Dakota Diabetes Coalition is proud to offer this column on diabetes and related concerns every other Friday.

Dr. Johnson is a family practice doctor in Grand Forks with a special interest in diabetes -- and a special knack for writing. As a member of the Dakota Diabetes Coalition, he has generously made himself available to answer questions through our listserv. If you have comments, or questions for Dr. Johnson to address in future columns, please contact gailhand@q.com

DAKOTA DIABETES COALITION

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A1C...

How low should a patient really go?

Some new studies presented at the American Diabetes Association meeting last summer prompted questions about treating A1C levels to previously established targets of <7%.

Let's review the pertinent data, both old and new, to help health care providers make good decisions regarding treatment of their patients with diabetes.

A recent ADA Position Statement, published in the December, 2008 issue of the journal Diabetes Care, is an excellent summary of this data with appropriate recommendations. Likewise, these were also presented at a recent endocrinology conference in San Francisco. In short, for most non-pregnant adults, an A1C of <7% is still a worthwhile target. Let's review the data from pertinent studies:

The Diabetes Control and Complications Trial, DCCT, was published in the New England Journal of Medicine in 1993. In this study, patients

with type 1 diabetes had about a 60% reduction in microvascular, eye, kidney or nerve) complications in the intensive treatment group of A1C ~7% over a 6½ year period. This initial study did not specifically address macrovascular disease such as heart disease and stroke.

The United Kingdom Prospective Diabetes Study (UKPDS, 1998) found similar results in reduction of microvascular complications in intensively treated type 2 diabetes patients. Microvascular complications were reduced by about 25%. However, reductions in macrovascular complications were not as pronounced in this study.

These two landmark studies were part of the basis for the establishment of the American Diabetes Association guideline of treating most non-pregnant adults to an A1C of <7%.

So, what about the relationship of A1C to macrovascular complications? Follow-up studies of the DCCT and UKPDS populations did show **a trend toward reduction of heart disease and stroke,** particularly in the DCCT patients with type 1 diabetes.

Data from three studies were all specifically designed to look at the relationship between **reduction of A1C and the risk of macrovascular** complications such as heart disease and stroke:

- **ACCORD**-Action to Control Cardiovascular Risk in Diabetes, 2008
- **ADVANCE**-Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation
- **VADT**-Veterans Affairs Diabetes Trial

These studies **did not establish a strong relationship** between lowering of A1C and reduction of macrovascular complications – in fact, in the ACCORD study, patients with aggressively lowered A1C had **a higher risk of macrovascular** complications.

ACCORD, ADVANCE and the VADT all looked at patients with type 2 diabetes, and most of these patients had cardiovascular disease risk factors, such as high blood pressure, abnormal cholesterol, and smoking.

All of these other risk factors were treated along with A1C, so it's very **likely that cardiovascular disease risk was different across all groups** -- not *just* those with lowered A1C's. Interestingly, in the ADVANCE study the group with intensively-treated A1C did have lower

rates of kidney disease, a microvascular complication, which is similar to previous studies.

A final study that should be considered is the Steno-2 study (2008), which targeted many risk factors in type 2 patients: A1C, blood pressure, cholesterol, and levels of another blood fat, triglyceride. This study showed that patients with intensive treatment of these risk factors had a **20% decrease in premature death.**

What are we left with to help patients? It's really reasonable to interpret this data as follows:

1) Reduction of A1C is an important tool in reducing microvascular, eye, kidney or nerve, complications in **both type 1 and type 2 diabetes.**

2) Reduction of A1C may reduce macrovascular, heart disease and stroke, **in type 1 patients.**

3) A1C reduction may give only **small** benefit in terms of macrovascular risk reduction in **type 2 patients** -- in fact, aggressive reduction of A1C in patients with strong cardiovascular disease risk factors and a history of poor diabetes control may possibly be **detrimental** (ACCORD). Additionally, aggressive reduction of A1C may **not be appropriate** in certain patient populations -- the **elderly**, those with **life expectancy of less than 3 years,** or those with significant **hypoglycemic unawareness.**

4) Aggressive treatment of other risk factors, such as **cholesterol, blood pressure and smoking are worthwhile strategies** to reduce macrovascular risk in diabetes.

Guidelines for treatment of risk factors in diabetes still have merit, but here's the take home point: **Remember to always address a patient's individual needs, and tailor treatments appropriately.**

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