Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20190657

Original Research Article

Comparative analysis of safety and efficacy of cefotaxime/sulbactam verses piperacillin/tazobactam combinations in the treatment of complicated urinary tract infections

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Received: 20 December 2018
Accepted: 12 January 2019

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ABSTRACT

Background: Complicated UTIs (cUTIs) are leading causes of the gram negative bacteraemia. The objective of this study was to compare efficacy and safety Cefotaxime/ Sulbactam (CTS) and Piperacillin/ Tazobactam (PT) combinations in complicated Urinary Tract Infections.
Methods: Total 80 patients admitted in the hospital due to cUTI were enrolled. 31 patients were given CTS while 49 patients were given PT. Clinical symptoms were registered and scored as mild (1) moderate (2) or severe (3). The follow-up of were done daily till the patient is discharged. Thereafter, one follow up visit was done within 4 to 9 days of after discharge, termed as test of cure (TOC), and, one late follow up visit after 6 to 8 weeks was done, known as late follow up visit (LFU). Clinical assessments and microbiological analysis were done at the time of TOC and LFU.
Results: At TOC visit, in CTS and PT groups, clinical scores were 1.25±3.47 and 0.86±2.35, respectively ($p<0.005$). Rate of clinical improvement at TOC visit was 92.00% and 92.68% while microbiological clearance was 84.00% and 87.80% with CTS and PT groups respectively. At LFU visit, clinical scores CTS and PT in groups were 1.30±3.56 and 1.32±3.37, respectively, suggesting significant improvement from baseline ($p<0.005$). Clinical cure rate at LFU visit was 88.00% and 87.80% while microbiological cure rate at LFU visit was 76.00% and 82.91% in CTS and PT groups respectively.
Conclusions: Results suggest that both regimens have no significant difference for the treatment of cUTI. CTS and PT both are equally efficacious in treatment of cUTI.

Keywords: Complicated UTI, Cefotaxime, Piperacillin, Sulbactam, Tazobactam, UTI

INTRODUCTION

Urinary tract infections (UTIs) are one of the leading causes of gram-negative bacteraemia for patients of all ages. Complicated UTIs (cUTIs) occur in patients who have a functionally, metabolically, or anatomically abnormal urinary tract. Complicated urinary tract infection (cUTI) is defined in various ways by different authors. It can be defined as urinary infection that occurs because of anatomically abnormal urinary tract and/or significant surgical or medical co morbidities.[1] It is also defined as that occurring in individuals with functional or structural abnormalities of the genitourinary tract.[2] Gram negative organisms are the most common uropathogen causing cUTI.[3] *E. coli* is the most common organism causing cUTI.[4] Mechanisms of infection include obstruction with incomplete urinary drainage, persistence of bacteria in biofilm on stones or indwelling devices or increased introduction of organisms into the genitourinary tract through instrumentation.[5]

The empiric use of antimicrobials in this group of patients will promote the emergence of organisms with increased antimicrobial resistance. Whenever possible,

empirical therapy should be avoided and antimicrobial therapy specific for the infecting organism(s) should be identified by urine culture sensitivity test, and, the antimicrobial therapy should be reevaluated when the culture and susceptibility testing results are available.[6] The primary objective of this study was to compare efficacy of Cefotaxime/ Sulbactam (CTS) and Piperacillin/ Tazobactam (PT) combinations in complicated Urinary Tract Infections. While, secondary objectives of this study were to evaluate sensitivity of causative organisms, to measure the safety of drugs, and, to generate guidelines to the prescribers.

METHODS

This continuous, longitudinal, prospective, single centred, cohort study included both, male and female gender of all ages, who were admitted in the wards Institute of Kidney Disease & Research Centre, Ahmedabad, was carried out for the duration of 18 months from December 2010 to July 2012. Patients with the following conditions were excluded: Treatment with another antimicrobial due to any other condition, uncomplicated UTI, renal transplantation, immunocompromised status, prostatitis, history of drug allergy.

