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Abstract

Background: Thrombocytopenia (TP) is one of the adverse effects associated with linezolid (LZD). The association between body mass index (BMI) and LZD induced TP has not been reported. The aim of this study was to identify the independent risk factors for LZD induced TP and particularly to evaluate whether low BMI is a risk factor.

Methods: A retrospective cohort study was conducted among 70 consecutive patients (pts) who received LZD therapy (1200mg/day) between July 2003 and August 2012 at St. Luke's International Hospital (530 beds, acute care teaching hospital in Tokyo). Pts who received LZD repeatedly and pts with hematologic malignancy or DIC were excluded. TP was defined as decreased platelet counts (more than 50% decrease from baseline). Laboratory data were obtained for each pt followed from baseline to 14 days after discontinuation of LZD. Bivariate analyses and multivariate analysis were performed categorizing BMI into the three groups: 1. BMI less than 20, 2. BMI equal to or more than 20 and less than 25, 3. BMI equal to or more than 25.

Results: The mean age of the 70 pts was 70 ± 17 years and 42 (60%) were male. The median period of LZD therapy was 16 days (range 4-65 days). LZD induced TP was found in 30 of 70 pts (43%). When evaluated by BMI category, 59% (13/22), 40% (12/30), and 28% (5/18) of pts with BMI less than 20, BMI equal to or more than 20 and less than 25, BMI equal to or more than 25, respectively, developed TP. Low BMI was significantly associated with TP in bivariate analyses ($p < 0.01$). Results of the multivariate analysis showed evidence of an association with increasing age [adjusted odds ratio (OR)=1.02, 95% confidence intervals (CI), 0.99-1.05] and increase in serum creatinine (OR=1.52, 95%CI, 0.98-2.63], and a significant association with BMI less than 20 (versus BMI equal to or more than 25 ,OR=7.20, 95% CI, 1.71-37.97).

Conclusion: BMI less than 20 was independently associated with LZD induced TP. Our results indicate that the platelet counts of pts with low BMI treated with LZD should be monitored closely due to a potential increased risk of TP.

Background

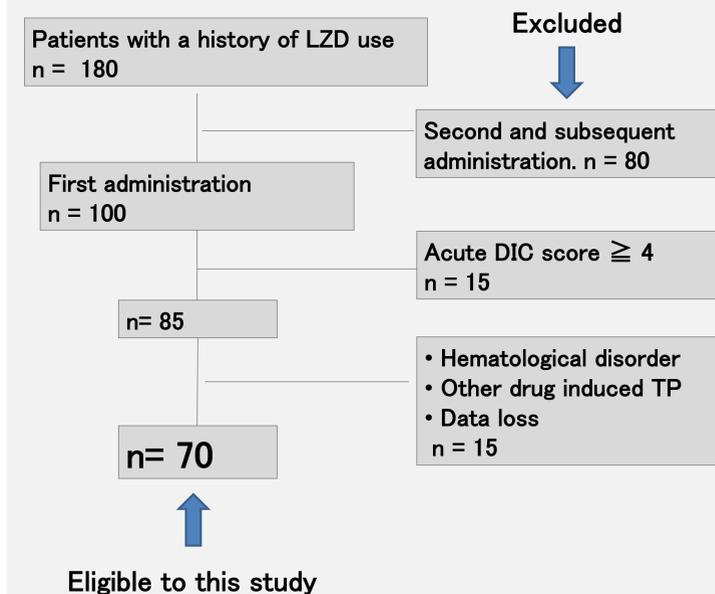
- Linezolid (LZD) is an antibiotic to treat infections caused by *methicillin-resistant Staphylococcus aureus* (MRSA) and *vancomycin-resistant Enterococci* (VRE)
- Dosage adjustment has been considered to be unnecessary in patients(pts) with renal failure and hepatic impairment and in pts with low body mass index.
- Thrombocytopenia (TP) is one of the major adverse effects associated with LZD use.

Purpose

- The association between the body mass index (BMI) and LZD induced TP has not been reported.
- The aim of this study was to identify the independent risk factors for LZD induced TP and particularly to evaluate whether low BMI is a risk factor.

