

TYPE 2 DIABETES: AN EVIDENCE-BASED APPROACH TO ITS MANAGEMENT BY THE FAMILY PRACTITIONER

The rising incidence of type 2 diabetes mellitus is linked to the increase in obesity.

GBOYEGA ADEBOLA OGUNBANJO

MB BS, MFGP (SA), MFamMed (MEDUNSA), FACRRM, FACTM, FAFP (SA)

Associate Professor and Deputy Dean: Research

Faculty of Medicine

University of Limpopo (Medunsa Campus)

Professor Ogunbanjo graduated from the College of Medicine, University of Lagos, Nigeria in 1982. After rural practice in Nigeria, he worked in Maputo, Mozambique, and then in Maseru,

Lesotho. He joined the Department of Family Medicine and Primary Health Care, Medunsa (now University of Limpopo, Medunsa Campus) in 1992.

He has many publications in local and international peer-reviewed medical journals, and is the associate editor of the South African Family Practice Journal, and International Journal of Medicine, UK. Areas of special interest are STIs including HIV/AIDS, tuberculosis, ethics, mental health, EBM and biostatistics.

Diabetes mellitus (DM) is rapidly emerging as a major public health problem in South Africa and other developing countries. The prevalence of diabetes in South Africa is highest in the Indian community (10%), and 5 - 6% in the African community. Type 2 diabetes accounts for 80 - 90% of all forms of DM and its prevalence is increasing as the prevalence of obesity increases. The association of co-morbid conditions such as obesity, overweight, hypertension, atherosclerosis and coronary artery disease makes it imperative that the family practitioner manages these patients in a comprehensive manner through a multidisciplinary approach. The availability of family support in enhancing patient compliance appears to be beneficial in the overall management of this metabolic syndrome.

DEFINITION AND CLINICAL PRESENTATION

Diabetes mellitus is a heterogeneous group of disorders caused by a relative or absolute insulin deficiency, resulting in abnormalities of carbohydrate and fat metabolism. The clinical presentation of polyuria, polydipsia, polyphagia, fatigue and irritability are typical for type 1 DM. For type 2 DM, many patients are relatively asymptomatic initially. Family practitioners should suspect type 2 DM in patients with risk factors of obesity, increasing age (> 40 years), positive family history of DM and a higher pre-diabetic fasting blood glucose. Symptoms of recurrent infections, visual difficulties, unexplained peripheral neuropathy, and signs of other insulin-resistance states such as polycystic ovarian syndrome and the metabolic syndrome X should alert the family practitioner to the probability of type 2 DM.

The pathophysiology of type 2 DM is primarily linked to obesity, insulin resistance and environmental factors such as inactivity and abundance of food (Fig. 1).

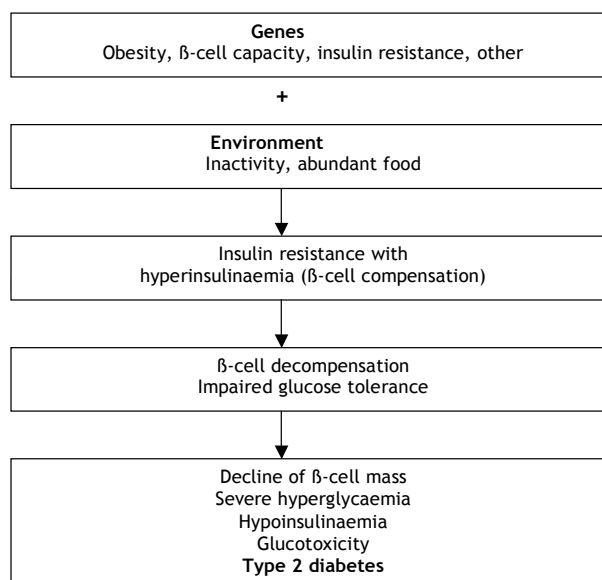


Fig. 1. Pathogenesis of type 2 diabetes mellitus. Source: <http://upp.spis.co.uk/images/bwplus/figures/large/ACE0202-01-021.jpg> (accessed 24 May 2006).

