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MEETING ABSTRACT

A3.31

Micafungin concentrations in human brain tissue and cerebrospinal fluid

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Background: The echinocandin micafungin (MICA) is recommended for treatment of invasive candidiasis. However, data on its tissue distributions in humans is limited. The penetration of MICA into the human CNS is of particular clinical relevance. Therefore, we quantified MICA in cerebrospinal fluid (CSF) and in brain tissue (BT) samples of adult patients who had been treated with MICA.
Methods: CSF samples were obtained from critically ill patients on MICA who had undergone lumbar puncture or external ventriculostomy for therapeutic purpose. BT specimens were taken at routine autopsies of patients who had died on MICA treatment or up to 30 days after MICA administration. MICA concentrations were measured with high-pressure liquid chromatography (HPLC) and UV detection. In CSF samples proteins were precipitated by acetonitrile, and subsequently samples were purified by solid-phase extraction. BT specimens were processed by protein precipitation with acetonitrile and mechanical homogenisation with a Precellys homogenizer. MICA quantification was validated according to guidelines of the European Medicine Agency (EMA). The lower limit of quantification (LOOQ) was 0.01 µg/ml in CSF and 0.1 µg/g in BT.
Results: BT was obtained from 7 autopsy cases. CSF was taken from 3 patients. MICA concentrations ranged from 0.17 to 2.8 µg/g in BT, and from 0.092 to 0.159 µg/ml in CSF. The simultaneous plasma levels were 1.155 to 9.759 µg/ml. MICA kinetics could be determined in CSF in one patient. C_{max} in CSF was amounted to 0.159 µg/ml and occurred 4 hours after the start of infusion and in plasma a C_{max} of 9.759 µg/ml was reached after 1 hour.
Discussion: MICA concentrations in CSF and BT were comparable with those of anidulafungin [1]. CSF levels are much lower than the simultaneous plasma concentrations and slightly below the BT concentrations. Based on our findings the achievement of therapeutic CNS concentrations of MICA cannot be anticipated in critically ill adults.
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Keywords: target-site pharmacokinetics – CNS penetration – echinocandins

Reference

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