
Poster

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

Chair: Hege Christensen, Norway

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[P26-6-9] Therapeutic drug monitoring of mycophenolic acid in plasma samples of patients with systemic lupus erythematosus and clinical implications

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Background

Mycophenolates were initially used in the organ transplant patients. Further, the use of mycophenolate mofetil (MMF) has extended to a broad range of autoimmune diseases including systemic lupus erythematosus (SLE). The American College of Rheumatology guidelines recommend usage of MMF preferentially instead of cyclophosphamide to lupus nephritis treatment. But still a clear inverse correlation between mycophenolic acid (MPA) area under the concentration-time curve (AUC) and SLE activity was not established. The aim of the study is the trial to define the cut-off value of abbreviated MPA AUC to flare prediction and remission maintenance in SLE.

Methods

An abbreviated 3-points concentration MPA AUC_{0-2h} values were measured in 12 patients undergoing MMF therapy. The study protocol was approved by the local ethics committee and informed consent was obtained from all patients before the study began. The abbreviated AUC values from 0 to 2 h of total MPA was calculated using the linear trapezoidal rule. Plasma samples were collected before 0 min, and at 30 and 120 min after dosing. MPA were measured using a validated HPLC-UV method. Standard curve of plasma samples was constructed by plotting the peak-area ratios versus concentrations in the range 0.1-30 mg/mL. The coefficient of variation was in the range 1.8 -5.1 %. The within- and inter-day variations for MPA concentrations were highly reproducible with relative standard deviations of 0.3 to 9.4 % and had very good accuracy with mean relative errors in the range of -3.4 to 5.2 %.

Results

The mean MPA±SD AUC_{0-2h} was 21.2±7.9 mg×h/mL (range: 5.2 -38.8 mg×h/mL) and mean MPA C₀ was 2.9 ±1.1 mg/mL. There was no significant correlation between patient`s MPA AUC_{0-2h} and MPA C₀ (r= 0.40; P=0.195) in opposition to a high correlation between MPA AUC_{0-2h} and MPA C_{0.5} (r=0.95; P<0.0001) .

Conclusions

For 12 SLE patients, the symptoms intensity of SLE under MMF therapy was significantly associated with lower MPA AUC_{0-2h} <15 ±4.9 mg×h/mL . Further studies on larger population are needed to confirm the ability of MPA pharmacokinetic parameters to predict clinical outcomes.