

Comparison of Efficacy of Intravenous Amikacin with Intravenous Cefoperazone/Sulbactam in Urinary Tract Infections Caused by Escherichia Coli Indiabetic Patients

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ABSTRACT

Objective: To compare the efficacy of I/V Amikacin with I/V Cefoperazone/Sulbactam in urinary tract infections caused by Escherichia coli in patients having diabetes mellitus.

Study Design: Randomized clinical trial study

Place and Duration of Study: This study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar during November 2014 to April 2015.

Materials and Methods: It was a randomized clinical trial and the sample size was 46 patients in each group, total sample size was at least n=92. Non probability consecutive sampling was used for sample collection. Routine investigations like Full Blood Count, Ultrasound of Urinary system, Renal Function tests, 24 hours urinary proteins and creatinine clearance, Random and fasting blood Sugar and HbA1c were done on the selected patients. The patients were then divided into two groups "Group-A" for Amikacin I/V 500mg BD and 'Group-B' for Cefoperazone/Sulbactam 2 Grams I/V BD, both groups receiving treatment for 07 days. The diagnosis of UTIs was based on mentioned criteria. Urine culture was performed by collecting clean-catch midstream urine in a sterile urine bottle or sending catheter tip, if patient was catheterized and then subjecting it to growth for bacteria using kled or MacConkey agar incubated at 37C° in incubator for 24 hours in hospital laboratory. At the end of study, difference of at least 10% in Efficacy of two groups(drugs) was considered as significant. P1=Efficacy of Amikacin (90%) and P2=Efficacy of Cefoperazone/Sulbactam(65%), Power of test(1-β)=90% and level of significance=0.05%.

Results: Our study shows that mean age in group A (I/V Amikacin) was 44 ± 2.77 years and mean age in group B (I/V Cefoperazone/Sulbactam) was 46 ± 3.12 years. In group A (I/V Amikacin) 32% patients were male, 68% patients were female. Whereas in group B (I/V Cefoperazone/Sulbactam) 30% patients were male, 70% patients were female. More over our study shows that I/V Amikacin was effective in 85% patients and was not effective in 15% patients whereas I/V Cefoperazone/Sulbactam was effective in 68% patients and was not effective in 32% patients

Conclusion: Our study concludes that I/V Amikacin was more effective than I/V Cefoperazone/sulbactam in urinary tract infections caused by Escherichia Coli in diabetic patients.

Key Words: Amikacin, Cefoperazone/Sulbactam, urinary tract infections, escherichia coli, diabetes mellitus.

Citation of articles: Nadeem M, Rehman M, Ullah I, Basharat A, Ullah I, Ghaffar T. Comparison of Efficacy of Intravenous Amikacin with Intravenous Cefoperazone/Sulbactam in Urinary Tract Infections Caused by Escherichia Coli Indiabetic Patients. Med Forum 2019;30(8):11-14.

INTRODUCTION

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Received: January, 2019

Accepted: March, 2019

Printed: August, 2019

The term Urinary Tract Infection (UTI) is the infection of urinary tract by pathogenic bacteria which includes patients having cystitis, prostatitis and pyelonephritis. Urinary tract infections are amongst the most prevalent infectious diseases affecting approximately 150 million people worldwide annually.¹ Most common causative organism for the urinary tract infection is Escherichia coli, which is responsible for up to 70% of the cases both in outpatient and inpatient. Other less common gram negative bacteria include Klebsiella spp., Enterobacter spp., Pseudomonas aeruginosa, Proteus spp. Gram positive bacteria accounts for 5 – 15% of UTIs and include Enterococcus spp., Staphylococci, and Streptococci.²

The resistance of bacteria causing urinary tract infection (UTI) to commonly prescribed antibiotics is

increasing both in developing as well as in developed countries. Resistance has emerged even to more potent antimicrobial agents.³ The antibiotics commonly used to treat UTIs are broad spectrum cephalosporins, fluoroquinolones and aminoglycosides.⁴ Sulbactam is a molecule that is administered in combination with β -lactam antibiotics to overcome the effects of β -lactamase. The addition of sulbactam to cefoperazone treatment augments the activity of cefoperazone against β -lactamase-producing bacteria).^{1,5}

