IL-1 Receptor Antagonist Therapy in Type 2 Diabetes

Impaired ß-cell function and decreased ß-cell mass due to apoptosis contribute to impaired insulin secretion in patients with type 2 diabetes. Interleukin-1 receptor antagonists (IL-1Ra) can block ß-cell apoptosis, and patients with type 2 diabetes are known to have reduced levels of IL-1Ra expression.

Anakinra is a recombinant human IL-1Ra that is currently used for moderate to severe rheumatoid arthritis. Thomas Mandrup-Poulsen, MD, PhD of the Steno Diabetes Center in Denmark presented results from a recent study examining anakinra in the treatment of type 2 diabetes. This was a randomized double-blind, placebo controlled trial conducted at 2 sites, the Steno Diabetes Center in Denmark and the University of Zurich, Switzerland. In this study, 70 patients with type 2 diabetes were treated with 100 mg/day of anakinra via self-administered subcutaneous injection once each morning.

Patients in this study had type 2 diabetes for a minimum of three months, were obese, and had an HbA1c > 7.5%. People with infectious disease or an immunodeficiency were excluded because IL-1Ra therapy is contraindicated in these patients. The treatment period was 13 weeks, with an additional 39 weeks of follow-up. During the study participants continued taking their regular diabetes treatments. The primary endpoint was the change between baseline and end of study HbA1c values. Secondary measures included home fasting blood glucose, oral glucose tolerance test (OGTT) results, ß-cell function, and insulin sensitivity. Sixty-four of the 70 patients were included in the analyses, 32 in the IL-1ra group and 32 in the placebo group.

There were no statistically significant differences in demographics between the two groups. The therapy was well tolerated and there were no differences in adverse events between the groups. The most common adverse event was injection site reaction (10/32 subjects). Treatment with anakinra reduced the HbA1c more than placebo over the 39 week study period (p=0.02). The change in the 2- hour OGTT plasma glucose in the anakinra group was significantly less than that in the placebo group at 13 weeks (p=0.04). In terms of ß-cell function, the change in the area under the curve for insulin during the IV stimulation test was statistically significant, favoring anakinra (p=0.031). There was no significant difference in insulin sensitivity between the two groups. These results suggest that IL-1Ra is worthy of further exploration in the treatment of diabetes.

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