The study included total 80 patients admitted in the hospital due to cUTI. Among of 80 patients, 31 patients were given CTS while 49 patients were given PT combinations. Patients were classified as having cUTI based on the criteria defined by Rubenstein and Schaeffer.[5] Informed consents were obtained from all patients. At admission detailed clinical history was taken. Five clinical symptoms (e.g., dysuria, frequency, suprapubic pain, back and/or flank pain) were registered and scored as mild (1) no significant interference with normal daily activities, moderate (2) significant interference with normal daily activities, or severe (3) preventing normal daily activities. The follow up were done daily till the patient is discharged. Thereafter, one follow up visit was done within 4 to 9 days of after discharge, termed as test of cure (TOC). One late follow up visit after 6 to 8 weeks was done, known as late follow up visit (LFU). Clinical assessments and microbiological analysis were done at the time of TOC and LFU. Efficacy and safety assessments were performed during treatment, at the time of discharge, at 1st and late follow up visit. The data was collected over a period of 18 months and at the end of this period, the data were analysed as following:

Clinical outcome

A) Clinical cure: resolution of all symptoms of patient at the TOC visit and no further use of additional antimicrobial therapy. B) Improvement: Each clinical symptom is decreased by at least one score. C) Failure: No change / increase in score of each symptom at the test-of-cure visit, or use of additional antimicrobial therapy for the current infection. D) Recurrence (at LFU only): Increase in score after clinical cure at TOC visit.

Microbiological outcome

a) Eradication*:* uropathogens reduced to $<10^4$CFU/mL. B) Persistence: $>10^4$CFU/mL of the original uropathogen.
b) Superinfection: $>10^5$CFU/mL of a uropathogen other than the baseline pathogen.
c) New Infection: A pathogen, other than the original microorganism found at baseline at a level $>10^5$CFU/mL, is present at a level $>10^5$ CFU/mL anytime after treatment is finished.
d) Recurrence: $>10^4$CFU/mL of the original uropathogen taken any time after documented eradication at the 5 to 9 day post-treatment visit, up to and including the 4 to 6 week post-therapy visit**.**

RESULTS

A total of 80 patients were recruited during the study period of eighteen months. Out of these patients, 31 patients were given CTS, while 49 patients were given PT combinations. A total number of 66 patients completed the study, of which 41 and 25 patients belonged to PT and CTS group respectively. A total of 14 patients did not complete the study. Out of these 14 patients, 9 patients were lost to follow up, 2 patients had required additional antibacterial drug and 1 patient were died. While in 2 patients culture sensitivity reports were not found.

Table 1: Age wise distribution of patients in study population.

Age (year)	Cefotaxime + Sulbactam (n=25)	Piperacillin + Tazobactam (n=41)
Mean (SD)	40.20 (16.75)	46.22 (17.81)
Range	1 to 61	1 to 67

Table 2: Gender wise distribution of patients in study population (values are expressed as absolute numbers and percentage in parenthesis).

Gender	Cefotaxime + Sulbactam (n=25)	Piperacillin + Tazobactam (n=41)
Male (%)	12 (48.00)	21 (51.12)
Female (%)	13 (52.00)	20 (48.78)

The mean age was 40.20±16.75 (33.28 to 47.11) and 46.22±17.81 years for CTS and PT, respectively (Table 1). Both treatment regimens were well matched with respect to age characteristics of the patients. These patients belonged to the age ranging from 1 to 67 years. Most common age group was 50 to 59 years of age. Male participants were 48.00% and 51.12% respectively for CTS and PT. While 52.00% and 48.78% were females in CTS and PT groups, respectively. Thus, both groups had

almost equal distribution of male and female population (Table 2) (Figure 1).

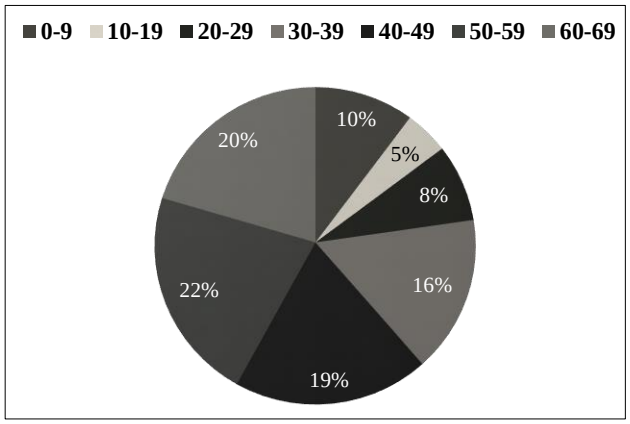

Figure 1: Age wise distribution of study population (values are expressed in percentage).

