Early Insulin Trumps Oral Therapy in Type 2

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Early, aggressive insulin therapy is probably the optimal treatment for patients with newly diagnosed type 2 diabetes who present with severe hyperglycemia, because it provides better short-term glycemic control and β-cell recovery than a regimen of oral antidiabetes drugs, a study has found.

After being stabilized on insulin, patients in the controlled trial who were randomized to a further 6 months of insulin therapy had significantly better glucose levels and β-cell function, Dr. Harn-Shen Chen and colleagues concluded.

"Our data demonstrated that intensive insulin therapy … can achieve optimal glycemic control in [these patients], but cannot induce long-term glycemic control," Dr. Chen of the Taipei Veterans General Hospital, Taiwan, and the coauthors wrote in Diabetes Care. "A 6-month course of further insulin therapy, compared with oral antidiabetes treatment, more effectively maintained adequate glycemic control accompanied with significant improvement of β-cell function" (Diabetes Care 2008;31:1927-32).

The investigators examined the effect of both treatments in 50 patients with newly diagnosed type 2 diabetes, all of whom were hospitalized with severe hyperglycemia—a fasting plasma glucose of more than 300 mg/dL, or random plasma glucose of more than 400 mg/dL. All patients received 10-14 days of intensive insulin treatment, with the goal of a preprandial blood glucose of 90-130 mg/dL and a bedtime blood glucose of 100-160 mg/dL. After stabilization, patients took an oral glucose tolerance test for baseline values, and were discharged on either insulin (30) or oral antidiabetic agents (20).

Insulin doses were titrated every 3 days to achieve a target blood glucose level of 90-130 mg/dL. Oral medications were titrated in several phases. Initially, overweight patients received metformin and lean patients received gliclazide-MR, both of which were titrated to achieve blood glucose of 90-130 mg/dL. In the second step, lean patients received metformin and overweight patients received gliclazide. In the third step, the drugs were titrated to a maximum of 120-mg/day gliclazide and 2,550-mg/day metformin in a split dose. After 6 months, the insulin-treated patients switched to an oral regimen. Both groups were assessed again at 12 months.

During the treatment period, the insulin dose decreased from a mean of 26 IU/day to 17 IU/day. Conversely, the oral medications had to be increased to achieve the target blood glucose level.

At the beginning of the treatment, both groups had stable hemoglobin A_{1c} (HbA_{1c}) of about 11%. At the end of the treatment, the HbA_{1c} level was significantly lower in the insulin group (6% vs 7.5%). At the 12-month follow-up visit, the HbA_{1c} level was still significantly better in the insulin group (6.8% vs 7.8%).

"The study showed that desired glycemic control was successfully achieved by intensive insulin therapy. … However, most of these subjects required pharmacologic therapy to maintain near-euglycemia in our study period," the authors noted. "A 6-month course of further insulin therapy, compared with [oral antidiabetes drug] treatment, could more effectively achieve a near-normal A_{1c} level."

β-Cell function was assessed by an oral glucose tolerance test at 6 months. All β-cell functions were significantly improved in both groups. However, when compared with the oral medications group, the insulin group had a significantly better insulin area under the curve, HOMA-β index, and insulinogenic index.

"Our results support the concept that correction of hyperglycemia can improve insulin secretion," the authors wrote. "Another possibility is that β-cell secretory capacity may have been restored by 'rested' β-cells, induced by insulin injection."

There were no severe hypoglycemic events in either group.

"Given the much greater efforts [required] on the part of both patients and physicians to initiate treatment with insulin, we need evidence, not hypotheses, to recommend this course," Dr. Mayer B. Davidson of Charles R. Drew University of Medicine and Science, Los Angeles, cautioned in an accompanying editorial.

The study was funded by the Taipei Veterans General Hospital and the Taiwan Department of Health. The authors reported no conflicts of interest. ■