Comparison of Treatment Modalities of Single Dose and Seven Day Courses in the Treatment of the Pregnant Women with Uncomplicated Urinary Tract Infection or Symptomatic Pregnant Women with 103-105/Ml Mid-Stream Bacteriuria

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Abstract

Objective: Comparison of bacteriologic efficacy of single dose, intramuscular 2 g-cefoxitin (Mefoxime®, Merck Sharp Dome) and 7 day courses of oral amoxicillin (2 g/ daily) (Largopen®, Bilim) in the treatment of the pregnant with uncomplicated urinary tract infection (Group 1) or symptomatic pregnant women with $10^{(3)}$-$10^{(5)}$/ml mid-stream bacteriuria (Group 2).

Methods: The pregnant women in the Group 1 and 2 between 6-34 (mean 20±1.61) gestation weeks were randomly selected for taking single dose, intramuscular 2 g-cefoxitin and 7 day courses of oral amoxicillin (2 g/ daily). Twenty-five patients were in cefoxitin group and 23 were in amoxicillin group. There was no clinic difference according to demographic and patient character between the groups (p>0.05). The pathogens were identified by using of urine culture and repeat urine cultures were performed 10 days after initiation of therapy for bacteriologic evaluation of the patients.

Results: Bacterial eradication rates were 16/20 (80%) after single dose, intramuscular 2 g- cefoxitin and 15/18 (83%) in 7 day courses of oral amoxicillin (2 g/ daily) in the Group 1. All pregnant women in the Group 2 were responded well to the treatment. There was no difference between single dose, intramuscular, 2g-cefoxitin and 7 day courses of oral amoxicillin (2 g/ daily) according to bacteriologic evaluation in the both groups (p>0.05). Although the sensitivity of cefoxitin and amoxicillin were 79% (15/19) and 94% (16/17) for *E. coli*, the most common pathogen, respectively, the difference was not statistically significant (p>0.05).

Conclusion: There was no difference between efficacy of single dose, intramuscular 2 g- cefoxitin and 7 day courses of oral amoxicillin (2 g/daily) therapy in the treatment of pregnants with uncomplicated lower urinary tract infection or symptomatic pregnant women with 10^3-10^5/ml mid-stream bacteriuria.

Keywords: Pregnancy, urinary tract infection, bacteriuria.

Komplike olmamış alt üriner sistem enfeksiyonu bulunan ve orta idrarda 103-105/ml bakteriürisi olan semptomatik gebelerde, tek doz ve yedi günlük tedavi yöntemlerinin karşılaştırılması

Amaç: Komplike olmamış alt üriner sistem enfeksiyonu olan (Grup 1) ve üriner sistem enfeksiyon şikayetleri olup orta idrarda $10^{(3)}$-$10^{(5)}$/ml bakteriürisi bulunan gebelerde (Grup 2) tek doz intramusküler 2 g-sefoksitin (Mefoxim®, Merck Sharp Dome) ile yedi günlük oral amoksisilin 2 g/ günlük (Largopen®, Bilim) tedavisinin bakteriyolojik etkinliklerinin karşılaştırılması.

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Yöntem: Grup 1 ve 2'de yer alan 6-34. haftalar arasındaki gebeler (ortalama gebelik haftası: 20.00±1.61), tek doz, intramusküler 2g-sefoksitin veya yedi günlük, oral, 2 g-amoksisilin almak için randomize edildi. Yirmibeş hasta sefoksitin, 23 hasta amoksisilin grubunda yer aldı. Çalışmaya alınan gruplar arasında demografik ve hasta karakterleri bakımından klinik farklılık yoktu (p>0.05). Patojenlerin tanımlanması idrar kültürü ile yapıldı ve tedavi başlangıcından 10 gün sonra hastalar bakteriyolojik değerlendirme için tekrar idrar kültürü ile değerlendirildi.

Bulgular: Grup 1 için, tek doz, intramusküler 2g-sefoksitin sonrası bakteriyel eradikasyon oranı 16/20 (%80), yedi günlük, oral, 2 g-amoksisilin sonrası ise 15/18 (%83) idi. Grup 2'de yer alan olguların tümü tedaviye yanıt verdi. Tedaviden sonra uygulanan bakteriyolojik değerlendirme sonucunda, Grup 1 ve 2'de yer alan gebelerin tedavi etkinlikleri arasında fark yoktu (p>0.05). En sık tespit edilen patojen olan *Escherichia coli*'ye olan duyarlılık, sefoksitin tedavisi alan gebelerde %79, amoksisilin tedavisi alan gebelerde ise %94 olarak gözlenmesine rağmen istatistiksel olarak anlamlı değildi (p>0.05).

Sonuç: Akut komplike olmamış alt üriner sistem enfeksiyonu veya üriner sistem enfeksiyon şikayetleri olup orta idrarda $10^{(3)}$-$10^{(5)}$/ml bakteriürisi bulunan gebelerde uygulanan tek doz, intramusküler, 2 g-sefoksitin ile yedi günlük, oral, 2 g-amoksisilin tedavilerinin etkinlikleri arasında fark gözlenmedi.

