A Comparison of Antibiotic Susceptibility Patterns of *Klebsiella* Associated Urinary Tract Infection in Spinal Cord Injured Patients with Nosocomial Infection

Farzin Khorvash[*1], Kamyar Mostafavizadeh[1], Sina Mobasherizadeh[2], and Mohaddeseh Behjati[3]

[1] *Department of Infectious Diseases, Isfahan University of Medical Sciences, Isfahan, Iran*

[2] *Department of Microbiology, Infectious Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*

[3] *Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran*

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Abstract- Just regarding different risk factors for antibiotic resistant uropathogenes, it seems justice to improve diagnostic power for drug resistant uropathogenes and well appropriate empirical therapy. 300 and 145 cases of clinicopathologically diagnosed nosocomial and spinal cord injured (SCI) associated urinary tract infection (UTI), respectively, were considered as our samples included in our 24 months study (2005 and 2006). 50 (16.6%) and 26 (17.9%) correctly diagnosed Klebsiella, respectively, were cultured from our specimens . MIC pattern of this uropathogenes for 8 antibiotics was determined by gradient concentration method. The prevalence of antibiotic resistant Klebsiella was more among nosocomial associated UTI rather than SCI UTI (P<0.05). According to susceptibility cut-off point criteria of CLSI M7-A6 (Clinical and Laboratory Standard Institute), Klebsiella resistance rate of nosocomial and SCI were 40% and 0 in amikacin (P <0.0001), 86.2% and 16.7% in ceftazidime (P<0.001), 69% and 25% in ceftriaxon (P<0.005), 5.1% and 0 in imipenem (P<0.0001), 50% and 25% in ciprofloxacin (P< 0.05), 81% and 22.2% in gentamicin 100%and 62.5% (P<0.001) in trimethoprim/sulfamethoxazole (P<0.05) respectively. Only resistance to nalidixic acid was mildly higher in SCI Klebsiella (68.8%, 66.7%). MIC 50 of all antibiotics except nalidixic acid and trimethoprim/sulfamethoxazole were higher in nosocomial Klebsiella (P<0.05). In conclusion although the whole risk factors for UTI in the cases of SCI associated UTI are more than for nosocomial UTI. Interestingly, the prevalence of Klebsiella resistant UTI was more in the second group.

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Key words: Klebsiella; urinary tract infection; spinal cord injuries**;** anti-bacterial agents

Introduction

Urinary tract infection (UTI), considered by the presence of 10^5 or more bacteria in the urine, impact a great burden in today's clinical practice (1). A considerable amount of risk factors, as hospitalization, underlying medical diseases, immune deficiency, indwelling catheters, spinal cord injury and others will help to this conflicting problem (2,3). Naturally, age, gender, general and sexual hygiene are other to contributors to the case of uncomplicated UTI which is occurring more commonly in young sexually active women (4). Now, it's well known that E-coli is the most common cause of UTI, all over the world and each kind of UTI 5, but other organisms are also growing as playing a role this regard. E-coli, Staphylococcus saprophyticus, Proteus mirabilis, Streptococcus agalactiae and Klebsiella spp are the most common known causes of UTI (6). Among two categories of UTI (uncomplicated and complicated UTI) (7), the latter needs some predisposing factors to be established. Surprisingly, especial pathogens seek specific co morbid conditions to be disaster well, such as Klebsiella spp which afflicts hospitalized (nosocomial infection) and also spinal core injured patients (8). Knowing the propensity of some organisms to some predisposed condition (ready environ-

***Corresponding Author:** Farzin Khorvash
Department of Infectious Diseases, Isfahan University of Medical Sciences, Isfahan, Iran.
Tel: +98 913 1190525, Fax: +98 311 6684510, E-mail: khorvash@med.mui.ac.ir

ments for catch up), may be beneficial guide toward necessary growth elements, adhesion molecules or perhaps better and discrete treatment. Despite of this glorified selection by organisms, antibiotic resistance is growing exponentially.

But for appropriate empirical therapy, understanding the antibiotic resistance profile and the drug of choice in nosocomial and SCI UTIs seems to be necessary. Risk factors such as catheterization, use of regular and potent antibiotics and other co morbid conditions are the same subject, but more prevalence of chronic and recurrent infections (9), asymptomatic bacteriuria (10), elevated intravesical pressure, more need for clean intermittent catheterization (CIC) (11), neurological bladder obstruction, reflux, stone formation (12) and other amplifying methods in the SCI UTI, let us suggest that antibiotic resistant is more common in SCI UTI rather than nosocomial ones.