Table 3: Details of presenting symptoms of the patients with cUTI (values are in absolute numbers). (Patients may have more than one presenting symptom.)

Symptoms	Cefotaxime + Sulbactam (n=25)	Piperacillin Tazobactam (n=41)
Dysuria	19	24
Suprapubic pain	22	17
Fever	23	16
Vomiting	8	9
Oliguria	9	9
Back pain	6	,0
Heamaturia	5	6
Anuria	3	5

Table 4: Complicating factors in study population (values are expressed as absolute numbers and percentage in parenthesis).

Complicating factors	Cefotaxime+ Sulbactam (n=25)	Piperacillin+ Tazobactam (n=41)
Male gender (M)	12(63.15)	21 (65.71)
Diabetes mellitus (DM)	12 (63.15)	18 (56.25)
Instrumentation (I)	14 (73.68)	10 (24.39)
Obstructive uropathy (OU)	14 (73.68)	14 (43.75)
Urogenital surgery (SX)	01 (05.26)	3 (09.37)
Functional/ anatomical abnormality (A)	06 (31.57)	5 (15.62)
Pregnancy (P)	01 (05.26)	2 (06.25)

It was observed that lower cUTI (80.12%) was more common clinical presentation than pyelonephritis (19.88%) in both treatment group. Amongst the patients suffering from lower cUTI, majority of the patients were symptomatic [75% and 79.16% in CTS and PT group respectively]. It was observed that dysuria (43 patients) was the most common presenting symptom for the patient with cUTI, followed by suprapubic pain (39 patients), fever (39 patients) and vomiting (17 patients) (Table 3).

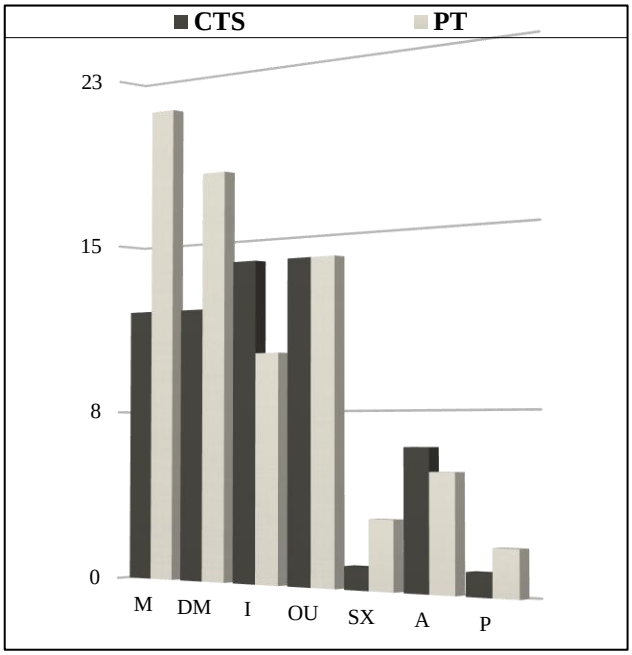

Figure 2: Complicating factors in patients of cUTI (values are expressed in absolute numbers).

Instrumentation and obstructive uropathy were found to be the two most common complicating factors in CTS (73.68%) group. However, Male gender was found to be the most common complicating factor in PT (65.71%) group (Figure 2) (Table 4).

Baseline characteristics

Clinical evaluation

At first visit, before starting the therapy, a clinical score was calculated according to the intensity of each symptom (presented by the patient. 1 - mild, 2 - moderate, 3 - severe). The sum of score of all presenting symptoms is considered as total clinical score. The mean baseline clinical score for CTS and PT were 10.57±2.02 and 10.89±2.23, respectively. When mean baseline clinical score of both the treatment groups was compared using ANOVA test, it was found that there was no significant difference between the both groups.

Microbiological evaluation

It was observed that gram negative organisms were the most common pathogens in both treatment groups. Amongst the organisms, *E-coli* and *P. aeruginosa* were the two most common organisms found in both treatment groups (Table 5).

Table 5: Organisms isolated from urine samples of patients with cUTI (values are expressed in percentage). [Patient may have more than one uropathogens.]