Anahtar kelimeler: Gebelik, üriner sistem enfeksiyonu, bakteriüri.

Introduction

Urinary system infection (USI) is an infection which is seen frequently in gestation and which proceeds symptomatically and asymptomatically. Infection in pregnants with USI is usually limited with lower urinary system and frequently the agent is Escherichia coli (*E.coli*). Enterobactery types (klebsiella, enterobacter, proteus), staphylococcus, B group streptococci are other frequently seen agents.[1] Urinary system infection is defined as pollacuria, pain in urinary bladder, dysuria and complaints as these and existence of 100.000/ml bacteria in culture taken from middle urine. As to its localization, it is named as upper or lower urinary infection.[1-3] In addition, it is shown that an active urinary infection may exist even with bacteria less than 100.000/ml in samples obtained from middle urine.[4] Appearance rate of symptomatic urinary infection in Turkish society is 4.7%.[5] The purpose is to decrease repeating risk by removing infection in pregnants with USI not complicated due to pyelonephritis growth in 20-40% of gestations who have lower urinary system infection complaint.[6,7]

Clinical researches for treatment by a single dose antibiotic of acute cystitis (lower urinary system infection) in young adults have been continued for twenty years.[8] This treatment method arouses interest in terms of increasing patient compatibility, decreasing of treatment cost and low prices.[9] While antibiotic resistance is decreased with single dose antibiotic treatment, only a few agents have high treatment activity.[10] Generally, the most effective single dose antibiotics are agents which are the most effective against general pathogens and which reach high urinary system concentration in USI.[11] Cefoxitin (Mefoxime®, Merck Sharp Dome) is a cephalosporin from second generation which is effective for E.coli, Enterobactery in urinary system infections and which is applied parenterally in wide spectrum and in beta lactam structure. Amoxicillin (Largopen®, Bilim) is a kind of antibiotic which is derivated from penicillin effective on urinary infections and threw from urinary system.

Our purpose in this work is to compare oral amoxicillin activity in 2 g/day (7 days) with 2 g single dose intramuscular cefoxitin in pregnants who had not complicated lower urinary infection and pregnants who had urinary system infection complaints and who had 103-105/ml bacteriuria in middle urine.

Methods

This prospective study was done by randomizing after including pregnants (n:10) who had urinary system infection complaints and who had 103-105/ml bacteriuria in middle urine or pregnants (n:38) who were found lower urinary system infection which were not acute complicated in Obstetric Clinic of Medicine Faculty of Kahramanmaras Sutcuimam University in between September 2002 and May 2004. Written consents were taken from patients and ethic committee of Medicine Faculty of Kahramanmaras Sutcuimam University for this work. Criteria for being includ-

ed to study are determined as pain in lower abdominal area pollacuria and/or pollacuria and/or fever complaints in last four days in addition to 105 CFU/ml (colony forming unit) in urinary culture for USI (Group 1). Pregnants who were found bacteriuria in middle urine (103-105 CFU/ml) and who had symptomatic complaints determined for USI infection were included into work (Group 2). Pregnants who had upper urinary system infection (pyelonephritis), who had allergic reaction against penicillin and who had drug within last week were not included into the work. Urine culture sampling for diagnosis was made by taking middle flow urine given after cleaning urethra entrance. Urine samples came to microbiological laboratory within one hour were incubated about 18-24 hours at 37°C by being planted into bloody agar and MacConkey agar basal mediums. Samples found production were defined by API (BioMérieux, France) system and its antibiograms were done. It was determined by urologist within the work whether the urinary system infection was complicated or not. Predisposing factors of patients were accepted as urinary system infections before gestation and urinary infections repeating in gestation. The treatment was arranged as giving 1g x 2 cefoxitin (n:25) totally 2 g intramuscular dose or 1 oral and daily 1 g x 2 totally 2 g amoxicillin (n:23) for 7 days. Activity of the treatment was evaluated as to bacteriological answers obtained ten days later from the beginning of the treatment. Same treatment was repeated for the patients who were observed production in cultures repeated after treatment and urine cultures were repeated 10 days later. The treatment was interpreted as successful for patients who were not observed production. Mann-Whitney and X_2 tests were used for statistical analyze. $p<0.05$ was deemed as significant. Results were given as ± average standard fault.

Results

Totally 48 patients were included into the evaluation for Groups 1 and 2. Demographic qualities of cefoxitin and amoxicillin groups are shown in Table 1. Isolated pathogens are shown in Table 2.

Table 1. Demographic qualities of cases included into work and patients within cefoxitin and amoxicillin groups.

