



# DIABETES, DRUGS AND DECISIONS

By Narendra Singh, MD

**As a kid growing up in Canada, we were all taught about the discovery of insulin by Banting and Best. Insulin has changed the lives of diabetics but it is not a cure.**

In fact, although insulin stabilizes blood sugars, it also causes weight gain and does not reduce heart attacks or improve survival in Type 2 diabetics. Type 1 diabetes is usually identified in childhood and felt to be an autoimmune condition that damages the pancreas where insulin is produced. Type 2 diabetes usually occurs in adulthood, often associated with obesity, and results from decreased insulin production and increased insulin resistance.

Diabetes increases the risk of heart attacks, strokes, renal failure, retinal damage, neuropathy limb amputations and premature death. The goal should always be to prevent diabetes with a combination of diet and exercise. During your annual physical the A1c should be measured. Normal A1c is less than 5.7%. Diabetes begins with an A1c greater than 6.5%. In between, is considered prediabetes. Many drugs have been developed for the treatment of Type 2 diabetes. They all lower A1c but work in different ways. Deciding which ones to use is somewhat challenging.

In general, our first line therapy is metformin. This drug lowers sugars, causes weight loss and improves survival. It should be used with some caution when the kidneys

are impaired. Metformin is also inexpensive. Another inexpensive class of medications are the sulfonylureas ( glyburide, glipizide, glimepiride). Although these drugs also improve sugars, they can be harmful to the heart and should only be considered if other agents are not affordable.

Glitazones have had a mixed history. The first one was taken off the market for liver toxicity, then rosiglitazone (Avandia) was shown to increase heart attacks and heart failure. Pioglitazone (Actos) however is safe for the heart but does cause fluid retention and may increase bladder cancer.

Next came the DPP4 inhibitors. In general, this class of medications is very well-tolerated and safe for the heart but two – saxagliptin and alogliptin can cause fluid retention. Sitagliptin (Januvia) and linagliptin (Trajenta) don't have this concern. While A1c is improved with DPP4's, survival is not.

GLP1 agonists are another class of medications that lower sugar and cause weight loss. They are administered as an injection – twice daily-exenatide (Byetta), daily-liraglutide (Victoza), or weekly extended release exenatide (Bydureon). Liralutide has been shown to also reduce cardiovascular events such as heart attacks and strokes. In its high dose formulation, it has been approved as a weight loss drug (Saxenda). Side-effects include nausea, diarrhea and gastric fullness.

The most exciting new class of drugs for diabetics are the SGLT2 inhibitors (gliflozins). Currently, there are three on the market—empagliflozin (Jardiance) canagliflozin (Invokana) and dapagliflozin (Farxiga). Sorry, I did not create these names! These drugs work by causing excess sugar to be excreted through the urine. In doing so, sugar levels, blood pressure and weight all come down. With empagliflozin these beneficial features result in a 38% reduction in cardiovascular deaths over three years. It is the first diabetes drug to be approved by the FDA to reduce mortality. Canagliflozin also has the same benefits on the heart but unfortunately increase limb amputations two-fold and therefore must be used with caution. Other side effects to watch for are bladder and yeast infections.

So, while diabetes prevention is the key, it's nice to know that many options beyond insulin now exist. ■

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