Pathogen	Cefotaxime+ Sulbactam (n=25)	Piperacillin+ Tazobactam (n=41)
	(%)	(%)
Gram negative		
Escherichia coli	43.75	41.46
Klebsiella pneumoniae	12.50	12.19
Pseudomonas aeruginosa	15.62	14.63
CUrobacterfreundii	0	02.43
Proteus Vulgaris	06.25	07.31
Morganelle	0	02.43
Enterobacter cloacae	0	02.43
Gram positive		
Staphylococcus aureus	12.50	07.31
Staphylococcus Saprophyticus	0	02.43
Streptococcus agalactiae	06.25	02.43
Enterococcus Faecalis	03.12	04.87

The mean duration of drug therapy was 11.32 days for CTS and 11.65 days in for PT respectively. Hence, the duration of drug therapy in all treatment group was found almost similar.

At TOC visit

Clinical evaluation

At TOC visit, the mean clinical score was found to be 1.25±3.48 and 0.86±2.30 in CTS and PT respectively. When mean clinical score at TOC was compared to baseline clinical score using paired t-test significant difference ($p<0.0001$) was found in both treatment groups. However, when compared both the groups for total clinical score at TOC visit by using ANOVA test, there was no significant difference between both treatment groups. Mean reduction in clinical scores between TOC visit and baseline were and 9.33±2.34 and 9.95±2.44 CTS and PT respectively. However no significant difference, when compared the both treatment groups for mean reduction in clinical score between two visits by using paired t test, was observed (Table 6).

Table 6: Comparison of the clinical score between baseline and TOC (Test of Cure) visit (values are expressed as mean (SD)). (*p<0.0001 (paired t-test). Significant difference as compared to baseline.)

Clinical evaluation	Cefotaxime + Sulbactam (n=25)	Piperacillin + Tazobactam (n=41)
Baseline	10.57(2.02)	10.89 (2.23)
TOC	1.25 (3.48)*	0.86 (2.35)*
Reduction in clinical score	9.33±2.34	9.95±2.44

Table 7: Microbiological evaluation at TOC in both treatment groups.

Pathogen	Cefotaxime + Sulbactam (n=25)			Piperacillin + Tazobactam (n=41)		
	Baseline C/S +ve	TOC C/S -ve	Conversion % (+ve to -ve)	Baseline C/S +ve	TOC C/S -ve	Conversion % (+ve to -ve)
Gram Negative						
Escherichia coli	10	9	90.00	17	15	88.23
Klebsiella pneumoniae	3	2	66.66	5	4	80.00
Pseudomonas aeruginosa	3	2	66.66	6	5	94.44
Citrobacter freundii	1	0	100	1	1	100
Proteus Vulgaris	2	2	100	3	3	100
Morganelle	0	0		1	1	100
Enterobacter cloacae	1	1	100	1	1	100
Gram positive						
Staphylococcus aureus	1	1	100	3	1	33.33
Staphylococcus Saprophyticus	1	1	100	1	1	100
Streptococcus agalactiae	1	1	100	1	1	100
Enterococcus Faecalis	2	2	100	2	2	100

Microbiological evaluation

At TOC visit, urine samples were also investigated for culture and sensitivity test, it was observed that urine samples were negative from 84% of samples in CPS and 87.80% of samples in PT group. In CTS group, urine sample from 2 patients were positive for the presence of microorganisms including *Pseudomonas aeruginosa* and *S. aureus* (one sample for each organism. In PT group, urine samples from 3 patients were positive for the

presence of microorganisms including *E. coli* (2 samples), *K. pneumoniae* (1 samples). They were resistant to PT. There were 7 cases of new infection (3 cases for PT and 4 for CTS) at the TOC visit. Majority of the pathogens (*E. coli, S. agalactie, K. pneumoniae and P. aeruginosa)* were resistant to respective treatment regimen. Prolong catheterization and diabetes mellitus were the predominant reasons for the growth of new uropathogens (Table 7).

At LFU visit

Clinical evaluation

At LFU visit, mean clinical score was found to be 1.30 (3.56) in CTS and 1.32 (3.37), in PT treatment groups. When compared mean clinical score at LFU visit using paired t-test, significant difference ($p<0.0001$) was found between baseline and LFU visit in both treatment group. However, when compared the mean clinical score of both treatment groups using ANOVA test, there was no significant difference between both treatment groups. The mean reduction in clinical score in both treatment group were 9.16 and 9.65 in CTS and PT respectively. When compared the mean reduction score of both treatment group using ANOVA TEST, there was no significant difference between both treatment groups (Table 8).

