klavulanat (58.1%) idi; fakat tüm *E. Coli* örnekleri karbapenem duyarlı idi. Enterokok grubunda vankomisin rezistansı bulunmazken; bu grupta nitrofurantoinin en etkili antibiyotik idi. Tüm stafilokok grubu vankomisin ve teikoplanine duyarlı iken bu gruptaki metisilin direnci sıklığı 33.3% olarak bulundu. Streptokokların tümü penisilinin yanı sıra levofloksasin (95.4%) ve sefotaksime de (93.9%) duyarlı idi. Bu grupta tetrasiklin rezistans oranı 75.1% olarak saptandı.

Sonuçlar: Komplike olmamış idrar yolu enfeksiyonlarında en sık saptanan etken patojen mikroorganizma *E. Coli*'dir (66.4%). Üriner enfeksiyonlarda genelde idrar kültürü sonucu olmadan tedaviye başlandığından antibiyotiklerin etkisi daha az olmaktadır.

Anahtar kelimeler: Üriner sistem enfeksiyonu, etyolojik ajanlar, antibiyotik duyarlılığı, geleneksel tedavi.

Abstract

Objective: To evaluate the frequency of the causative pathogens for the uncomplicated urinary tract infections, the efficacy of antimicrobial agents and the antimicrobial resistance of common pathogens.

Materials and methods: The culture-antibiogram results of patients with probable uncomplicated urinary tract infections were retrospectively analysed. Three urine samples were routinely collected by the mid-stream "clean catch" method. The samples were tested microbiologically by standard procedures. Antibiotic susceptibility was analysed by Kirby-Bauer technique.

Results: 2850 urine cultures were analysed. The most commonly isolated pathogen was *E. Coli* (%66.4). *E. Coli* most commonly had antibiotic resistance for ampicillin (63.2%) and amoxicillin clavulanat (58.1%); but all *E. Coli* samples were susceptible for Carbapenems. Vancomycin resistance was not found in Enterococcus spp and Nitrofurantoin was the most effective antibiotic against this group. All Staphylococcus spp. were susceptible for Vancomycin and Teicoplanin and the resistance rate of Methicillin was 33.3%. All of Streptococcus spp. had susceptibility for Penicillin and the other susceptible antibiotics were Levofloxacin(95.4%) and Cefotaxime(93.9%). Tetracycline resistance in this group were 75.1%.

Conclusion: The most common etiologic pathogene in uncomplicated UTI is *E. Coli*(66.4%). The conventional antibiotics for UTI are less effective and the treatment commonly starts without any results of urine culture.

Key words: Urinary tract infection, etiologic agents, antibiotic susceptibility, conventional management.

Introduction

Urinary tract infection(UTI) is a common cause of the hospital admissions and the morbidity in general population, and also it is the most common cause of the nasocomial infection(1).

UTI is more commonly seen in women; 20% of women have a urinary infection at least once in their lifetime, and approximately 3% of female population undergo at least one or more recurrent UTI episodes in a year (2). Although it is not common in young men, the incidence increases with aging because of the diseases such as neurogenic bladder and prostate enlargement which are commonly occurred in aging period of male(3). The probability of the occurrence of UTI increases in patients who are catheterised or who perform self catheterisation and who had undergone urinary tract interventions(4).

The most frequently isolated pathogenic microorganism in UTI is *Escherichia Coli* (% 75-95) and other common microorganisms are *Klebsiella* spp., *Proteus* spp., *Staphilococcus Saprophyticus*, *Pseudomonas* spp. (5, 6). The common symptoms are dysuria, frequency, urgency and suprapubic pain and they are very valuable in the diagnosis. Although the UTI is commonly diagnosed by direct microscopic urine analysis and urine culture tests, and also leucocyte esterase technique is used as a screening method to help the diagnosis in many centers(5, 7). Recurrent UTI, especially which involves the upper urinary tract and is not treated and/ or properly followed up, may cause irreversible damage of the upper urinary tract and thus hypertension and renal insufficiency may be seen(8).

The treatment of UTI usually begins in the form of the empirical treatment and continues according to the culture and antibiogram results. In this approach, the most important problem is antibiotic resistance and therefore the treatment failure. Many current studies have been performed about the responsible microorganisms of the UTI and their resistance mechanisms with the aim of to find the correct antibiotic agent for the empiric treatment(9- 11). The success of the treatment is based on the sensitivity of the microorganisms to the therapeutic agents and the ability of these agents to overcome the resistance mechanisms(12).

