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Original Research Paper

Clinical Research

EFFECTIVENESS AND SAFETY OF POLYMYXIN WITH CEFTRIAXONE-SULBACTAM-EDTA FOR CARBAPENEM RESITANT INFECTIONS: A RETROSPECTIVE OBSERVATIONAL STUDY.

Dr. Rahul Kishore	Attending Consultant, Dept of Critical Care Medicine, Max Smart Super Speciality Hospital, Press Enclave Marg, New Delhi.
Dr Arun Dewan	Principal Director, Dept of Critical Care Medicine, Max Smart Super Speciality Hospital, Press Enclave Marg, New Delhi.
Dr Ritesh Aggarwal	Associate Director, Dept of Critical are Medicine, Max Smart Super Speciality Hospital, Press Enclave Marg, New Delhi

KEYWORDS :

INTRODUCTION

Bacterial septicemia and sepsis are the oldest and most elusive disorders and can become life threatening if managed inappropriately. Sepsis is widely prevalent in patients with skin, lungs, abdomen and urinary tract infections and requires rapid diagnosis, initiation of rational antibiotic and supportive therapy to save the lives of patients. Antimicrobial therapy remains gold standard for the management of sepsis patients. However, rapid development of multi-drug resistance (MDR) in microbes has limited there use in this deadly indication. Prevalence of drug resistance in sepsis is particularly important because of rising number of cases and high mortality rate associated with this serious malady.

In Indian hospitals, extended-spectrum beta lactamase (ESBL) and Metallo-beta lactamase (MBL) producing Gram-negative microbes are the most prevalent organisms responsible for rendering many antibiotics worthless. Rising incidences of these difficult to treat infections exposed patients to highly reserve antibiotics like carbapenem and colistin which further complicated resistance scenario. Recent reports of resistance to colistin and carbapenem posed serious therapeutic crisis to health care workers and risk of 'Pan resistance' i.e. resistance to all antimicrobials seems a reality.

Newer therapeutic strategies are needed to be explored to avoid the problems of developing resistance and to save the future of antibiotics. Previous reports suggested that rational combination therapy of 2 or more antibiotics may be a suitable approach to reduce the frequency of drug resistance in microbes.

Carbapenem-resistant Enterobacteriaceae (CRE) refers to Enterobacterales that exhibit resistance to at least one of the carbapenem antibiotics, namely ertapenem, meropenem, doripenem, or imipenem, or that produce carbapenemase – an enzyme conferring resistance to carbapenem antibiotics. The prevalence of CRE has risen in recent times due to the inappropriate use of antibiotics. These organisms are notorious for causing a wide array of nosocomial infections. Within this group of pathogens, antimicrobial resistance can stem from inherent characteristics or be acquired over time. Infection with CRE strains has been associated with prolonged hospital stay, increased mortality rate, and elevated direct or indirect healthcare expenses. Anti-microbials with different target of actions provides additional mechanism of action and may confer synergistic action.

An antibiotic adjuvant entity (AAE) of ceftriaxone, sulbactam and disodium edetate is developed for the MDR ESBL and MBL producing pathogens. The rationale behind addition of sulbactam and disodium edetate (EDTA) with ceftriaxone was to provide multiple mechanisms of antibacterial actions. Sulbactam, a BLI can be effective against various beta lactamase producing microbes. EDTA delivers its antibacterial action through antibiofilm and metal chelating property. It also enhances the penetration of drug by increasing the membrane porosity, which in turn decreased minimum inhibitory concentration (MIC) values of drugs. This combination of ceftriaxone, sulbactam and disodium edetate has been approved by the Indian regulatory authority; Drug Controller General of India (DCGI) for the treatment of MDR ESBL/MBL associated infections.

Polymyxin B belongs to the class of polymyxins, which is a polypeptide group of antibiotics. Polymyxins share their structure with cationic antimicrobial peptides (CAMPs) like defensins and gramicidins. CAMPs represent the first line of defense against bacterial infections. Polymyxins are cationic polypeptides that consist of a cyclic heptapeptide possessing a tripeptide side chain acylated at the N-terminus by a fatty acid tail.3,4 N-terminal fatty acyl segment is hydrophobic and is associated with both toxicity and the antimicrobial property. Polymyxin B is administered directly as an active antibiotic. The outer membrane of gram-negative bacteria is the target for polymyxins. Because of an electrostatic interaction occurring between the - diaminobutyric acid (Dab) residue of the positively charged polymyxin on one side and the phosphate groups of the negatively charged lipid A membrane on the other side, divalent cations are displaced from the negatively charged phosphate groups of membrane lipids.

