Thrombocytopenia and Anemia Associated with Linezolid in Patients with Kidney Failure

To the Editor—Recently, Wu et al. [1] published a retrospective study that compared the tolerability and efficacy of linezolid therapy for patients with end-stage renal disease (ESRD) and non–end-stage renal disease. They included 91 patients receiving linezolid therapy for ~15 days, 28 of whom had ESRD. Independent risk factors associated with thrombocytopenia were high pretreatment disease severity score ($P = .001$), central catheter–related infection ($P = .046$), and ESRD ($P = .007$). ESRD was also associated with anemia ($P = .006$). In our opinion, this study presented important methodological limitations.

First, important baseline differences between groups could affect the results. Patients in the ESRD group were older than patients in the non-ESRD group (72.1 years vs. 56.8 years; $P < .001$). Older patients ($>60$ years old) could have more than double incidence of thrombocytopenic purpura than younger patients [2]. Therefore, it seemed logical to suppose that the ESRD group, because it is the older group, would have a higher rate of thrombocytopenia than the non-ESRD group and that thrombocytopenic patients would be older than non-thrombocytopenic patients, as actually occurred. A similar argument could be applied to the severity score.

Second, one-third of thrombocytopenic patients in the study already had low platelet counts before starting linezolid therapy, but 1 safety criterion for discontinuing therapy was a platelet count of $<100 \times 10^9$ platelets/L. It seems contradictory that, in some cases, linezolid therapy was discontinued when patients became thrombocytopenic and that, in other cases, linezolid therapy was initiated for patients who already had thrombocytopenia. Even so, the authors had not considered that low counts of platelets and RBCs at the beginning of linezolid therapy could determine, respectively, a higher risk of developing thrombocytopenia and anemia [3, 4] rather than ESRD. Because it was assumed that nonthrombocytopenic patients did not have initial low platelet counts (the contrary was not directly stated in the study), patients with initial low platelet counts developed thrombocytopenia (14 [28.6%] of 49 patients) more often than not (0 of 42 patients, $P < .0001$). The OR for the null hypothesis was 6.72 (95% CI, 2.14–21.07), higher than the OR for ESRD (6.14; 95% CI, 1.63–23.26). In relation to anemia, Wu and colleagues did not show the number of patients who were anemic before starting linezolid therapy.

Third, other causes of thrombocytopenia aside from ESRD were not well ruled out. At least 98 drugs can cause thrombocytopenia, but the drugs most frequently reported with definite evidence are heparin, quinidine, quinine, rifampin, and trimethoprim-sulamethoxazole [5]. The administration rate of these later drugs should be studied in each group, especially heparin, which is widely used in patients with ESRD who are undergoing dialysis. In a similar way, the use of drugs that contribute to anemia and iron or epoetins that increase hemoglobin levels should also be studied. Whole blood, RBC, and platelet transfusions were not included in the study, either.

Finally, the SDs for several important variables were proportionally high. This indicated a wide dispersion of data and a nonhomogeneous group of patients included in the study. This was the case for age, blood urea nitrogen, creatinine level, m-SOFA score, and duration of the antibiotic treatments. In our opinion, a new study with better methodological structure should be conducted to confirm the results presented. Until then, the results of Wu and colleagues should be considered with care.

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Javier Mateu de Antonio, Santiago Grau, José-Antonio Morales-Molina, and Mónica Marín-Casino
Pharmacy Department, Hospital del Mar, Barcelona, Spain

References


Reprints or correspondence: Dr. Santiago Grau, Pharmacy Dept., Hospital del Mar, Passeig Maritim, 25-29, 08003 Barcelona (sgra@imar.imim.es).

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