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Case Study

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HYPERSENTIVITY DUE TO LINEZOLID IN ELDERLY PATIENTS: A CASE REPORT

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INTRODUCTION

Linezolid is recognized as the inaugural member within the oxazolidinone antibiotics category. Initially developed in 1978 for its efficacy in managing plant diseases, oxazolidinones demonstrated enhanced antibacterial properties compared to their precursor compounds six years later. These improved characteristics marked the oxazolidinone compounds as the primary lead entities in the oxazolidinone family. Linezolid was introduced in 1996 and has since been acknowledged as a leading compound. The US Food and Drug Administration granted approval for Linezolid in 2000. Over the past four decades, oxazolidinones have been recognized as a genuinely novel class of antibiotics now employed in clinical settings.[1]

Linezolid works by inhibiting bacterial protein synthesis by interfering with the translation. Linezolid binds to the site on the bacterial 23S ribosomal RNA of the 50S subunit, which prevents the formation of a functional 70S initiation complex. This leads to inhibition of protein production and prevents bacterial multiplication.

Linezolid is also a reversible, non-selective monoamine oxidase inhibitor. Blocking monoamine oxidase (MAO) results in elevated levels of neurotransmitters such as epinephrine, norepinephrine, dopamine, and serotonin within the central and sympathetic nervous systems. This inhibition can also lead to decreased sensitivity of alpha- and beta-adrenergic receptors, as well as serotonin receptors. In the gastrointestinal tract and liver, MAO inhibition can lead to the absorption of substantial quantities of tyramine from the diet, posing a risk of life-threatening hypertension.[2]

The efficacy of linezolid in the treatment of multidrug-resistant Gram-positive bacterial infections has been demonstrated in various Phase II or III studies focused on methicillin-resistant staphylococcus or vancomycin-resistant enterococcus infections. Linezolid effectively treats bacteremia caused by vancomycin-resistant E. faecalis or faecium.[3]

Although linezolid has been proposed for treating Gram-positive community-acquired pneumonia, it may not be the favored antibiotic for this indication. Its efficacy, as demonstrated in numerous studies, does not consistently establish superiority over third generation cephalosporins like ceftriaxone followed by cefpodoxime. Moreover, success has been observed with linezolid in the treatment of community-acquired lung disease in children caused by pathogens such as S. pneumoniae, group A streptococci, or methicillin-resistant S. aureus.[4]

In a double-blind, randomized study conducted across multiple centers, the efficacy of linezolid was compared to that of oxacillin. Patients were given either intravenous linezolid at a dose of 600 mg twice daily or intravenous oxacillin at a dose of 2 g every six hours. Additionally, both treatment groups were offered an oral switch. Whether administered intentionally for treatment or in patients eligible for evaluation, linezolid demonstrated clinical and microbiological efficacy equivalent to that of oxacillin. The tolerance profiles of the two medications were also found to be similar.[5]

In case reports involving spondylodiscitis arising from methicillin-resistant S. aureus and vancomycin-resistant enterococcus bacteremia, a six-week course of linezolid monotherapy was employed in conjunction with surgical intervention.[6]

In a comparison study involving pediatric skin infections caused by S. aureus or S. pyogenes, linezolid and cefadroxil were found to be equivalent in both efficacy and tolerability.[7]

In cases of skin infections caused by both aerobic and anaerobic bacteria, including Fusobacterium, Prevotella, and Peptostreptococcus, particularly those resulting from

animal bites, linezolid, demonstrating efficacy similar to macrolides, might be considered following bacteriological confirmation. Linezolid also exhibits activity against Pasteurella.[8]

Allergic/hypersensitivity reactions to linezolid are infrequent. Some of the instances have been documented of immediate hypersensitivity reactions to linezolid, presenting symptoms such as urticaria, skin flushing, and angioedema. In a case study, rash and pruritis were reported in 1.7% of 828 patients and also two cases of anaphylactoid-type of reactions in the patients who underwent linezolid treatment.[9]

Yang & Xu[10], also reported a case of patient who developed urticaria and angioedema post 12hrs linezolid.

