

To examine the Antimicrobial Sensitivity Pattern of the Gram Negative Isolates and to Study the in vitro effect of Ceftriaxone-Subactam EDTA on these Isolates in Tertiary Care Hospital

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Abstract

Objective: To examine the antimicrobial sensitivity pattern of the Gram Negative isolates and to study the in vitro effect of Ceftriaxone-Subactam EDTA on these isolates. **Place and Duration of Study:** This was an observational study conducted at Dr. S.S. Tantia medical College Hospital and Research Center, Sriganganagar, Rajasthan between January 2023 to September 2023. **Material and Methods:** Bronchoalveolar lavage, body fluids, urine, pus, tissue, etc., of patients attending the hospital during the study period were included in the study. Susceptibility testing was performed using Kirby Bauer disk diffusion method and the results were interpreted as per Clinical Laboratory Standards Institute (CLSI) guidelines. The data was analyzed using SPSS Version. **Result:** A total of 1126 samples were received in the laboratory for culture and sensitivity. In vitro susceptibility test results of ceftriaxone sulbactam EDTA combination disks (Venus Remedies Limited, India) were interpreted as per manufacturer's instructions, instructions, ≥ 21 mm susceptible, 14-20mm intermediate and ≤ 13 resistant. **Conclusion:** CSE emerged as a potent antimicrobial against the MDR pathogen in our study, showed excellence in vitro activity. Thus, CSE can prove itself to be an affordable, promising option for the treatment of MDR gram negative pathogens.

Keywords: Ceftriaxone sulbactam EDTA, Multi drug Resistant, Gram Negative Bacterial

Introduction

With the upsurge of multi drug resistant (MDR) gram negative bacteria, the treatment of the patients harboring these pathogens has become a therapeutic challenge for the physicians. (1,2,3) The South east Asian region, particularly India, has been facing a rapid increase in the incidence of ESBLs as well as MBLs. (4,5,6,7) With no new antimicrobials in the pipeline, a new concept of using certain adjuvant with antimicrobials is undergoing research. These adjuvant increase the penetrability of the drug to the target site, hence potentiates the antimicrobial action. CSE-Ceftriaxone Sulbactam EDTA is one such drug, the activity of which is being tested widely. EDTA- Ethylenediaminetetraacetic acid is a well known chelating agent which binds with the metal ions and catalyzes resistance breaking mechanisms.(1,8,9) This study was conducted in a district in the North region of Rajasthan with the aim to examine the antimicrobial sensitivity pattern of the Gram Negative isolates and to study the in vitro effect of Ceftriaxone-Subactam EDTA on these isolates.

Materials and Methods

The study was conducted at a tertiary care Centre Dr S.S. Tantia medical College Hospital and Research Center in Sriganganagar, Rajasthan between January 2023 to September 2023. Gram-negative bacterial isolates obtained from various clinical samples like cerebrospinal fluid, blood, sputum, endotracheal aspirates, Bronchoalveolar lavage, body fluids, urine, pus, tissue, etc., of patients attending the hospital during the study period were included in the study. All clinical samples were processed aerobically as per the standard guidelines.(10,11) The bacterial isolates obtained in culture were identified by conventional biochemical techniques. Antimicrobial susceptibility testing was performed using Kirby Bauer disk diffusion method and the results were interpreted as per Clinical Laboratory Standards Institute (CLSI) guidelines.(12) In-vitro susceptibility test results of ceftriaxone-sulbactam-EDTA combination disks (Venus Remedies Limited, India) were interpreted as per manufacturer's instructions, instructions, ≥ 21 mm susceptible, 14-20mm intermediate and ≤ 13 resistant. Screening of isolates for ESBL production was performed as per the Clinical Laboratory Standards Institute (CLSI) guidelines. Isolates exhibiting zone size ≤ 25 with ceftriaxone (30 μ g), ≤ 22 for ceftazidime (30 μ g), and ≤ 27 with cefotaxime (30 μ g) were considered as possible ESBL producers. Extended-

spectrum beta-lactamase production was confirmed by disk potentiation test using ceftazidime (30 µg) and cefotaxime (30 µg) antibiotic disks with and without clavulanic acid (10 µg) and by double disk susceptibility test (DDST).(12)

