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Linezolid associated with lactic acidosis

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Background: Adverse events reported owing to linezolid (LZD) administration include thrombocytopenia. LZD-associated lactic acidosis (LA) was first reported in 2003; however, there are no data on the incidence and risk factors for LZD-associated LA despite LA being a serious problem. To identify incidence and risk factors for LA caused by LZD, we conducted a retrospective cohort study among patients who were administered either LZD or vancomycin (VCM). A case-control study of LZD-associated LA in the LZD group was also conducted.

Material/methods: We conducted a multimethod investigation including a retrospective cohort and a case-control study. We included patients ≥20-years-old who were administered either LZD or VCM over 3 days from January 2014 to March 2016 at a tertiary care hospital in Tokyo, Japan. A retrospective cohort study examined the incidence of LA after administration of either LZD or VCM evaluated using the propensity scores-matched analysis. The following data were collected: age, sex, underlying diseases, laboratory data including blood gas analysis, sequential organ failure (SOFA) score, incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from blood cultures, duration of antibiotic administration, incidence of LA, and 30-day mortality after antibiotic administration. LA was defined as a serum pH of ≤7.35 and serum lactate ≥36 mg/dL. A case of antibiotic-associated LA was defined as a patient first presenting with LA after antibiotic administration. To evaluate the risk of incidence of LZD-associated LA, LA patients in the LZD group was compared with non-LA patients in the same group. There were individually matched in a 1:2 ratio by age (within a 10-year-old range) and sex.

Results: Ninety-six patients were included in the LZD group and 315 patients in the VCM group. Differences were identified between the LZD and VCM groups by univariate analysis of chronic kidney

disease, chronic obstructive pulmonary disease, SOFA score, incidence of MRSA isolated from blood cultures, and duration of antibiotic administration. After matching by propensity score, incidence of LA was higher in the LZD group than in the VCM group (8.6%(6/70) vs. 1.4%(1/70); odds ratio (OR), 6.5; 95% confidence interval (CI), 0.7-301.7; p=0.05). Within the LZD group, LA patients (11) were compared with non-LA patients (22) by univariate analysis of SOFA score (>11 or not), renal function (estimated glomerular filtration rate >30 or not), and duration of LZD administration (≥7 days or not); ORs (95%CI) were 2.6 (0.4-17.9; p=0.25), 6.5 (0.9-71.6; p=0.03), and 1.9 (0.3-13.6; p=0.44), respectively.

Conclusions: Use of LZD was associated with a higher incidence of LA compared with use of VCM. When LZD is administered to patients with renal failure, blood gases should be checked routinely.