Best post-transplant drug regimen identified for patients with new kidneys

29 July 2011

For the thousands of patients who receive kidney transplants in the United States each year, preventing organ rejection without compromising other aspects of health requires a delicate balance of medications. Immunosuppresive drugs that protect transplanted organs can also cause serious side effects, including compromising patients' immunity to infection, cancer, and other threats. Finding the best combination and dosage of drugs has often proved difficult for physicians.

A new multi-year study has now shown that using tacrolimus (TAC) and mycophenolate mofetil (MMF) in combination provided the best long-term benefits and the least amount of side effects after a kidney transplant. The results, which come from the longest randomized study to date that has analyzed transplant drugs, provide valuable guidance to physicians who care for for kidney transplant patients. The study, conducted by Giselle Guerra, MD, and colleagues at the University of Miami, appears in an upcoming issue of the *Journal of the American Society Nephrology* (*JASN*), a publication of the American Society of Nephrology.

To compare therapies, Dr. Guerra studied 150 kidney transplant recipients who received one of three common immunosuppressive treatment regimens: tacrolimus + MMF, tacrolimus + sirolimus, or cyclosporine + sirolimus. Tacrolimus and cyclosporine are in a class of drugs called calcineurin inhibitors; they can prevent early organ rejection but can be toxic to the kidneys. Sirolimus and MMF do not damage the kidneys. Patients often receive low doses of calcineurin inhibitors plus sirolimus or MMF in order to gain the most benefit without serious risk to their kidneys. All patients in the study also received another immunosuppressive drug called daclizumab shortly after transplantation, as well as steroids long term; they were followed for an average of eight years after transplantation.

Among the major findings:

- Survival of transplanted organs was similar in all groups of patients.
- Significantly fewer patients treated with tacrolimus + MMF (12%) experienced acute rejection, compared to those treated with tacrolimus + sirolimus (30%) or cyclosporine + sirolimus (28%).
- Patients taking tacrolimus + MMF also had better kidney function during the first 36 months.
- Patients taking tacrolimus + MMF or cyclosporine + sirolimus were less likely to die with a functioning transplant (12% and 4% respectively), compared to those treated with tacrolimus + sirolimus (26%).
- Patients who took sirolimus were more likely to develop viral infections, discontinue treatment, and need cholesterol-lowering medications, compared to patients who were not taking sirolimus.

Taken together, these results suggest that transplant patients do better over the long term with tacrolimus + MMF than with either tacrolimus + sirolimus or cyclosporine + sirolimus. "We have been able to prove that the use of low-dose tacrolimus and MMF is safe and provides excellent outcomes over time to renal transplant patients," said Dr. Guerra.

Provided by American Society of Nephrology