Investigation of Saliva as an Alternative to Plasma Monitoring of Voriconazole

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Therapeutic drug monitoring (TDM) of voriconazole is increasingly being implemented in clinical practice. However, as blood sampling can be difficult in paediatric and ambulatory patients, a non- invasive technique for TDM is desirable. The aim of this study was to compare the pharmacokinetics of voricona- zole in saliva with the pharmacokinetics of unbound and total voriconazole in plasma in order to clinically validate saliva as an alternative to plasma in voriconazole TDM. In this pharmacokinetic study, paired plasma and saliva samples were taken at steady state in adult haematology and pneumology patients treated with voriconazole. Unbound and bound plasma voriconazole concentrations were separated using high-throughput equilibrium dialysis. Voriconazole concentrations were determined with liquid chromatography–tandem mass spectrometry. Pharmacokinetic parameters were calculated using log-linear regression. Sixty-three paired samples were obtained from ten patients (seven haematology and three pneumology patients). Pearson's correlation coefficients (R values) for saliva versus unbound and total plasma voriconazole concentrations showed a very strong correlation, with values of 0.970 (p \ 0.001) and 0.891 (p \ 0.001), respectively. Linear mixed modelling revealed strong agreement between voriconazole concentrations in saliva and unbound plasma voriconazole concentrations, with a mean bias of -0.03 (95 % confidence interval -0.14 to 0.09; p = 0.60). For total concentrations below 10 mg/L, the mean ratio of saliva to total plasma voriconazole concentrations was 0.51 ± 0.08 (n = 63), which did not differ significantly (p = 0.76) from the unbound fraction of voriconazole in plasma of 0.49 ± 0.03 (n = 36). Conclusions Saliva can serve as a reliable alternative to plasma in voriconazole TDM, and it can easily be implemented in clinical practice