

A20 - How often do we need to adjust the dose of linezolid in critically ill patients to get the target?

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Introduction:

Critically ill patients present unpredictable changes in the pharmacokinetics of different drugs¹ including linezolid (LZD)², increasing the risk of toxicity due to accumulation and the risk of underdosing with therapeutic failure. This study aimed to assess the importance of TDM of LZD in patients admitted to an Intensive Care Unit (ICU) of a tertiary hospital.

Methods:

Retrospective study of patients admitted to a multipurpose ICU between 2022/11 and 2023/07, who received treatment with LZD and performed TDM. To determine LZD exposure, minimum concentrations (C_{min}) and maximum concentrations (C_{max}) were measured after a minimum of 3 treatment administrations. The primary endpoint were the achievement of a C_{min} of LZD between 2-8 mg/L and $AUC > 100 \mu\text{g/mL}\cdot\text{h}$. Secondary endpoints included analysis of TDM-guided dose adjustments.

Results:

A total of 56 patients were included (Table 1). Most patients upon admission had medical pathologies (53.4%). The median duration of LZD treatment in the ICU was 8 days [4.0-10.5]. The therapeutic range was achieved at the first measurement in 16/56 patients (28.6%) with a median C_{min} 2.6 [1.5–6.9] mg/L, median AUC 137.5 [88.0–250.8] $\mu\text{g/mL}\cdot\text{h}$. After TDM-guided dose adjustments, a total of 26 patients (46.4%) were within therapeutic range after a median of 2.8 [1.5-3.8] days. After 2 TDM adjustments, 31 patients (55.4%) were within therapeutic range after a median of 1.6 [1.0–2.9] days. In 21 patients (37.5%), therapeutic levels were not reached, 25% had subtherapeutic levels and 12.5% had toxic levels. In 19 patients (33.9%) after reaching therapeutic levels, maintaining dose and administration interval resulted in toxic or subtherapeutic levels.

Conclusion:

Use of TDM in critically ill patients under LNZ treatment increases the probability of reaching the therapeutic target, reducing the risk of underdosing.

References:

- [1] – Abdul-Aziz MH, et al. Intensive Care Med. 46(6):1127-1153, 2020.
- [2] – Dong H, et al. Int J Antimicrob Agents. 38(4):296-300, 2011.

Table:

Age, years Median [IQR]	64.5 [53.5 - 74.0]
Male, n (%)	42 (75.0%)
Body mass index, Kg/m ² , Median [IQR]	30.9 [27.9 - 34.9]
SOFA Score, Median [IQR]	11.0 [9.0 - 13.5]
SAPS 3, Median [IQR]	73.0 [60.3 - 82.8]
Creatinine Clearance mL/min, Median [IQR]	32.6 [7.0 - 82.9]

Renal replacement therapy, n (%)	24 (42.9%)
Septic shock n (%)	51 (91.1%)

Demographic and clinical characteristics of LZD-TDM patients. IQR – Interquartile range