

DRUG MONITORING IN CLINICAL PRACTICE

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INTRODUCTION

Linezolid (LNZ) is usually used in drug-resistant gram-positive infections. Is typically given at 600mg/2id, the exposure can differ significantly between patients and can result in treatment failure or toxicity, such as thrombocytopenia¹.

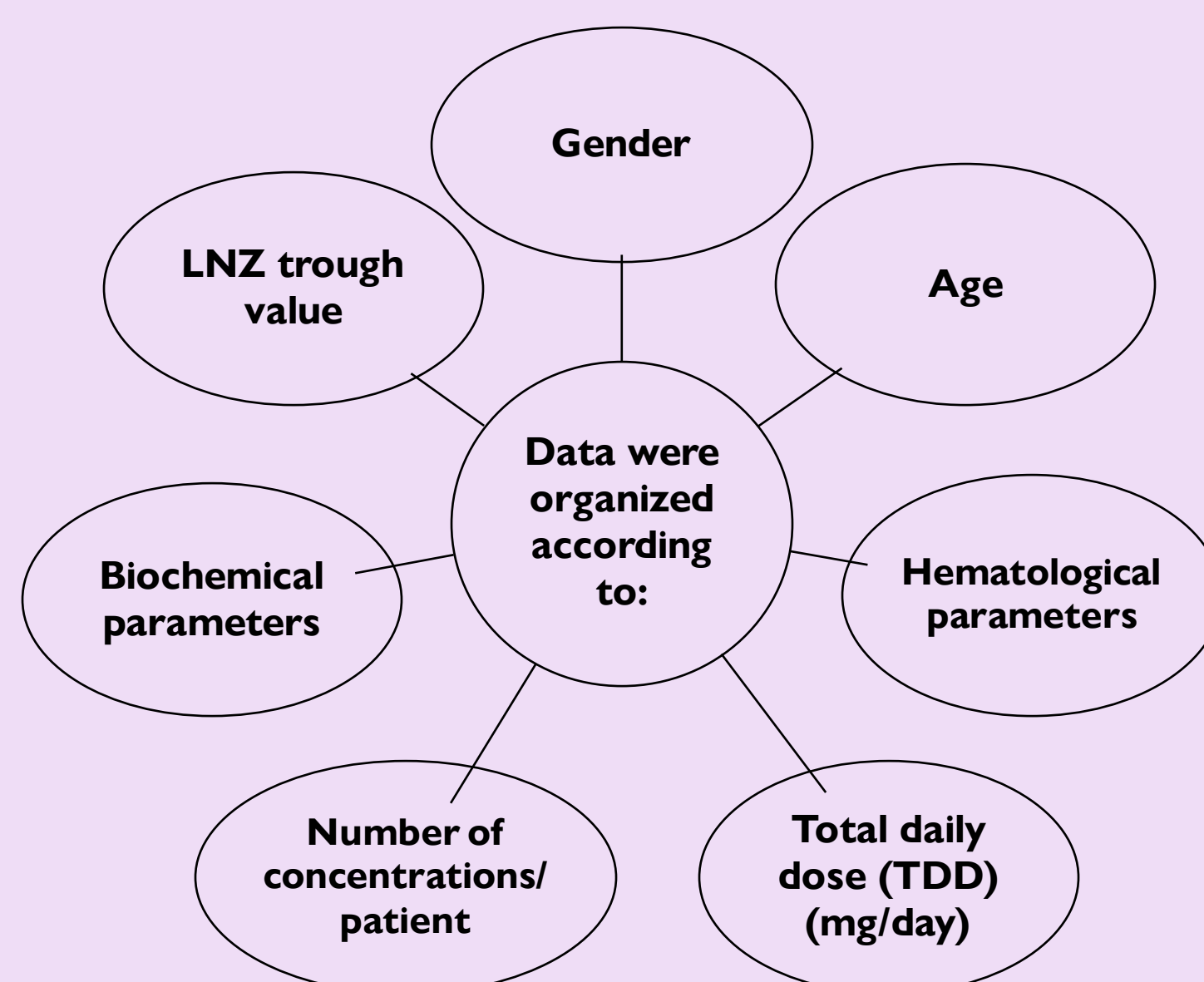
OBJECTIVE

Characterization of the hospitalized population under LNZ therapy according to the protocol of the Advanced Pharmacokinetics and Personalized Therapeutics Unit (UFAP) of the Pharmacy Department of our hospital, regarding:



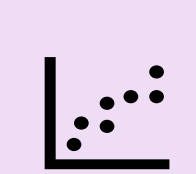
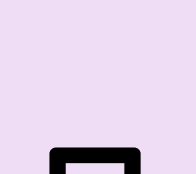
- Demographic characteristics, pharmacotherapeutics and serum levels observed;
- Evaluate the correlation between the trough concentrations obtained and the clinical parameters.

