High plasma linezolid concentration and impaired renal function affect development of linezolid-induced thrombocytopenia.

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Abstract

OBJECTIVES: Thrombocytopenia is sometimes observed during linezolid therapy. Here, we aimed to investigate the factors affecting linezolid-induced thrombocytopenia.

METHODS: A prospective observational study was performed between October 2009 and February 2011; 30 patients were included. Plasma linezolid trough concentrations were measured on days 3, 7 and 14 after initial drug administration. Platelet counts and haemoglobin levels were also monitored.

RESULTS: Thrombocytopenia occurred in 17 patients (56.7%). Median linezolid trough concentrations on day 3 were significantly higher in patients with renal impairment (creatinine clearance <60 mL/min) than in patients without renal impairment (14.7 versus 4.8 mg/L; P<0.0001). Median linezolid trough concentrations on day 3 in patients who developed thrombocytopenia were also significantly higher than those in patients who did not (13.4 versus 4.3 mg/L, P<0.0001). Development of thrombocytopenia occurred significantly more frequently in patients with linezolid trough concentration >7.5 mg/L (OR, 90.0; P<0.0001) and renal impairment (OR, 39.0; P=0.0002). The Kaplan-Meier plot showed that the median time from the initiation of therapy to development of thrombocytopenia was 11 days.

CONCLUSIONS: Patients with renal impairment are more likely to have a high plasma linezolid concentration. In addition, a high plasma linezolid concentration and renal impairment significantly affected the development of linezolid-induced thrombocytopenia. Further studies are required to evaluate whether therapeutic drug monitoring-guided dosage adjustment of linezolid decreases the adverse effects while maintaining treatment efficacy in patients with renal dysfunction.

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