

The Case of the Vanishing Voriconazole

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Objective

Describe a **potential drug-drug interaction between voriconazole and linezolid** resulting in subtherapeutic voriconazole concentrations.

Clinical Features

A 63-year-old male presented with fever and altered neurology. Relevant medication history included immunosuppression for chronic GvHD after allogeneic bone marrow transplant for Non-Hodgkin's Lymphoma 19 years ago. In addition to broad spectrum antibiotics, he was escalated to voriconazole (from fluconazole prophylaxis). He had two appropriately timed voriconazole trough concentrations of 5.8 mg/L and 6.5 mg/L (range 1.0 - 5.5 mg/L), and the dose remained unchanged as the patient was admitted to ICU and commenced on linezolid for empiric therapy of MRSA.

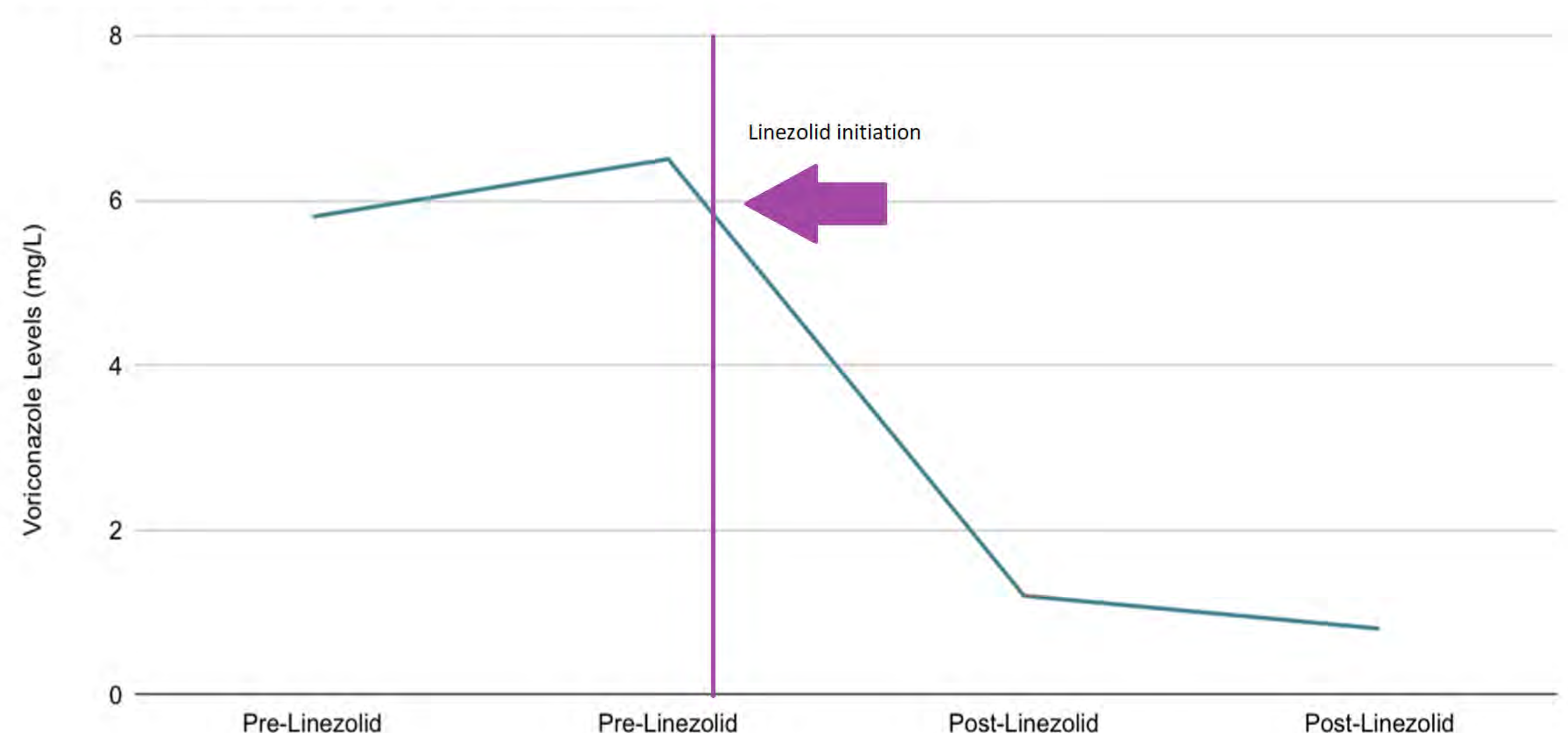
Literature Review

A single centre observational study of 5 patients showed increased voriconazole clearance by 250-700% with concurrent linezolid use¹. There has been no proven mechanism yet for this drug-drug interaction.

Pharmacist Interventions, Case Progress and Outcomes

The potential interaction was discussed on the specialist ID/ICU round and the ICU pharmacists organised voriconazole therapeutic drug monitoring (TDM). Without changing the voriconazole dose, 5 days after linezolid commencing the voriconazole concentration dropped to 1.2 mg/L. No dose change was made (as still in therapeutic range) and another TDM was organised, this time dropping to a subtherapeutic voriconazole concentration of 0.8 mg/L. The patient clinically improved and the linezolid was then ceased and voriconazole de-escalated to fluconazole.

Voriconazole Levels Pre- and Post-Linezolid



Discussion

As antimicrobial resistance developed, the role of drugs with activity against resistant organisms (such as linezolid) will increase. Understanding potential drug interactions is a fundamental role of the pharmacist. This interaction between linezolid and voriconazole is not documented in drug interaction software and could result in both subtherapeutic concentrations, and supratherapeutic voriconazole concentrations after ceasing linezolid.

Therefore, it is important that pharmacists are aware of the interaction and undertake voriconazole TDM if concurrent linezolid use is unavoidable.