HIGHLIGHT

Type 2 diabetes – preventable, but how?

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The prevalence of diabetes is rapidly increasing worldwide and has been estimated to double within the next 25 years, presumably affecting almost 300 million people in 2025 (1). More than 80% will suffer from type 2 diabetes, which is caused by combined defects in insulin secretion and action. Tuomilehto *et al.* (2) recently showed for the first time in a properly designed and conducted randomised, controlled trial that the disease may be prevented. In the Finnish Diabetes Prevention Study they were able to lower the cumulative incidence of diabetes by 58% by the use of lifestyle counselling in subjects with impaired glucose tolerance (IGT) and a high risk for diabetes.

Although there is ample evidence that a genetic predisposition is important in the development of type 2 diabetes, the rapid increase in prevalence in almost every region of the world shows that environmental factors are of major importance. Epidemiological studies have clearly identified overweight and a sedentary lifestyle as two of the most important environmental factors associated with the development of the disease (3–5). Not surprisingly, weight reduction and physical exercise have therefore long been advocated by many to prevent type 2 diabetes. However, as is the case for prevention of cardiovascular disease, it has been difficult to prove scientifically that preventive strategies based on changes in lifestyle significantly lower the incidence of type 2 diabetes (6).

Ten years ago, Eriksson & Lindgarde (7) in Malmö, Sweden reported the results of a 6-year, non-randomised, lifestyle intervention study in subjects with IGT. The counselling emphasised primarily the importance of physical exercise, but the participants also received dietary advice. The incidence of type 2 diabetes was significantly reduced from 4.3% per year to 1.3% per year. Furthermore, in a follow-up study performed after 12 years and published in 1998 (8), the authors reported a reduced mortality rate from 14% in IGT subjects who had not received any special advice to 6.5% in subjects who had participated in the intervention programme. It is noteworthy that active intervention only lasted for 6 years and during the last 6 years of follow-up the intervention group had not received any specific lifestyle counselling.

In 1997 Pan *et al.* (9) reported from China that lifestyle counselling based on diet and exercise (alone or in combination) reduced the progression to diabetes in 577 IGT subjects from almost 68% to around 43%

during a 6-year study period. The subjects attended prevention clinics that were randomly allocated to perform counselling on diet, exercise, both or none (control group), but subjects were not randomly allocated to different follow-up groups on an individual basis.

With this background, it is with considerable enthusiasm that we now receive the report from The Finnish Diabetes Prevention Study Group (2). They have found that lifestyle intervention with counselling on diet and physical exercise was able to reduce the incidence of diabetes by 63% in men and 54% in women during a 4-year period. The study randomly allocated 523 subjects with IGT to one of two treatment groups in five centres in Finland between 1993 and 1998. The subjects in the intervention group were given detailed advice about diet and exercise, aimed at reducing weight by 5% or more and increasing the level of physical activity. The dietary advice was tailored to each subject and given during seven sessions with a nutritionist during the first year of the study and one session every 3 months thereafter. Total intake of fat should be less than 30% of energy consumed, and intake of saturated fat less than 10%. Fibre intake was recommended to increase to at least 15 g/1000 kcal. Moderate exercise for at least 30 min per day was advocated, especially in the form of endurance exercise, to improve cardio-respiratory fitness.

The results showed that the mean weight in the intervention group decreased by 4.2 ± 5.1 kg after 1 year and by 3.5 ± 5.5 kg after 2 years, compared with a reduction of 0.8 ± 3.7 kg and 0.8 ± 4.4 kg in the control group. Both fasting glucose levels and glucose levels 2 h after an oral glucose tolerance test decreased significantly during the study in the intervention group, but increased in the control group. Diabetes was diagnosed in 27 subjects in the intervention group and 59 in the control group, giving a cumulative incidence of diabetes after 4 years of 11% (95% confidence interval 6–15%) in the intervention group and 23% (17–29%) in the control group. When the subjects were ranked according to their success in achieving the goals of the intervention advice, there was a strong inverse correlation between the success score and the incidence of diabetes. Diabetes did not develop in any of the 49 subjects in the intervention group who reached at least four of the primary goals (weight reduction >5%, fat intake <30% of energy

intake, saturated-fat intake <10% of energy intake, fibre intake ≥ 15 g/1000 kcal and exercise >4 h/week). In the control group, 15 subjects achieved at least four of the primary goals, and none developed diabetes. A total of 40 subjects withdrew from the study, 27 for personal reasons.

The authors conclude that it is possible to prevent one case of diabetes for every five subjects with IGT who are subject to non-pharmacologic intervention for 5 years in a primary health care setting. This should be good news for subjects with IGT, for health personnel involved in preventive medicine and, not least, for health authorities facing the increasing burden of diabetes on health care budgets. However, some consideration of the interpretation of the results may be justified. First, the preventive effect was shown in a high-risk population estimated to have a cumulative incidence of diabetes of 35% during a 6-year period. To identify subjects in this risk category will require extensive use of oral glucose tolerance tests in high-risk subjects. The prevalence of IGT among adults in Europe varies between 3 and 10% (10), and it has been estimated that screening of a high-risk population yields one subject for every ten screened who may be suitable for an intervention programme (11).