Method

- Study design: Retrospective cohort study
- Study period: April 2003 ~ October 2012
- Setting: St Luke's International Hospital, Tokyo, Japan (530 beds, tertiary-level community teaching hospital)
- Patients: Total 70 patients aged over 18-year-old who received LZD therapy for the first time were eligible. Patients with repeated LZD Therapy, DIC or hematological malignancy were excluded.
- Definition of TP: decline of platelet count more than 50% from baseline. Laboratory data were followed from baseline to 14 days after discontinuation of LZD.
- We categorized the patients by BMI into three groups: BMI < 20, $20 \leq \text{BMI} < 25$, and $\text{BMI} \geq 25$.
- Analysis: Unadjusted and adjusted logistic regression Model. All P-value was calculated by two-tailed and less than 0.05 was considered to be significant.



Results

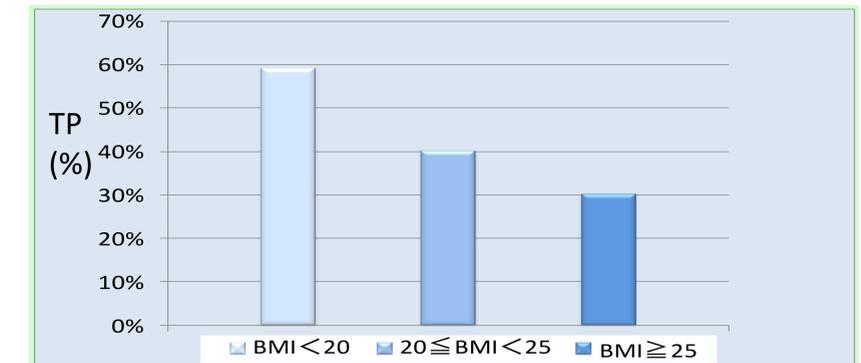
Table 1. Patients characteristics(N=70)

| | TP(+) n=30 (43%) | TP(-) n=40 (57%) | P value |
|--|-------------------------|-------------------------|----------------|
| Age, median (range) | 72.0 (28-85) | 69.5 (24-102) | 0.296* |
| Male, n (%) | 20 (66.6) | 22 (55) | 0.321 |
| BMI, median (range) | 20.45(14.8-27.3) | 22.2(16.1-45.2) | 0.0013* |
| Total dose (g) median (range) | 16.8 (3.6-56.4) | 16.8 (4.8-75.6) | 0.68 |
| Cr (mg/dl) baseline median (range) | 1.16 (0.39-7.47) | 0.99 (0.24-3.93) | 0.16* |
| Plt ($10^4/\text{mm}^3$) baseline median (range) | 25 (6.5-69.4) | 24 (7.5-55.6) | 0.336* |

Table 2. Multivariate analysis

| | Adjusted OR (95% CI) | P value |
|--|--------------------------|---------------|
| Age | 1.02 (0.99-1.05) | 0.30 |
| Cr | 1.52 (0.98-2.63) | 0.06 |
| BMI ≥ 25 | | |
| $20 \leq \text{BMI} < 25$ | 2.79 (0.72-13.21) | 0.14 |
| BMI < 20 | 7.20 (1.71-37.97) | 0.0064 |
| Total dose | 1.01 (0.96-1.05) | 0.78 |

Table 3. Relationship between BMI and TP



Summary of Results

- LZD induced TP was found in 43% (30 of 70) of the pts in total.
- When evaluated by BMI category, The results were as follows :
 - 59% (13/22) of pts with BMI < 20,
 - 40% (12/30) of pts with $20 \leq \text{BMI} < 25$
 - 28% (5/18) of pts with $\text{BMI} \geq 25$ developed TP.
- Low BMI and high Cr were significantly associated with TP by bivariate analyses ($p < 0.01$).
- Multivariate analysis showed evidence of a significant association with BMI < 20 (versus $\text{BMI} \geq 25$,OR=7.20, 95% CI, 1.71-37.97).

Conclusions

- BMI less than 20 was independently associated with LZD induced TP.
- Our results indicate that the platelet counts of pts with low BMI who receive treatment with LZD should be monitored closely due to a possible increased risk of TP.