Comparative Efficacy of Ceftaroline with Linezolid against Staphylococcus Aureus and Methicillin Resistant Staphylococcus Aureus

Amira Hafeez, Tehmina Munir, Sabahat Rehman, Sara Najeeb, Mehreen Gilani, Mahwish Latif, Maliha Ansari and Nadia Saad

ABSTRACT

Objective: To compare the in vitro antimicrobial efficacy of ceftaroline with linezolid against Staphylococcus aureus and methicillin resistant Staphylococcus aureus.

Study Design: Quasi-experimental study.

Place and Duration of Study: Microbiology Department, Army Medical College, Rawalpindi, from January to December 2013.

Methodology: Clinical samples from respiratory tract, blood, pus and various catheter tips routinely received in the Department of Microbiology, Army Medical College, Rawalpindi were inoculated on blood and MacConkey agar. Staphylococcus aureus was identified by colony morphology, Gram reaction, catalase test and coagulase test. Methicillin resistant Staphylococcus aureus detection was done by modified Kirby Bauer disc diffusion method using cefoxitin disc (30µg) and the isolates were considered methicillin resistant if the zone of inhibition around cefoxitin disc was ≤ 21 mm. Bacterial suspensions of 56 Staphylococcus aureus isolates and 50 MRSA isolates were prepared, which were standardized equal to 0.5 McFarland's turbidity standard and inoculated on Mueller-Hinton agar plates followed by application of ceftaroline and linezolid disc (Oxoid, UK), according to manufacturer's instructions. The plates were then incubated at 37°C aerobically for 18 - 24 hours. Diameters of inhibition zone were measured and interpreted as per Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: Out of 106 isolates all of the 56 Staphylococcus aureus (100%) were sensitive to ceftaroline and linezolid. However, out of 50 methicillin resistant Staphylococcus aureus, 48 (96%) were sensitive to ceftaroline whereas, 49 (98%) were sensitive to linezolid.

Conclusion: Ceftaroline is equally effective as linezolid against Staphylococcus aureus and methicillin resistant Staphylococcus aureus.

Key Words: Ceftaroline. Methicillin resistant Staphylococcus aureus. Linezolid.

INTRODUCTION

Staphylococcus (S.) aureus is an important cause of infections worldwide. For the last many years Methicillin Resistant Staphylococcus aureus (MRSA) has become a frequent offender in hospital settings and represents about 33% to 55% of all isolated S. aureus strains from hospital and 60% from critical care units. Clinicians face a great challenge while treating patients with MRSA infections especially Community Acquired Pneumonia (CAP) because of limited treatment options. MRSA infections not only cause increased morbidity and mortality but also contributes to increasing healthcare costs.

Cephalosporins have been used for more than 40 years against Gram-positive and Gram-negative bacterial infections until now since S. aureus has developed increase in resistance to beta-lactams. Vancomycin and linezolid are preferred medicines in the USA and Europe for the treatment of infections caused by MRSA especially nosocomial pneumonia. Linezolid is the first oxazolidinone and is bacteriostatic. It has very good clinical results but adverse effects like thrombocytopenia and myelosuppression may occur. Although many new agents to combat MRSA have been introduced during the last decade including, daptomycin, tigecycline, and telavancin but their usage has been mitigated because of concerns regarding adverse effects, drug interactions, and high drug prices. Newer antimicrobials are needed as there is ongoing emergence of multidrug-resistant Gram-positive organisms.

Ceftaroline is newer addition in cephalosporin family. It has a wide-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria including MRSA, which makes it an ideal treatment option for complicated Skin and Skin Structure Infections (cSSSI) and community-acquired pneumonia. Ceftaroline is a bactericidal agent and like all other beta-lactam it inhibit
cell wall synthesis. It has high affinity to bind to Penicillin binding proteins 2a making it effective against MRSA\textsuperscript{8}. By using animal models the in vivo efficacy of ceftaroline has also been demonstrated and results are very promising. These were followed by Phase-III clinical trials for treatment of cSSSI and CAP and results are very promising.\textsuperscript{9}

Ceftaroline has been placed as a member of a new subclass of antimicrobials, cephalosporins with anti-MRSA activity by The Clinical and Laboratory Standards Institute (CLSI).\textsuperscript{10} Currently, no data is available on the spectrum of activity of this novel antibiotic in our region as the antibiogram of bacteria vary from region to region. This study was done to compare in vitro antimicrobial efficacy of ceftaroline with linezolid against \textit{S. aureus} and MRSA.

**METHODOLOGY**

This quasi-experimental study was done in the Department of Microbiology, Army Medical College, Rawalpindi, National University of Science and Technology, Islamabad. Clinical samples from respiratory tract, blood, pus and various catheter tips received were inoculated on Blood and MacConkey agar. These were then incubated at 37°C for 18 - 24 hours. \textit{Staphylococcus aureus} was identified by its colony morphology, positive Gram reaction, positive catalase and coagulase test.