According to Bishop et al[11], one out of 44 patients developed a severe skin rash requiring discontinuation of linezolid treatment.

CASE STUDY

A 75yrs old male patient K/C/O Diabetes, hypertension and thryoidism for more than 20years was presented to outpatient department with C/O injury on right elbow and left knee, he had a H/O fall from a table while working in his home, he took home treatment initially such as cleaning the wound with antiseptic liquid and covering it with a cotton, later on he went to his diabetologist where was prescribed with Tab Lizofine 600 (Linezolid) twice daily for 5days, Tab Chymoral forte (Trypsin-Chymotrypsin) thrice daily for 5days, Tab P-650 (Paracetamol) thrice daily, Tab Allegra 120 (Fexofenadine Hydrochloride) once daily for 5days, T-bact ointment, Tab Augmentin-CV 625 (Amoxicillin clavulanate) twice daily for 5days.

Patient was not informed about any specific diet as he was already following a diabetic diet, patient started taking the treatment, and he was also seeing the betterment of his condition, his wounds were also healing well with the regular use of the medications and the ointments given, from the 3rd day his treatment he started experiencing severe itching on his right forearm, and it gradually increased into stiffness and redness of his right forearm, itchiness was so severe that upon itching patient was observing peeling of the skin, on observing this reaction on his forearm, the patient again went back to his diabetologist, after examining his condition he was advised to stop his previous prescription and was advised with a new prescription which included Tab Augmentin-CV 625 (Amoxicillin clavulanate) twice daily for 5days, Tab Allegra 120 (Fexofenadine Hydrochloride) once daily for 5days, Tab Chymoral forte (Trypsin-Chymotrypsin) thrice daily for 5days, Tab Medrol 4mg (Methylprednisolone) twice daily for 5days, Tab Atarax 10mg (Hydroxyzine hydrochloride) twice daily for 5days and Calamine lotion for local application.

The wounds were already healed to good condition but not completely healed, and after the using the updated prescription good changes were seen on the affected site, stiffness was decreased, redness and itching were gradually decreasing, and the patient was advised no to itch on his hand, as the skin was getting peeled off which may result in another wound, he was advised to apply the calamine lotion on the affected part which gave him additional comfort.

DISCUSSION

linezolid, an oxazolidinone antibiotic used for gram positive infections, methicillin-resistant staphylococcus aureus (MRSA), bacterial pneumonia, bacteremia, bone and joint infections, skin and soft tissue infections. Linezolid, being a promising antibiotic for various conditions as discussed above, may also lead to some of the severe hypersensitivity reactions mentioned in the case presented above.

Kim FS et al[12], reported a case of 64-year-old male was admitted to the hospital after developing a petechial rash following linezolid treatment. The patient exhibited non-blanching petechiae and purpura across his entire body, with no signs of active bleeding.Changes in the condition of the patient were noted upon discontinuation of linezolid.

According to a study conducted by Cattaneo D et al[13], about the results of 5 years of therapeutic drug monitoring of linezolid focused on elderly patients, revealed that the administering the standard dose of 600 mg of linezolid twice daily to elderly patients may elevate the likelihood of excessive exposure to the treatment, consequently raising their susceptibility to drug-related hematological toxicity.

CONCLUSION

linezolid, an oxazolidinone antibiotic used for gram positive infections, methicillin-resistant staphylococcus aureus (MRSA), bacterial pneumonia, bacteremia, bone and joint infections, skin and soft tissue infections. Hypersensitivity to linezolid is a rare reaction but is more seen in the geriatric/elderly patients. As discussed in the above case linezolid even in the standard dose may be leading to harmful hypersensitivity reactions in the adults. Alternate option as drug of choice for the indication and if prescribed when no other option available, the patient must be explained about the outcome and allergic reactions if any.

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