Multiple drugs

X S

Various toxicities: case report

A woman in her fifties developed unpleasant taste, nausea and vomiting during treatment with itraconazole for antifungal prophylaxis. Subsequently, she developed decreased level of γ-glutamyl transferase for antifungal prophylaxis. Additionally, she developed decreased level of itraconazole following concomitant administration of itraconazole for antifungal prophylaxis and, vonoprazan and famotidine. Additionally, she developed increased level of tacrolimus following concomitant administration of itraconazole for antifungal prophylaxis and immunosuppressive therapy with tacrolimus [*not all indications routes and dosage stated*].

The woman had a history of COVID-19 and subsequent COVID-19-related respiratory failure. After 104 days from the onset of COVID-19, she received living-donor lobar lung transplantation (LDLLT). Hence, she was admitted. Subsequently, on POD 1, she started receiving immunosuppressive therapy with tacrolimus, mycophenolate mofetil and unspecified corticosteroids. Notably, during the first 3 months, her tacrolimus trough levels were maintained at 10–20 ng/mL. Additionally, on post operative day 20, she started receiving antifungal prophylaxis with oral itraconazole 200 mg/day solution. However, she developed unpleasant taste, nausea and vomiting which was attributed to itraconazole.

Hence, on post operative day 23, the woman's treatment with itraconazole was discontinued temporarily. Thereafter, on post operative day 33, her treatment with oral itraconazole 200 mg/day solution was restarted. However, on post operative day 55, the serum concentrations of itraconazole and hydroxy-itraconazole were 240 ng/mL and 358 ng/mL, respectively which was below the target concentration 750 ng/mL as the summation. Thus, itraconazole was stopped. Subsequently, on postoperative day 57, she started receiving voriconazole 600 mg/day tablet which was decreased to 400 mg/day on post operative day 58–63. Subsequently, on post operative day 64−70, voriconazole was increased to 500 mg/day and finally, on post operative day 71−74, it was increased to 600 mg/day. However, her serum γ-glutamyl transferase level showed an increase which was attributed to voriconazole. Hence, her treatment with voriconazole was stopped. Subsequently, on post operative day 75, her treatment with oral itraconazole solution was restarted. However, he again experienced nausea and vomiting, Therefore, on post operative day 78, the oral itraconazole solution was replaced with itraconazole tablet 300 mg/day. Concomitantly, she also started receiving vonoprazan. However, on post operative day 82, the serum concentrations of itraconazole and hydroxy-itraconazole were below the detection limit. Subsequently, on post operative day 82, the dose of the itraconazole tablet was increased to 400 mg/day. Thereafter, on post operative day 83, vonoprazan was replaced with famotidine. However, still the bioavailability of itraconazole was low. Therefore, on post operative day 84, she started receiving itraconazole with POKKA LEMON obtained from POKKA SAPPORO Food & Beverage Ltd., Nagoya, Japan and CHELATE LEMON obtained from POKKA SAPPORO Food & Beverage Ltd. commercially available acidic beverages. Eventually, at POD 125 the serum concentrations of itraconazole and hydroxy-itraconazole were 341 ng/mL and 673 ng/mL, respectively. Additionally, it was reported that, on post operative day 117, she developed cytomegalovirus. Ultimately, it was reported that, there was decrease in level of itraconazole following concomitant administration of itraconazole and, vonoprazan and famotidine. Moreover, the concentration/dose ratio of tacrolimus increased 6.9-fold following concomitant administration of itraconazole with lemon beverages which was considered to be an effect of itraconazole and furanocoumarin of citrus fruits [*duration of treatments to reactions onset not stated; not all outcomes stated*].

Umemura K, et al. Improved absorption of itraconazole tablet by co-administration with lemon beverages in a lung transplant recipient: A case report. Journal of Infection and Chemotherapy 28: 1203-1207, No. 2, Aug 2022. Available from: URL: http://www.journals.elsevier.com/journal-of-infection-and-chemotherapy/ 803675057