Distribution evaluation of tacrolimus in the ascitic fluid of liver transplant recipients with liver cirrhosis by a sensitive UPLC-MS/MS method

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Abstract

Background: Tacrolimus (TAC), an important immunosuppressant for liver transplantation, has a narrow therapeutic index and large individual differences in pharmacokinetics. Ascitic fluid is commonly drained after liver transplantation. However, the distribution of TAC in ascitic fluid and the influence of drained ascitic fluid on whole-blood TAC are unclear. Methods: The ascitic fluid samples from twenty liver transplant recipients who were received TAC treatment within 12h after the transplantation surgery were collected for consecutive 24h in different days after the surgery. The distribution of TAC in ascitic fluid were evaluated by using a sensitive UPLC-MS/MS method. Chromatographic separation was achieved on an Agilent ZORBAX Eclipse Plus Phenyl-Hexyl column (2.1×100mm, 3.5μm). Mass spectrometry was performed in multiple reaction monitoring (MRM) conditions of transitions m/z 821.4-768.5 for TAC. Results: The concentrations of TAC in ascitic fluid samples range from 0.2 to 3.0 ng/mL, accounting for 1.19-31.87% of whole-blood TAC concentrations. A linear mixed model showed a statistically significant positive correlation between the steady-state trough blood concentration of TAC (C0) and the corresponding amount of TAC excreted in the ascitic fluid for 24 consecutive hours, especially after normalization by the daily dose per unit body weight (D/W). Conclusions: These data suggested that the distribution of TAC in ascitic fluid has great individual differences. The whole-blood TAC concentration, D/W and other confounding factors may contribute to the excretion of TAC in ascitic fluid, but the influence of TAC excretion in drained ascitic fluid on the whole-blood TAC concentration is negligible.

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