METHODS

This was an observational and retrospective study between March 2022 and August 2023. Data were collected from the patient's clinical files and from the UFAP clinical pharmacokinetic monitoring platform.



The UFAP protocol considers:

-  Sample collections are carried out in a steady state;
-  A trough is collected immediately before the administration;
-  The adjustment was based on a mono-compartmental model and linear kinetics;
-  Statistical analysis was performed using Microsoft Excel®.

RESULTS

Main outcome measures: Comparing the therapeutic regimens between the first and the last dosing, according to the therapeutic range (2-8mg/L) for the LNZ minimum concentrations.

- 152 patients (96 men and 56 women)
- 295 LNZ concentrations (± 2 per patient)
- Age: 69 ± 15 years
- Initial dose of 600mg bid.



- Infratherapeutic (<2mg/L)
- Within therapeutic range (2-8mg/L)
- Supratherapeutic (>8mg/L)

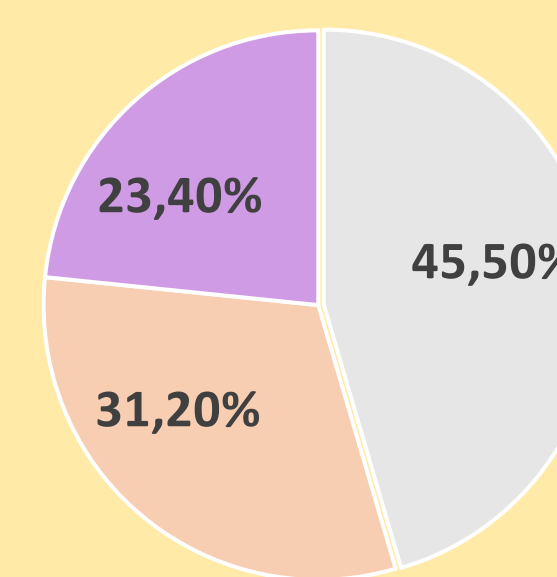


Figure 1- Distribution of the LNZ concentrations before pharmaceutical intervention

- A total of 77 patients underwent more than one measurement.
- Only around 31.20% of the concentrations were within the therapeutic range (figure 1).

After pharmaceutical intervention, 50% of patients had a change in LNZ TDD, thus increasing the percentage of concentrations within the therapeutic range to 36.4% (figure 2).

