Is prevention of type 2 diabetes possible?

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Type 2 diabetes has reached epidemic proportions in Australia and around the world. Prevention and treatment of this costly disease have become an important focus of healthcare. Lifestyle and pharmacological interventions have been shown to be effective in the prevention of diabetes.

Key points

- **A number of type 2 diabetes prevention trials have shown that diabetes can be prevented with varying degrees of success depending on the intervention.**
- **Interventions for the prevention of diabetes fall into two categories: lifestyle and pharmacological.**
- **Current recommendations for diabetes prevention include the referral of high-risk patients to a lifestyle modification program.**
- **Pharmacological treatment may be considered in patients not responding to a lifestyle modification program, although adverse effects should be carefully weighed against the benefits.**
- **Awareness and education will play a major role in diabetes prevention as we move into the future.**

ENDOCRINOLOGY TODAY 2013; 2(3): 32-34

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Diabetes is associated with high morbidity, mortality and cost and is frequently asymptomatic until complications develop. The prevalence of diabetes is reaching epidemic proportions in both the developed and developing worlds, and it is estimated that up to half of people with diabetes are unaware of their condition. For these reasons diabetes prevention has become an important focus for healthcare providers and patients at risk of developing diabetes.

Is prevention possible?

A number of type 2 diabetes prevention trials performed over the past 20 years that have shown that diabetes can be prevented with varying degrees of success depending on the intervention. These interventions fall into two broad categories: lifestyle and pharmacological.

For lifestyle intervention four major studies are notable. The China Da Qing Diabetes Prevention Study was the first large-scale diabetes prevention trial. Completed in 1992, it investigated Chinese people with impaired glucose tolerance.[1] After a six-year lifestyle intervention program there was a 51% reduction in diabetes compared with the control group. Similarly, the Diabetes Prevention Program (DPP) in the USA,[2] the Finnish Diabetes Prevention Study (DPS)[3] and the Indian Diabetes Prevention Programme (IDPP)[4] all showed a decreased incidence of diabetes with lifestyle intervention of 58%, 58% and 28%, respectively, compared with controls (see Figure).[5] In general, lifestyle modification in these studies consisted of dietary and exercise counselling with weight reduction goals of 5% body weight and regular moderate exercise. Patient contact was variable over the course of these trials, ranging from monthly to six monthly.

Diabetes prevention trials focusing on pharmacological intervention have been performed with nearly every class of glucose-lowering agent available. The most significant of these include metformin, which showed a 31% decrease in the incidence of diabetes in the DPP,[5] and a 26% decrease in the IDPP.[4] The Study

to Prevent Noninsulin-dependent Diabetes Mellitus showed that acarbose reduced the incidence of diabetes by 25%.[6] The glitazones have proved very effective with reductions in diabetes ranging between 55% and 78%, although these agents have unfortunately been associated with significant adverse effects.[7,8] Ongoing trials with insulin, incretin-based therapies and combination therapies are under way. Bariatric surgery has also been shown to be highly effective in preventing diabetes in the morbidly obese.[9]

Diabetes prevention programs are effective in reducing the incidence of diabetes over a few years and there is increasing evidence that the benefits of lifestyle modification programs are sustainable. Follow up of the Da Qing study showed a 43% decrease in the incidence of diabetes compared with the control group up to 14 years after the intervention.[10] Similarly, the Finnish DPS study showed a 36% reduction and the US DPP a 34% reduction after extended follow up.[11,12]

With regards to diabetes complications, it is important to note that these trials were not designed or powered to look at microvascular or macrovascular events. Cardiovascular outcomes from these trials so far have shown little change despite improvements in cardiovascular risk factors. The Da Qing study follow up showed no significant reduction in cardiovascular events or mortality.[10] There was a significant 47% reduction in severe retinopathy but no decrease in neuropathy or nephropathy.[13] Similarly, the DPS, DPP and IDPP have all shown decreases in cardiovascular risk factors but not, as yet, events.

How do we manage high-risk patients?

Lifestyle intervention

Current recommendations for diabetes prevention include the referral of high-risk patients to a lifestyle modification program. The Prevention of Type 2 Diabetes Prevention Program is an initiative of the council of Australian Governments that was set up to detect people at high risk of developing diabetes and to provide advice and access to lifestyle modification program interventions where appropriate. There are some government subsidised lifestyle modification programs available in Australia run by accredited lifestyle modification program providers (http://www.measureup.gov.au/internet/abhi/publishing.nsf/Content/OrderGP).

There are also diabetes prevention resources available for primary care including Medicare item numbers for assessment of disease risk, and resources such as Lifescript (http://www.health.gov.au/lifescripts) and RESET. Further information is available on the Department of Health and Ageing website (http://www.health.gov.au/).

These lifestyle modification programs generally should be trialled for at least six months before pharmacological intervention. These programs focus on weight loss, diet, physical activity and behavioural therapy. Further information regarding local lifestyle modification programs is usually available through local divisions of general practice.