From the isolated \textit{S. aureus} MRSA was detected by modified Kirby-Bauer disc diffusion method. Isolate suspension was applied on Mueller-Hinton agar as per manufacturer's instructions. The plates were then incubated at 37°C for 18 - 24 hours. \textit{Staphylococcus aureus} was identified by its colony morphology, positive Gram reaction, positive catalase and coagulase test. Isolated \textit{S. aureus} MRSA was detected by modified Kirby-Bauer disc diffusion method. Isolate suspension was applied on Mueller-Hinton agar followed by application of cefoxitin disc (30µg) incubated at 37°C for 18 - 24 hours. The isolates were considered methicillin resistant if the zone of inhibition around cefoxitin disc was ≤ 21 mm. Duplicate sample from same patient during same episode of illness was excluded.

Antimicrobial susceptibility testing of the isolates was done by Modified Kirby-Bauer disc diffusion method. Bacterial suspensions of isolated 56 \textit{Staphylococcus aureus} and 50 MRSA equivalent to 0.5 McFarland turbidity standard were prepared. Inoculation on MHA plates was done which was followed by application of ceftaroline (30µg) and linezolid (30µg) disc (Oxoid, UK) according to manufacturer's instructions. The plates were then incubated at 37°C aerobically for 18 - 24 hours. Zone diameters were measured and interpretation was done as per CLSI guidelines. The isolates were considered resistant to ceftaroline and linezolid if the zones of inhibition around the disc were ≤ 20 mm for both and susceptible if zone was ≥ 24 mm for ceftaroline and ≥ 21 mm for linezolid respectively.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21. Frequencies and percentages were calculated for categorical data like sensitivity and resistance. Chi-square test (Fisher's Exact test) was used to compare sensitivity between the two groups. P-value of less than 0.05 was considered as significant.

**RESULTS**

Out of a total of 106 isolates all of 56 isolates of \textit{S. aureus} (100%) were sensitive to ceftaroline and linezolid both. However, out of 50 MRSA isolates, 48 (96%) were sensitive to ceftaroline, whereas 49 (98%) were sensitive to linezolid. Sensitivities of both the drugs were similar with insignificant statistical difference (p = 1.000).

**DISCUSSION**

It is the need of the hour to discover and develop new antibiotics to combat the increasing resistance of bacteria to currently available drugs.\textsuperscript{11} Ceftaroline may be a useful alternative treatment option since there are reports of decreased susceptibility to vancomycin and the report documenting emergence of both chromosomal and transferable resistance to linezolid.\textsuperscript{12} Ceftaroline is currently the only approved beta-lactam antimicrobial by Food and Drug Administration (FDA) which has activity against MRSA. Although it is indicated for the treatment of CAP and cSSSI, recent reports suggest that different infections including osteomyelitis and endocarditis caused by MRSA may also be treated.\textsuperscript{13}

\textit{S. aureus} was found to be 100% sensitive to ceftaroline and to linezolid both which showed these to be highly effective and promising treatment option. Similar results were seen from surveillance studies conducted in different parts of the world. A surveillance study conducted in Canada by Karlowsky \textit{et al}. showed 100% sensitivity of \textit{S. aureus} to ceftaroline and linezolid both.\textsuperscript{14} Same 100% sensitivity to both was seen in Europe in 2010 by a study done by Farrel \textit{et al}.\textsuperscript{15} However, by 2013 a surveillance study done in USA conducted by Sader \textit{et al}. reported 98.5% sensitivity of \textit{S. aureus} to ceftaroline and 99.93% to linezolid which is lower than this study.\textsuperscript{16}

MRSA showed different results. Out of 50 samples 48 isolates i.e 96% were sensitive to ceftaroline and 49 isolates 98% sensitivity to linezolid. Different surveillance studies done in different parts of the world showed different results demonstrating the demographic variation. In a study, conducted by Ge Yigong \textit{et al}. who studied isolates from USA and Europe causing CAP demonstrated 98% sensitivity of MRSA to ceftaroline and 98.4% to linezolid.\textsuperscript{17} Slightly lower sensitivity of MRSA against ceftaroline being 97.5% was shown by Sader \textit{et al}. who studied isolates from hospitals in USA during a period of 2008 - 2011 whereas sensitivity to linezolid was 99.93% which was higher than this study.\textsuperscript{16}

In another study by Farrel \textit{et al}. evaluated different antibiotics against major pathogens causing skin and soft tissue infections in Europe documented 88.8%
sensitivity of MRSA to ceftaroline which is quite low as compared to the present findings whereas 100% sensitivity to linezolid was documented which was higher than these results.\textsuperscript{18} Higher sensitivities of ceftaroline and linezolid was documented by Richter \textit{et al.} to MRSA as compared to these findings of being 98% to ceftaroline and 99.9% to linezolid.\textsuperscript{19} In another study by Sader \textit{et al.}\textsuperscript{20} in which they studied pathogens causing skin and soft tissue infections and Community Acquired Respiratory Tract Infection (CARTI) from Asia Pacific Region and South America in 2010 showed quite low sensitivity to ceftaroline being only 80.6% whereas linezolid showed 100% sensitivity.

**CONCLUSION**

Ceftaroline is as effective as linezolid against \textit{S. aureus} and MRSA.

**REFERENCES**


