fect" that extends protection against cardiovascular disease beyond the initial period of intensive glycemic control.

The group with early-onset diabetes in the present study clearly had higher average glucose levels for a relatively longer duration than did the later-onset group. In addition, the early-onset group may have had a higher incidence of neuropathy – including damage to the autonomic nerves, which is itself a risk for cardiovascular events – and cerebral and peripheral arterial disease as well, each factor increasing the relative risk for such an event.

Therefore, it is hardly surprising that those patients exposed to a longer duration of diabetes are at higher risk for cardiovascular disease. In fact, VA-HIT (Veterans Affairs High-Density Lipoprotein Intervention Trial) showed that after 16 years duration of diabetes, the positive impact of intensive insulin therapy was outweighed by the risk of adverse outcomes, another indication of the importance of considering duration of diabetes as a risk factor for complications, and a limitation on our ability to achieve the best outcomes for that patient.

Clearly more studies are needed to explore the point raised again by Dr. Wannamethee and colleagues.

Although such observational studies as theirs have many methodological flaws that limit our ability to generalize the findings, I think that his findings are credible, and fit well with what has been previously published. ■

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Novel Long-Acting Insulin Effective

BY MIRIAM E. TUCKER

FROM THE LANCET

Using the ultra-long-acting basal insulin degludec three times a week produced glycemic control comparable with that of daily insulin glargine in patients with inadequately controlled type 2 diabetes, in a phase II study.

"A three times a week, weekend-off, dosing regimen might appeal to some people with type 2 diabetes who are inadequately controlled on oral antidiabetic drug treatments, potentially helping with acceptance and early initiation of insulin therapy," explained Dr. Bernard Zinman of the University of Toronto and his associates (Lancet 2011[doi:10.1016/S0140-6736(10)62305-7]).

Novo Nordisk's insulin degludec is formulated in such a way that dosing could be reduced to just three times a week in previously insulin-naive patients with type 2 diabetes – thereby reducing the risk for hypoglycemia and potentially improving adherence to insulin treatment, the authors wrote.

The trial results were first reported at the annual scientific sessions of the American Diabetes Association (CLINICAL ENDOCRINOLOGY NEWS, August 2010, p. 19)

The 16-week, randomized, parallel-group trial of 245 patients was done at 28 clinics in four countries. All patients had type 2 diabetes, were insulin naive, and had been treated with one or two oral antidiabetic agents for more than 2 months.

The subjects were randomized to one of four groups: insulin degludec either three times a week (900 nmol/mL formulation, once daily (600 nmol/mL), or once daily (900 nmol/mL); or insulin glargine once daily (600 nmol/mL formulation). All four drug regimens were given in combination with metformin.

Mean hemoglobin A_{1c} and fasting plasma glucose concentrations were similar between the treatment groups. Reductions in HbA_{1c} from baseline were between 1.3% and 1.5% (to 7.2%-7.5%) and did not differ significantly between the groups. Fasting plasma glucose concentrations dropped 3.4-4.2 mmol/L from baseline and also did not differ between treatment groups.

The rates of hypoglycemia were low in all of the treatment groups, with 77%-92% reporting no episodes. However, the proportion of patients who had hypoglycemia in the once-daily 600-nmol/mL insulin degludec group was lower than was the proportion in the insulin glargine group and the insulin degludec three times a week group, with odds ratios of 0.26 and 0.31, respectively.

Adverse events were mild or moderate in severity, with no apparent treatment-specific pattern. Dr. Zinman has been a consultant to, an adviser for, and received grant support from Novo Nordisk, GlaxoSmithKline, Merck, Eli Lilly, Amylin, and Boehringer Ingelheim. ■