Poster

[P26-6] P26-6: Immunosuppressive drugs (5): Clinical practice

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[P26-6-5] Clinical pharmacokinetics of mycophenolic acid: a comparison between the two formulations of mycophenolate mofetil (Cellcept and Myfenax) and the enteric-coated mycophenolate sodium (Myfortic) in adult renal transplant recipients in the early transplant period

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Background

In our hospital, a generic version of mycophenolate mofetil –MMF- (Myfenax®) has been introduced very recently. Aims:1) To determine and compare the pharmacokinetic profiles of the two formulations of MMF, the original(Cellcept®) and the generic version(Myfenax®), and of the enteric-coated mycophenolate sodium-EC-MPS (Myfortic) and 2)To assess the best correlation between individual concentrations and the area-under-the-curve (AUC_{0-12}) in order to predict the exposure of mycophenolic acid (MPA) in a population of adult renal transplant recipients 15 days after transplantation.

Methods

Retrospective study of Caucasian cadaveric renal transplant patients who were co-treated with tacrolimus and steroids. All patients received the same MMF (Cellcept® or Myfenax®) or EC-MPS (Myfortic®) dosage for at least 1 week before each profile. A dose correction of 360 mg of EC-MPS=500 mg of MMF was applied. Plasma levels were measured by MEIA on a VIVA® Analyzer.

Pharmacokinetic profiles were obtained at two weeks post-transplant. Blood samples were taken pre-dose and 1, 2, 3, 4, 6 and 8 h after the morning oral dose. AUC_{0-12} was calculated using the linear trapezoidal rule. Statistical analysis was performed using SPSS 19.0 with the Bonferroni multiple comparison test and the Pearson linear correlation coefficient (r^2).

Results

Fifty-two patients (20 with Cellcept®, 11 with Myfenax® and 21 with Myfortic®), age 53±12 years, weight 76 ±13 kg were included.

The AUC_{0-12} was comparable for the three formulations (Cellcept®, Myfenax® and Myfortic®) without any significant differences: 74.58±28.36; 59.74±15.28 and 83.15± 33.11 ng.h/mL, respectively. Similarly, the trough concentration showed comparable values: 4.66±2.51; 4.26±2.51 and 5.25±2.52 ng/mL, respectively.There was a good correlation between the C_{trough} and AUC_{0-12} at steady state: r^2=0.608, 0.748 and 0.453, respectively; however, 3h and 8h-post dose (C_3 and C_8) showed the best correlation for Cellcept® (r^2=0.714 and 0.655) and 2h-post dose (C_2) for Myfortic® (r^2=0.657).

Conclusions

In the early transplant period, with the administration of equivalent doses of the two formulations of MMF (Cellcept® and Myfenax®) and of EC-MPS (Myfortic®) similar levels of exposure to MPA were observed. For these drugs, trough level monitoring was a good way to predict the degree of exposure (AUC_{0-12}), and the generic version of MMF (Myfenax®) presented the best correlation.