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Research Article

Analysis of Hematological Picture in Patients on Linezolid: A Prospective, Observational Study

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Abstract

OBJECTIVE: To evaluate the impact of Linezolid therapy on haematological parameters, including haemoglobin levels, total leukocyte count, and platelet count, and identify patterns and predictors of haematological toxicity.

METHODS: This prospective, observational study was conducted at the Department of Pharmacology after obtaining institutional ethics committee approval. Thirty-six patients over 18 years who had received Linezolid therapy for at least five days were enrolled. Patients with pre-existing haematological disorders, recent chemotherapy, viral diseases, pregnancy, or hypersensitivity to Linezolid were excluded. Baseline haematological parameters were recorded and compared to values after 5–7 days of therapy. Haematological toxicity was defined as thrombocytopenia (≥25% reduction in platelet count or ≤125×10⁹/L), anaemia (>25% reduction in haemoglobin), and leukopenia (<4×10⁹/L). Data were analysed using paired t-tests and the Wilcoxon Signed Ranks Test, with $p < 0.05$ considered statistically significant.

RESULTS: The mean age of participants was 49.39 ± 13.43 years, with 63.9% males. Linezolid therapy resulted in significant reductions in haemoglobin (12.71 ± 1.64 g/dL to 11.30 ± 1.74 g/dL; $p = 0.0034$), total leukocyte count (15.15 ± 3.14×10⁹/L to 10.96 ± 3.48×10⁹/L; $p = 0.0011$), and platelet count (361.50 ± 75.63×10⁹/L to 306.53 ± 76.22×10⁹/L; $p = 0.0021$). Thrombocytopenia occurred in 33.33% of patients, anaemia in 16.67%, and leukopenia in none. Longer therapy duration was associated with increased toxicity risk.

CONCLUSION: Linezolid therapy significantly impacts haematological parameters, with thrombocytopenia being the most frequent adverse effect. Regular monitoring and individualised treatment strategies are essential for minimising haematological toxicity and optimising Linezolid's clinical use.

KEYWORDS: Linezolid, Haematological toxicity, Thrombocytopenia

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1. INTRODUCTION

Linezolid, a synthetic antibiotic, is the first member of the oxazolidinone class and has been a significant advancement in the treatment of severe infections caused by Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecium (VRE).[1,2] It achieves its antibacterial action by binding to ribosomal RNA on the 30S and 50S subunits, inhibiting bacterial protein synthesis.[3] Linezolid's unique mechanism of action and its efficacy against drug-resistant pathogens have made it a vital tool in antimicrobial therapy, especially in settings with limited treatment options.[4,5]

Despite its clinical benefits, Linezolid use has been associated with adverse haematological effects, such as anaemia, leukopenia, and thrombocytopenia.[6,7] Among these, thrombocytopenia is the most commonly reported, with an incidence of 0.3% to 10% during Phase 3 clinical trials.[8] These cytopenias are often reversible upon discontinuation of the drug, yet they can complicate treatment courses, particularly in patients with pre-existing haematological vulnerabilities or prolonged Linezolid therapy.[9,10] Understanding these adverse effects mechanisms and clinical manifestations is critical for optimising its use while minimising patient harm.

Emerging research suggests that Linezolid-induced haematological toxicity primarily arises from interfering with mitochondrial protein synthesis. The structural similarity between bacterial and mitochondrial ribosomes allows Linezolid to bind to mitochondrial ribosomes, leading to mitochondrial dysfunction in hematopoietic cells. This mechanism underpins the drug's potential to induce pancytopenia, particularly in patients undergoing extended treatment durations. [11,12] Additionally, evidence indicates that Linezolid may reduce peripheral blood cell survival rather than suppress bone marrow production, further contributing to its haematological impact.[13] Given the growing use of Linezolid in managing resistant infections and its associated haematological risks, there is a pressing need to evaluate its effects on haematological parameters systematically. This study aims to analyse key haematological indices in patients receiving Linezolid therapy, including haemoglobin levels, total leukocyte count, and platelet count. By providing insights into the patterns and predictors of haematological toxicity, the findings could inform clinical strategies to enhance the safety and efficacy of Linezolid treatment.

2. MATERIALS AND METHODS

This prospective, observational study was conducted in the Department of Pharmacology after obtaining clearance from the Institutional Ethics Committee [IEC/HIMS/RR600/04-10-2024]. Patients aged over 18 years of either sex who had been on Linezolid therapy for at least five days were recruited after providing written informed consent. Participants with pre-existing haematological disorders, a history of chemotherapy, viral diseases, pregnancy or lactation, steroid use, or hypersensitivity to Linezolid were excluded to eliminate confounding factors.