The second concern is whether the effect obtained represents prevention of diabetes or merely a delay of the onset of hyperglycaemia. Will these measures prevent the vascular complications of the disease? It is reasonable to expect that the onset of microvascular complications will be significantly delayed, as the frequency of these complications is closely related to the degree and duration of hyperglycaemia (12, 13). However, the effect of similar preventive measures on cardiovascular disease are more uncertain. Hyperglycaemia is only one out of several important risk factors for macrovascular disease in diabetes (14, 15) and cardiovascular disease is prevalent in IGT subjects even before they develop diabetes (16). Although the lifestyle changes introduced in the study have the potential to lower several of the known modifiable risk factors for macrovascular disease, it remains to be proven whether these measures will prevent cardiovascular morbidity and mortality.

The optimistic results of lifestyle counselling shown by Tuomilehto and co-workers (2) increase the focus on the results of two large multi-centre studies evaluating whether pharmacological treatment with metformin (17) or acarbose (11) will prevent diabetes in subjects with IGT. The data from these studies are awaited next year, and will raise an important discussion about how diabetes can be prevented in a most cost-effective way. Lifestyle counselling can be quite expensive and hopefully the Finnish Diabetes Prevention Study Group will provide some health economic data from their study. Furthermore, the discussions concerning the best way to prevent diabetes should include considerations about

the 'medicalisation' of healthy subjects and the possible side-effects of drugs.

The last, and possibly most important concern, is whether the results from this individually tailored lifestyle counselling in a high-risk population performed by highly qualified and motivated physicians and nurses can be reproduced in an ordinary General Practice setting. If so, this would be a major step towards the prevention of type 2 diabetes. It also remains to be studied whether population-based programmes aimed at changing lifestyle in a healthy direction can achieve similar results as individual counselling. So far, such population-based strategies aiming at reducing cardiovascular disease have been rather disappointing (18). The study by Tuomilehto *et al.* (2) adds important knowledge about preventing type 2 diabetes, and further studies will show whether we are able to implement such strategies in a way that will prevent the global epidemic of diabetes.

References

- King H, Aubert RE & Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998 **21** 1414–1431.
- Tuomilehto J, Lindström J, Eriksson J, Valle T, Hämäläinen H, Ilanne-Parikka P *et al.* Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine* 2001 **344** 1343–1350.
- Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS *et al.* Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991 **338** 774–778.
- Chan JM, Rimm EB, Colditz GA, Stampfer MJ & Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care* 1994 **17** 961–969.
- Ohlson LO, Larsson B, Bjorntorp P, Eriksson H, Svaldsudd K, Welin L *et al.* Risk factors for type 2 (non-insulin-dependent) diabetes mellitus. Thirteen and one-half years of follow-up of the participants in a study of Swedish men born in 1913. *Diabetologia* 1988 **31** 798–805.
- Nilsson P & Berglund G. Prevention of cardiovascular disease and diabetes: lessons from the Malmo Preventive Project. *Journal of Internal Medicine* 2000 **248** 455–462.
- Eriksson KF & Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. *Diabetologia* 1991 **34** 891–898.
- Eriksson KF & Lindgarde F. No excess 12-year mortality in men with impaired glucose tolerance who participated in the Malmo Preventive Trial with diet and exercise. *Diabetologia* 1998 **41** 1010–1016.
- Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX *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.
- King H & Rewers M. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. WHO Ad Hoc Diabetes Reporting Group. *Diabetes Care* 1993 **16** 157–177.
- Chiasson JL, Gomis R, Hanefeld M, Josse RG, Karasik A & Laakso M. The STOP-NIDDM Trial: an international study on the efficacy of an alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design, and preliminary screening data. Study to Prevent Non-Insulin-Dependent Diabetes Mellitus. *Diabetes Care* 1998 **21** 1720–1725.

- 12 Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. *Diabetes Care* 1995 **18** 258–268.
 - 13 Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal* 2000 **321** 405–412.
 - 14 Laakso M. Hyperglycemia and cardiovascular disease in type 2 diabetes. *Diabetes* 1999 **48** 937–942.
 - 15 Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR & Holman RR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). *British Medical Journal* 1998 **316** 823–828.
 - 16 Fontbonne A, Thibault N, Eschwege E & Ducimetiere P. Body fat distribution and coronary heart disease mortality in subjects with impaired glucose tolerance or diabetes mellitus: the Paris Prospective Study, 15-year follow-up. *Diabetologia* 1992 **35** 464–468.
 - 17 The Diabetes Prevention Program Research Group (TDPPR) The Diabetes Prevention Program. Design and methods for a trial in the prevention of type 2 diabetes. *Diabetes Care* 1999 **22** 623–634.
 - 18 Thelle D. Prevention of cardiovascular diseases – a scientific dilemma. *Scandinavian Cardiovascular Journal* 2000 **34** 103–105.
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