Steroid-Dependent Nephrotic Syndrome: Rituximab versus Tacrolimus

Rituximab appears more effective than tacrolimus in children with corticosteroid-dependent nephrotic syndrome (CDNS), reports a trial in *JAMA Pediatr*.

The randomized, open-label trial included children and adolescents (aged 3 to 16 years) with CDNS. The patients, seen at a tertiary care center in India over a 16-month period, had received no previous corticosteroid-sparing therapy. They were randomly assigned to tacrolimus, along with tapering alternate-day prednisolone, for 12 months; or a single course of rituximab, two 375 mg/m² infusions. Twelve-month relapse-free survival was compared between groups.

Of 176 patients screened, 120 were enrolled in the study; all but 3 had 1-year follow-up data. The two treatment groups had similar characteristics. Fifty-three percent were boys, and the mean age was 7.2 years. Mean duration of CDNS was 2.5 years in the tacrolimus group and 2.3 years in the rituximab group; 25% of patients in both groups had a disease duration of less than 1 year. Both groups had a median of 4 relapses; mean cumulative prednisolone dose in the previous year was 246 mg/kg in the tacrolimus group and 239 mg/kg in the rituximab group.

The 12-month relapse-free survival rate was 90.0% for children assigned to the rituximab group, versus 63.3% for those assigned to the tacrolimus group. In a Cox proportional hazards regression model, the relative risk of relapse was five times higher with tacrolimus compared to rituximab. The median time to first relapse was 40 weeks with rituximab versus 29 weeks with tacrolimus. Multiple relapses occurred in only 2 patients in the rituximab group, compared with 10 in the tacrolimus group.

Despite a higher rate of mild to moderate infections in the tacrolimus group (43.3% versus 21.7%), both treatments were well tolerated. The mean 12-month cumulative corticosteroid dose was 25.8 mg/kg with rituximab versus 86.3 mg/kg with tacrolimus.

The B-lymphocyte-depleting antibody rituximab has emerged as an alternative to the calcineurin inhibitor tacrolimus for children with CDNS. This trial—performed in an area with a high incidence of childhood idiopathic nephrotic syndrome—suggests that rituximab is more effective than tacrolimus as first-line corticosteroid-sparing therapy for pediatric CDNS. In addition to higher relapse-free survival, rituximab reduces corticosteroid exposure and is well-tolerated, without nephrototoxic effects [Basu B, et al. Efficacy of rituximab vs tacrolimus in pediatric corticosteroid-dependent nephrotic syndrome: a randomized clinical trial. *JAMA Pediatr* 2018; 172:757–764].

**Findings**

**Second-Line Sulfonylureas Increase Risks in Type 2 Diabetes**

Sulfonylureas are widely used as second-line oral antidiabetic therapy, despite potential cardiotoxicity and hypoglycemia risk. A new UK population-based cohort study suggests that such second-line treatment with sulfonylureas is associated with increased risks of myocardial infarction, death, and severe hypoglycemia. The study was published in the *British Journal of Medicine*.

Using the UK Clinical Practice Research Datalink, the researchers identified 77,138 patients with type 2 diabetes who started metformin monotherapy between 1998 and 2013. In a prevalent new-user design, the analysis included 23,592 patients who added or switched to sulfonylureas as second-line therapy and the same number of patients who remained on metformin.

The two groups were matched for high-dimensional propensity score, hemoglobin A1c, and number of previous metformin prescriptions. The two groups were compared for risk of myocardial infarction, ischemic stroke, death from cardiovascular causes, death from any cause, or severe hypoglycemia.

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