Is a Lower HgA1c Worth the Risk?

Casey Mapes, MD

Story from the Front Lines

A man in his 70s with a history of ischemic stroke, hypertension, OSA, and Type 2 Diabetes Mellitus presented for follow-up. He reported feeling more fatigued and irritable in the past year. He hadn't been checking his blood sugars, but had continued his metformin, glimepiride, and 50 Units of glargine. His HgA1c came back at 5.5%, down from 7.0% 18 months prior, and 8.7% 3 years prior. He denied any loss of consciousness or known hypoglycemic events. He was reluctantly agreeable to resumption of blood sugar checks. His glargine was cut in half and ultimately discontinued entirely as his fasting blood sugars were in the low 100s off of insulin.

Teachable Moment

Goal HbA1c for diabetics has been debated for many years with numerous studies looking at microvascular and macrovascular outcomes with standard (HbA1c <9%) vs. intensive (HbA1c <7%) glycemic control. There is consistent data that intensive glycemic control results in more hypoglycemic events[1-4], with a relative risk of 1.5 to 3[5]. But is the increased risk of hypoglycemia offset by improvements in other outcomes? None of the 4 most prominent trials showed statistically significant reduction of major cardiovascular events within their study periods of 3-10 years[1-4]. There was risk reduction in long-term, observational follow-up starting at 10 years in 3 of these trials[5,6], but only mortality benefit in the UKPDS trial[6], which had a younger patient population and recently diagnosed diabetics[4]. The rest of the trials had older patient populations (average age in the 60s) that had already had diabetes for 10 years[1-3]. Regarding microvascular benefits, only the secondary outcome of a reduction in albuminuria was seen during the initial study periods[1-4]. However, there was decreased microvascular complications beyond 8 years in the follow-up period of UKPDS[1-4]. Thus, tight glycemic control doesn't seem to have clinically important benefits for at least 8 to 10 years. This suggests we should be more cautious with diabetic control in older patients, particularly those with limited life expectancy due to other co-morbidities. Despite this data, it seems there has been little relaxation in treatment, as a study found no changes from 2001 to 2010 in the proportion of adults with HbA1c less than 7% overall or among those with poor health[7]. The patient described above likely will have no mortality benefit from aggressive control based on his age and co-morbidities. It would have been appropriate to reduce his regimen when he last presented 18 months prior, particularly with the down trending HbA1c. Lastly, patient preferences and behaviors must be considered. This patient preferred not to check blood sugars, so continuing insulin could carry significant risk to the point that a higher A1c would be tolerable. He may not have had a severe hypoglycemic episode, but his increased fatigue and irritability was possibly attributable to lower blood sugars.

1. Duckwork W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, et al. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2009 Jan 8;360(2):129-39.
2. Gerstein HC, Miller ME, Byington RP, et al. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008; 358(24):2545–2559.
3. Patel A, MacMahon S, Chalmers J, et al. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008; 358(24): 2560–2572.
4. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998; 352(9131):837–853.
5. Lipska KJ, Krumholz H, Soones T, Lee SJ. Polypharmacy in the aging patient: A review of glycemic control in older adults with type 2 diabetes. JAMA. 2016 Mar 8;315(10):1034-45.
6. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil AW. 10-Year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008 Oct 9;359(15):1577-89.
7. Lipska KJ, Ross JS, Miao Y, Shah ND, Lee SJ, Steinman MA. Potential overtreatment of diabetes mellitus in older adults with tight glycemic control. JAMA Intern Med. 2015 Mar;175(3):356-62.