Insulin, cardiovascular disease and malignancy, where do we stand?

The major randomized clinical trials assessing the effects of vascular disease and glycemic control (DCCT and UKPDS) have shown that tight glycemic control prevents or postpones the onset of microvascular disease (retinopathy, neuropathy, nephropathy). Death and disability from diabetes however result mainly from macrovascular disease, for which coronary artery disease (CAD) is a major contributor. The evidence for glycemic control and CAD was less forthcoming, falling just short of statistical and clinical significance. A series of studies were therefore carried out to see whether really tight glycemic control would make a difference to the occurrence of CAD. It did, but not in the direction one anticipated. A large scale trial compared the effect of achieving euglycemia on the occurrence of coronary events in elderly people with a risk of vascular disease. It had to be prematurely terminated because those in the intensive treatment arm who had lower glycosylated hemoglobin were found to have more number of coronary events. The results of the ORIGIN trial, published early this year showed that CAD was not prevented by euglycemia, but to allay the suspicions raised by ACCORD trial, showed that it was not increased either.

Similarly, the association of insulin analogs with cancer made a dramatic appearance based on epidemiological studies. There is well known risk of some forms of cancer with diabetes, and vice versa. Also, in our glucose-centric view of insulin action, its effect on cell proliferation via insulin like growth factor has been overlooked. A Lancet consensus statement gave clinical guidelines that the use of insulin should not be deterred by the possible risk of future malignancy, although those with cancer or at risk need to be carefully evaluated about the use of insulin. In addition patients with diabetes mellitus should also be monitored for the occurrence of cancer. The ORIGIN study, which was caught by the insulin analog-cancer imbroglio also found that those using cancer did not have a greater prevalence of cancer in the period under follow up.

Biography

GR Sridhar did his MD (Medicine) from Andhra University and DM (Endocrinology) from All India Institute of Medical Sciences. He is Director of Endocrine and Diabetes Centre, Visakhapatnam. A Fellow of the Royal College of Physicians and Surgeons (Glasgow) and of American College of Endocrinology, he was the President of Research Society for the Study of Diabetes in India (2010) and is currently the Vice President of Endocrine Society of India. He was the founding editor of Indian Journal of Endocrinology and Metabolism. A contributor to major medical textbooks in India, he has more than 250 peer-reviewed publications.

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