The lipopolysaccharide (LPS) is therefore destabilized consequently increasing the permeability of the bacterial membrane leading to leakage of the cytoplasmic content and ultimately causing cell death. The endotoxin of gram-negative pathogens corresponds to the lipid. A portion of the LPS; polymyxins have the ability to bind to and neutralize this LPS molecule released during cell lysis.

Inhibition of vital respiratory enzymes (inhibition of type II nicotinamide adenine dinucleotide–quinone oxidoreductases [NDH-2]) in the bacterial inner membrane is another proposed mechanism of action. Even though the LPS is the initial target, the exact mode of action of polymyxins still remains uncertain.

Polymyxins have a narrow antibacterial spectrum including most members of the Enterobacteriaceae and common nonfermentative gram-negative bacteria including Acineto-bacter baumannii, Pseudomonas aeruginosa, and Steno-trophomonas maltophilia. Proteus spp., Morganella morganii, Providencia spp., Serratia marcescens, Pseudo-monas mallei, Burkholderia cepacia, Chromobacterium spp., Edwardsiella spp., Brucella, Legionella, Campylobacter, and Vibrio cholerae are intrinsically resistant to the drug. Gram-negative cocci (Neisseria spp.), gram-positive bacteria, and anaerobic bacteria are not covered by polymyxins.

The present study was designed to evaluate the effectiveness and safety of the combination of Polymyxin with Ceftriaxone-Sulbactam-EDTA(CSE) for Carbapenem -resistant infections.

