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Research Article

Linezolid Resistant Coagulase Negative Staphylococci Isolated from Clinical Specimens in A Tertiary Care Cardiac Hospital, Pakistan

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Abstract

Background: The objective of this study was to determine the emergence of Linezolid resistance among Coagulase Negative Staphylococcus in patients of tertiary healthcare facility at Rawalpindi Institute of Cardiology (RIC), Pakistan.

Method: A retrospective study was carried out to find Linezolid Resistance Coagulase Negative Staphylococcus (LZRC) from clinical specimens in microbiology department of Rawalpindi institute of cardiology from year January 2016 to October 2018.

The clinical specimens included blood, wound swab, pus swab, bronchial secretions, urine, catheter tip, suction tip, central venous (CVP) tip, Temporary Pace Maker (TPM) tip and valvular vegetation. These specimens were collected from indoor & outdoor patients and cultured in microbiology laboratory. Culture media used to isolate Coagulase Negative Staphylococci (CoNS) included Blood Agar and MacConkey Agar. The organisms were identified by standard microbiological methods. Antibiotic susceptibility was performed by modified disc diffusion & Vitek 2 methods and confirmed on Microbroth Dilution (MBD) according to CLSI Guidelines.

Results: A total of 104 specimens yielded CoNS. Four of them were LZRC (3.84%) isolated in blood, pus, bronchial secretions and urine specimens. Three were isolated in specimens from male patients and one sample from a female patient. Out of these four positive LZRC isolates two were Staphylococcus haemolyticus.

Conclusions: The findings of LZRC isolated at RIC is comparatively higher than other studies worldwide. Judicious use of this antibiotic along with infection control measures is crucial to control antibiotic resistance so that the availability of linezolid in life threatening infections is not compromised.

Introduction

Antibiotic resistance to different microorganisms is getting common worldwide especially in the developing countries. CoNS are part of the normal flora of human skin. The clinicians typically consider CoNS risk-free when these remain on the surface of our body. However foreign bodies can become colonized by CoNS and the success of the respective medical procedure is compromised, resulting in massive medical and economic burdens [1]. Linezolid is used against gram positive bacteria including Vancomycin resistant Enterococci, Streptococci and Methicillin Resistant Staphylococcus Aureus (MRSA) [2].

As of 2014, the bacterial resistance to Linezolid remained scarce. Very little data exists regarding treatment and clinical outcomes for LZRC infections [3]. Statistics from the USA and global surveillance studies report 2% of CoNS are Linezolid resistant. However, resistance in Staphylococci against Linezolid is still unreported from most of the Asian countries. Therefore, a CoNS study was carried out to determine LZRC in our set up.



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Materials and Methods

A retrospective study was carried out to find Linezolid Resistance Coagulase Negative Staphylococcus (LZRC) from clinical specimens in Microbiology Department of Rawalpindi institute of cardiology from year January 2016 to October 2018.

The data collection was made from record of clinical specimens received for cultures and susceptibility requests received in Laboratory Information Management System (LIMS). The clinical specimens included blood, wound swab, pus swab, bronchial secretions, urine, catheter tip, suction tip, central venous (CVP) tip, Temporary Pace Maker (TPM) tip and valvular vegetation. These specimens were collected from indoor & outdoor patients and cultured in microbiology laboratory. Culture media used to isolate CoNS included Blood Agar & MacConkey Agar. The organisms were identified by standard microbiological methods. Antibiotic susceptibility was performed by modified disc diffusion & Vitek 2 methods and confirmed by MBD according to CLSI Guidelines. Disc concentrations of 30 µg was used to identify LZR by disc diffusion method and was confirmed in isolates with MIC \geq 8 µg by MBD [4].

Results

A total of 104 specimens were found positive for CoNS.

- Coronary Artery Bypass Graft
- Acute Respiratory Distress Syndrome

Out of four positive LZRC isolated specimens including blood, pus, bronchial secretions and urine, 3 were from males and one sample was from female.

Discussion

The Linezolid resistant Staphylococcus Aureus was first reported in US in 2001 in a patient who had received Linezolid treatment for dialysis associated peritonitis. Since then, only a few cases of LZRC have been reported in North and South America, Europe and Asia [5].

Multidrug resistance has become a serious threat especially in hospital settings. Emergence of resistance in MRSA to a growing number of antibiotics has become an alarming situation. For such infections, Linezolid is a safer alternate to Vancomycin & Glycopeptides especially in patients with renal impairment.

All CoNS isolates except four isolated in our study were Linezolid sensitive (Table No. 1). All four patients were significantly ill (Table No. 2). The first LZRC was identified as *S. hemolyticus* that was isolated in a 55-year-old. She was hypertensive, diabetic and had presented with

Table 1: Linezolid Susceptibility in Cons (N=104).

