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Managing diabetes

MANAGEMENT ISSUES – STARTING TREATMENT WHERE THE TYPE OF DIABETES IS NOT CLEAR

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Diabetes mellitus is classified as primary (type 1 and type 2 diabetes), secondary and other types. Primary diabetes constitutes the majority of cases of diabetes seen in clinical practice,[1,2] of which more than 90% will be type 2. A distinction between type 1 and type 2 diabetes is important, as therapy differs.

Type 1 diabetes is characterised by an early age of onset (under 35 years), lean body mass, absolute insulinopenia, susceptibility to ketosis, presence of autoantibodies and insulin dependence, with insulin therapy being life-saving. In contrast late age of onset, obesity, insulin resistance, hyperinsulinaemia (earlier on) and control by diet with or without oral agents are the hallmarks of type 2 diabetes.[1,2]

In the majority of cases classification into type 1 and type 2 diabetes can be made on clinical grounds. However, there are instances when a distinction is not clear-cut. Evaluation of endogenous insulin secretion in response to beta-cell secretagogues (e.g. glucagon) and measurement of islet cell autoantibodies (e.g. glutamic acid decarboxylase (GAD) antibodies and islet-cell antibodies) may be helpful, but these tests are not widely available.[2] In addition, GAD antibodies are not as common in non-Caucasoids as in Caucasoids with type 1 diabetes.[2] Hence clinical judgement will often be the determining factor in deciding on the type of diabetes and with which form of therapy to start.

A subacute onset, obesity and a family history of type 2 diabetes in a first-degree relative will favour a diagnosis of type 2 diabetes. Co-existing hypertension or dyslipidaemia would also support this diagnosis. Type 2 diabetes commonly presents in persons older than 35 years, but it may also present in adolescence or earlier, particularly in the obese. In recent years there has been a significant increase in the incidence of type 2 diabetes with onset in youth.[3] Type 1 diabetes may also present in middle age or later (latent autoimmune diabetes of adults (LADA)).[1,2]

While presentation with ketoacidosis classically occurs in type 1 diabetes, many patients may have a subacute onset characterised by polyuria, polydipsia, polyphagia and loss of weight with a good appetite. Absence of a family history, younger age and lean body mass would suggest type 1 diabetes and insulin therapy should be commenced.

Hyperosmolar non-ketotic coma may be a presenting feature of type 2 diabetes. In such cases insulin therapy is instituted in the acute phase, after which control will be achieved with oral hypoglycaemic agents.

Occasionally patients with newly diagnosed type 2 diabetes present with profound loss of weight. In such cases insulin therapy should be instituted for about 3 months, after which oral agents may be substituted.

In summary, where a clinician is in doubt as to the type of diabetes, leanness or obesity, presence or absence of a family history of diabetes and to an extent age will help decide which therapy to institute.

References

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PREVENTION OF TYPE 2 DIABETES — EVIDENCE FROM RECENT TRIALS

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Diabetes presents a significant burden to individuals, families, communities and the health services due to its morbidity, premature mortality and economic costs. This burden is likely to increase given the projected rates of rise in prevalence of diabetes throughout the world, particularly in developing countries. Of note is that even impaired glucose tolerance is associated with increased mortality.

Given the consequences of diabetes and the evidence that treatment does not avert all its sequelae, it is not surprising that attention has been given to prevention of this disease. A number of well-designed and conducted studies which examine whether type 2 diabetes can be prevented or delayed have recently been reported involving people at high risk for diabetes. These are summarised in Table I.

Da Qing Study[1]

This study was conducted in the city of Da Qing, China, on 530 people with impaired glucose tolerance (2-hour glucose level of 7.8 - 11 mmol/l in an oral glucose tolerance (OGTT) test. The participants were randomised to one of four groups: diet alone, exercise alone, diet and exercise, and control. At 6 years the intervention reduced the risk of development of diabetes by 31%, 46% and 42% respectively compared with the control group, with no significant difference between groups.

Finnish Diabetes Prevention Study (DPS)[2]

The DPS randomised 522 overweight people (body mass index (BMI) $\geq$ 25, mean BMI 31), aged 40 - 60 years (mean age 55 years) with impaired glucose tolerance to a lifestyle intervention or control group. Multiple sessions of individualised counselling were used in the intervention group with the goal of achieving a reduction of weight of 5%, a total fat intake of < 30% of energy consumed, a saturated fat intake of < 10% of energy consumed, an increase in fibre of at least 15 g/1 000 kilocals and moderate exercise of at least 30 minutes per day. At a mean of 3.2 years, the risk of diabetes was reduced by 58% in the intervention group. The reduction in incidence of diabetes was directly associated with the degree of success in achievement in the goals set for lifestyle changes.