Review of Literature

1. In a study by Vijayakumar M et al A total of 89 patients were enrolled, with 59 (66%) patients receiving CAZ-AVI + AZT and 30 receiving polymyxins. Baseline demographics and clinical characteristics were similar between the two groups. The Cox multivariate regression analysis showed a statistically significant difference in clinical failure on day 14 with the CAZ-AVI + AZT group vs polymyxins (HR = 0.78, 95% CI 0.63-0.95, p = 0.018). There was no difference in microbiological failure (HR = 1.08, 95% CI 0.66-1.77, p = 0.76), microbiological relapse (HR = 0.75, 95% CI 0.36-3.02, p = 0.62), and hospital mortality (HR = 1.04, 95% CI 0.75-1.43, p = 0.796) between the two groups. [11]
2. In a retrospective study in 2023 by Parikshit S Prayag et al, out of total 104 patients, 78 (75%) were in the CAZ-AVI group. There was no significant difference in the underlying comorbidities between the two groups. The incidence of nephrotoxicity was significantly higher in the polymyxin group (p = 0.017). Ceftazidime-avibactam-based therapy was 66% less likely to be associated with day 14 mortality (p = 0.048) and 67% less likely to be associated with day 28 mortality (p = 0.039) as compared with polymyxin-based therapy.
3. Demosthenes Makris et al in 2018 conducted an open label prospective study including 74 patients who developed microbiologically documented VAP due to A. baumannii with carbapenem-resistant strains but susceptible to colistin and ampicillin-sulbactam concluded that a Combination therapy with colistin and a high dose of ampicillin/sulbactam was associated with a more favourable clinical response to VAP due to carbapenem-resistant A. baumannii than colistin monotherapy.
4. In The meta-analysis including 39 studies conducted by Samir Samal et al in 2021 of polymyxin monotherapy vs. combination therapy in multidrug-resistant infections yielded an odds ratio (OR) of 0.81 (95% confidence interval [CI]: 0.65-1.01) with minimal heterogeneity (I^2 = 40%), whereas pooled analysis of this comparison in studies that included carbapenem as combination therapy yielded an OR of 0.64 (CI: 0.40-1.03; I^2 = 62%). Likewise, the pooled analysis of the RCTs yielded an OR of 0.82 (95% CI: 0.58-1.16, I^2 = 22%). All these showed no statistical significance. However, it was seen that polymyxin combination therapy was more effective in multidrug-resistant infections compared to polymyxin monotherapy. The effectiveness was more glaring when carbapenems were used as the combination drug instead of any other antibiotic and more so in many in vitro studies that used polymyxin combination therapy.
5. Mohd Amin Mir et al in 2019 conducted a double blind noninferiority randomised trial of 230 patients, 74/143 and 69/143 were treated with CSE and meropenem respectively. Of these, 98% were ceftriaxone non-susceptible and 83% were ESBL-positive at baseline. Noninferiority of CSE to meropenem was demonstrated for both the US Food and Drug Administration defined co-primary endpoints of (1) symptomatic resolution at test-of-cure: 71/74 (95.9%) patients vs 62/69 (89.9%) [treatment difference, 6%; 95% CI, -2.6% to 16%] and (2) both symptomatic resolution and microbiological eradication at test-of-cure: 70/74 (94.6%) vs 60/69 (87.0%) (treatment difference, 7.6%; 95% CI, -2.0% to 18.4%). Microbiological eradication at test-of-cure (European Medical Agency's primary endpoint) was observed in 70/74 (94.6%) vs 61/69 (88.4%) [treatment difference, 6.2%; 95% CI, -3.2% to 16.6%] patients treated with CSE and meropenem respectively. Safety profile of CSE was consistent with that of ceftriaxone alone.
6. Xiaojuan Xin et al in 2013 conducted a multicentre clinical study including 285 patients to evaluate the efficacy and safety of this therapy in the treatment of respiratory and urinary infections caused by ceftriaxone-resistant bacteria in comparison with the effect of cefoperazone/sulbactam on cefoperazone-resistant bacteria and concluded that Ceftriaxone/sulbactam is as effective and well-tolerated as cefoperazone/sulbactam for the treatment of intermediate and severe bacterial infections caused by resistant strains.
7. Umakant Nagashetty Patil,Kiran Lakkol and Jambulingappa in 2012 conducted A retrospective observational study including 18 patients admitted in intensive care unit (ICU) at tertiary health care site in India, concluded and recommended the use of combination of ceftriaxone, sulbactam and disodium edetate (EDTA) for the treatment of MDR septicaemia associated with ESBL and MBL producing microbes.
8. Manu Chaudhary et al in 2016 conducted a post marketing surveillance study including 2500 patients were included in the study suffering from various bacterial infections and treated with Elores (CSE1034) and concluded that CSE-1034 was found to be an effective and safe option against Pip tazo and meropenem in management of patients with multi-drug resistant (MDR) bacterial infections under routine ward settings.
9. Marco Falcone et al in 2020 conducted a prospective observational study including patients admitted to 3 hospitals in Italy and Greece. The primary outcome measure was 30-day all-cause mortality. Secondary outcomes were clinical failure at day 14 and length of stay after BSI diagnosis and concluded that the CAZ-AVI + ATM combination offers a therapeutic advantage compared to OAAs for patients with BSI due to MBL-producing Enterobacterales although further studies are warranted.
10. Sunita Gupta, Taranpreet Kaur in 2016-2017 conducted a Retrospective Analysis of the efficacy of ceftriaxone-sulbactam-EDTA combination for suspected Biofilm infections and concluded that cse 1034 should be a choice of treatment for beta lactam/beta lactamase inhibitor combinations for patients suspected of biofilm infections.

Lacunae In Existing Knowledge

There are limited studies on the use of Polymyxin and Ceftriaxone sulbactam EDTA as a combination therapy to treat infections caused by carbapenem resistant organisms.

Research Question

Is Polymyxin and Ceftriaxone sulbactam EDTA combination effective and safe to treat infections caused by carbapenem resistant organisms.

Hypothesis

Polymyxin and Ceftriaxone-Sulbactam-EDTA combination therapy is effective and safe for the treatment of infections caused by carbapenem resistant organisms.

Aim and Objectives

Aim: - To Study the Effectiveness and safety of Polymyxin with Ceftriaxone- Sulbactam-EDTA(CSE) for carbapenem-resistant infection.