The study's sample size was calculated based on previous literature using the formula n=4pq/d2, yielding a derived sample size of 36. Eligible patients were enrolled, and their demographic information and baseline haematological parameters, including haemoglobin levels, total leukocyte count, and platelet count, were recorded. These parameters were reassessed after 5–7 days of Linezolid therapy to detect significant haematological changes.

Haematological toxicity was defined using specific criteria: thrombocytopenia as a reduction of ≥25% in platelet count from baseline or a count of ≤125×109/L; anaemia as a decrease of >25% in haemoglobin levels from baseline; and leukopenia as a total leukocyte count of <4×109/L. These thresholds provided a structured framework to systematically evaluate the haematological impact of Linezolid therapy.

Data collected during the study were entered into Microsoft Excel and analysed using SPSS software (version 20.0). Quantitative data were expressed as means and standard deviations (Mean ± SD), and categorical variables were analysed using frequency distributions and percentages. Comparative analysis of haematological parameters before and after Linezolid therapy was performed using the Wilcoxon Signed Ranks Test and paired t-tests. A p-value <0.05 was considered statistically significant, ensuring a robust assessment of the observed haematological changes.

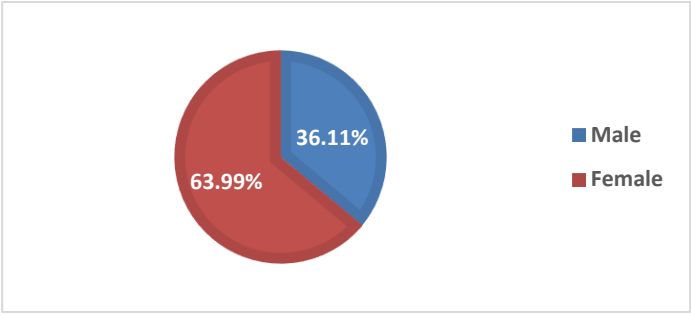
3. RESULTS

A total of 36 patients were included in the study, with a mean age of 49.39 ± 13.43 years, ranging from 25 to 78 years. Most participants were male (63.9%), while females comprised 36.1% of the study population. (Figure 1) Baseline demographic characteristics and haematological parameters were collected and compared to follow-up values after 5–7 days of Linezolid therapy. (Table 1).

Table 1: Descriptive Statistics of Study Population

Variable (n=36)	Minimum	Maximum	Mean	Std. Deviation
Age (years)	25	78	49.39	13.43
Hemoglobin (g/dL)	10.2	14.5	12.71	1.64
Total Leukocyte Count (×10⁹/L)	8.2	20.7	15.15	3.14
Platelet Count (×10⁹/L)	240	500	361.50	75.63

Figure 1: Gender Distribution



The analysis revealed a significant reduction in haemoglobin levels, total leukocyte count, and platelet count during the follow-up period. The mean haemoglobin level decreased from 12.71 ± 1.64 g/dL at baseline to 11.30 ± 1.74 g/dL, reflecting an 11% reduction (p = 0.0034). Similarly, the mean total leukocyte count dropped from 15.15 ± 3.14 × 10⁹/L to 10.96 ± 3.48 × 10⁹/L, a 13% reduction (p = 0.0011). Platelet counts demonstrated the most pronounced decrease, falling from 361.50 ± 75.63 × 10⁹/L to 306.53 ± 76.22 × 10⁹/L, corresponding to a 27% reduction (p = 0.0021). (Table 2).

Table 2: Haematological Parameters at Baseline and Follow-Up

Parameter	Baseline	Follow-up	% Reduction	p-value
Haemoglobin (g/dL)	12.71 ± 1.64	11.30 ± 1.74	11%	0.0034
Total Leukocyte Count (×10⁹/L)	15.15 ± 3.14	10.96 ± 3.48	13%	0.0011
Platelet count (×10⁹/L)	361.50 ± 75.63	306.53 ± 76.22	27%	0.0021

Among the haematological abnormalities, thrombocytopenia was the most frequently observed, with 33.33% of patients experiencing a reduction of ≥25% in platelet counts or levels ≤125 × 10⁹/L. Anaemia, defined as a >25% reduction in haemoglobin, was observed in 16.67% of patients, while leukopenia (total leukocyte count <4 × 10⁹/L) occurred in none. These findings highlight the diverse spectrum of haematological toxicity associated with Linezolid therapy. (Table 3).

Table 3: Frequency of Haematological Abnormalities

Abnormality	Frequency (n)	Percentage (%)
Thrombocytopenia	12	33.33%
Anemia	6	16.67%
Leukopenia	0	0%

The analysis of additional variables, such as treatment duration and concomitant antibiotic use, showed a correlation between longer Linezolid therapy and increased risk of haematological toxicity. These results underscore the importance of monitoring haematological parameters in patients receiving Linezolid, particularly those requiring prolonged therapy or those with baseline vulnerabilities.