Because obesity or weight gain has such an important role in the pathophysiology of diabetes, there is an urgent need to implement nutrition strategies to prevent, ameliorate and manage these problems. It is important to differentiate type

Table I. General characteristics of type 1 and type 2 diabetes mellitus

	Type 1 DM	Type 2 DM
Genetic locus	Chromosome 6	Chromosome 7 (MODY)
Age of onset	Below 40 years	Above 40 years
Body habitus	Normal to wasted	Obese
Plasma insulin	Low to absent	Normal to high
Plasma glucagon	High, suppressible	High, resistant
Acute complication	Ketoacidosis	Hyperosmolar coma
Insulin therapy	Responsive	Responsive to resistant
Sulphonylurea therapy	Unresponsive	Responsive

MODY = maturity-onset diabetes of the young.

1 DM from type 2 DM. Table I gives a very simple set of general characteristics to differentiate one from the other.

PHYSICAL EXAMINATION AND INVESTIGATIONS

Apart from the general examination of the patient, special focus should be on the determination of the patient's body mass index (BMI), blood pressure, fundoscopy, and the presence or absence of peripheral pulses and sensations. A thorough examination of both feet for any evidence of peripheral neuropathy, arterial disease and ulcers is mandatory in all diabetic patients. The use of the office pin (usually unsterile) to test for pain sensation in the diabetic foot should be avoided owing to the risk of initiating foot ulcers.

At the primary care level, a simple urine dipstick (urinalysis) is usually a first indication of possible diabetes, although many substances, ageing, and pregnancy affect the amount of glucose in the urine. The preferred and reliable method of diagnosis is to measure the plasma glucose level. For the diagnosis of DM, the patient must satisfy one of the criteria for plasma

glucose levels as shown in Table II. Haemoglobin A_{1c} is the best measure of diabetic control, should be checked every 3 - 6 months and kept under 7% to minimise complications.

MANAGEMENT

The goals of management for type 2 DM are to:

- reduce diabetic symptoms
- prevent acute and chronic complications
- promote education and self-care
- control co-morbid conditions
- improve quality of life and productivity.

Dietary therapy

The reduction of diabetic symptoms in type 2 DM patients involves good control of the diet, which should be in consultation with a dietician to customise the diet for each patient. The recommended diet should contain 50 - 65% carbohydrate, 30% total fat, with saturated fat less than 10%, and protein 10 - 20% of the daily energy intake. The minimum number of meals per day should be 3, correlating to the duration of peak action of the medication(s).

The moderate use of sweeteners is

acceptable, and alcohol consumption is allowed in well-controlled diabetic patients provided it does not exceed 6 - 10% of the total daily energy intake, and is taken with meals. In practical terms, a maximum of 2 alcoholic drinks per day are allowed.

In the Finnish Diabetes Prevention Programme, the risk of developing diabetes was reduced by 58% over a 6-year period through an intervention fostering weight loss and increased physical activity. The US Diabetes Prevention Program also reported a 58% reduction in risk for diabetes in subjects with lifestyle intervention compared with the control group. These individuals increased their physical activity by ~50%, lost 6% of their initial body weight and maintained a weight loss of ~3.5% at 4 years.

Exercise

Exercise has a glucose-lowering effect and should be recommended for the improvement of diabetic control. The exercise programme begins at low intensity, increases gradually and takes place after meals to reduce postprandial hyperglycaemia. Patients with type 2 DM with plasma glucose values above 16.7 mmol/l should not exercise until their control has improved. Self-monitoring of blood glucose is useful during exercise to avoid hypoglycaemia.

Oral hypoglycaemic drugs

These drugs are the mainstay of drug therapy in type 2 DM. The modes of action of the various oral hypoglycaemic drugs are shown in Table III.