Objectives: -

1. To study the Effectiveness of Polymyxin with Ceftriaxone-Sulbactam-EDTA(CSE) for carbapenem- resistant infection.
2. To study the Safety of Polymyxin with Ceftriaxone-Sulbactam-EDTA(CSE) for Carbapenem- resistant infection.

Methodology

Study Venue:- Department of Critical Care Medicine, Max Smart Super Specialty Hospital, New Delhi

Study Design:- Retrospective Observational Study.
Duration of Study:- 24 months
Sample Size:- To estimate the sample size for the above study, following parameters are considered: -
The proportion of improvement for CSE in Carbapenem resistant infection(p) =60%
(Based on the pilot basis from ICU)
Assuming absolute margin of error (d)= 10%
The required sample size (n) based on formula = $(1.96^2p*q)/(d^2)$ where q = 1-p
we get n= (3.8416*.6*.4)/(.01) = 92

Allowing 10% of noncompliance, we need to recruit 101 patients of resistant infection cases to estimate the efficacy and safety in terms of cure rate with test drug.

Statistical Analysis
Efficacy of test drug will be calculated in terms of success rate (p) with 95% CI of p. Side effects will be seen and presented in percentages separately for patients with test drug only.

Inclusion Criteria
1. Age >18 years
2. Pneumonia, Urinary tract infection or Bloodstream infection (BSI) due to carbapenem-resistant Enterobacteriaceae (E coli, Klebsiella, Enterobacter) or Carbapenem-resistant Acinetobacter (CRAB) or carbapenem-resistant Pseudomonas. Carbapenem resistance is defined as phenotypic resistance to carbapenems (Meropenem, Imipenem, Doripenem, or Ertapenem MIC ≥ 1 mcg/ml)
3. Organism is sensitive to CSE (Elores)

Exclusion Criteria
1. Polymicrobial cultures
2. Patients who received 72 hours or more of antibiotic treatment for carbapenem-resistant infection within 96 hours of enrolment
a. Ceftazidime Avibactam alone or in combination
b. OR Polymyxin B/Colistin alone or in combination
c. OR Fosfomycin/Minocycline/Tigecycline/Ampicillin-Sulbactam alone or in
d. Combination.
3. Pregnant or breastfeeding females
4. Neutropenia (TLC <500cells/mm3)
5. Presence of any of the following clinical syndromes due to carbapenem-resistant bacteria as a pathogen which requires a duration of antibiotic > 14 days: Endocarditis, Osteomyelitis, Prosthetic joint infections, Meningitis or other CNS infections.
6. Presence of concurrent infections (bacterial or fungal) at any other body site.
7. Refractory shock or comorbid condition such that the patient is not expected to survive more than 48 hours of eligibility assessment.
8. Where the source control of infection is required (catheter/device/prosthesis removal, surgical procedure etc), but not performed due to any reason.

Patient Evaluation
Patient fulfilling the above-mentioned inclusion criteria will be enrolled in the study after explaining pertinent details of the study with conmsent waiver attached.

History Taking
1. Chief complaints of the patient.
2. History of present illness -
3. Past history- history of any trauma, surgery
4. Treatment history.
5. Family History:
6. Personal History

Detailed Methodology
Patients with culture proven infections with Carbapenem Resistant organisms in lungs (Bronchoalveolar Lavage or Sputum), urine and blood were further evaluated for Ceftriaxone sulbactam EDTA sensitivity. Those patients who were sensitive to the drug were started on combination of injections polymyxin and Ceftriaxone sulbactam EDTA and were closely observed clinically and through lab investigations. SOFA score was calculated for each patient every day all patients were closely observed for a significant change in SOFA score. Any side effects to the medications were also looked for. In Patients who did not improve and deteriorated while on this combination with a significant change in SOFA Score, antibiotics were changed as per the sensitivity report. Also in patients who developed notable side effects, antibiotics were changed. The end ponts were Change in SOFA score, Duration of ICU stay, Need for change or addition of other antibiotics, Side effects due to the medication and Mortality.