Table 8: Comparison of the clinical score between baseline and LFU visit (values are expressed as mean (SD)).

Clinical socre	Cefotaxime + Sulbactam	Piperacillin + Tazobactam
Baseline	10.57 (2.02)	10.89(2.23)
LFU	1.30 (3.56)*	1.32(3.37)*
Reduction in clinical score	9.16	9.65

Microbiological evaluation

When urine samples were investigated at LFU visit, 76% samples were negative from patients of CTS while 88.91% samples were negative from patients of PT (Table 9). At LFU visit, culture sensitivity reports of 4 patients shown the presence of microorganism in PT group. The organisms were *E. coli* [2 samples], *K. pneumoniae* [1 sample] *and p. aeruginosa* [1 sample]. In CTS group also culture sensitivity reports of 3 Patients were positive including 1 sample each for *Pseudomonas aeruginosa*, *s. aureus and K. pneumoniae;*. Suggesting resistance of these organisms.

Safety

A total of 10 adverse events were reported among both treatment groups. The number of reported adverse event were 6 and 4 in CTS and PT group respectively. All these adverse events were no serious and mild to moderate in nature. The causality assessment done by using WHO-UMS scale (Table 10) (Table 11).

Table 9: Evaluation of clinical and microbiological response at TOC and LFU visit (values are expressed in percentage).

Treatment group	CTS (n=25) TOC	PT (n=41) TOC	CTS (n=25) LFU	PT (n=41) LFU
	(%)	(%)	(%)	(%)
Clinical improvement	92.00	92.68	88.00	87.80
Microbiological cure	84.00	87.80	76.00	82.92

Table 10: Adverse drug reactions observed in patients treated with both treatment groups (values are expressed as absolute numbers.

Adverse event	Cefotaxime + Sulbactam (n=25)	Piperacillin+ Tazobactam (n=41)
Headache	2	1
Nausea	1	0
Vomiting	1	1
Diarrhea	0	1
Rashes	0	0
Pain at the site of injection	2	0
Hypoprothrombinemia	0	1

Table 11: Causality assessment of ADRs.

	Number of ADRs	
(WHO-UMC criteria)	Cefotaxime + Sulbactam	Piperacillin + Tazobactam
Certain/ Definite	0	0
Probable	3	2
Possible	2	1
Unlikely/ Doubtful	1	1
Conditional/ Unclassifiable	0	0
Unassessible	0	0
Total	6	4

DISCUSSION

It is estimated that 150 million UTIs occur yearly on a global basis, resulting in more than 6 billion dollars in direct health care expenditures.[7] In the year 1997 UTI accounts approximately 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalisations in the United States.[8] Furthermore, the direct and indirect costs associated with community-acquired UTIs in the USA alone exceed an estimated US $1.6 billion.[9] There is lack of data about drug pattern of antimicrobial agents for cUTI. The objective of this study was to provide a summary of the existing efficacy data pertaining to the use of antimicrobial combinations for the treatment of cUTI. While our search of the literature

revealed that there are only few publications meeting the criteria for microbiological and clinical cure rates in patients of cUTI. Hence the present study was carried out with the aim to compare the efficacy and safety of antimicrobial combinations in patients with cUTI.

In this study, a total of 56 patients were enrolled. Patients were divided in two groups: 1) CTS (n=25), 2) PT (n=41). The mean age for patients was and 40.20±16.75 and 46.22±17.81 years for CTS and PT, respectively. Male patents were 53.13% and 51.12%, while female patients were 46.87% and 48.78% in CPS and PT, respectively. In all patients with cUTI, symptomatic UTIs (77.70%) were commoner than asymptomatic UTI (22.30%). Male gender was the most common complicating factor for cUTI. Dysuria was the commonest presenting symptom followed by suprapubic pain and fever.

The baseline clinical score in CTS was having 10.57±2.02, while PT group had mean value of 10.89±2.23. Most common organisms in both groups were *E. coli* (40.00% and 41.46% in CTS and PT group respectively) followed by *P. aeruginosa* (14.63% and 12.00% in CTS and PT group respectively.

