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Therapeutic Drug Monitoring

The Influence of Proinflammatory Cytokines on Voriconazole Trough Concentration in Patients With Different Forms of Hematologic Disorders

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Abstract

Even though multiple factors are involved in the high fluctuation of voriconazole (VCZ) plasma concentration, little is known regarding the influence of proinflammatory cytokines on VCZ concentration. The aim of this study was to investigate the influence of proinflammatory cytokines, namely, interleukin (IL)-1β, IL-6, IL-18, interferon-γ, tumor necrosis factor-α, and transforming growth factor (TGF)-β1 on VCZ trough concentration (VCZ-C_{min}) in Chinese patients with different forms of hematologic disorders. A total of 250 plasma samples from 113 patients were analyzed for VCZ-C_{min} and proinflammatory cytokines using a validated liquid chromatography–tandem mass spectrometry and enzyme-linked immunosorbent assay methods, respectively. Patient demographics and clinical characteristics were obtained from hospital records. VCZ-C_{min} was significantly correlated with IL-18 in acute myeloid leukemia (r = 0.456; $P < .0001$), acute lymphoblastic leukemia (r = 0.317; $P = .019$), and chronic myeloid leukemia (r = 0.737; $P = .004$) while VCZ-C_{min} and TGF-β1 were correlated (r = 0.436; $P < .001$) in acute myeloid leukemia patients only. VCZ-C_{min} at different concentration range showed significant inhibitory effect of IL-6. A backward multiple linear regression model revealed patient age (coefficient [β] = 0.025; $P = .04$), gamma-glutamyl transferase (β = 0.003; $P = .023$), IL-6 (β = –0.001; $P = .024$), proton pump inhibitor coadministration (β = 1.518; $P = .002$), and cytochrome P450 (CYP) 2C19 polymorphism as predictors of VCZ-C_{min}; however, these factors explained only 29% of VCZ-C_{min} variation. In conclusion, IL-18 and TGF-β1 have correlation with VCZ-C_{min} in Chinese patients with leukemia. Apparently, VCZ may have an inhibitory effect on IL-6 levels. Furthermore, patient age, gamma-glutamyl transferase, IL-6, PPI coadministration, and cytochrome P450 2C19 polymormorphism partially predicted the VCZ-C_{min}. Therapeutic drug monitoring of VCZ in Chinese patients is highly encouraged.