Oral biguanides, e.g. metformin, are used in overweight or obese patients with normal renal function particularly for their anorexic side-effect, while sulphonylureas are prescribed for other type 2 DM patients. The UK Prospective Diabetes Study (UKPDS) documented that metformin remains the only glucose-lowering drug to reduce the risk of macrovascular complications, and to prolong life in patients with type 2 DM. It proposes that all patients without contraindications to metformin, and

Table II. Plasma glucose measurement criteria for the diagnosis of diabetes mellitus

One random plasma glucose measurement > 11.1 mmol/l
or
Two fasting plasma glucose levels > 7.8 mmol/l
or
Glucose tolerance test (75 g load) in which any glucose level between time zero and 2 hours > 11.1 mmol/l

TYPE 2 DIABETES

Diabetes mellitus is a heterogeneous group of disorders caused by a relative or absolute insulin deficiency, resulting in abnormalities of carbohydrate and fat metabolism.

Because obesity or weight gain has such an important role in the pathophysiology of diabetes, there is an urgent need to implement nutrition strategies to prevent, ameliorate and manage these problems.

The use of the office pin (usually unsterile) to test for pain sensation in the diabetic foot should be avoided owing to the risk of initiating foot ulcers.

without insurmountable tolerability issues, should therefore receive metformin as first-line therapy. Both groups of drugs can be used in patients who do not achieve adequate glycaemic control with either, and there is no benefit prescribing two sulphonylurea agents.

Insulin therapy

Insulin is used when glycaemic control is not achieved on both diet and oral hypoglycaemic agents. With twice-daily biphasic insulin mixtures (30/70), the starting dose should be 0.2 U/kg/day increasing to a maximum of 0.6 U/kg/day, with two-thirds of the total daily dose before breakfast and the remaining one-third before supper, while all oral hypoglycaemic agents are stopped.

Education and family support

This type of support includes adequate knowledge about diabetes, its

management and complications. Home self-monitoring of blood glucose and identification of signs of hypo/hyperglycaemia should be known by the patient and family members. Health promotion focusing on good nutrition, hygiene, dental care and active lifestyle cannot be overemphasised. Motivational interviews with patients and their families help them gain insight into accepting the disease, to appreciate the value of compliance and to resolve conflicts that may arise with modification of patient and family dietary habits.

Management of co-morbid conditions

The approach to management of co-morbid conditions should be as follows:

- **Hypertension.** ACE inhibitors are used as first-line therapy, with or without low-dose thiazide diuretics, if clinical proteinuria is



I  my grandchildren

present, e.g. hydrochlorothiazide 12.5 mg daily. Calcium-channel blockers may be useful in patients of African origin.

- **Dyslipidaemia.** Statins (HMG-CoA reductase inhibitors) are

the rational choice for type 2 diabetics with moderately or severely elevated low-density lipoprotein (LDL) cholesterol. They lower LDL cholesterol by 30 - 60%.

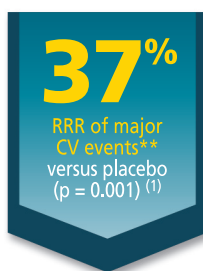
- **Peripheral neuropathy.** Painful peripheral neuropathies can be treated with low-dose tricyclic antidepressants, such as amitriptyline 50 mg at night.
- **Heart failure.** Combined neurohormonal blockade using ACE inhibitors and aldosterone antagonists is essential in the treatment of heart failure in type 2 DM patients. β -blockers should be avoided owing to the increased incidence of hypoglycaemia, worsening dyslipidaemia, and decreased insulin sensitivity.
- **Peripheral arterial disease** can be prevented by the oral administration of aspirin 325 mg daily.
- **Pregnancy.** The use of oral hypoglycaemic agents should be stopped, preferably before conception, to reduce the prevalence of congenital anomalies associated with these agents. Insulin

