



Drug Monitor

Stop the Posttransplant Corticosteroids Sooner?

Immunosuppressive drug treatment is known to contribute to weight gain in renal transplant recipients—which is particularly problematic given the high incidence of cardiovascular disease and death in this population. Researchers from the University of Cincinnati and The Christ Hospital in Cincinnati, OH and Fujisawa Healthcare Inc. in Deerfield, IL suggest that withdrawing corticosteroids early (within seven days after the transplant) can help keep the weight gain down.

They compared data from several prospective clinical trials, in which a total of 169 patients had early corticosteroid withdrawal (CSWD) following renal transplant, with that of a historic control group of 132 renal transplant recipients who were given long-term corticosteroid therapy (LCST). They found that the mean weight gain was approximately 30% higher among the LCST patients at three, six, and 12 months—and about 33% faster. In fact, early CSWD patients tended to lose weight in the first month posttransplant, while LCST patients gained. At one year, the LCST group had a significantly higher mean weight gain of 7.7 kg, compared with 2.4 kg in the early CSWD group.

Subset analysis showed that both groups had similar proportions of patients who lost weight overall but that the early CSWD group had more patients whose weight remained stable (defined as a gain or loss of less than 5 kg) and fewer who gained weight. Female patients, white patients, those with a pretransplant body mass index greater than 30, and recipients of living-donor transplants appeared to benefit most from early withdrawal.

The connection between corticosteroids and greater weight gain was reinforced by the finding that, when patients in the early CSWD group were treated with corticosteroids for acute rejection, their patterns of weight changes reverted to those seen in LCST patients. The researchers also point out that results from previous studies, in which corticosteroid therapy was withdrawn three to seven months after the transplant, suggest that the later the drugs are stopped, the smaller the benefit. They call for more studies to clarify the risks and benefits of early withdrawal in specific patient populations.

Source: *Transplantation*. 2005;80:26–33.

Oral Contraceptives and the Diabetic Kidney

Oral contraceptive (OC) use may be a risk factor for diabetic nephropathy, say researchers from Brigham and Women's Hospital and the Joslin Diabetes Center in Boston, MA; the Steno Diabetes Center in Gentofte, Denmark; and the University of Aarhus in Aarhus, Denmark. In their two-part study, the rate of macroalbuminuria was almost nine times as high in diabetic women who used OCs than in those who didn't.

The first part of the study involved 92 women with and without diabetes: 41 nondiabetic OC nonusers, 10 nondiabetic OC users, 29 diabetic OC nonusers, and 12 diabetic OC users. (Diabetic patients in this part of the study included 28 with type 1 diabetes as well as 13 with type 2.) The researchers measured renal plasma flow (RPF) response to captopril as an index of renin-angiotensin system (RAS) activation—which has been linked to nephropathy.

Both diabetic and nondiabetic women who were using OCs showed an increased RPF response, compared to those who were not using OCs. In fact, OC use in the absence of diabetes increased angiotensin-dependent control of the renal circulation to levels observed in diabetic women who did not use OCs. But the diabetic patients who used OCs had, by far, the most pronounced RPF response, which was significantly greater than that seen in both the diabetic and nondiabetic OC nonuser groups.

Based on these results, the researchers decided to follow up on 117 women with newly diagnosed type 1 diabetes for approximately 20 years to determine the long-term effects of OC use on the diabetic kidney. This prospective cohort included 33 OC users and 81 nonusers. Over time, 18% of the OC users developed macroalbuminuria compared with 2% of the nonusers ($P = .003$). After controlling for other risk factors, OC use remained a significant predictor of progression to macroalbuminuria, with a relative risk of 8.9. All of the patients who developed macroalbuminuria fulfilled the criteria for diabetic nephropathy.

The findings could have wide reaching implications, the researchers say, considering that at least 20% of diabetic women use OCs. They point out that no contraceptive methods are contraindicated in diabetic women; in fact, contraception is particularly advocated for these women because of the possibility of serious complications with an unexpected pregnancy. Until larger studies are performed, the researchers recommend caution and surveillance when OCs are used in the context of diabetes. ●

Source: *Diabetes Care*. 2005;28:1988–1994.