Glycemic Control in Diabetes

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One of the central issues in the treatment of patients with diabetes is whether tight glycemic control will reduce Cardio-vascular Disease (CVD) morbidity and mortality. The Diabetes control and complications trial (DCCT) conclusively showed that the greater the average blood glucose in patients with type 1 diabetes, the greater the risk of developing neuropathy, retinopathy and nephropathy.[1] The Diabetes control and complications trial-Epidemiology of Diabetes Interventions Complications (DCCT-EDIC) trial showed that a history of tight glycemic control significantly reduces the rate of CVD.[2]

Data from the Stockholm diabetes intervention study indicated that, in patients with type 1 diabetes, tight control retards the development of atherosclerosis as measured by the development of carotid intima – media thickening.[3] In the United Kingdom Prospective Diabetes Study (UKPDS), a comparison between an intensive treatment group and a conventional treatment group demonstrated a 16% reduction in the risk of fatal and non fatal MI (p=0.052), but all cause mortality did not differ between the two groups.[4] The 10 years follow up of the UKPDS trial showed a reduction of 15% in myocardial events and 13% of death from any cause.[5]

While The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) study concluded that lowered HbA1c value to 6.5% yielded a 10% relative reduction in the combined outcome of major macrovascular and microvascular events primarily as a consequence of a 21% relative reduction in nephropathy.[6] The study also showed no significant effects of the type of glucose control on major macrovascular events (p=0.32), death from cardiovascular causes (p=0.12) or death from any cause (p =0.28).

In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, the mean baseline for HbA1c in the intensive therapy group was 8.3+ 1.1%, while it was 8.3+1.1% in the standard group therapy.[7] During the follow up period, (mean of 5.6 years) the study asked whether a therapeutic strategy targeting normal HbA1c of 6.5% would reduce the rate of cardiovascular events with strategy targeting HbA1c on the range of 7-7.9% in the middle aged and older patients with type 2 diabetes. The investigators in the study concluded that intensive therapeutic strategy increase did not significantly reduce major cardiovascular events. The investigators were forced to end the intensive therapy arm earlier (after 3.5 years) due to high mortality rate in this arm.

The Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes-Steno-2 study compared the effect of a targeted intensified multifactorial intervention with that of conventional treatment on modifiable risk factors for CVD in patients with type 2 diabetes and microalbuminuria during a mean duration of 7.9 years.[8] The multifactorial intensified treatment approach to neutralize the modifiable risk factors (hypertension, dyslipidemia and microalbuminuria) trial succeeded to reduce the risk of cardiovascular and a microvascular event by approximately 50% and the Number Needed for Treatment (NNT) was 5. The target goal for HbA1c in the intensive group was <6.5% and in the conventional group was 6.5-7.5%.

The Glucose Control and Vascular Complications in Veterans with type 2 diabetes Trial (VADT) compared the effects of intensive therapy versus standard glucose control on cardiovascular events.[9] This study showed that after a median follow up period of 5.6 years and median HbA1c of 8.4% in the standard treatment group and a median HbA1c of 6.9% in the intensive treatment group, there was no significant effect on the rate of major cardiovascular events, death or microvascular complications was noticed between the two groups.

Recently, an interesting article by Victor and Merce published in the Annals of internal medicine reviewed the most available trial on types of glucose control regimens, and concluded that such tight glycemic control regimens burden patients with complex treatment regimens, hypoglycemia, weight gain and costs and offer uncertain benefits in return.[10] The authors also recommended keeping HbA1c between 7-7.5% in patients with diabetes.

In my opinion, tight glycemic control targets (HbA1c 6.5-7%) can be kept during the early period of diabetes care and levels between 7-7.5% as a target ca be accepted later on.

Acknowledgements

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