Poster

[P27-2] P27-2: Anti-infective drugs (7): Antifungals

Chair: Yoh Takekuma, Japan

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[P27-2-7] Usefulness of therapeutic drug monitoring of voriconazole in patients with liver cirrhosis (Child-Pugh class C)

Takehiro Yamada[1], Shungo Imai[2], Yuki Tazawa[3], Keisuke Kagami[4], Kenichiro Yamashita[5], Tsuyoshi Shimamura[6], Ken Iseki[7] (1.Hokkaido University Hospital, 2.Hokkaido University Hospital, 3.Hokkaido University Hospital, 4.Hokkaido University Hospital, 5.Hokkaido University Graduate School of Medicine, 6.Hokkaido University Hospital, 7.Faculty of Pharmaceutical Sciences, Hokkaido University)

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Background

Voriconazole (VRCZ) is a triazole antifungal agent. However, exposure to this drug is associated with an enhanced risk of serious side effects. The package insert of VRCZ recommends reduction of the maintenance dosage by 50% for patients with mild (Child-Pugh class A) to moderate (Child-Pugh class B) hepatic impairment. However, the optimal dose for patients with more severe liver cirrhosis, Child-Pugh class C, is not apparent. In such a situation, therapeutic drug monitoring (TDM) of VRCZ will be useful tool for the appropriate dose-setting of this agent.

Methods

We retrospectively evaluated 4 cases with Child-Pugh class C (score 10-12), they all received orally VRCZ treatment. They all were patients who were waiting or have received liver transplantation. The plasma VRCZ level was determined by using high-performance liquid chromatography and UV detection. This study was carried out in accordance with the guidelines for human studies, and the study protocol was approved by the ethics committee of the Hokkaido University Hospital.

Results

Two of 4 patients with Child-Pugh class C treated VRCZ with ordinary loading dose (orally 300 mg twice daily) on the day 1, then maintenance dose for 75 mg twice daily, the first TDM performed on the day 3. Their plasma trough levels of VRCZ were 3.26 mg/L, 4.20 mg/L, respectively. After the first TDM, the maintenance dose of VRCZ was decreased up to 25 and 50 mg twice daily, respectively. The each mean trough VRCZ levels after the first TDM were 2.17 mg/L and 2.09 mg/L, they were all in the target trough value recommended in Japanese TDM guideline. The remaining patient received no loading dose, started from 50 mg twice daily. All the 4 patients did not show level in the toxic range (more than 5.0 mg/L as trough level of VRCZ).

Conclusions

The maintenance dose of VRCZ for all 4 patients with Child-Pugh C needed reduction compared with that for Child A or B patients. The results of this study will provide useful information on the optimal dosage settings of VRCZ for patients with Child–Pugh class C hepatic impairment.