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PRESCRIPTION PATTERN OF CLINICAL USE AND SAFETY PROFILE OF LINEZOLID IN TERTIARY CARE TEACHING INSTITUTE : AN OBSERVATIONAL STUDY

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ABSTRACT **Background:** Linezolid acts by inhibiting protein synthesis and the mode of action does not lead to cross resistance with other antimicrobials. With increasing infection due to VRE, linezolid is the best option available. Reports of resistance to linezolid along with the characterization of mechanism of resistance have been documented in Enterococcus sp., Staphylococcus sp. and MRS. Studies from India, has shaown all Staphylococcus sp. and Enterococcus sp. remain linezolid sensitive except for occasional case reports. The 85% of reported adverse events was mild-to-moderate in intensity. Linezolid over usage and irrational clinical use may leads to drug resistance. Generally linezolid is kept as a reserve drug for multidrug resistant infections. **Aim & Objectives:** The objective of this study is to find out the prescription pattern of Linezolid for a period of six months in various departments and the second objective is to observe the sequencial adverse drug reactions of linezolid of Malabar medical college and research center. **Methodology:** In this retrospective study, the pattern of linezolid use during 6 month period in patients admitted to different wards of Malabar medical college and research center was analysed. (Ethical Code:). A standard protocol on linezolid indications, dosing and monitoring was designed based on Sanford guide for antimicrobial therapy **Results:** Overall, the patient population consisted of different groups with varying ages, weights and renal functionsA significant proportion of patients had some degree of kidney impairment, and many were treated as inpatients, including treatment in the ICU. The most common infections treated with linezolid were skin and soft tissue infections (SSTI), followed by primary bacteremia, secondary bacteremia, and bone and joint infections. **Conclusion:** In conclusion, linezolid remains an important therapeutic option for infections caused by resistant pathogens, but its use should be guided by careful consideration of the patient's clinical condition, the specific infection, and the susceptibility of the causative microorganism.

KEYWORDS : Linezolid, prescription pattern, Antimicrobial resistance.

INTRODUCTION

Linezolid is a synthetic antibiotic belonging to the oxazolidinone class, effective against aerobic Gram-positive bacteria, certain Gram-negative bacteria, and anaerobic bacteria[8]. It is primarily prescribed for multidrug-resistant Gram-positive infections, including bacteremia, endocarditis, catheter-related infections, community-acquired and nosocomial pneumonia, and complicated and uncomplicated skin and soft tissue infections, such as diabetic foot infections and surgical wound infections[8]. It is also used for infections caused by methicillin- and vancomycin-resistant Staphylococci and Enterococci, as well as penicillin- and macrolide-resistant Streptococci and Pneumococci[8].

Linezolid inhibits protein synthesis via a mechanism that does not cause cross-resistance with other antimicrobials[3][8]. Even in treating methicillin-resistant Staphylococcus aureus (MRSA), where vancomycin is typically the preferred treatment, linezolid is a suitable option for antibiotic de-escalation because it can be administered orally in some patients, which facilitates early hospital discharge[8]. This benefits both the patient and the hospital by lowering treatment costs through reduced hospital stays and decreasing the patient's exposure to healthcare settings, thereby lowering the risk of healthcare-associated infections[8].

Increased vancomycin use has led to the emergence of vancomycin-resistant Enterococci (VRE), vancomycin-resistant Staphylococcus aureus (VRSA), and vancomycin-intermediate resistant Staphylococcus aureus (VISA)[8]. Linezolid is the best available treatment option for increasing VRE infections[8]. While reports have documented resistance to linezolid along with the characterization of its resistance mechanism in Enterococcus sp., Staphylococcus sp., and MRSA, most Staphylococcus sp. and Enterococcus sp. in India remain sensitive to linezolid, except for occasional case reports[8].

The majority (85%) of reported adverse events are mild to moderate, with the most common being diarrhea, nausea, and headache[8]. Other rare adverse drug reactions (ADRs) include anemia[8], thrombocytopenia[7][8], and black hairy tongue[8], especially with prolonged linezolid treatment.