Results

During the study period, a total of 1126 samples were received in the laboratory for culture and sensitivity. Out of these, a total of 252 gram negative isolates were obtained. Most common organism was found to be *Escherichia coli* (74) followed by *Klebsiella spp* (52), *Pseudomonas* (46) *Acinetobacter spp* (43), *Citrobacter spp*(25), *Proteus spp* (12) (Fig 1)

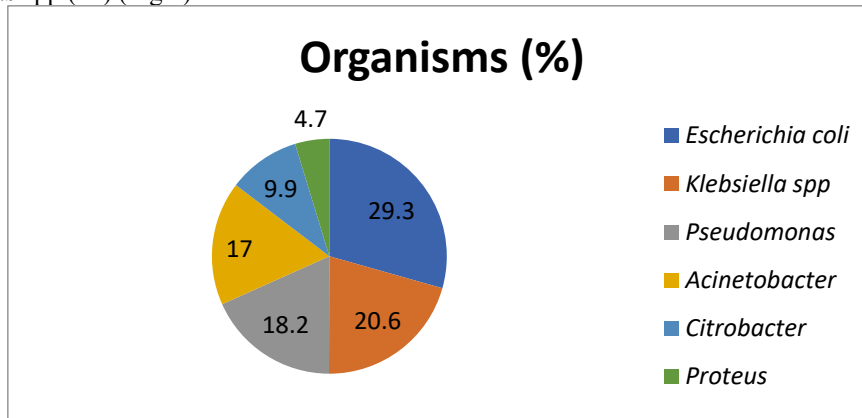


Fig 1 Distribution of gram negative organism included in the study

Maximum isolates were obtained from urine(98) followed by respiratory samples(74), pus(32), blood (25), csf (8) and others (15)

All the clinical isolates were sensitive to Ceftriaxone-Sulbactam EDTA (Elores). Maximum resistance was observed for 3rd generation cephalosporins (75%) followed by aminoglycosides (69%), fluoroquinolones (65%), piperacillin-tazobactam (55%), carbapenems (42%) and tigecycline (10%). The prevalence of ESBL and MBL was 65% and 48% in our study. As per the CLSI 2020 guidelines, colistin was reported as intermediate in all the isolates. (Fig 2)