Outcome Measures
1. Change in SOFA score
2. Duration of ICU stay.
3. Need for change in antibiotics.
4. Need for additional antibiotics.
5. Side effects observed
6. Mortality

Stastical Analysis
Frequency Table
Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	58	58.0	58.0	58.0
	Female	42	42.0	42.0	100.0
	Total	100	100.0	100.0	

Diagnosis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	PNEUMONIA	69	69.0	69.0	69.0
	SEPSIS	10	10.0	10.0	79.0
	UTI	20	20.0	20.0	99.0
	UROSEPSIS	1	1.0	1.0	100.0
	Total	100	100.0	100.0	

Culture Report

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	BAL - ACINETOBACTER	23	23.0	23.0	23.0
	BAL--KLEBSEILLA	24	24.0	24.0	47.0
	BAL-PSEUDOMONAS	5	5.0	5.0	52.0
	SPUTUM-KLEBSIELLA	7	7.0	7.0	59.0
	URINE-E COLI	9	9.0	9.0	68.0
	SPUTUM-PSEDOMONAS	5	5.0	5.0	73.0
	SPUTUM- E COLI	5	5.0	5.0	78.0
	URINE KLEBSIELLA	12	12.0	12.0	90.0
	BLOOD -KLEBSIELLA	5	5.0	5.0	95.0
	BLOOD-ACINETOBACTER	4	4.0	4.0	99.0
	BLOOD-E COLI	1	1.0	1.0	100.0
	Total	100	100.0	100.0	

Need for Additional Antibiotics or Change of Antibiotic

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	YES	18	18.0	18.0	18.0
	NO	82	82.0	82.0	100.0
	Total	100	100.0	100.0	

Mortality

		Frequency	Percent	Valid Percent	Cumulative Percent

Valid	YES	11	11.0	11.0	11.0
	NO	89	89.0	89.0	100.0
	Total	100	100.0	100.0	

Side Effects Noted

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	HYPERSENSITIVITY	1	1.0	1.0	1.0
	NO	99	99.0	99.0	100.0
	Total	100	100.0	100.0	

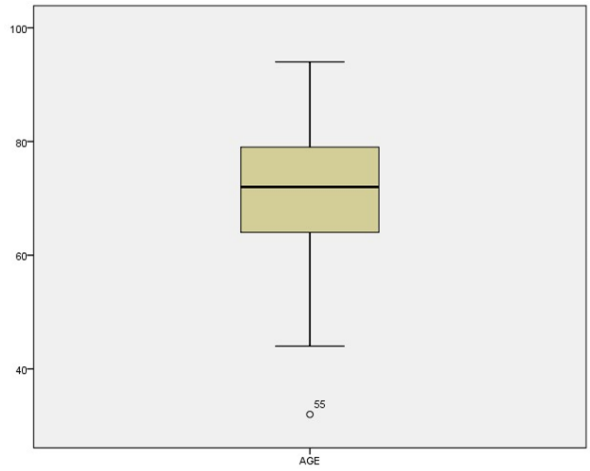
Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	32	94	70.47	12.081
DURATION OF ICU STAY (DAYS)	100	3	25	7.39	3.175
Valid N (listwise)	100				

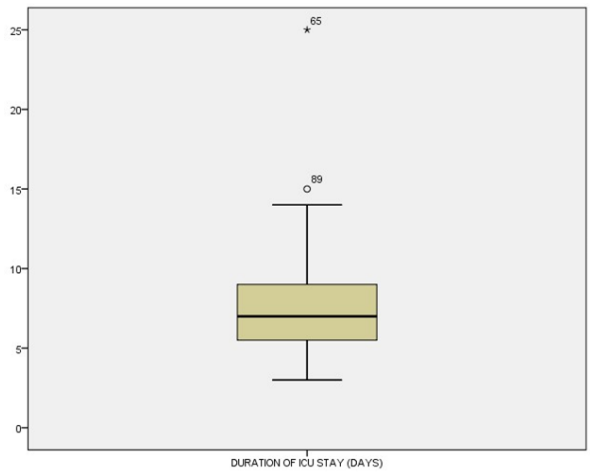
Descriptives for Age and Duration of Stay