Herein, the aim of this study is to investigate the probable differences between antibiotic resistance profile in nosocomial and SCI UTIs. It will help us in better empirical therapy and to diminish the spent time and cost for proper diagnosis and full treatment.

Patients and Methods

From 2005 to 2006, in Al-Zahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran, 300 and 145 cases of clinicopathologically diagnosed nosocomial and SCI associated UTI, respectively, were selected rondomly. Mean age of them was 45±12 and 40±10,respectivly. The inclusion criteria for nosocomial UTI (sample A) were dysuria, fever, urine color changes, unexplained nausea and vomiting, absence of fever and UTI signs and symptoms in pre- and early 48h of hospitalization. The inclusion criteria for SCI associated UTI (sample B) were fever, complaining from dysuria, urine color changes, unexplained nausea and vomiting. To overcome missing the patient due to absent dysuria sensation from neuerosensory deficits in these patients, each positive urine culture for Klebsiella in clinically suspicious patients, was also included. The exclusion criteria were recent use of antibiotics and presence of the other uropathpgenes rather than Klebsiella, for both groups. The collected urine for analysis was drawn by from Crede maneuver, clean intermittent catheterization (CIC), indwelling catheter, supra pubic aspiration and also clean cached mid-stream urine. Then, standard urine analysis and culture (UA/UC) on selected medium was established for all as base line data. All Klebsiella species were detected by biochemical assays, and their MIC pattern to ten regularly used antibiotics was determined by the use of gradient concentration method (E-Test; AB BIODISK Co.Sweden). Quality control assessment was performed by E.coli ATCC25922 .SPSS 13 and WHO net 5 software were used for data analysis.

Results

Out of 300 urine cultures in group A 50 (16.6%) and 145 urine specimens in group B 26 (17.9%) were Klebsiella. As susceptibility cut-off point criteria from NCCLS (National Committee for Clinical Laboratory Standard), Klebsiella resistant nosocomial and SCI associated UTIs were 40% and 0 in Amikacin (P <0.0001), 86.2% and 16.7% in Ceftazidime (P<0.001), 69% and 25% in Ceftriaxon (P<0.005), 5.1% and 0 in Imipenem (P<0.0001), 50% and 25% in Ciprofloxacin (P< 0.05), 81% and 22.2% in Gentamicin 100%and 62.5% (P<0.001) in Trimethoprim/Sulfamethoxazole (P<0.05) respectively. Only resistance

to Nalidixic acid was mildly higher in SCI Klebsiella (68.8%%, 66.7%). MIC 50 of all antibiotics except Nalidixic acid and Trimethoprim/ Sulfamethoxazole were higher in nosocomial Klebsiella (P<0.05). The information derived from E-test is arranged in table 1. Our data demonstrates that Klebsiella resistant UTI was more prevalent in hospitalized cases in comparison with SCI associated ones. This difference should be considered significant (P<0.05).

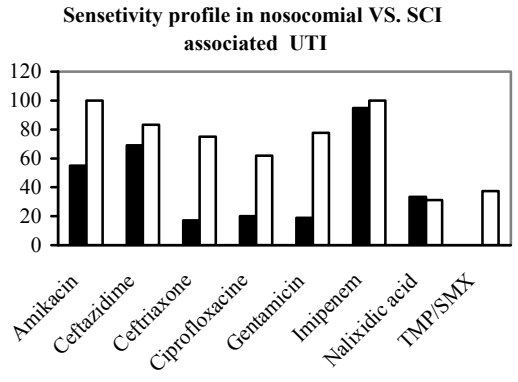

Figure 1. Sensitivity profiles

Table 1. Susceptibility pattern of isolated Klebsiella in two groups

Drug-name	Break-point		%R	%I	%S	%R 95%C.I.	MIC50	MIC90	MIC-range	P
Amikacin	S<=16 R>=64	A	40	5	55	25.3-56.6	16	256	0.125-256	<0.0001
		B	0	0	100	0.0-28.3	1	3	0.25-6	
Ceftazidime	S<=8 R>=32	A	86.2	6.9	6.9	67.4-95.5	256	256	0.25-256	<0.001
		B	16.7	0	83.3	4.4-42.3	.75	96	0.125-256	
Ceftriaxone	S<=8 R>=64	A	69	13.8	17.2	49.1-84.1	256	256	0.094-256	<0.005
		B	25	0	75	6.7-57.2	.38	256	0.047-256	
Ciprofloxacin	S<=1 R>=4	A	50	30	20	20.1-79.9	2	32	0.5-32	< 0.05
		B	25	6.2	68.8	8.3-52.6	.19	32	0.032-32	
Gentamicin	S<=4 R>=16	A	81	0	19	57.5-93.7	96	G256	0.19-1024	<0.001
		B	22.2	0	77.8	3.9-59.8	.75	32	0.064-32	
Imipenem	S<=4 R>=16	A	5.1	0	94.9	0.9-18.6	0.5	2	0.125-24	<0.0001
		B	0	0	100	0.0-69.0	.125	.25	0.023-0.25	
Nalidixic acid	S<=16 R>=32	A	66.7	0	33.3	12.5-98.2	256	256	6-256	>0.05
		B	68.8	0	31.2	41.5-87.9	256	256	2-256	
TMP/SMX	S<=2 R>=4	A	100	0	0	73.2-100	32	32	16-32	<0.05
		B	62.5	0	37.5	25.9-89.8	32	32	0.25-32	

