



PRESS RELEASE

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IMMUNOSUPPRESSIVE DRUG'S BLOOD LEVEL VARIABILITY MAY IDENTIFY PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS AT RISK OF REJECTION

Tacrolimus variability linked to likelihood of developing antibodies against transplanted kidney.

Highlights

- Kidney transplant recipients typically take the immunosuppressant drug tacrolimus to prevent rejection, and some patients experience large fluctuations in blood levels of tacrolimus even when the dose is unchanged.
- In a recent study, pediatric kidney transplant recipients with such variability had higher risks of developing antibodies against the transplanted kidney, putting them at risk of rejection.

Washington, DC (July 26, 2022) — Although kidney transplantation is the most effective treatment for children with kidney failure, rejection of the transplanted organ by the recipient's immune system is a major concern. Transplant recipients must take life-long immunosuppressant drugs, most commonly tacrolimus, and some patients experience large fluctuations in blood levels of tacrolimus even when the dose is unchanged—a phenomenon called high tacrolimus inpatient variability. In a recent study published in *CJASN*, pediatric kidney transplant recipients with such variability had higher risks of developing antibodies against the transplanted kidney, thereby putting them at risk of rejection.

For the study, researchers assessed trends in tacrolimus inpatient variability among 426 children who underwent kidney transplantation at Lucile Packard Children's Hospital Stanford from 2004–2018. The blood of 220 of these children was also screened over a median of nearly 4 years for the presence of antibodies against the transplanted kidney (or donor-specific antibodies) that can contribute to rejection.

Patients who formed donor-specific antibodies had patterns of higher tacrolimus inpatient variability in the first two years after transplantation and rising variability even in the years before such antibodies were detected. "Tacrolimus variability is a potential real-time non-invasive tool that can serve as an important biomarker to predict long-term graft outcomes," said co-lead author Vaka K. Sigurjonsdottir, MD, of Stanford University School of Medicine and University of Miami. "Non-adherence [when patients don't take their medications as prescribed] is thought to be the most important determinant of high

tacrolimus variability in adolescents and young adults. We are currently conducting a prospective study to investigate this relationship in this age group, whom we already know is at the highest risk of rejection due to high prevalence of non-adherence.”

The authors note that tacrolimus inpatient variability can be easily incorporated into a hospital’s electronic health record to quickly identify high-risk transplant patients, allowing for early intervention to prevent rejection.

“These early interventions can include more frequent phone calls, in-person visits, or further engaging the patients’ families to improve medication adherence, likely the most modifiable determinant of tacrolimus variability,” said co-lead author Kim H. Piburn, DO, of Stanford University School of Medicine. “High tacrolimus inpatient variability may be due to periods of under-immunosuppression, thus putting patients at risk for donor-specific antibody formation and rejection. Minimizing variation in tacrolimus drug levels through these interventions may potentially help improve graft outcomes.”

An accompanying editorial noted that a multidisciplinary team approach to the long-term care of pediatric, adolescent, and young adult kidney transplant recipients should include repeated assessments of impediments to adherence to immunosuppression. “These might be a combination of medical insurance issues, socioeconomic factors, side effects of medications, scheduling problems and behavioral issues,” the authors wrote.

Additional study authors include Olafur S. Indridason, MD, MHS, Lynn Maestretti, MPH, MMS, PA-C, Mary Victoria Patton, MS, CPNP, Anne McGrath, MS, CPNP, CEN, Runolfur Palsson, MD, Amy Gallo, MD, Abanti Chaudhuri, MD, and Paul C. Grimm, MD.

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The article, titled “Patterns in Tacrolimus Variability and Association with De Novo Donor-Specific Antibody Formation in Pediatric Kidney Transplant Recipients,” will appear online at <http://cjasn.asnjournals.org/> on July 26, 2022, doi: 10.2215/CJN.16421221.

The editorial, titled “Pathophysiological Implications of Variability in Blood Tacrolimus Levels in Pediatric and Adolescent Kidney Transplant Recipients,” will appear online at <http://cjasn.asnjournals.org/> on July 26, 2022, doi: 10.2215/CJN.06640622.

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