At TOC visit, in CTS and PT groups, clinical scores were 1.25±3.47 and 0.86±2.35, respectively; suggesting significant improvement from baseline ($p<0.005$). Rate of clinical improvement at TOC visit was 92.00% and 92.68% while microbiological cure rate was 84.00% and 87.80% with CTS and PT groups respectively. At LFU visit, clinical scores CTS and PT in groups were 1.30±3.56 and 1.32±3.37, respectively. Clinical cure rate at LFU visit was 88.00% and 87.80% while microbiological cure rate at LFU visit was 76.00% and 82.91% in CTS and PT groups respectively. All these results suggest that both regimens have no significant difference for the treatment of cUTI and thus they are equally effective for the treatment of cUTI.

Demographic characteristics

The demographic results of our study revealed that the mean age of patient was 40.20±16.75 and 46.22±17.81 CTS and PT, respectively. Study carried out in New Jersey, USA had mean value 51.2±21.1 and 51.1±21.0 for the doripenam and levofloxacin group with cUTI, which was higher as compared to mean age of our study.10 The reason for higher mean age value is they excluded patients lesser than 18 years of age, while in our study we included all the patients suffering from cUTI irrespective of their age. Eight patients less than 10 years of were included in present study. cUTI is very common in age group of 45-50 years because the complicating factors like DM, prostate hypertrophy are very common in these age groups.[10]

In our study male to female ratio were 0.93 and 1.05:1 in CTS and PT group respectively. Similar outcome was seen in study conducted in Orlando clinical research centre, Florida showed ratio of 1.27:1 and 1.38:1 in cUTI patients treated with gatifloxacin and ciprofloxacin respectively.[11] Any UTI present in male is to be considered as cUTI. The other reason behind high male female ratio in our study is many patients were having benign prostatic hypertrophy. Male gender is one of the complicating factors in cUTI.[12] Our study also observed the male patients (52%) were more common than female (48%) patients.

In our study majority of patient population had symptomatic UTIs (77.70%). While only 22.30% patient had asymptomatic UTI. Study conducted in USA revealed that 90% patients were symptomatic.13 These results show that majority of patients with cUTI are symptomatic. The reason behind less symptomatic patients were: 1) we have enrolled those patients who are positive for organisms with culture and sensitivity irrespective of their clinical features. 2) Sample size was quite small as compared to other multi-centre study.

E. coli (40.23%) was the most frequently isolated uropathogen and was identified in samples from nearly half of the population. The second most common organisms were *P. aeruginosa* (13.31%). A review by Lindsay Nicolle reported *E.coli* as the most common uropathogen with a worldwide Prevalence rate of 21-54%.[14] The results from worldwide review are similar to the present study. Similar findings were obtained in one Tunisian hospital, they reported the most frequently isolated organisms were *Gram-negative rods* (80.8%).[15] All these data suggests that gram negative bacteria are the most common organisms causing cUTI and among all these gram negative organisms *E.coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* are the most common organisms. Though *E.coli* was the most frequently isolated organisms, percentage of *E.coli* positive were less in our study as compared to other studies. In our study the number of female patients was less as compared to other studies and females are likely to have more *E.coli* induced cUTI female patients. This could be due to the close proximity of the urethral catheter to the anal passage.

It is also observed that there is significant difference between the clinical score of first visit and TOC visit showing the efficacy of both treatment groups. The microbiological cure rate observed was negative from 84.00% and 87.80% in CTS and PT groups, respectively.

Five clinical trials, involving different antimicrobial agents including Carbenicillin, Cefoperazone, Ceftazidime, Ceftriaxone and combination of Piperacillin/ Tazobactam studies, reported variable microbiological and clinical cure rate on short term follow up of patients (5 to 9 days after the discontinuation of antimicrobial therapy). Evaluation of these studies is frequently compromised by variability in study subjects, small sample size, lack of blinding or placebo control, variable follow-up and exclusion of patients with resistant isolates. Published reports describing comparative studies of

adequate sample size with at least short-term follow-up e.g. five to nine days post-therapy. The microbiological cure rate ranges from 50% (Carbenicillin) to 85.90% (Ceftriaxone) while clinical cure rate ranges from 30.20% (Carbenicillin) to 84.90% (Ceftriaxone) in these studies. In present study the microbiological cure rate of CTS group (84%) was comparable with that of ceftriaxone reported by cox et al.[11] However the clinical cure rate in both groups of present study was found higher than the clinical cure rate reported by all five studies. Reason for higher microbiological and clinical cure rate is, antimicrobial combinations were used which expands the spectrums of antimicrobial agents. Secondly the selection of antimicrobial combination was done in accordance with urine culture and sensitivity reports and the causative organism were sensitive to the given antimicrobial combination (Table 12).