In this study, we evaluate the frequencies of the patho-

genic microorganisms which are commonly responsible for the uncomplicated urinary tract infections in daily practice, the effectiveness of antimicrobial agents and the antimicrobial resistance of the common microorganisms.

Materials and methods

In this study, we retrospectively evaluated the urine culture of 2850 outpatients who had uncomplicated UTI symptoms between March 2008 and July 2010. Mid-stream urine samples were routinely taken 3 times from the patients who have symptoms suggestive of urinary tract infection. Urine samples were analyzed by direct microscopic examination and using standart microbiologic tests. These samples were incubated in MacConkey and blood agar medium at 37 C in the dark environment, and after that they were treated with loop technique. The bacterial growth in the cultures were followed.

The results of the cultures were evaluated according to the defined standards and interpreted as significant or insignificant growth. The growth of $\geq 10^5$ colonies of bacteria in the media was regarded as significant bacteriuria. The patients with significant bacteriuria and patients who were symptomatic but had lower colony accounts were regarded as infected. Identification of the microorganisms in the culture were performed by using routine examination techniques. In case of three or more different microorganisms were identified, the culture was regarded as contamination, therefore antibiotic susceptibility test was not done and the sample was excluded from the study.

Antibiotic susceptibility tests and their results were interpreted by using Kirby Bauer technique. All first and second generation antibiotic susceptibility tests were done by using disc diffusion method and standardized for all samples. The data were collected in excel format and analyzed. First and second generation antibiotic susceptibilities were calculated against the each microorganisms in the culture, and the results were evaluated.

Results

Between March 2008 and July 2010, a total of 2850 urine cultures, consist of 883 men (31%) and 1967 women (69%) were examined. There were no significant urinary tract infections in 2308(81%) of the cultures. 542 urine cultures had significant proliferation of pathogen microorganisms. While only one microorganism was

isolated in 447 cultures, two microorganisms were simultaneously identified in 18 cultures. In 77 (2.7%) urine samples, three or more microorganisms were found, and these cultures were accepted as contamination and excluded from the study.

A total of 483 microorganisms were isolated from the significantly proliferated cultures and these were grouped as *Escherichia coli* 321 (66.4%), *Candida* spp. 48 (9.9%), *Enterococcus* spp. 30 (6.2%), *Klebsiella* spp. 23 (4.7%), *Proteus* spp. 27 (5.6%), *Pseudomonas Aeruginosa* 19 (3.9%), *Staphylococcus* spp. 15 (3.1%), respectively.

Antibiotic susceptibility of each microorganisms were evaluated separately for each antibiotic. In Enterobacteriaceae spp., seven of them (2.2%) were ESBL positive. According to the antibiogram sensitivity tests, this group was commonly resistant to the ampicillin (63.2%) and amoxicillin clavulanat (58.1%), respectively. Ciprofloxacin sensitivity was 83.7% in this group. This group showed complete sensitivity against carbapenems. In enterococci group, there was no resistance to vancomycin. The resistance within this group were against tetracycline (84.7%), ciprofloxacin (38.9%) and penicillin derivatives (36.4%), respectively. However, nitrofurantoin (87.3%) was the most sensitive antibiotic in this group.

According to the antibiotic susceptibility tests for *Pseudomonas Aeruginosa*, the most effective antibiotics against this bacteria were carbapenems (95.3%) and amikacin (94.2%), respectively. This microorganism commonly developed resistance to the gentamicin group (52%). In this group, it was determined that 7 (%36.9) microorganisms had chromosomal beta lactamase positive. In case of *Staphylococci* group, culture antibiogram results showed that all of this group was sensitive to vancomycin and teicoplanin. Beside of these antibiotics, this microorganism group had also common sensitivity against gentamycin (%88.3) and trimethoprim / sulfamethoxazole (83.7%). It has been found that 29.6% of staphylococcus group were resistant to meticillin.

Although streptococcal microorganisms were entirely sensitive to penicillin derivatives, except these group of antibiotics the higher sensitivity were seen against levofloxacin (95.4%) and cefotaxime (93.9%). These microorganisms commonly developed resistance against tetracycline (75.1%).

Discussion

In this study, we evaluated the urine cultures of 2850 patients who had the symptoms of UTI. We have found that the urine cultures were sterile or there were no significant microorganisms in the cultures of 2308 of all patients (%81). Therefore there was no need to use antibiotics and/or antibiotic usage would not be useful in most of the patients who have the symptoms of urinary tract infection.

