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Influence of renal graft function on mycophenolic acid pharmacokinetics during the early period after kidney transplant.

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Abstract

OBJECTIVES: Mycophenolate mofetil, the prodrug of mycophenolic acid, is widely used for maintenance immunosuppressive therapy in renal transplant recipients. The effect of renal graft function on mycophenolic acid pharmacokinetics parameters is still controversial. The aim of this study is to investigate the impact of renal graft function on mycophenolic acid pharmacokinetics during the early posttransplant period. MATERIALS AND METHODS: Our study was done on ١٣ patients with severe renal impairment (glomerular filtration rate < ٣٠ mL/min, impaired group) and ١٣ patients with normal graft function (glomerular filtration rate < ٧٠ mL/min, control group), at a steady mycophenolic acid plasma level, during the first month after transplant. All patients received a fixed dose of mycophenolate mofetil (١ g twice daily) in combination with cyclosporine and steroids. Mycophenolic acid plasma levels were determined by a validated high-performance liquid chromatography method. Mycophenolic acid area under the time concentration curve from ٠ to ١٢ hours and apparent mycophenolic acid plasma clearance (CL/f) were measured for each patient. RESULTS: Mycophenolic acid area under the time-concentration curve (٠-١٢ h), mycophenolic acid area under the time-concentration curve (٦-١٠ h), first peak concentration (Cmax١), and secondary peak concentration (Cmax٢) were higher in the impaired group, while mycophenolic acid plasma clearance was higher in the control group (P < .٠٥). Trough levels (C٠) were similar for both groups (P < .٠٥). There was a negative correlation between glomerular filtration rate and area under the time-concentration curve (r=-٠,٤٢٢, P = .٠٤), while there was a positive correlation between glomerular filtration rate and mycophenolic acid plasma clearance (r=٠,٤٦٣, P = .٠٢). CONCLUSIONS: Mycophenolic acid pharmacokinetics parameters in normal renal function patients and severe renal impairment patients are different, and renal graft function correlates with total mycophenolic acid area under the time-concentration curve and apparent mycophenolic acid plasma clearance. However, the necessity of dosage adjustment based on renal graft function requires further studies.

Reaxys Database Information

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Indexed Keywords

EMTREE drug terms: cyclosporin; drug derivative; immunosuppressive agent; mycophenolic acid; mycophenolic acid ٢ morpholinoethyl ester; prednisone

EMTREE medical terms: area under the curve; article; blood; clinical trial; controlled clinical trial; controlled study; drug combination; female; glomerulus filtration rate; high performance liquid chromatography; human; kidney; kidney transplantation; male; metabolic clearance rate; pathophysiology; postoperative period; prospective study

MeSH: Area Under Curve; Chromatography, High Pressure Liquid; Cyclosporine; Drug Therapy, Combination; Female; Glomerular Filtration Rate; Humans; Immunosuppressive Agents; Kidney; Kidney Transplantation; Male; Metabolic Clearance Rate; Mycophenolic Acid; Postoperative Period; Prednisone; Prospective Studies
Medline is the source for the MeSH terms of this document.

Chemicals and CAS Registry Numbers: cyclosporin, ٧٩٢١٧-٦٠-٠; mycophenolic acid, ٢٣٠٤٧-١١-٢, ٢٤٢٨٠-٩٣-١; mycophenolic acid ٢ morpholinoethyl ester, ١١٦٦٨٠-٠١-٤, ١٢٨٧٩٤-٩٤-٥; prednisone, ٥٣-٠٣-٢;Cyclosporine, ٥٩٨٦٥-١٣-٣;