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Meeting abstract

Voriconazole and target-site penetration into human tissue

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Background

Voriconazole (VOR) is an azole antifungal drug with broad activity against *Candida albicans*, non-albicans *Candida* and *Aspergillus* species. Oral and parenteral formulations have similar pharmacokinetics and are used for the treatment of life-threatening invasive fungal infections.

Materials and methods

Target-site penetration was evaluated in autopsy samples (lung, brain, kidneys, liver, spleen, heart) of two patients who had died during treatment with VOR. Patient 1 had obtained a single-dose of VOR (200 mg), the interval between the last administration and death was 36 hours. Patient 2 was on VOR therapy under steady-state (day 10, cumulative dose 3,800 mg). He died 12 hours after the last VOR infusion. Tissue samples were obtained during routine autopsy, homogenized, purified and quantified by HPLC.

Results

The VOR concentrations in patient 2 exceeded those measured in patient 1 in all tissue samples. The highest levels were determined in the liver (4.21 ± 0.77 g/L) and the kidneys (6.89 ± 0.06 g/L). Mean VOR lung concentration amounted to 1.30 ± 0.63 g/L (patient 1: 0.72 to 0.76 g/L; patient 2: 1.47 to 2.04 g/L). After a single administration VOR tissue levels in the brain were below the limit of detection (<0.25 g/L) and achieved concentrations of 3.34 ± 0.18 g/L under steady-state conditions. In the different areas of the brain (cortex, hippocampus, nucleus caudatus, medulla oblongata and cerebellum) similar VOR concentrations were found. VOR levels amounted to 1.31 ± 0.03 g/L and 2.95 ± 0.05 g/L in samples of the spleen of patient 1 and 2, respectively. In the myocardium samples of patient 1 VOR was not detectable, but reached a mean concentration of 2.44 ± 0.25 g/L in patient 2.

Conclusion

Even after a single administration, VOR could be detected in most tissues. Obviously, the drug accumulates in the organs of its elimination, the liver and the kidneys. The penetration into the brain and into the myocardium is probably slower. The maximum lung concentrations appear to be below the levels achieved in other tissues. However, the levels may exceed the minimal inhibitory concentrations of most relevant fungal pathogens.