Neither mycophenolate acyl-glucuronide levels nor their areas under the curve are responsible for the gastrointestinal side effects in kidney transplant recipients receiving EC-MPA: a prospective trial.

Abstract:
Since previous in vitro studies suspected the metabolite mycophenolate acyl-glucuronide (AcMPAG) to be responsible for the gastrointestinal side effects, we examined the correlation between AcMPAG blood levels and patient gastrointestinal satisfaction inquiries using a standardized, validated questionnaire. We enrolled 63 renal transplant patients, however, two discontinued the study and 16 were excluded because of inadequate completion of the questionnaires or missing blood values or discontinuation of enteric coated mycophenolic acid (EC-MPA) therapy, severe side effects or viral infections. The final responses of 45 people were subjects to statistical analysis. Gastrointestinal side effects were examined using the Gastrointestinal Symptom Rating Scale (GSRS) completed at three times: T1 (3-5 days after transplantation), T2 (10-15 days), and T3 (3 months). The GSRS results generated two groups of patients based on cutoff values set at a score of 4 points for each item. Scores less than 4 were assumed to be “no side effects”; >=4, “side effects.” AcMPAG was measured by mass spectroscopy on blood samples obtained at fixed times generating three pharmacokinetic profiles per patient. There was no relation between high AcMPAG blood concentrations
and gastrointestinal dissatisfaction. Neither Ac-MPAG area under the curve (AUC) in the absorption phase nor AcMPAG peak values correlated with gastrointestinal dissatisfaction. There was no significant correlation between mean AcMPAG and GSRS scores, although previous studies had suggested AcMPAG maximum values or alternatively AcMPAG AUC in the absorption phase to relate to side effects.