	Cefoxitin	Amoxicillin	P*
Age	25,60+1,17	25,78+,99	.906
Gravida	2,08+0,34	1,86+0,25	.626
Parity	0,92+0,21	0,69+0,21	.463
Abortus	0,48+0,18	0,17+8,08	.306
Predisposing factor	1,48+,37	0,86+0,31	.610
Gestational week	20,68+1,55	19,30+1,68	.551

*: p<0.05 significant

While there was no production in culture repeated after treatment within 16 (80%) of 20 patients who were in Group 1 and took cefoxitin, this rate was observed as 15/18 (83%) in amoxicillin group (p>0.05). No production was observed in culture repeated after treatment in any patient within Group 2 and had treatments of cefoxitin (n:5) and amoxicillin (n:5).

Most frequently observed pathogen E.coli sensitivity was observed as 79% in pregnants who had cefoxitin treatment and observed as 94% in pregnants who had amoxicillin treatment (p>0.05).

There was predisposing factor in all pregnants who did not respond first treatment within both cefoxitin and amoxicillin groups. Patients within cefoxitin group (n:10) and within amoxicillin group (n:6) had predisposing factor. No response was taken from 4/10 (40%) cases in cefoxitin group who had predisposing factor and from 3/6 (50%) cases in amoxicillin group who had predisposing factor.

Table 2. Isolated pathogens in cefoxitin and amoxicillin groups.

Isolated pathogens	Cases having cefoxitin and USI (n: 20)	Cases having cefoxitin and ASB (n: 5)	Cases having amoxicillin and USE (n: 18)	Cases having amoxicillin and ASB (n: 5)
Escherichia coli	14 (%70)	5 (%100)	12 (%66)	5 (%100)
Klebsiella spp.	5 (%25)	0	3 (%17)	0
Proteus mirabilis	1 (%5)	0	0	0
B group streptococci	0	0	3 (%17)	0

USI: Urinary system infection, **ASB:** Asymptomatic bacteriuria

Discussion

Mechanical and hormonal changes such as gathering of urine relatively within urethras, not completely emptying urinary bladder, increasing of bladder residual volume and vesico-ureteral reflux, increase of PH in urine cause urinary system infection in pregnants.

When treatment type is taken into consideration, factors such as activity, price, tolerance of drug etc. become important. For that reason, single dose application for treatment of lower urinary system infections without complication in gestation was tried with many combination.[6-10] However; single dose application is an arguable subject today even particularly agents including beta lactam are used in high dose.[11] Although a great success is obtained by applying a few agent (trimethoprim, fluoroquinolon etc.) as single dose, it is not preferred due to the fact that sulphonamides cause neonatal hyperbilirubinemia by using in the last two gestational week and fluoroquinolons has teratogenic effects on bone-cartilage system.[9]

We have not met any information in the literature about comparison of the activity of single dose (2 g) cefoxitin and amoxicillin treatments. In our work, we found that activity of single dose (2 g) cefoxitin for treatment of cases within Groups 1 and 2 is not different than amoxicillin's activity ($p>0.05$). Though predisposing factors showed a different distribution in both groups, all cases who were included to work and who did not respond to treatment had predisposing factors [4/10 (40%) in cefoxitin group and 3/6 (50%) in amoxicillin group]. Mc Fadyen et al[12] suggested to prefer short-term and single dose application for not complicated cases.

Stamm et al[4] stated that evaluation of sample taken from bladder by suprapubic catheterization is the most sensitive method for observing urethra infection and they also showed that sensitivity and specificity are insufficient to find urethra infection in asymptomatic cases which had bacteria less than 150/ml in samples taken from middle urine. However, they emphasized that middle urine samples more than 10^2/ml are together with high sensitivity (95%) and specificity (85%) for estimating urethra infection in symptomatic cases. There were 10 cases in our study who had 103-105 bacteria in their middle urine and who had symptomatic complaints for urinary system infection. It was observed that all cases who did not have predisposing factor responded to treatment ten days later and they did not have any urinary system complication in the following periods of gestation.

Kutlay et al[5] found treatment activity as 83% in their work in which they evaluated asymptomatic (n:43) cases with bacteriuria and symptomatic (n:19) cases with bacteriuria by giving single dose amoxicillin or oral first generation oral cephalosporin. This treatment activity was similar with the result (15/18, 83%) we obtained in amoxicillin group in our work.

While success was 15/19 (79%) by applying single dose cefoxitin to *E. coli* which was most isolated pathogen in pregnants who had 103-105/ml bacteriuria in middle urine and who had urinary system infection complaints and in urinary system infections not complicated, it was found as 16/17 (94%) in amoxicillin group ($p>0.05$).

Responding to treatment of single dose or to seven day treatment by pregnants who had both urinary system infection complaints and 103-105/ml bacteriuria in middle urine and similarity of bacteriological results (80% and 83%) of both cefoxitin and amoxicillin groups by evaluating all pathogens are may be used by patient's preference that single dose application does not include predisposing risk factor. Additionally, being not significant statistically of treatment results against *E. coli* which is the most frequently met pathogen in urinary infections supports our opinion.

Conclusion

Single dose (2 g) cefoxitin may be applied in the non-existence of predisposing factors in pregnants who 103-105/ml bacteriuria in middle urine and urinary system infection complaints and in cases who had lower urinary system complaints without complication.

Refeences

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