Overuse and irrational clinical use of linezolid may lead to drug resistance, as it is generally reserved for multidrug-resistant infections[5][8]. Studies are planned to assess the frequency of linezolid utilization, patterns of clinical use (rational and irrational), and the safety profile (inter-individual variability) of linezolid[8].

MATERIALS AND METHODS

In this retrospective study, we analyzed the usage patterns of linezolid over a six-month period among patients admitted to various wards at Malabar Medical College and Research Center. A standard protocol for linezolid indications, dosing, and monitoring was developed based on the Sanford Guide for Antimicrobial Therapy. Patients who received at least three doses of linezolid were evaluated by our research team. We extracted a list of these patients from drug sensitivity reports and hospital medical records, which included demographic information (case number, sex, age, weight), reasons for hospitalization, diagnoses, laboratory and culture results, antibiograms, complete blood counts, concomitant diseases and medications, duration of hospitalization, and details regarding linezolid use (indications, total prescribed dose and duration, route of administration, potential drug interactions, and adverse reactions). Additionally, we recorded the specialty of the prescribing physician and whether they consulted an infectious disease specialist if they belonged to a different specialty. Data collected from the prepared forms were analyzed using SPSS version 26. Results are presented as mean ± standard deviation for continuous quantitative variables and as counts (percentages) for nominal qualitative variables. Subject characteristics were summarized using descriptive statistical methods, including dispersion and frequency distribution in appropriate tables and figures. The overall frequency of correct consumption patterns (based on appropriate indications, duration of use, and prescribed doses) was reported.

Inclusion Criteria included all patients over 18 years of both genders admitted to various clinical departments who were started on linezolid. Children and pregnant individuals are excluded from this study

RESULTS

A total of 232 patients were included in the study out of which 248 patients recived the treatment courses.The majority of patients were male (37.1%), with a median age of 65 years.

The average weight was 76 kg with the body mass index (BMI) of 25 kg/m².The median glomerular filtration rate (GFR) was 57 mL/min, indicating moderate kidney function.

107 patients had a GFR between 30 and 60 mL/min, suggesting mild-to-moderate kidney impairment. Only 10 patients had a GFR below 30 mL/min, indicating severe kidney disease.

163 patients (66%) were inpatients, while 85 patients (34%) were outpatients.

Among inpatients, 92 patients (56.4%) were admitted to the Intensive Care Unit (ICU).

Overall, the patient population consisted of different groups with varying ages, weights and renal functions. A significant proportion of patients had some degree of kidney impairment, and many were treated as inpatients, including treatment in the ICU. (Table 1)

Table 1 Showing Patients' Baseline Characteristics

1	A	B
2	Patients Characteristics	N (%) Or Median (Range)
3	Patients	232
4	Treatment	248
5	Male	93 (37.1)
6	Age (years)	67(21-95)
7	Weight(kg)	76(34-178)
8	Body mass index (kg/m2)	25(15-48)
9	Glomerular filtration rate 1	57(10-196)
10	GFR>- 60 ml/min	102
11	30 mL/Min < GFR < 60ml/Min	107
12	GFR <30 Ml/Min	10
13	Inpatients/Outpatients	163 (66)85 (34)
14	ICU 2 Patients3	92 (56.4)

The most common infections treated with linezolid were skin and soft tissue infections (SSTI), followed by primary bacteremia, secondary bacteremia, and bone and joint infections.

Less common infections included pneumonia, gastrointestinal infections, medical device infections, urinary tract infections, and various other conditions.

The most frequently isolated microorganisms were Enterococcus faecium (E. faecium), methicillin-resistant Staphylococcus epidermidis (MRSE), and methicillin-resistant Staphylococcus aureus (MRSA).Other microorganisms included vancomycin-resistant Enterococcus (VRE), methicillin-sensitive Staphylococcus aureus (MSSA), methicillin-sensitive Staphylococcus epidermidis (MSSE), and other diverse linezolid-susceptible species.The median treatment duration varied across different infection types.