Many clinicians routinely apply the empirical treatment and then evaluation is done. This approach is incorrect according to our study. Instead of this management, urine cultures should be done before the empirical treatment and treatment can be rearranged after the culture results, but if the symptoms are severe, the empirical treatment should be immediately started after taking a urine culture. If the symptoms are mild, antibiotic therapy should be started according to the culture results. Out of 2850 patients who were included into the study, 1967 were women (69%) and 883 were men (31%). As it is seen, the admissions of UTI were higher in women than men.

Regarding the frequency of the microorganisms isolated in urine cultures, we have found that *Escherichia coli* 321(66.4%), *Enterococcus* spp. 30(6.2%), *Proteus* spp. 27 (5.6%), *Klebsiella* spp. 23 (4.7%), were the most common microorganisms in Enterobacteriaceae group and this results were consistent with the previous studies(10, 13, 14). Also in our study the most common cause of uncomplicated urinary tract infection was *E. Coli* (66.4%). Several factors that facilitate the microorganism to hold on the urothelioma are responsible for the frequency of the Enterobacteriaceae group as a frequent causative agent. These factors that allow these gram-negative aerobic bacterias to attach and colonize on to the urothelium are bacterial adhesion, pili, fimbria, and P1 blood group phenotype (15).

The antibiotic susceptibility of *E.coli* group were different in several studies. In one study, antibiotic susceptibility of *E.coli* was found as; ampicillin(72.6%), cotrimoxazol(77.9%) and norfloxacin(78.4%), respectively(14). While in contrast, the resistance against ampicillin was very high in some studies(10,16,17) and also increased resistance against norfloxacin and ciprofloxacin have been reported in some studies, too(9, 11). In our

study, *E. coli* group showed resistance against ampicillin (%63.2) and amoxicillin clavulanat (58.1%), respectively, unlike to other studies in the literature. All of *E. coli* group was susceptible to carbapenems. Ciprofloxacin sensitivity was 83.7% in this group and this group of therapeutic agents were accepted as highly effective agents.

In *Enterococcus* group, the resistance against Vancomycin was not seen. In this group the antibiotic resistance was seen commonly against tetracycline (84.7%), ciprofloxacin (38.9%) and penicillin derivatives (36.4%) respectively. Nevertheless nitrofurantoin was the most susceptible agent against this group (87.3%). Nitrofurantoin has shown significant activity against *E. faecalis* in various studies which was in concordance to our study (16, 18, 19).

In several studies, it was shown that *Pseudomonas aeruginosa* was a common causative agent of the UTI in the hospital and showed resistance against first generation antibiotics such as ampicillin but usually it was sensitive to amikacin, piperacillin, ciprofloxacin and gentamycin (16, 20). In our study, the most effective antibiotics against *Pseudomonas Aeruginosa* were carbapenems (95.3%) and amikacin (94.2%) similar to other studies, but in contrast to the literature, the resistance was most commonly developed against gentamycin (52%). It has been found that 7 of this group (%36.9) had the positivity of chromosomal beta lactamase.

Except *Staphylococcus aerious* which shows high sensitivity to oxacillin, other gram positive microorganisms that isolated from urinary tract were commonly resistant against the most of the agents that were used for the treatment of UTI. In this study all of the *Staphylococcus* group was sensitive to the vancomycin and teicoplanin in terms of culture and antibiogram results. Except these antibiotics, they were also highly sensitive to gentamycin (88.3%) and trimethoprim / sulfamethoxazole (83.7%), on the other hand %29.6 of *Staphylococcus* group showed methicillin resistance. Although streptococcal microorganisms were entirely sensitive to penicillin derivatives, except these group of antibiotics the higher sensitivity were seen against levofloxacin (95.4%) and cefotaxime (93.9%) in our study. And it has been found that these microorganisms commonly developed resistance against tetracycline (75.1%).

In conclusion, the most frequent microorganism observed in uncomplicated urinary tract infections was *Escherichia coli* (66.4%). And the *Enterobacteriaceae* species beside of *E. coli* and *Enterococci* must be also kept in mind as the infective agents. In addition, the empirical treatment can be used just in patients with severe and bothersome symptoms after taking a urine culture, and also the curative treatment should be done according to the culture antibiogram results to increase the effectivity of antibiotics and to decrease the cost of the treatment although in practice usually the opposite is done.

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