Females are more susceptible to UTI than males and the most effective drug (effective on isolated E.coli) is Amikacin (from amino-glycosides group).⁶ Highest percentages of susceptibility by E.Coli was seen for amikacin (96.6%), ciprofloxacin (95.1%), and gentamicin (92.9%).⁷ So there is a strict need for developing specific guidelines for antibiotic prescriptions for UTI and directing the attention of the authorities to the development of increasing antibiotic resistance of uropathogens. Escherichia coli was found to be resistant to Amikacin in less than 10% of cases (hence 90% Efficacy) and resistance of 35% was shown by cefoperazone/sulbactam group (hence 65% Efficacy).⁸ Amikacin is very cost-effective and has a good efficacy against E.coli UTIs in previous different studies. The current study is designed in this regard, to find statistics about the efficacies of Amikacin and Cefoperazone/Sulbactam for the treatment of UTIs in diabetic patients in our local population, to find the local statistics about efficacy of the two drugs so that we will be able to formulate a proper protocol for the empirical treatment of UTI in diabetic patients. Therefore a prospective randomized control trial will prove the efficacy of amikacin in treating Diabetic patients having UTI.

MATERIALS AND METHODS

This study was conducted in Department of Medicine, Khyber Teaching Hospital, Peshawar. It was Randomized Clinical Trial. Using WHO Calculator, sample size was 46 patients in each group, total sample size was at least $n=92$, $P1$ =Efficacy of Amikacin and $P2$ =Efficacy of Cefoperazone/Sulbactam, Power of test $(1-\beta)=90\%$ and level of significance = 0.05%. Non probability consecutive sampling technique was used. Patients included in this study were known diabetics having UTI (Urinary symptoms with >10 WBCs/HPF and E.Coli growth on urine culture) aged 20-60 years and who have already taken oral antibiotics without response at least 48 hours before sending Urine C/S. Patients excluded were those who were hypersensitive to Amikacin Or Cefoperazone/Sulbactam, having impaired renal functions, chronic renal failure or diabetic nephropathy, pregnant females in their first trimester, terminally ill or immune-compromised patients (except having Diabetes Mellitus) like HIV, Malignancies etc.

Ethical approval was taken for this study. Routine investigations like Full Blood Count, Ultrasound of Urinary system, Renal Function tests, 24 hours urinary proteins and creatinine clearance, Random and fasting blood Sugar and HbA1c were done on the selected patients.

The patients were then divided into two groups by lottery method: "Group-A" for Amikacin I/V 500mg BD and "Group-B" for Cefoperazone/Sulbactam 2 Grams I/V BD, both groups receiving treatment for 07 days. Detailed history and examination of patients was recorded. The diagnosis of UTIs was based on mentioned criteria. Urine culture was performed by collecting clean-catch midstream urine in a sterile urine bottle or sending catheter tip, if patient was catheterized and then subjecting it to growth for bacteria using kled or MacConkey agar incubated at 37°C in incubator for 24 hours in hospital laboratory. At the end of study, difference of at least 10% in Efficacy of two groups (drugs) was considered as significant.

The data collected from the patients through proformas was entered and analyzed in statistical package for social sciences (SPSS) latest version. Mean \pm SD was calculated for numerical variable like age and duration of diabetes mellitus. Frequencies and percentages were calculated for categorical variable like gender, efficacy and urine culture. Chi-Square test was applied to compare the efficacy of both the drugs keeping the P Value ≤ 0.05 , was significant. Efficacy was stratified for UTIs isolates to see the effect modification of age and gender. Final results were presented as tables and graphs.

RESULTS

Our study shows that mean age in group A (I/V Amikacin) was 44 year \pm 2.77 and mean age in group B (I/V Cefoperazone/Sulbactam) was 46 year \pm 3.12. In group A (I/V Amikacin) 32% patients were male, 68% patients were female. Where as in group B (I/V Cefoperazone/Sulbactam) 30% patients were male, 70% patients were female.

Urine culture among two groups was analyzed as urine culture was done in all the patient of group A and group B and escherichia coli was found positive. (as shown in table no 3)

Table No. 1: Age Distribution (n=92)

AGE	GROUP A	GROUP B
20-30 years	5(12%)	4(9%)
31-40 years	14(30%)	15(32%)
41-50 years	16(35%)	16(35%)
51-60 years	11(23%)	11(24%)
Total	46(100%)	46(100%)
Mean and SD	44 year \pm 2.77	46 year \pm 3.12

Group A: I/V Amikacin

Group B: I/V Cefoperazone/Sulbactam

Chi Square test was applied in which P value was 0.002

Efficacy among two groups was analyzed as I/V Amikacin was effective in 39(85%) patients and was not effective in 7(15%) patients. Whereas I/V Cefoperazone/ Sulbactam was effective in 31(68%) patients and was not effective in 15(32%) patients. (as shown in table no 4.

