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ERTAPENEM SUSCEPTIBILITY OF EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING E COLI AND K PNEUMONIAE

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ABSTRACT

Background: Multidrug resistant organism such as extended spectrum beta-lactamase (ESBL) – producing E. coli and K. pneumoniae are increasing in critical ill patients. Carbapenem [Imipenem and Meropenem] are the antibiotics of choice to treat them. Ertapenem, newest Carbapenem has limited clinical data regarding its efficacy against these organisms.

Objectives: Objective of study is to compare susceptibility of ertapenem to imipenem and organisms are susceptibility of ertapenem to imipenem could be used as a surrogate for ertapenem susceptibility.

Materials and Methods: 53 ESBL isolates (n==26 E –coli and n==27 K. pneumoniae) collected from critical care unit specimen were identified tested susceptibility by Vitek 2 compact (Biomerieux India pvt. LTD.)

Result: 100% of clinical isolates tested were susceptible to ertapenem. 100% of same isolates were also susceptible to imipenem.

Conclusion: 100% susceptibility, suggest that ertapenem may be an alternative to other carbapenem for the treatment of infection caused by ESBL_ producing E-coli and K.pneumoniae.

Key words: Escherichia coli, Ertapenem, ESBL, Imipenem and K. pneumonias

INTRODUCTION

Extended spectrum B – Lactamase (ESBLS) continue to be major problem in clinical setup world over conferring resistant to the extended spectrum cephalosporins.[1-3] Extended spectrum beta – lactamase producing Escherichia coli and Klebsiella pneumoniae are resistant to almost all antibiotics excluding Carbapenem (imipenem and ertapenem), are drug of choice to treat infection caused by ESBL producing organisms.[4,5] There is limited clinical data regarding ertapenem a relative new Carbapenem against ESBL-producing organisms.[6-8] However the ease of once daily dosing and reduced cost of ETP (ertapenem) make this drug a desired alternative in the treatment of these patients.

The aim of this study is to evaluate ETP susceptibility of ESBL – Producing E Coli and Klebsiella pneumoniae of clinical isolates. A secondary aim is to compare ITP (imipenem) and ETP susceptibilities to determine if ITP can be used as a surrogate for ETP susceptibility.

MATERIAL AND METHOD

All isolates taken from clinical specimens from critical care unit were screened for ESBL production and tested for antimicrobial susceptibility by using Vitek 2 compact (Biomerieux India pvt.LTD). Isolates which are ESBL-producers by Vitek 2 compact are submitted for disk diffusion confirmatory testing. Phenotyping confirmatory disk diffusion testing is done on presumptive ESBL-

producing organisms in accordance with the clinical and laboratory standard institute (CLSI) guidelines.

ETP susceptibility is determined using Vitek 2 compact (Biomerieux India pvt. LTD) Isolates are revived from freezer stocks by passing twice to 5% sheep blood agar plate (Hi media) then processed in vitek2 compact as per --- manufacturer instruction for identification and susceptibility testing.

Susceptibility data to ETP is determined as per the clinical and laboratory standards institute (CLSI) interpretive criteria. For ETP, sensitive is defined as MIC </=2 µg/ml intermediate 4 µg/ml and resistant >/= 8 µg/ml. Data compiled for 53 clinical isolates (n=26 E. coli, n= 27 Klebsiella pneumoniae) included specimen site for each isolates.