Table III. **Modes of action of oral hypoglycaemic drugs**

Oral hypoglycaemic drugs	Mode of action
Sulphonylureas e.g. gliclazide, glibenclamide	Enhance insulin secretion (side-effects include hypoglycaemia and weight gain)
Biguanides e.g. metformin	Decrease hepatic glucose output and increase peripheral utilisation of glucose (side-effects include anorexia, diarrhoea, vomiting, and lactic acidosis in renal impairment)
Alpha-glucosidase inhibitors e.g. acarbose	Delay absorption of simple sugars at the brush border of the small intestines (side-effects include hypoglycaemia)
Thiazolidinedione agents e.g. pioglitazone	Enhance insulin action via direct stimulation of receptors in the nucleus of hepatic and skeletal muscle cells (increased insulin sensitivity)

CARDS*

Lipitor 10 mg, through its lipid-lowering action, significantly reduced cardiovascular events in type 2 diabetic patients ⁽¹⁾



* 2 838 type 2 diabetic patients randomised to placebo or Lipitor 10 mg daily. Patients had no history of CHD, an LDL-C \leq 4.14 mmol/l and at least one of the following: retinopathy, albuminuria, current smoking or hypertension. Median duration of follow-up was 3.9 years. ** Primary endpoint was time to first occurrence of the following: acute CHD events, coronary revascularisation, or stroke

HELPING YOUR PATIENTS DO WHAT THEY LOVE IS THE HEART OF CV SUCCESS



LIPITOR
atorvastatin 10, 20, 40, 80 mg

Power. Evidence. Confidence.

References: 1. Colhoun HM, Betteridge DJ, Durrington PN, et al on behalf of the CARDS Investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004;364:685-696. 2. Lee JD, Morrissey JR, Mikhailidis DP, Patel V. CARDS on the table: should everybody with type 2 diabetes take a statin? *Current Med Res Opin* 2005;21(3):357-361. **[S4] Lipitor 10, Lipitor 20, Lipitor 40, Lipitor 80 Tablets.** Each Lipitor 10, 20, 40 and 80 tablets contains atorvastatin calcium trihydrate, equivalent to 10 mg, 20 mg, 40 mg and 80 mg atorvastatin respectively. Reg. No.: Lipitor 10: 3177.5/0357, Lipitor 20: 3177.5/0358, Lipitor 40: 3177.5/0359, Lipitor 80: 3177.5/0210. **Pharmacological Classification:** A: 7.5 Serum-cholesterol reducers. **Indications:** Lipitor is indicated as an adjunct to diet for reduction of elevated total-cholesterol, LDL-cholesterol, apolipoprotein-B, and triglyceride levels in patients with primary hypercholesterolaemia; mixed dyslipidaemia; and heterozygous familial hypercholesterolaemia. **Contra-indications:** Hypersensitivity to any component of this medication. Active liver disease or unexplained persistent elevations of serum transaminases. Lipitor is contra-indicated in pregnancy, in breast feeding mothers and in women of childbearing potential not using adequate contraceptive measures. An interval of one month should be allowed from stopping Lipitor treatment to conception in the event of planning a pregnancy. Safety and efficacy have not yet been established in children. **Warnings:** **Liver Effects:** Persistent elevations (> 3 times the upper limit of normal (ULN) occurring on 2 or more occasions) in serum transaminases occurred in 0.7% of patients who received atorvastatin in clinical trials. Active liver disease or unexplained persistent transaminase elevations are contra-indications to the use of Lipitor (see **Contra-Indications**). **Skeletal Muscle:** Rhabdomyolysis with or without renal impairment has been reported with the use of HMG-CoA reductase inhibitors. Myalgia has been reported in patients treated with Lipitor (see **Adverse Reactions**). **Dosage:** The patient should be placed on a standard cholesterol-lowering diet before receiving Lipitor and should continue on this diet during treatment with Lipitor. The usual starting dose is 10 mg once a day. Doses should be individualised according to the baseline LDL-C levels, the goal of therapy, and patient response. Adjustment of dosage should only be made after an interval of 4 weeks or more. The maximum recommended dose is 40 mg once a day. The maximum dose for treating patients with homozygous FH is 80 mg. Doses may be given at any time of day with or without food. **Side-Effects and Special Precautions:** The most frequent adverse effects associated with Lipitor therapy, in patients participating in controlled clinical studies were: diarrhoea, constipation, flatulence, dyspepsia, abdominal pain, headache, nausea, myalgia, arthralgia, asthenia, insomnia and rash. The following side-effects have also been reported in clinical trials: muscle cramps, myositis, myopathy, paraesthesia, peripheral neuropathy, pancreatitis, hepatitis, cholestatic jaundice, anorexia, vomiting, alopecia, pruritus, impotence, hyperglycaemia and hypoglycaemia. Allergic reactions have been reported rarely. Lipitor may cause elevation of creatine phosphokinase and dose-related increases in transaminase levels may occur (see **Warnings**). **Licence Holder:** Pfizer Laboratories (Pty) Ltd, Reg No 1954/000781/07, 102 Rivonia Road, Sandton, 2196. Tel (011) 320 6000. Please refer to detailed package insert for full prescribing information. PI REF 06/1997 115/LIP/10/2005/JA