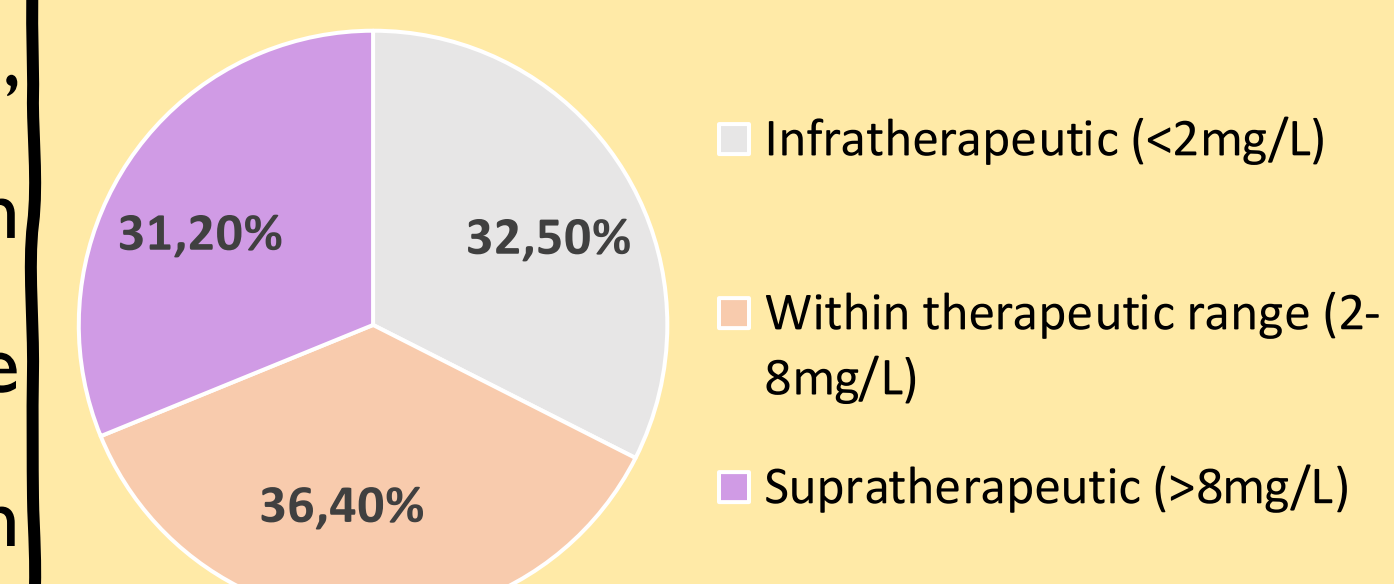


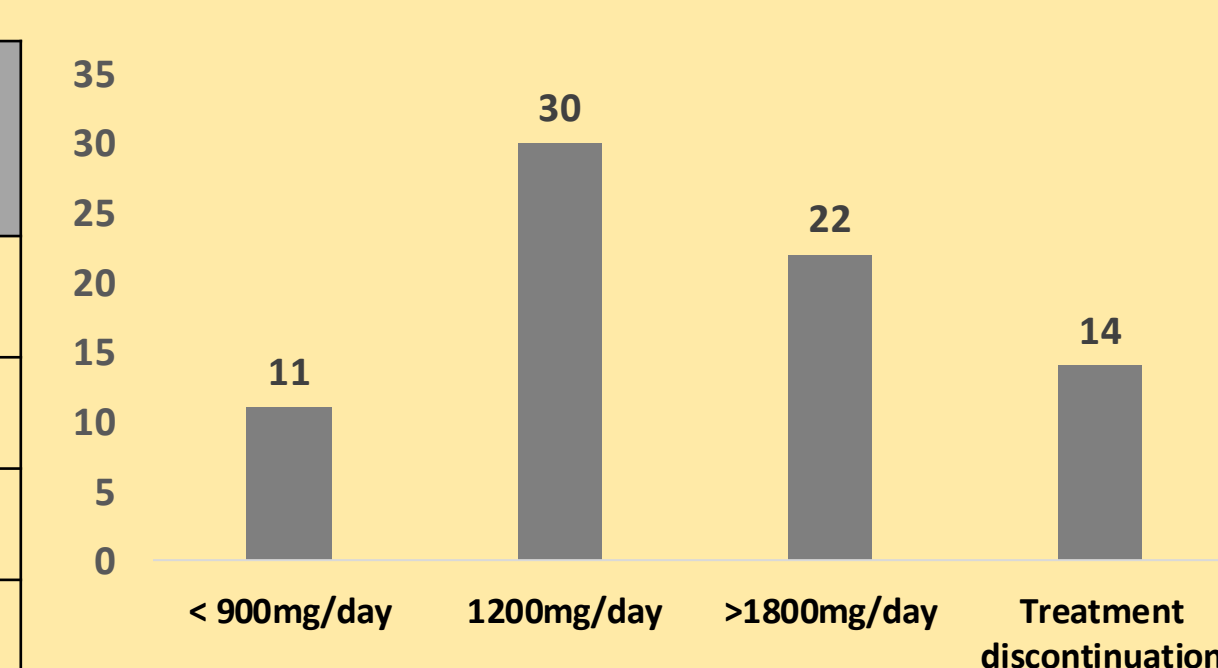
Figure 2- Distribution of the LNZ concentrations after pharmaceutical intervention

Significant correlations were identified between LNZ trough concentrations and platelets count ($r=-0.2$), glomerular filtration rate (GFR) ($r=-0.3$) and aspartate amino transferase ($r=-0.3$). With the decrease of GFR, lower mean values of platelets count were identified (table 1).

Table 1- Correlation between the GFR and platelets mean values

Glomerular filtration rate	Platelets mean values
>90mL/min	105.1 \pm 10.6x10 ⁹ /L
60-90mL/min	77.8 \pm 8.8 x10 ⁹ /L
30-59mL/min	46.1 \pm 9.3 x10 ⁹ /L
<30mL/min	19.3 \pm 6.9 x10 ⁹ /L

Table 2- TDD of linezolid in the last treatment measurement



CONCLUSION

In this study, therapeutic drug monitoring of linezolid was a useful tool to optimize antimicrobial therapy, reducing underexposure to linezolid. Patients with lower GFR are at greater risk of thrombocytopenia, underlining the importance of linezolid dosage individualization.