LINEZOLID USE IN PATIENTS WITH LOW BODY WEIGHT: IS REALLY A NEED TO REDUCE THE DOSE TO PREVENT HAEMATOLOGICAL TOXICITY?

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BACKGROUND

A major concern of the use of linezolid is its haematological toxicity. Some factors such as body weight (BW) <55 kg have been related to a higher risk of thrombocytopenia[1]. Recently, a reduced linezolid dose of 20mg/kg has been recommended for patients with a BW <55 kg[1]. The aim of this study is to evaluate the use and tolerability of linezolid at the standard dose (1200 mg/day) in underweight (<55 kg) patients in clinical practice.

MATERIAL/METHODS

All hospitalized underweight patients treated with linezolid and undergoing therapeutic drug monitoring (TDM) were consecutively included during October 2010-November 2015. The study was performed in a university hospital in which TDM of linezolid is routinely performed.

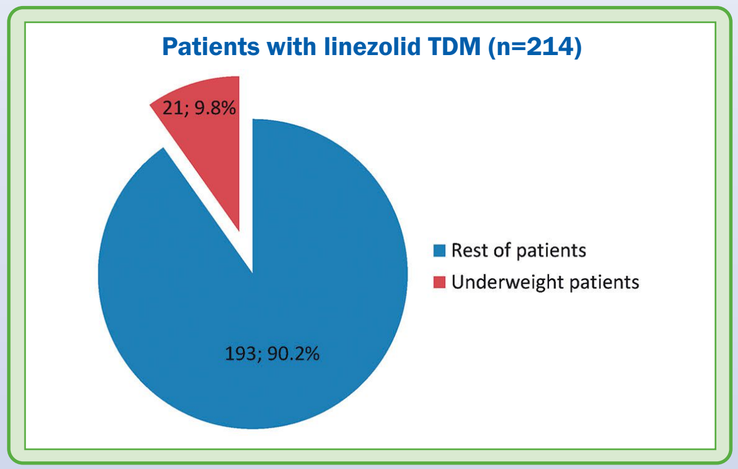
Plasma levels were obtained pre-dose (trough or Cmin) or at the end of the 1h infusion (peak or Cmax), both at steady state, and concentrations were determined by HPLC. Therapeutic levels were considered as trough concentrations between 4-7.5 mg/L and overexposure as trough values >7.5 mg/L and/or a peak concentration ≥30 mg/L.

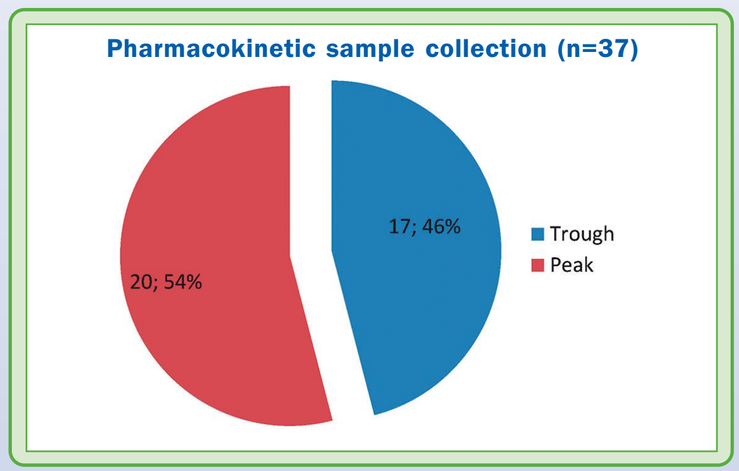
Haemoglobin and platelet count were measured at the beginning and end of linezolid treatment; and at the day of sample extraction (median 6th day of treatment).

Thrombocytopenia was defined as a decrease in platelet count to <75% of the baseline level and anaemia a decrease of ≥2 g/dL in haemoglobin from the baseline value[2]. All quantitative data are expressed as median (interquartile range).

RESULTS

Twenty-one underweight patients were included.





Characteristics of the patients (n=21)

Age (years), median (IQR)	66.0 (48.0-75.0)
Sex (male), n (%)	11 (52.4)
BW (kg), median (IQR)	50.0 (46.0-55.0)
Surgical unit, n (%)	9 (42.9)
Dose (mg/kg/day), median (IQR)	21 (100)
Dose (mg/kg), median (IQR)	24 (21.8-26.1)

The median dose of linezolid/kg BW was similar between patients with and without haematological toxicity (24.0 vs 24.5 mg/kg, p=0.999). A higher frequency of thrombocytopenia was present within patients with high trough levels (6/7 (85.7%) vs 3/10 (30%), p=0.05)

Pharmacokinetic data and haematological toxicity

Trough (mg/L), median (IQR)	5.5 (2.1-16.6)
Peak (mg/L), median (IQR)	23.9 (15.9-31.3)
Therapeutic levels, n (%)	3/17 (17.6)
Trough <4 mg/L, n (%)	7/17 (41.2)
Trough >7.5 mg/L, n (%)	7/17 (41.2)
Peak >30 mg/L, n (%)	7/20 (35.0)
Anaemia, n (%)	7 (33.3)
Thrombocytopenia, n (%)	12 (57.1)
Both anaemia and thrombocytopenia	14 (66.7)

CONCLUSIONS

All our underweight patients received a dose higher than that recommended for patients with a body weight <55 kg (20 mg/kg) and more than 50% presented haematological toxicity. However, more than 40% of the patients did not reach therapeutic trough levels.

Despite the results of this study seem to suggest the need to reduce the linezolid dose in underweight patients to prevent haematological toxicity, there is some concern regarding the associated higher risk of underexposure and clinical failure with this strategy.

BIBLIOGRAPHY

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