is the treatment of choice for diabetes in pregnancy. Folate supplementation (5 mg daily) should be added to the treatment.

During follow-up visits, the family practitioner should perform the following:

- Eye examination – visual acuity, fundoscopy and cataracts.
- Examination of the feet – peripheral neuropathy, circulation impairment and ulcers.
- Dental examination – check for caries.
- Glycosylated haemoglobin (Hb A_{1c}) measurement – best measure of diabetic control. It should be checked every 3 - 6 months and kept under 7% to minimise complications.
- Fasting serum lipid profile – especially the total cholesterol/high-density lipoprotein ratio, which is a risk determinant for heart disease.
- Reinforcement of DM knowledge and practice related to the diet, optimal weight maintenance,

exercise, alcohol and smoking (as applicable).

- Assessment of the BMI, blood pressure, urinalysis for glucose, protein and ketones.
- ECG measurement – absence or presence of cardiac ischaemia or infarction.

CONCLUSION

The management of type 2 DM should involve continuous professional training for family practitioners in the management of non-communicable chronic diseases, because the interplay of other conditions with diabetes requires up-to-date evidence-based knowledge of the disease and the assistance of other health care professionals with specific qualifications and skills. The early involvement of the family in the management of the type 2 diabetic patient is rewarding, as compliance to management is enhanced.

Further reading

Colditz GA, Willet W, Rotnitzky A, Manson J. Weight gain as a risk factor for clinical diabetes mellitus in women. *Ann Intern Med* 1995; **122**: 481-486.

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.

Fonarow GC. An approach to heart failure and diabetes mellitus. *Am J Cardiol* 2005; **96** (suppl): 47E-52E.

Maggio C, Pi-Sunyer F. The prevention and treatment of obesity. Application to type 2 diabetes. *Diabetes Care* 1997; **20**: 1744-1766.

Society of Endocrine and Metabolic Diseases of South Africa (SEMDSA), in association with DESSA, SADA, ADSA. Guidelines for the management of type II (non-insulin-dependent) diabetes mellitus at primary health care level in South Africa. *S Afr Med J* 1997; **87** (4): 497-512.

Tuomilehto J, Lindstrom J, Ericsson J, *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.

UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998; **352**: 854-865.

IN A NUTSHELL

The presence of glycosuria is a strong indicator of diabetes.

The prevalence of type 2 diabetes mellitus (DM) is increasing as the prevalence of obesity increases.

All adults older than 45 years should be screened every 3 years by means of a fasting plasma glucose test.

A healthy diet with just enough calories to maintain ideal body mass index (20 - 24) plus regular exercise is the cornerstone of treatment for both types 1 and 2 diabetes mellitus.

Haemoglobin A_{1c} is the best measure of diabetic control, should be checked every 3 - 6 months and kept under 7% to minimise complications.

Control of blood pressure, lipid levels and smoking cessation are important measures in reducing the chance of macrovascular complications.

Family practitioners should endeavour to understand the context of their diabetic patient's illness by assessing cultural beliefs including dietary practices, look for any evidence of depression, family dysfunction and available financial resources.