A: Nosocomial cases B: Spinal cord injury cases R: Resistant
S: Sensitive I: Intermediate MIC: Minimal Inhibitory Concentration

Discussion

Urinary tract infection (UTI) is still a problem not infrequently encountered in the clinical practice (6). The most common type of UTI is uncomplicated one which is more common in sexually active females (4). Etiology is influenced by different factors, but it's commonly believed that the most common cause of community acquired, nosocomial and SCI UTI are Ecoli, Klebsiella and Klebsiella respectively (6,13). The mass of recent reports have shown increasing resistance to commonly-used antibiotics. Since the rate of resistance has considerable variations, in our study we have assesed antibiotic resistant Klebsiella UTI in nosocomial and SCI cases. Regarding complicated cases, UTIs are the most common hospital-acquired infections (14), and the great workload in microbiological laboratories, is attributed to this. It s now estimated that about $2 billion a year in the United States is spent for prolonged hospitalization due to nosocomial UTI (15). Klebsiella spp. in nosocomial UTI showed an overall increase in resistance to antibiotics and advent of multiple antibiotic resistant strains were not uncommon (16). In comparison with available published data, Issack H demonstrated that all of the Klebsiella organisms were sensitive to Gentamicin, but only 19% of our cases were sensitive to it (17) Rizivi MF demonstrated a maximum sensitivity to Imipenem by klebciella strains (5). Also, our data demonstrated that 94.9 of our Klebsiella strains were sensitive to Imipenem. Leblebicioglu H. demonstrated that 6.25, 40.6, 59.4% of Klebsiella spp. were resistant to carbapenems, quinolones and Ceftriaxon, respectively (18). Our data shows that 94.9, 20 and 17.2 of our Klebsiella strains were resistant to carbapenems, quinolones and ceftriaxone, respectively. The other spectrum of complicated UTI, is SCI associated UTI. Today s, a decrease in mortality rate due to urinary tract complications in spinal cord injured patients have been occurred (19), but one of a leader causes of their mortality, is still UTI. There is not enough data for comparisons. Although the data about SCI associated UTI are less available, but as a rule of thumb, we can consider that the prevalence of antibiotic resistant Klebsiella in the SCI associated UTI is less that nosocomial UTI (P<0.05). Considering repeated UTIs, chronic use of antibiotics, greater need for catheterization, concurrent neurological and bladder problems and immobility in spinal core injured patients, make us think that the risk of antibiotic resistant Klebsiella, is more in the case of SCI associated UTI, rather than nosocomial UTI. But it is not clear why this is not so in reality. Perhaps differencies in pathogenecity, vi-

rulence and underlying co morbidities is somehow involved.

Today s, the increasing antibiotic resistance of common uropathogens, such as Klebsiella pneumoniae, can complicate the therapeutic outcomes. Economic factors will attract our attentions to cost-effective therapy. Correct, adequate and cost-effective treatment is the great matters of fact that each physician should take them into account before starting the treatment. Seeking empirical therapy to bridge the patient to treatment, bypassing the great costs and time spent to microbiological data, especially in underdeveloped countries, it seems necessary to asses common uropathogenes for antibiotic susceptibility patterns. The levels and patterns of resistance of those organisms even help us making guidelines for better monitoring of trends over time. Herein, considering our data, the need for more investigations to understand the cause of the superiority of resistance in the cases of SCI associated UTI comparing nosocomial UTI seems to be necessary. The answer will help us try to eliminate the disasters underlying matter. In conclusion, Although the whole risk factors for UTI in the cases of SCI associated UTI are more than for nosocomial UTI, interestingly, the prevalence of Klebsiella resistant UTI was more in the second group. More data are needed to identify the cause of such a sophisticated difference.

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