Drug-Drug Interaction of Miconazole Oral Gel with Tacrolimus and Cyclosporine after Oral Administration
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Purpose
Oral gel form of miconazole is used to treat oral or esophageal candidiasis. We recently encountered a case with dermatomyositis in which an increase in the blood concentration of tacrolimus was observed after the administration of miconazole oral gel. Although azole antifungal agents have been shown to affect the pharmacokinetics of calcineurin inhibitors such as tacrolimus and cyclosporine by inhibiting drug metabolism, there are few clinical reports on drug interactions between miconazole oral gel and calcineurin inhibitors. In the present study, the effects of miconazole oral gel on the blood concentrations of tacrolimus and cyclosporine were investigated.

Methods
In this retrospective study, eighteen patients concomitantly administered miconazole oral gel and tacrolimus and fifteen patients concomitantly administered miconazole oral gel and cyclosporine were evaluated. The dose-adjusted blood concentrations of tacrolimus or cyclosporine were compared before and after the initiation of miconazole oral gel.

Results
The trough blood concentration/dose ratio of tacrolimus increased from 0.10 ± 0.07 kg/L to 0.19 ± 0.13 kg/L (n = 21, p<0.001) by the co-administration of miconazole oral gel. The trough blood concentration/dose ratio of cyclosporine also increased from 0.036 ± 0.015 kg/L to 0.045 ± 0.023 kg/L (n = 15, p<0.01) by the co-administration of miconazole oral gel. The degree of increases in the blood concentrations of tacrolimus and cyclosporine showed wide inter-individual variability (range -44 to 216% and -34 to 195%, respectively). No significant difference was found in the peak concentration/dose ratio of cyclosporine before and after the co-administration of miconazole oral gel (0.15 ± 0.04 and 0.20 ± 0.10 kg/L, n = 5).

Conclusion
These results suggest that miconazole oral gel affects the pharmacokinetics of tacrolimus and cyclosporine after oral administration. Detailed monitoring of the blood concentrations of these drugs followed by dose adjustments are needed for each patient due to the difficulties associated with accurately predicting the degree of the effects of miconazole oral gel.