DIABETES

Basal insulin and n-3 fatty acids—no effect on cardiovascular outcomes

Neither provision of basal insulin nor of n-3 fatty acids to patients with poor glycaemic control who are at a high risk of adverse cardiovascular events confers significant cardiovascular protection. These findings of a two-by-two factorial study conducted by the ORIGIN trial investigators have been published in *The New England Journal of Medicine*.

The presence of elevated fasting glucose levels is a known cardiovascular risk factor and the researchers hypothesized that provision of basal insulin (insulin glargine) to at-risk patients to normalize fasting glucose levels could reduce the incidence of cardiovascular events. Results of previous studies have been conflicting, with some reports showing an association between insulin treatment and increased mortality,

cardiovascular disease or cancer, whereas in other trials insulin reduced the incidence of myocardial infarction and mortality.

n-3 fatty acids have been shown to reduce the incidence of cardiovascular events in certain groups of at-risk individuals. However, the cardiovascular effects of these compounds in patients with impaired fasting glucose levels or reduced glucose tolerance was not known.

Over 12,500 individuals aged ≥ 50 years who had impaired glucose tolerance, impaired fasting glucose levels or a diagnosis of type 2 diabetes mellitus (receiving no more than one oral glucose-lowering drug), with history or known risk of cardiovascular events were recruited to this study. The patients were randomized to receive insulin glargine at a dose titrated to achieving a fasting plasma glucose level of < 5.3 mmol/l or to standard care. The patients were also randomized to take a dietary supplement of 1 g of n-3 fatty acids daily or placebo. The study had a median follow-up period of 6.2 years.

The researchers found that an individualized insulin-glargine regime had a neutral effect upon cardiovascular outcomes and development of cancers. Patients who did not have diabetes mellitus at the study outset were 28%

less likely to develop this condition while receiving insulin glargine than while receiving standard care. However, patients receiving insulin glargine were more than twice as likely to experience severe hypoglycaemia than those receiving standard care. Patients receiving insulin glargine also gained a median of 1.6 kg of body weight, whereas those receiving standard care lost a median of 0.5 kg.

Dietary supplementation with n-3 fatty acids had no significant effect on the incidence of death due to cardiovascular causes, major cardiovascular events or death from any cause. These results were independent of treatment with or without insulin glargine.

Overall, neither basal insulin treatment nor this level of n-3 fatty acid supplementation appear to be beneficial in patients at high risk of cardiovascular events who have poor glycaemic control.

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Original articles The ORIGIN Trial Investigators. Basal insulin and cardiovascular and other outcomes in dysglycemia. *N. Engl. J. Med.* doi:10.1056/NEJMoa1203858 | The ORIGIN Trial Investigators. n-3 fatty acids and cardiovascular outcomes in patients with dysglycemia. *N. Engl. J. Med.* doi:10.1056/NEJMoa1203859