Age

			Statistic	Std. Error
AGE	Mean 95% Confidence Interval for Mean 5% Trimmed Mean	Lower Bound Upper Bound	70.47	1.208
			68.07	
			72.87	
			70.89	
	Median			
			72.00	
	Variance		145.949	
	Std. Deviation			
			12.081	
	Minimum		32	
	Maximum		94	
	Range		62	
	Interquartile Range			
			15	
	Skewness		-.578	.241
	Kurtosis		.266	.478
DURATION OF ICU STAY (DAYS)	Mean .31795% Confidence Interval for Mean 5% Trimmed Mean Lower Bound Upper Bound 6.76 8.02 7.10 Median 7.00 Variance 10.079 Std. Deviation 3.175 Minimum 3 Maximum 25 Range 22 Interquartile Range 4 Skewness 2.197 .241 Kurtosis 8.728 .478		7.39	



Duration of ICU Stay (days)



Need for Additional Antibiotics or Change of Antibiotic * Mortality Crosstabulation

		MORTALITY		Total
		YES	NO	
NEED FOR ADDITIONAL YES ANTIBIOTICS OR CHANGE OF ANTIBIOTIC NO	Count	11_a	7_b	18
	% within MORTALITY	100.0%	7.9%	18.0%
	Count	0_a	82_b	82
	% within MORTALITY Count	0.0% 11	92.1% 89	82.0% 100
Total	% within MORTALITY	100.0%	100.0%	100.0%

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
For cohort MORTALITY = NO	.389	.218	.694
N of Valid Cases	100		

It indicates that additional antibiotic or change in antibiotic is a protective effect in survival of a patients not responding to the under study drug combination.

Comparison of duration of stay between Mortality status using t test

Group Statistics

	MORTALITY	N	Mean	Std. Deviation	Std. Error Mean
DURATION OF ICU STAY (DAYS)	YES	11	9.09	2.468	.744
	NO	89	6.83	2.170	.230

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
DURATION OF ICU STAY (DAYS)	Equal variances assumed	.758	.386	3.210	98	.002	2.259	.704	.863	3.656
	Equal variances not assumed			2.901	11.990	.013	2.259	.779	.562	3.957

Cross Table for No Mortality cases(89)

Culture Report * Diagnosis Crosstabulation

			DIAGNOSIS				Total
			PNEUMONIA	SEPSIS	UTI	UROSEPSIS	
CULTURE REPORT	BAL - ACINETOBACTER	Count	17	0	0	0	17
		% within DIAGNOSIS	27.9%	0.0%	0.0%	0.0%	19.1%
	BAL--KLEBSEILLA	Count	22	0	0	0	22
		% within DIAGNOSIS	36.1%	0.0%	0.0%	0.0%	24.7%
	BAL-PSEUDOMONAS	Count	5	0	0	0	5
		% within DIAGNOSIS	8.2%	0.0%	0.0%	0.0%	5.6%
	SPUTUM-KLEBSIELLA	Count	7	0	0	0	7
		% within DIAGNOSIS	11.5%	0.0%	0.0%	0.0%	7.9%
	URINE-E COLI	Count	0	0	9	0	9
		% within DIAGNOSIS	0.0%	0.0%	45.0%	0.0%	10.1%
	SP UTUM PSEDOMONAS	Count	5	0	0	0	5
		% within DIAGNOSIS	8.2%	0.0%	0.0%	0.0%	5.6%
	SPUTUM- E COLI	Count	5	0	0	0	5
		% within DIAGNOSIS	8.2%	0.0%	0.0%	0.0%	5.6%
	URINE KLEBSIELLA	Count	0	0	11	1	12
		% within DIAGNOSIS	0.0%	0.0%	55.0%	100.0%	13.5%
	BLOOD KLEBSIELLA	Count	0	5	0	0	5
		% within DIAGNOSIS	0.0%	71.4%	0.0%	0.0%	5.6%
	BLOOD - ACINETOBACTER	Count	0	1	0	0	1
		% within DIAGNOSIS	0.0%	14.3%	0.0%	0.0%	1.1%
	BLOOD-E COLI	Count	0	1	0	0	1

Comparison of Duration of Stay, Need for Additional Antibiotics Among Patients Discharged from ICU (89)

Group Statistics

	NEED FOR ADDITIONAL ANTIBIOTICS OR CHANGE OF ANTIBIOTIC	N	Mean	Std. Deviation	Std. Error Mean
DURATION OF ICU STAY (DAYS)	YES	7	9.14	2.340	.884
	NO	82	6.63	2.052	.227