Table 12: Comparative clinical trials of complicated urinary tract infection (cUTI).

Clinical trial		Outcomes (% cure rate)			
		Short-term 5-9 days post therapy		Long-term 4-6 weeks post therapy	
	Regimen	Micro biological	Clinical	Micro biological	Clinical
Cox et al[11]	Ceftriaxone 1g od x 3 d oral	84.90	84.90	NS	NS
Naber et al[16]	Piperacillin/tazobactam 2g/0.5g q8h, 5d - 14d (161)	57.80	83.00	49.10	65.20
Horowitz et al[17]	Ceftazidime 500mg ql2h, 7 d - 12 d (27)	74.00	NS	42	NS
Nishiura et al[18]	Cefoperazone 1g bid, 5 d (116)	68.20	59.50	NS	NS
Nishiura et al[18]	Carbenicillin 2g bid, 5 d (116)	50.00	30.20	NS	NS

bid Twice a day; Cli-Clinical; d-Days; IV-Intravenous; Micro-Microbiological; NS-Not stated; od-Once daily; po-per oral; q6h-Every six hours; q8h-Every eight hours; ql2h-Every 12 hours.

The study conducted by Naber et al has used Piperacillin/tazobactam combinations.[16] The clinical cure rate was 83% and 65.20% at TOC visit and LFU visit respectively while microbiological cure rate was 57.8% and 59.1% at TOC visit and LFU visit respectively. The cure rates were higher in our study for same Piperacillin/tazobactam combinations. The reason for higher cure rate in our study was high number of P. aeruginosa which were highly sensitive to Piperacillin/tazobactam combinations. Another reason for high cure rate was strict inclusion criteria.

In our study, 3 patients (*Pseudomonas aeruginosa*, *s. aureus and K. pneumoniae)* had persistence of infection in patient treated with CTS group. While, 4 patients were resistant to PT group including *E. coli* (2 samples), *K. pneumoniae* (1 sample) and *p. aeruginosa* (1 sample). There were total 4 cases of new infection with PT and 1 cases with CTS group, at the LFU. Majority of the pathogens (*E. coli* and *P. aeruginosa*) were resistant to respective treatment regimen. All these results were similar to or better than those reported in previous studies of patients with cUTI.[11,19]

The numbers of reported adverse events were 6 and 4 in CTS and PT group respectively. All these adverse events are mild to moderate. All the reactions were non-serious in nature and all patients recovered from them. Both treatment groups were well tolerated. Out of total 10 adverse drug events, 5 events were probable in nature and 3 events were possible with given treatment drug. While 2 events were unlikely of doubtful with the given treatment drug.

CONCLUSION

UTIs are very high but data regarding the treatment of cUTI and adherence to available guidelines are lacking especially in India. This study had tried to assess the clinical and antimicrobial activity of Cefotaxime /Sulbactam and Piperacillin + Tazobactam combination therapy for the cUTI. The study concluded that both the combination, CTS and PT, are equally efficacious in treatment of cUTI. Long follow up, involvement of all age groups, measurement of clinical scoring system were the main pillars of our study which strengthen our study. The study population was quite small which limited our study. Furthermore the study was observational study and decision of drug selection was taken by clinicians in nephrology unit. Management of cUTI especially in Indian setup (limited resources, lack of laboratory investigations, and sensitivity of organisms) should be outlined in a clear manner. Better and judicious use of drugs depends on the prominence on proper diagnosis, proper treatment, continuous medical education and availability of locally effective guidelines. We recommend further extensive study involving parameters like tolerability of drugs and pharmacoeconomics evaluation.

Funding: No funding sources
Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Makwana SP, Solanki MN. Comparative analysis of safety and efficacy of cefotaxime/sulbactam verses piperacillin/tazobactam combinations in the treatment of complicated urinary tract infections. Int J Basic Clin Pharmacol 2019;8:512-9.