4. DISCUSSION

The present study, focusing on the haematological effects of Linezolid, observed a significant reduction in haematological parameters such as haemoglobin levels, total leukocyte count, and platelet count during therapy, with thrombocytopenia being the most frequently recorded adverse effect (33.33%). These findings align with various previous studies, though they also reveal unique insights compared to the broader body of literature. The thrombocytopenia incidence in the present study (33.33%) corresponds closely to findings by Moraza L *et al.* [14], who reported a 42% incidence of haematological toxicity among Linezolid-treated patients. They noted that platelet reduction was the most frequent adverse effect, consistent with the 27% reduction observed in the present cohort. Similarly, Gerson SL *et al.* [15] highlighted reversible myelosuppression as a key side effect of Linezolid, particularly after two weeks of therapy, which supports the present study's findings on therapy duration as a critical factor for adverse outcomes.

Lima LS *et al.* [16] further demonstrated that renal impairment significantly increases the risk of thrombocytopenia in Linezolid-treated patients. This result parallels the present study's observation of higher vulnerability in patients with baseline haematological abnormalities or prolonged treatment duration. This highlights the critical importance of monitoring renal function and haematological parameters during therapy, especially in high-risk populations.

Thirot H *et al.* [17] conducted a retrospective study in Belgian hospitals and found that prolonged treatment (>10 days) and renal dysfunction were strong predictors of thrombocytopenia. These findings align with the present study, which identified therapy duration as a key determinant of haematological toxicity. Furthermore, Thirot H *et al.* [17] emphasised the high prevalence of off-label use of Linezolid and its association with adverse drug reactions, underlining the importance of adhering to the recommended treatment guidelines.

In a study by Zou F *et al.* [4] using the FDA Adverse Event Reporting System (FAERS), thrombocytopenia and anaemia were identified as the most frequent haematological adverse events associated with Linezolid. Zou F *et al.* [4] also noted the rapid onset of these toxicities, typically occurring within the first month of therapy, which is consistent with the present study's timeline of observed haematological changes within 5–7 days. The early identification of these effects emphasises the necessity for close haematological monitoring, even in the initial phases of treatment.

Cai Y *et al.* [18] evaluated haematological toxicity in a controlled setting with healthy volunteers, finding transient reductions in haemoglobin and red blood cell counts following a single dose of Linezolid. Although these effects normalised within 48 hours, the study highlights Linezolid's potential for haematological impact even in short-term use, contrasting with the cumulative effects observed in clinical patients during prolonged therapy. This underscores the multifactorial nature of Linezolid-associated haematological toxicity, influenced by patient health status, baseline conditions, and therapy duration.

While the overall findings of the present study align with the aforementioned research, it also offers unique insights. Notably, the observed frequency of anaemia (16.67%) was lower than that of Moraza L *et al.* [14] (25%). This discrepancy could be attributed to patient demographics, baseline health conditions, or study design differences. Furthermore, leukopenia was notably absent in the present cohort, diverging from findings in studies such as Gerson SL *et al.* [15] and Lima LS *et al.* [16], where white blood cell reductions were a significant concern. This divergence highlights the variability in haematological responses to Linezolid among different populations and clinical settings.

Another unique aspect of the present study was the detailed treatment duration analysis and its direct correlation with haematological toxicity. Longer therapy was associated with an increased risk of adverse events, a finding corroborated by

multiple studies but explored in greater depth here. This focus on therapy duration strengthens the argument for tailored dosing and treatment duration to mitigate toxicity risks.

The consistent finding across studies, including the present one, is the pivotal role of monitoring in minimising Linezolid-induced haematological toxicity. Early detection and intervention can prevent progression to severe conditions, such as Grade 3 thrombocytopenia, as categorised by Lima LS *et al.* [16] and Moraza L *et al.* [14] Incorporating regular haematological assessments, particularly for at-risk patients with renal impairment or pre-existing haematological abnormalities, is crucial. Including pyridoxine as a potential protective agent, as explored by Moraza L *et al.* [14] represents an area for further investigation. While its efficacy remains inconclusive, exploring adjunct therapies to counteract haematological toxicity could provide valuable avenues for improving patient outcomes.

5. CONCLUSION

Linezolid therapy is associated with significant haematological toxicities, particularly thrombocytopenia, influenced by treatment duration and patient-specific factors like renal function. Regular monitoring and personalised approaches remain critical for ensuring its safe and effective use.

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