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
DURATION OF ICU STAY (DAYS)	Equal variances assumed	.176	.676	3.073	87	.003	2.509	.816	.886	4.131
	Equal variances not assumed			2.748	6.811	.029	2.509	.913	.338	4.680

Diagnosis* Need for Additional Antibiotics or Change of Antibiotic Crosstabulation

			NEED FOR ADDITIONAL ANTIBIOTICS OR CHANGE OF ANTIBIOTIC		Total
			YES	NO	
DIAGNOSIS	Pneumonia	Count	5	56	61
		% within Need For Additional Antibiotics Or Change Of Antibiotic	71.4%	68.3%	68.5%
	Sepsis	Count	1	6	7
		% within Need For Additional Antibiotics Or Change Of Antibiotic	14.3%	7.3%	7.9%
	Uti	Count	0	20	20
		% within Need For Additional Antibiotics Or Change Of Antibiotic	0.0%	24.4%	22.5%

	Uro-sepsis	Count	1	0	1
		% within Need For Additional Antibiotics Or Change Of Antibiotic	14.3%	0.0%	1.1%
Total		Count	7	82	89
		% within Need For Additional Antibiotics Or Change Of Antibiotic	100.0%	100.0%	100.0%

Diagnosis* Need for Additional Antibiotics or Change of Antibiotic Crosstabulation

			Need For Additional Antibiotics Or Change Of Antibiotic		Total
			YES	NO	
DIAGNOSIS	Pneu-monia	Count	5	56	61
		% within DIAGNOSIS	8.2%	91.8%	100.0 %
	Sepsis	Count	1	6	7
		% within DIAGNOSIS	14.3%	85.7%	100.0 %
	UTI	Count	0	20	20
		% within DIAGNOSIS	0.0%	100.0%	100.0 %
	Uro-sepsis	Count	1	0	1
		% within DIAGNOSIS	100.0%	0.0%	100.0 %
Total		Count	7	82	89
		% within DIAGNOSIS	7.9%	92.1%	100.0 %

Analysis or Mortality cases

Diagnosis* Need for Additional Antibiotics or Change of Antibiotic Crosstabulation

			Need For Additional Antibiotics Or Change Of Antibiotic	Total
			YES	
DIAGNOSIS	Pneu-monia	Count	8	8
		% within Need For Additional Antibiotics Or Change Of Antibiotic	72.7%	72.7%
	Sepsis	Count	3	3
		% within Need For Additional Antibiotics Or Change Of Antibiotic	27.3%	27.3%
Total		Count	11	11
		% Within Need For Additional Antibiotics Or Change Of Antibiotic	100.0%	100.0%

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE(yrs.)	11	56	94	74.18	10.235
Valid N (listwise)	11				

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	6	54.5	54.5	54.5
	Female	5	45.5	45.5	100.0
	Total	11	100.0	100.0	

Diagnosis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Pneumonia	8	72.7	72.7	72.7
	Sepsis	3	27.3	27.3	100.0
	Total	11	100.0	100.0	

Culture Report

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Bal-Acineto-bacter	6	54.5	54.5	54.5
	Bal-klebseilla	2	18.2	18.2	72.7
	Blood-Acinetobacter	3	27.3	27.3	100.0
	Total	11	100.0	100.0	

Need for Additional Antibiotics or Change of Antibiotic

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	YES	11	100.0	100.0	100.0

Culture Report* Diagnosis Crosstabulation

			DIAGNOSIS		Total
			PNEUMONIA	SEPSIS	
Culture Report	Bal - Acineto-bacter	Count	6	0	6
		% within DIAGNOSIS	75.0%	0.0%	54.5%
	Bal-- klebseilla	Count	2	0	2
		% within DIAGNOSIS	25.0%	0.0%	18.2%
	Blood-Acineto-bacter	Count	0	3	3
		% within DIAGNOSIS	0.0%	100.0%	27.3%
Total		Count	8	3	11
		% within DIAGNOSIS	100.0%	100.0%	100.0 %

Crosstab

			MORTALITY		Total
			YES	NO	
SEX	Male	Count	6	52	58
		% within MORTALITY	54.5%	58.4%	58.0%
	Female	Count	5	37	42
		% within MORTALITY	45.5%	41.6%	42.0%
Total		Count	11	89	100
		% within MORTALITY	100.0%	100.0%	100.0%

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Contingency Coefficient	.025	.806
N of Valid Cases		100	

a. Not assuming the null hypothesis.
b. Using the asymptotic standard error assuming the null hypothesis.