Diabetes Prevention Programme (DPP)[3]

The DPP was conducted in the USA in 3 234 subjects with impaired glucose tolerance who were aged at least 25 years (mean age 51 years) with a BMI $\geq$ 24 in non-Asians or BMI $\geq$ 22 in Asians (mean BMI 34) and a fasting glucose of 5.3 - 6.9 mmol/l. Overall the participants were younger in the DPP than the DPS but more obese and included approximately 45% from Afro-American and Hispanic communities. Subjects were randomised to one of three interventions:
- standard lifestyle intervention plus metformin 850 mg twice daily
- standard lifestyle recommendations plus placebo twice daily or
- an intensive programme of lifestyle modification.

The goals in the intensive lifestyle modification group were to achieve and maintain a weight reduction of at least 7% of initial body weight through a low-fat low-calorie diet and moderate physical activity of at least 150 minutes per week. This intensive programme was delivered by means of a 16-lesson curriculum taught by case managers on a one-to-one basis during the first 6 months. Subsequent regular sessions were continued throughout the duration of the study.

The intensive lifestyle intervention was significantly more effective in reducing diabetes incidence (58% reduction) than metformin (31% reduction) compared with placebo

Table I. Randomised type 2 prevention trials

	Da Qing	DPS	DPP	STOP-NIDDM	TRIPOD
No. of patients	530	522	3 234	1429	236
Age (mean)	45	55	51	54	34
BMI (mean)	25.8	31	34	31	30
Entry criteria Fasting glucose (mmol/l)		< 7.8	≥ 5.3 - 6.9	5.6 - 7.7	Previous gestational diabetes
2-hr glucose post GTT (mmol/l)	7.8 - 11	7.8 - 11	7.8 - 11	7.8 - 11	
Intervention	Diet Diet + exercise Exercise	Intensive diet plus exercise	Intensive diet plus exercise Metformin 850 mg bd	Acarbose 100 mg tds	Troglitazone 400 mg daily
Results (percentage reduction compared with placebo)	Diet 31% Exercise 46% Diet plus exercise 42%	Intensive diet plus exercise 58%	Intensive diet plus exercise 58% Metformin 31%	25%	56%

at an average follow-up of 2.8 years. When metformin was withdrawn for a 2-week period and the OGTT repeated, its effect on the incidence of diabetes was reduced from 31% to 25% in the metformin arm.

On average 74% of the lifestyle group maintained the exercise goal and 50% the weight reduction goal.

STOP-NIDDM Trial[4]

This trial randomised 1 429 subjects with impaired glucose tolerance and a BMI of 25 - 40 who were aged 40 - 70 years and had a fasting blood glucose of 5.6 - 7.7 mmol/l to either placebo or acarbose (an alpha glucosidase inhibitor) in a dose of 100 mg three times daily. The subjects had a mean BMI of 31 and mean age of 55 years. After a mean follow-up of 3.3 years, there was a 25% reduction in progression to dia-

betes in the acarbose group.

Troglitazone in Prevention of Diabetes (TRIPOD) Study)[5]

The TRIPOD study evaluated the effects of pharmacological intervention on progression to diabetes in 236 Hispanic women with previous gestational diabetes. They were randomised to troglitazone (a thiazoledinedione now withdrawn from commercial sale due to hepatotoxicity) in a dose of 400 mg daily or placebo. During a median follow-up at 2.5 years there was a 56% reduction in the progression to diabetes. Furthermore these effects persisted after an 8-month washout period. This might suggest that troglitazone may affect the natural history of glucose intolerance.

Conclusion

Type 2 diabetes can clearly be delayed, but whether it can be pre-

vented, or whether the delay reduces long-term mortality or morbidity remains to be proven. The use of simple clinical indicators to identify patients at high risk for diabetes are much more practical than the use of OGTTs to determine the presence of impaired glucose tolerance. These indicators include BMI ≥ 25, family history of diabetes, decreased physical activity, previous gestational diabetes, polycystic ovarian syndrome, age more than 45 years, hypertension, and raised cholesterol. Such patients should be afforded basic instruction on increased physical activity, healthy eating, and modification of other risk factors for ischaemic heart disease. At present, phamacotherapy is not warranted except in those individuals requiring specific therapy for fertility in polycystic ovarian syndrome.

References available on request.