Table No. 2: Gender Distribution (n=92)

Gender	Group A	Group B
Male	15(32%)	14(30%)
Female	31(68%)	32(70%)
Total	46(100%)	46(100%)

Group A:I/V Amikacin

Group B: I/V Cefoperazone/Sulbactam

Chi Square test was applied in which P value was 0.002

Table No. 3: Urine Culture (n=92)

Urine Culture	Group A	Group B
Yes	46(100%)	46(100%)
No	0(0%)	0(0%)
Total	46(100%)	46(100%)

Group A:I/V Amikacin

Group B: I/V Cefoperazone/Sulbactam

Chi Square test was applied in which P value was 0.000

Table No. 4: Efficacy (n=92)

Efficacy	Group A	Group B
Effective	39(85%)	31(68%)
Not effective	7(15%)	15(32%)
Total	46(100%)	46(100%)

Group A:I/V Amikacin

Group B: I/V Cefoperazone/Sulbactam

Chi Square test was applied in which P value was 0.004

DISCUSSION

Urinary tract infections are amongst the most prevalent infectious diseases affecting approximately 150 million people worldwide annually. UTIs occur more in young to middle age patients than in pediatric patients and affects females more commonly.¹In pregnant women, prevalence rate of UTI is 29.57%.¹¹

The most common cause of UTI in men and women with and without DM is *E. coli*.^{4,9,10} Diabetic patients are at a higher risk of developing acute pyelonephritis, renal abscess, abnormalities of bladder scarring and pyelitis.⁹ Most common causative organism for the urinary tract infection is *Escherichia coli*, which is responsible for up to 70% of the cases both in outpatient and inpatient.^{4,9} Other less common gram negative bacteria include *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, *Proteus* spp. Gram positive bacteria accounts for 5 – 15% of UTIs and include *Enterococcus* spp., *Staphylococci*, and *Streptococci*.^{9,10}

Antimicrobial resistance among uropathogens causing community and hospital acquired urinary tract infections is increasing.^{12,13}The emergence of resistance to the described antibiotics in the management of UTIs

is indeed a serious public health problem in the developing countries like Pakistan, where apart from high level of poverty, ignorance and poor hygienic practices, fake and spurious drugs of questionable quality are often in circulation. Furthermore, common usage antibiotics have a high rate of resistance.^{14,15}If urgent measures are not taken to arrest the situation, we may see the return of the era of search for new drugs to fight bacterial infections causing UTI.

In our study, Urinary tract infections with *E. Coli* were seen more in individuals 44 to 46 years of age, with a female preponderance, as in group A (I/V Amikacin) 32% patients were male, 68% patients were female whereas in group B (I/V Cefoperazone/Sulbactam) 30% patients were male, 70% patients were female. Moreover, our study shows that I/V Amikacin was effective in 85% patients and was not effective in 15% patients. Whereas I/V Cefoperazone/Sulbactam was effective in 68% patients and was not effective in 32% patients. *Escherichia coli* was found to be resistant to Amikacin in less than 10% of cases(hence 90% Efficacy) and resistance of 35% was shown by cefoperazone/sulbactam group(hence 65% Efficacy). A study conducted in India shows that Amikacin sensitivity was 64.7% in *E. Coli* strains that were multiple drug resistant.¹⁶

In another study conducted by Fawwad A et al, *E. coli* strains were mostly susceptible to imipenem (100%) followed by ertapenem and piperacillin/tazobactam (95%), sulbactam / cefoperazone (76%), amikacin (90%) and aztreonam (62%).¹⁷

CONCLUSION

Our study concludes that I/V Amikacin was more effective than I/V Cefoperazone/sulbactam in urinary tract infections caused by *Escherichia Coli* in diabetic patients.

Author's Contribution:

Concept & Design of Study: Mohammad Nadeem
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Revisiting Critically: Mohammad Nadeem, Mujeeb-ur-Rehman

Final Approval of version: Mohammad Nadeem

Conflict of Interest: The study has no conflict of interest to declare by any author.

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