Diagnosis* Mortality
Crosstab

			MORTALITY		Total
			YES	NO	
Diagnosis	Pneumonia	Count	8	61	69
		% within MORTALITY	72.7%	68.5%	69.0%
	Sepsis	Count	3	7	10
		% within MORTALITY	27.3%	7.9%	10.0%

	UTI	Count	0	20	20
		% within MORTALITY	0.0%	22.5%	20.0%
	Urosepsis	Count	0	1	1
		% within MORTALITY	0.0%	1.1%	1.0%
Total		Count	11	89	100
		% within MORTALITY	100.0 %	100.0%	100.0%

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Contingency Coefficient	.244	.098
N of Valid Cases		100	

a. Not assuming the null hypothesis.
b. Using the asymptotic standard error assuming the null hypothesis.

Culture Report* Mortality Crosstab

			MORTALITY		Total
			YES	NO	
Culture Report	Bal - Acinetobacter	Count	6	17	23
		% within MORTALITY	54.5%	19.1%	23.0%
	Bal-klebseilla	Count	2	22	24
		% within MORTALITY	18.2%	24.7%	24.0%
	Bal-pseudomonas	Count	0	5	5
		% within MORTALITY	0.0%	5.6%	5.0%
	Sputum-klebsiella	Count	0	7	7
		% within MORTALITY	0.0%	7.9%	7.0%
	Urine-e Coli	Count	0	9	9
		% within MORTALITY	0.0%	10.1%	9.0%
	Sputum-psedomonas	Count	0	5	5
		% within MORTALITY	0.0%	5.6%	5.0%
	Sputum- E Coli	Count	0	5	5
		% within MORTALITY	0.0%	5.6%	5.0%
	Urine Klebsiella	Count	0	12	12
		% within MORTALITY	0.0%	13.5%	12.0%
	Blood - klebsiella	Count	0	5	5
		% within MORTALITY	0.0%	5.6%	5.0%
	Blood-Acinetobacter	Count	3	1	4
		% within MORTALITY	27.3%	1.1%	4.0%
	Blood-e Coli	Count	0	1	1
		% within MORTALITY	0.0%	1.1%	1.0%
Total		Count	11	89	100
		% within MORTALITY	100.0%	100.0%	100.0%

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Contingency Coefficient	.470	.002
N of Valid Cases		100	

a. Not assuming the null hypothesis.
b. Using the asymptotic standard error assuming the null hypothesis.

Symmetric Measures

		Value	Approx. Sig.

a. Not assuming the null hypothesis.
b. Using the asymptotic standard error assuming the null hypothesis.

Side Effects Noted * Mortality Crosstab

			MORTALITY		Total
			YES	NO	
Side Effects Noted	Hyper-sensitivity No	Count	0	1	1
		% within MORTALITY	0.0%	1.1%	1.0%
		Count	11	88	99
		% within MORTALITY	100.0%	98.9%	99.0%
Total		Count	11	89	100
		% within MORTALITY	100.0%	100.0%	100.0%

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Contingency Coefficient	.035	.724
N of Valid Cases		100	

a. Not assuming the null hypothesis.
b. Using the asymptotic standard error assuming the null hypothesis.

Summary

In The Retrospective study carried out on 100 patients with carbapenem resistant infections, we found that the combination of Ceftriaxone Sulbactam EDTA showed favourable clinical outcome as 81 patients were effectively treated with this combination.11 patients had mortality while in 8 patients the antibiotic had to be changed and 1 patient showed hypersensitivity reaction to the drug combination. Thus, the Combination of Ceftriaxone sulbactam and EDTA is an effective and safe combination for carbapenem resistant infections.

CONCLUSION

Based on our study, we conclude that combination of Polymixin with Ceftriaxone-sulbactam-EDTA was associated with a more favourable clinical response to infections caused by Carbapenem Resistant Organisms. It is an Effective and a Safe choice.

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