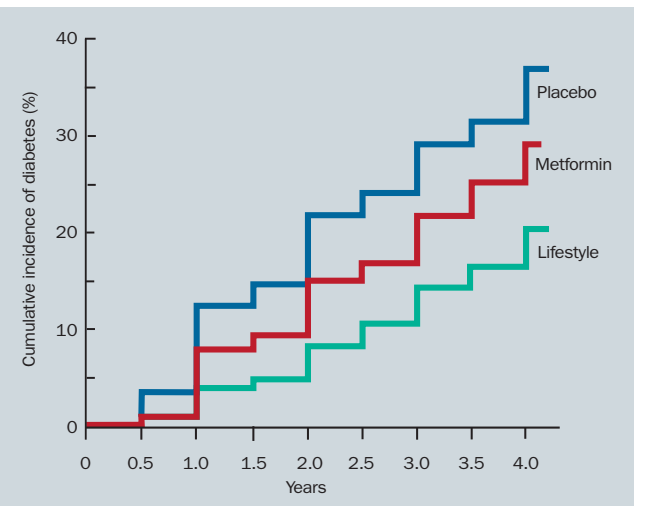

Figure. Cumulative incidence of diabetes according to study group.[5]
Reproduced with permission from Knowler WC, Barrett-Connor E, Fowler SE, et al. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.[5]

Pharmacological intervention

Pharmacological intervention may be considered for diabetes prevention in patients not responding to a lifestyle modification program, although adverse effects should be carefully weighed against benefits. Metformin is commonly used in this setting because its side effects are infrequent and mostly consist of mild gastrointestinal intolerance. Use of metformin in people with prediabetes or for the prevention of diabetes is not recognised by regulatory authorities in Australia and this off-label use should be discussed with the patient. Other agents such as glitazones, sulfonylureas and insulin are not generally recommended in this setting, particularly as they promote weight gain, hypoglycaemia and, in the case of the glitazones, fluid retention and bone loss. Acarbose has been used successfully in clinical trials but has a high side effect profile and is generally not well tolerated for prolonged periods.

In clinical practice, the use of glucose-lowering agents for diabetes prevention may be considered but is not currently recognised as best practice. Patients who are unable or unwilling to participate in lifestyle modification programs should be monitored for the development of both diabetes and cardiovascular disease. Attention to cardiovascular risk reduction is of primary importance in people at high risk of developing diabetes. Glucose levels should be monitored at least annually with fasting glucose or glucose tolerance testing. Subsequent development of diabetes should then be managed according to clinical guidelines, including the use of glucose-lowering agents if necessary for adequate glycaemic control.

Prevention at a community level

It is unlikely that lifestyle modification programs will make a significant impact on the rate of diabetes in the community, and despite strong messages from the health sector we continue to see further rises in this epidemic. At a community level health promotion activities are needed to help in the prevention of diabetes. Programs for diabetes prevention are currently in place in schools, work places and in the mainstream media. Awareness and education will play a major role as we move into the future. Our society is currently designed around busy city living and this has created a 'toxic' environment that promotes obesity and its metabolic consequences. Urban planning and legislation need to be considered by the government to address the complex issues surrounding poor diet and lack of regular exercise in the modern world.

Are these interventions cost effective?

The costs associated with the management of diabetes are high and increase with complications. The direct and indirect health cost per patient in Australia is estimated at about AU$4000 per year for diabetes with no complications and over AU$9000 for patients with diabetes and both microvascular and macrovascular complications. Similar to all medical treatments, the cost of the intervention to prevent diabetes needs to be carefully evaluated for its economic impact and value for money. Several cost effectiveness studies have been published showing that lifestyle modification programs are more cost effective than pharmacological therapy. An Australian study has shown the cost per quality-adjusted life year of a lifestyle modification program is about AU$50,000 making this a cost-effective intervention.[14] A recent US publication from the DPP showed that lifestyle modification programs and metformin represent good value for dollars spent with both programs costing US$10,000 per quality-adjusted life year gained.[15]

Conclusion

Diabetes prevention in high-risk patients is effective using lifestyle modification programs or pharmacotherapy with most glucose-lowering agents. Lifestyle modification programs are cost effective in high-risk groups and recommended for at least six months before consideration of pharmacotherapy for diabetes prevention. Pharmacological agents such as metformin are used off label for diabetes prevention and their use in this setting must be carefully weighed against adverse effects. Education, health promotion and government interventions at a society level will be important to slow the progressive rise of diabetes and its consequences as we move into the future. **ET**

References

1. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997; 20: 537-544.
2. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006; 29: 2102-2107.
3. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344: 1343-1350.
4. Ramachandran A, Snehalatha C, Mary S, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2006; 49: 289-297.
5. Knowler WC, Barrett-Connor E, Fowler SE, et al. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.
6. Chiasson JL, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 2002; 359: 2072-2077.
7. Gerstein HC, Yusuf S, Bosch J, et al. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet 2006; 368: 1096-1105.
8. Knowler WC, Hamman RF, Edelstein SL, et al. Prevention of type 2 diabetes with troglitazone in the Diabetes Prevention Program. Diabetes 2005; 54: 1150-1156.
9. Long SD, O'Brien K, MacDonald KG, et al. Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes. A longitudinal interventional study. Diabetes Care 1994; 17: 372-375.
10. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008; 371: 1783-1789.
11. Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, Christophi CA, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009: 374: 1677-1686.
12. Lindström J, Peltonen M, Eriksson JG, et al; Finnish Diabetes Prevention Study (DPS). Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). Diabetologia 2013; 56: 284-293.
13. Gong Q, Gregg EW, Wang J, et al. Long-term effects of a randomised trial of a 6-year lifestyle intervention in impaired glucose tolerance on diabetes-related microvascular complications: the China Da Qing Diabetes Prevention Outcome Study. Diabetologia 2011; 54: 300-307.
14. Colagiuri S, Walker AE. Using an economic model of diabetes to evaluate prevention and care strategies in Australia. Health Aff (Millwood) 2008; 27: 256-268.
15. Diabetes Prevention Program Research Group. The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: An intent-to-treat analysis of the DPP/DPPOS. Diabetes Care 2012; 35: 723-730.

COMPETING INTERESTS: None.