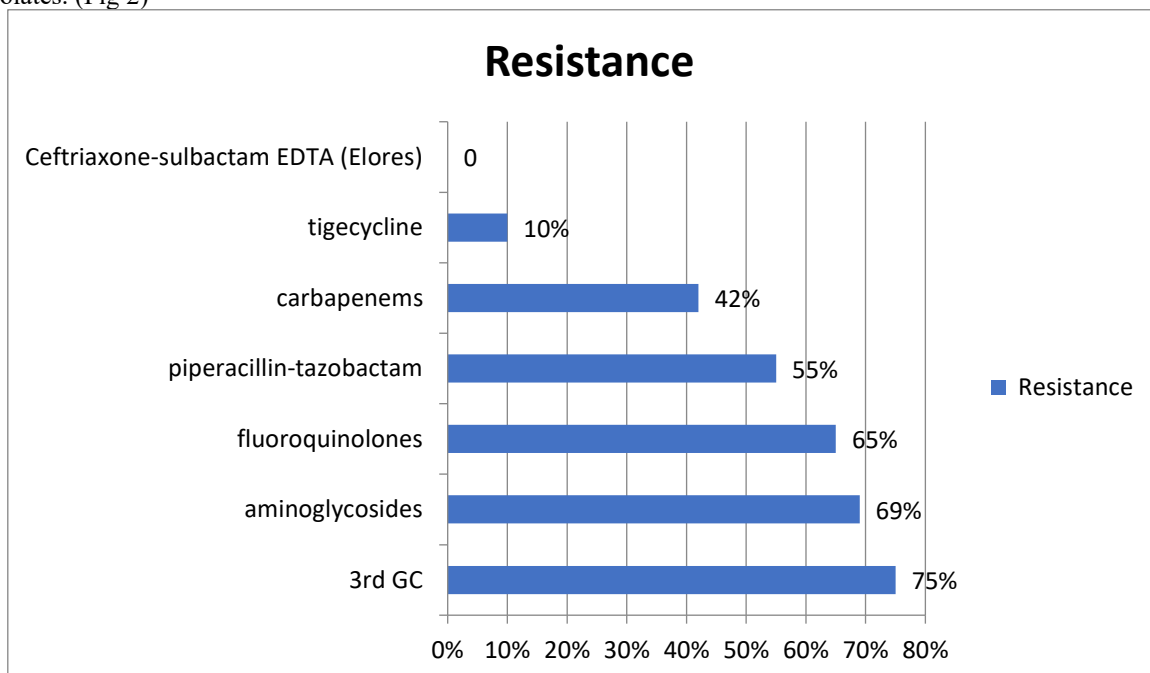


Fig 2 Resistance pattern of the isolates

Discussion

With the increasing trends in antibiotic resistance patterns, there is a constant need to explore newer drug alternatives. Colistin and Tigecycline are the reserved drugs which are now being used rampantly due to the increasing prevalence of MBLs and ESBL. Various BL/BLI combinations such as amoxicillin-clavulanic acid, Piperacillin–tazobactam are also now emerging as resistant drugs in many scenarios. Various other combinations are also in the pipeline. (7,13)

Ethylenediaminetetraacetic acid (EDTA) is a well-known chelating agent. When combined with an antibiotic, it enhances the penetration by binding with the metal ions that compete with antibiotics for the cell wall receptors. It does not have antimicrobial activity, but it acts as a potentiator and enhances the activity of antimicrobial (13-18)

In a study conducted in Lucknow, the prevalence of ESBL and MBL producers was 57% and 43%, respectively. (7) These results were comparable to our study where we observed a resistance of 65% for ESBLs and 48% for MBLs. Another study in Kolkata demonstrated MBL prevalence to be 42.1% which was also comparable to our study. (2) A study from New Delhi demonstrated the prevalence of MBL in *K.pneumoniae* to be 79% (3). This was higher than our study results as the study isolates included only *K.pneumoniae*..

In the study by Singh *et al* ceftriaxone sulbactam EDTA (CSE) combination was the most effective antibiotic showing 94% sensitivity for carbapenem-sensitive Enterobacteriaceae and 97% for carbapenem resistant *Acinetobacter* and *Pseudomonas* spp. (7)

Chaudhuri S *et al.* has also demonstrated very good sensitivity of CSE for various isolates of gram negative bacteria from different samples. (13)

Our study has demonstrated 100% sensitivity to CSE. As this drug is introduced for the first time in this region, it was found to show very good in vitro susceptibility results. CSE can be a very good option for treating infections resistant to carbapenems and in using the carbapenem sparing approach in lesser resistant infections.

Limitations

The present study was conducted on a small scale in a remote region. Hence, a larger study with a larger population should be planned to understand the exact scenario. The clinical efficacy of CSE should be tested and be compared with other newer agents like ceftazidime–avibactam, ceftolozane–tazobactam, etc.

Conclusion

CSE emerged as a potent antimicrobial against the MDR pathogen in our study. It showed excellent in vitro activity for Enterobacteriaceae, *Pseudomonas* as well as *Acinetobacter*. The results were good for all the types of samples tested. Thus, CSE can prove itself to be an affordable, promising option for the treatment of MDR gram negative pathogens.

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