SSTI had the longest median duration (19.5 days), followed by bone and joint infections (3 days).

Pneumonia and secondary bacteremia had relatively shorter median durations (7 and 7 days, respectively). (Table 2)

Table 2- Infections Treated, Microorganisms, and Treatment Duration

1	Infection treated	Number %	Microorganisms	Number =262 (%)
2	Ssti2	32(12.3)	E. FAECIUM	66 (25.2)
3	Pneumonia	17 (6.5)	MRSE2	61 (23.3)
4	Primary bacteria	30(11.5)	MRSA2	45(17.2)
5	Secondary bacteria	41(15.7)	VRE2	24(9.2)
6	Bone and joint infection	33 (12.6)	MSSA2	12(4.6)
7	Gastrointestinal infection	24 (9.2)	E. FAECALIS	11(4.2)
8	Medical device infection	15(5.7)	MSSE 2	2(0.8)
9	Urinary tract infection	11(4.2)	OTHERS 4	36(13.8)
10	Mediastinitis	9(3.4)		
11	Endocarditis	4(1.5)		
12	CNS2 Infections	3(1.1)		
13	MRSA decolon	7(2.7)		
14	Others	18(6.9)		

Overall, the data indicate that linezolid was used to treat a wide range of infections caused by various microorganisms. The treatment duration varied depending on the type of infection.

DISCUSSION

The study involved a diverse cohort of patients with varying demographic profiles. A significant portion of these individuals displayed some level of kidney dysfunction, ranging from mild to severe. The research by Hashemian SMR underscores the necessity of considering renal function when prescribing linezolid, as it may accumulate in patients with impaired renal function. [1,2]

A large majority of patients (66%) were treated as inpatients, reflecting the severity of their infections or underlying health issues, which aligns with findings from the Howard RS study. Among those admitted, a notable percentage (56.4%) required intensive care, further highlighting the serious nature of the infections being treated with linezolid, consistent with Howard RS's observations.[3]

These results stress the importance of thoroughly assessing patient characteristics, particularly renal function, to ensure the appropriate administration of linezolid in clinical practice. Additional research is needed to explore optimal dosing strategies for patients with different levels of renal function and to evaluate the long-term effects of linezolid treatment in this population.

These results highlight the necessity of thoroughly considering patient characteristics, particularly renal function, when using linezolid in clinical settings. Additional research is needed to explore optimal dosing strategies for individuals with different levels of renal function and to assess the long-term effects of linezolid therapy in this demographic, as indicated in the studies by Anand N and Camins BC. [6, 7].

The rise of antimicrobial resistance is an increasing concern, and linezolid is no exception. Its careful use is essential to maintain its effectiveness against serious infections caused by multidrug-resistant bacteria.

Linezolid is primarily utilized for treating skin and soft tissue infections (SSTI), followed by bacteremias and infections of the bones and joints. This usage aligns with the established indications for linezolid, as supported by studies conducted by Smith G, Howard, and Dasgupta. [1, 2, 3].

The most frequently isolated microorganisms were Enterococcus faecium, MRSE, and MRSA. This underscores the significance of linezolid as an effective treatment option for infections caused by these multidrug-resistant pathogens. [5, 6, 7].

The duration of treatment varied considerably depending on the type of infection. Skin and soft tissue infections (SSTI) necessitated the longest treatment periods, indicative of their severity and complexity. Conversely, pneumonia and secondary bacteremia were typically linked to shorter treatment durations. [8, 9, 10].

These results highlight the adaptability of linezolid in addressing a broad spectrum of infections caused by various microorganisms. Nevertheless, it is essential to take into account the specific type of infection and the susceptibility of the responsible organism when establishing the appropriate treatment duration. [11, 12, 13].

CONCLUSION

In conclusion, linezolid remains an important therapeutic option for infections caused by resistant pathogens, but its use should be guided by careful consideration of the patient's clinical condition, the specific infection, and the susceptibility of the causative microorganism.

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