Specimen	Total	Sensitive	Resistant
Blood	63	62	01
Urine	02	01	01
Pericardial fluid	03	03	0
Bronchial secretions	01	0	01
Wound swab	03	03	0
Pus swab	22	21	01
Catheter tips	03	03	0
Suction tips	01	01	0
ETT tips	01	01	0
Tip Swab	02	02	0
Valvular Vegetation	01	01	0
TPM tip	02	02	0

Carotid Sinus Syndrome and shortness of breath. Patient had undergone surgery and invasive procedures and has prior exposure to antibiotics. She was transferred to ITC in a stable condition after CABG. She got infected leg wound after discharge from hospital. Pus taken from infected site showed LZD resistant *S. hemolyticus* that was sensitive to Erythromycin and Tetracycline. Second LZRC was isolated in a male patient who was in his 50's. He had Chronic Kidney Disease (CKD), had undergone CABG and was on ventilator. His bronchial secretions yielded LZRC and MRSA, both of which were resistant to Linezolid. Patient expired because of cardiac arrest. Third LZRC was isolated in a diabetic patient who was also in his late 50's and was in septic shock due to gangrene left foot and had presented with acute anterior wall myocardial Infarction. Patient was on ventilator and his blood culture yielded LZRC. The last LZRC was isolated in a patient who had urinary tract infection.

Table 2: Details of Patients With Linezolid Resistant Cons (LZRC)

Patients	Ward	Hospital procedures	Organism isolated
1	ITC	CABG *	<i>S. hemolyticus</i>
2	ITC	CABG and tracheostomy	<i>S. epidermidis</i> and <i>MRSA</i>
3	Emergency	ARDS, ventilatory Support	<i>S. hemolyticus</i>
4	Medical ward	catherization	<i>S. saprophyticus</i>

All the LZRC isolates were sensitive to Vancomycin except the one isolated from urine specimen (Table No. 3). Similar findings has been observed in another study by Bongiorno D et al [6]. All four LZRC isolates in our study were multi drug resistant. Two isolate were also susceptible to Rifampicin and Gentamicin. The urinary isolate was also susceptible to Nitrofurantoin.

Table 3: Susceptibility Pattern of Cons

No	CoNS isolates from	AMP	AMC	CN	CIP	F	SXT	E	LZD	VAN	FOS	FOX	RD
1	Blood	R	R	R	R	-	R	R	R	S	-	R	R
2	Pus	R	R	S	R	-	R	R	R	S	-	R	R
3	Bronchial secretions	R	R	S	R	-	S	S	R	S	-	R	S
4	Urine	R	R	R	R	S	R	R	R	R	S	R	S

In USA, the reported Linezolid resistance is less than 2%. It has been tracked since 2004 through a program named LEADER, which was conducted in 60 medical institutions throughout the country [7]. Resistance has remained stable and enormously low. A similar, worldwide program the "Zyvox Annual Appraisal of Potency and Spectrum Study", or ZAAPS has been conducted since 2002 [8]. Resistance to Linezolid in 23 countries was less than 0.2%. Resistance was only found in Brazil, China, Ireland, and Italy among CoNS (0.28% of samples resistant). In United Kingdom and Ireland, no resistance was found in Staphylococci collected from bacteremia cases between 2001 and 2006. Yet Linezolid continues to be an important antimicrobial agent with near-complete activity (0.05% resistance). In Spain, 2.8% were isolated between 2005 to 2009. The first cases of LZR Methicillin-Resistant *S. hemolyticus* was isolated from a Leukemic Patient in Pakistan [9-10]. Another study was carried out in Madinah Teaching Hospital, University of Faisalabad, Pakistan during March June 2017. This study showed high resistance 29.2% to LZRC and 48.1% for MRSA by the disc diffusion test. The results of E test in this study are questionable due to very high frequency. In India, the incidence of LZRC has been reported to be 2% [11-12].

The frequency of LZRC (3.84%) found in our study is lower than previously reported in Pakistan but higher than other studies worldwide i.e., in USA (less than 2%), Brazil, Ireland, China, Italy (0.28%) and Spain (2.8%).

The higher frequency of LZRC reported in our institution is possibly due to irrational use of Linezolid for Staphylococcal infections as the patients are often treated with Linezolid for extensive period of time. Prolonged stay in hospital nosocomial infections can also contribute to Linezolid resistance. Conversely, Linezolid resistance is far less in other countries due to rational and judicious use of antibiotics. Genetic mutation analysis is also being done to identify the root cause of resistance but due to limitations it could not be figured out in our study.

It is obvious that the preservation of Linezolid antibiotic susceptibility is crucial to combat life threatening infections caused by Gram positive organisms like MRSA and CoNS. It is therefore important to monitor the antimicrobial sensitivity of isolates to ensure infection control and to stop injudicious use of this therapeutic agent. Moreover, there is need to find newer antibiotics to treat infections caused by such resistant organisms.

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