Type 2 Diabetes:

The Whys and Hows of Prevention

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Type 2 diabetes has become an epidemic. It is estimated that the incidence of Type 2 diabetes will increase 72% between 2003 and 2025, rising from 189 million people to 324 million people around the world. In North America, there will be a 59% increase from 25 million people to 39.7 million people.[1] The estimated lifetime risk of developing diabetes for US citizens born in 2000 is 32.8% for men and 38.5% for women.[2]

Based on a 2002 study in the US by the American Diabetes Association, it was estimated that the cost of diabetes in Canada will rise from $13.2 billion in 2002 to $19.2 billion by 2020.[3]

Five conditions to developing a prevention program

The American Di… have…

…ally development and …tory of the disease should be established to allow prediction and proper disease progression follow-up. There is evidence showing the development of Type 2 diabetes and its strong relation to hyperglycemic states of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), especially if other factors such as age, family history, waist-to-hip ratio, body mass index (BMI), high blood pressure and abnormal lipid levels are taken into consideration.

What else do the studies show about diabetes prevention and treatment?

In established cases of Type 2 diabetes, studies like the United Kingdom Prospective Diabetes Study (UKPDS) 35 have shown that control of blood glucose can somewhat prevent the development and progression of diabetic complications. However, this beneficial effect of treatment is more marked for the microvascular complications than for the macrovascular ones. For instance, it is estimated (by UKPDS 35) that a 1% drop in glycated hemoglobin (A1C) will … decrease microvascular endpoints … will decrease myocardial …

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…over …test was in the …ance (7.8 mmol/L to …and by 99% if it was in the diabetic …ge (≥ 11 mmol/L), indicating that even small changes in glucose metabolism is associated with major deleterious effects.

Thus, a very important question can be raised:

Can we prevent or delay the development of Type 2 diabetes mellitus and hopefully prevent or delay the development of its complications?

3. There should be a test to detect the predisease state that is safe, acceptable, widely available and predictive. Two tests meet these criteria: measurement of fasting plasma glucose (FPG) and the two-hour value in the oral glucose tolerance test (OGTT).

4. There should be safe, effective and reliable methods to prevent or delay the disease from occurring.There are now interventions capable of at least delaying the onset of Type 2 diabetes.

5. The effort to find individuals who are at high risk of getting the disease and the cost of the interventions should not be burdensome and should be cost-effective. This condition has yet to be established. There is support for opportunistic screening (*i.e.*, screening during routine health-care system encounters) as the most cost-effective way to find individuals at risk for diabetes. It is usually recommended to use the standard FPG value and/or the plasma glucose values obtained two hours after a 75-g glucose load. More recently, Johnson *et al*. used a simulated program and concluded that a random plasma glucose cut point of 7.2 g performed every three years would provide a good yield and minimize false-positive screening tests and costs in a US population aged 45 to 74 years, but this remains to be confirmed.[5]

Furthermore, in order to be more cost-effective, screening should also be done in subjects who are at higher risk. The Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada offers some recommendations:

- All individuals should be evaluated annually for risk on the basis of demographic and clinical criteria.
- Screening, using an FPG, should be performed every three years for individuals older than age 40, but more frequent and/or earlier testing with an FPG or a two-hour plasma glucose (2hPG) in a 75-g OGTT should be considered in people with additional risk factors for diabetes:
  - First-degree relative with diabetes
  - Member of high-risk population (*e.g.*, people of Aboriginal, Hispanic, Asian, South Asian or African descent)
  - History of IGT or IFG
  - Presence of complications associated with diabetes
  - Vascular disease
  - History of gestational diabetes
  - History of delivering of a macrosomic infant
  - Hypertension
  - Dyslipidemia
  - Overweight
  - Abdominal obesity
  - Polycystic ovary syndrome
  - Acanthosis nigricans
  - Schizophrenia
- Testing with a 2hPG in a 75-g OGTT should be considered in individuals with an FPG of 5.7 mmol/L to 6.9 mmol/L in order to identify individuals with IGT or diabetes.