Specimen location for ESBL isolates

Isolates	Urine	Blood	Pus	Sputum	HV
E. coli	7	1	12	2	1
K.pneumoniae	10	1	10	4	1

HV= High vaginal

RESULTS

All (100 %) of ESBL producing clinical isolate show susceptibility to ETP as per CLSI criteria ETP MICs ≤ 0.5 For E. coli and ≤ 0.5 for K. pneumoniae

Table 1: Antibiotic susceptibility of E. Coli and Klebsiella pneumonia

Drug name	Sensitivity (%)	
	E.coli	*K. pneumonia*
Ampicillin	0%	0%
Ampicillin salbactum	3%	0%
Piperacillin /tazobactum	100%	96.29%
Cefazolin	0%	0%
Cefotetan	19.23%	33.30%
Ceftazidine	0%	0%
Ceftriaxome	0%	0%
Cefepime	3%	0%
Aztreoman	3%	0%
Imipenem	100%	100%
Ertapenem	100%	100%
Amikacin	100%	100%
Gentamycin	46.15%	22.22%
Tobramycin	23.7%	14.81%
Ciprofloxacin	3%	3.7%
Levofloxacin	3%	18.51%
Nitrofurantoin	34.61%	22.22%
Trimethoprim sulfamethoxazole	38.41%	25.90%

All (100%) of ESBL isolate susceptible to ETP out of 53 samples. In regards to susceptibility of ESBL producing organism to other antibiotic 3% E. coli and 18.5% K. pneumonia are susceptible to quinolone such as levofloxacin. ESBL E. coli and K. pneumoniae are 100% and 81.48% sensitive to amikacin respectively, cephalosporin sensitivity shows approximately 96.15% & 100% resistant to cefepime in E. coli & K. pneumoniae respectively and 100% resistant to ceftazidime for all clinical specimen.

DISCUSSION

100% of the clinical isolate of ESBL producing E. coli and k. pneumoniae tested were susceptible to ertapenem in this study with MIC of <0.5 µg/ml for E. coli and K. pneumoniae, prior study also showed similar ETP efficacy in vitro[1,9].

Various studies report in vivo ETP susceptibility of clinical isolates. Livermore et al. tested 181 ESBL-producing clinical Enterobacteriaceae isolates (all Klebsiella spp.) taken from ICU patients and found ertapenem to inhibit 90% of isolate but found to be less active against ESBL non-producers [1]. Betetriu et al. tested 70 clinical ESBL-producing Enterobacteriaceae isolates which were found to be 98.6% susceptible to ertapenem at 10^4 and 10^6 inoculum with MICs ranging from 0.03-0.12 mg/L[9-13]. In our study inoculum size is held constant and plays no role in evaluation of ETP susceptibility, so no inferences can be made based on inoculum size.

Susceptibility of ESBL producing isolates in this study differed in regard to aminoglycoside and quinolone sensitivity. Overall 100% of clinical isolates show sensitive to amikacin, while less than 20% are sensitive to levofloxacin suggesting that aminoglycosides may be appropriate empiric adjunct therapy if concern over ESBL- producing organisms. Our data in conjunction with other studies suggest that ETP may be an alternative to other Carbapenem in the treatment of infections cause by ESBL- producing organisms. Ertapenem use to treat these infection would offer the benefit of ease of administration with once daily dosing (t ½ - 4-4.5 hrs.) and reduced cost. These advantages to the use of ETP are of particular value to clinicians & patients. All isolates tested are susceptible to ertapenem and imipenem which has also been observed in prior studies[1, 9]. However due to lake of resistant isolates we are unable to confidently conclude whether IPM susceptibility could accurately predict ETP susceptibility.

CONCLUSION

The result of our data shows that ESBL K. pneumoniae and E. coli clinical isolates showed uniform ertapenem susceptibility. This suggests that ertapenem with its ease of dosing and im-

proved cost, may be an acceptable alternative to other Carbapenem in the treatment, but it should be used with caution after further susceptibility testing clinical trials assessing the use of ertapenem to treat serious infection caused by ESBL isolates are needed.

ESBL E.coli susceptibilities to ertapenem and other antibiotics. yello represents percentage of isolates sensitive to antibiotics. pink represents percentage of intermediately sensitive antibiotics.

ESBL K. pneumoniae susceptibilities to ertapenem and other antibiotics. Blue represents percentage of isolates sensitive to antibiotics. Red represents percentage of intermediately sensitive antibiotics.

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