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How should diabetes be prevented?

Traditionally, lifestyle modifications (diet and exercise) have been the cornerstone of diabetes prevention. More recently, pharmacologic interventions have been studied.

Lifestyle intervention

The largest intervention study was the Diabetes Prevention Program (DPP), conducted in 3,234 subjects with impaired glucose tolerance, a mean age of 50.5, a mean BMI of 34 and a mean follow-up period of 2.8 years.

The intensive lifestyle intervention included structured education and individualized medical nutrition therapy, resulting in 150 minutes of physical activity per week and a 7% weight loss. The participants in the control group were given only information on healthy eating habits and exercise. The absolute risk of developing diabetes was 11% per year in the control group and diminished to 4.8% with lifestyle intervention—a 58%

Lifestyle modification or medication: which one?

Since greater benefits in diabetes prevention were observed in the studies with weight loss and physical activity, the American Diabetes Association recommends that modest weight loss (5% to 10% body weight) and modest physical activity (30 minutes daily) should be the recommended goals for the prevention of Type 2 diabetes. It is also suggested that health-care providers urge, at every opportunity, all overweight or sedentary individuals to adopt the appropriate lifestyle changes. However, one must realize that the lifestyle interventions, which were effective in the Diabetes Prevention Program (DPP) and in the Finnish Diabetes Prevention Study (DPS) were intensive, interdisciplinary and individualized in such a way as to achieve the weight loss.

The cost of lifestyle intervention was $3,540 per participant for three years in the DPP. Truly implementing these lifestyle modifications will require more than what is usually done by a physician during a standard medical visit.

Nevertheless physicians must realize that they have a crucial role to play in diabetes prevention. In a recent review on diabetes prevention, Davies *et al*. concluded that since the most beneficial population-based measures are to encourage increased physical activity and decreased consumption of energy-dense foods, needing the government and research to influence changes in transport, food and education policy, particularly targeting school children and young people. Obviously, this should be part of the program that must be developed and implemented to stop the growing obesity problem in many parts of the world, including Canada.

reduction in incidence, which can also be translated by the fact that seven subjects with IGT would need to be treated for three years with the lifestyle intervention to prevent one case of diabetes.

A similar 58% annual reduction in incidence was also observed in the Finnish Diabetes Prevention Study (DPS), conducted in 522 subjects older (mean age of 55) and somewhat less obese (mean BMI of 31) than those in the American study. The intervention study was designed to add 210 minutes of physical activity per week and to lose at least 5% of body weight.

Pharmacologic interventions

In the DPP, metformin, 850 mg, twice daily was also given to a group of subjects. The incidence of diabetes was diminished to 7.8% per year—a 31% annual reduction in comparison to the 11% incidence found in the placebo group. Fourteen subjects with IGT would need to be treated with metformin for three years to prevent one case of Type 2 diabetes. Moreover, placebo was as effective as metformin in subjects with a BMI less than 30, who were older than age 60 or who had an FPG less than 6.1 g.

In the Study TO Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial, 1,429 subjects with IGT received either acarbose, an a-glucosidase inhibitor, or placebo over a mean period of 3.3 years. The incidence of diabetes was diminished by 25% by the active drug, the incidence of diabetes per year in each group being 12.7% and 9.7%, respectively. Based on the cumulative incidence of diabetes in each group, 11 subjects with IGT would need to be treated with acarbose for 3.3 years to prevent one case of diabetes.

Along with the two studies carried out with agents currently in use for diabetes treatment, other drugs have also been associated with a reduced incidence of diabetes in comparison to others. This has been the case in different studies conducted with many angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists, with the weight loss medication orlistat and even with pravastatin in hyperlipidemic patients, but, in the last case, 111 subjects will need to be treated for 5.5 years to prevent one case of diabetes.

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