Management of Non-Insulin-Dependent Diabetes Mellitus in Europe: A Consensus Statement*

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ABSTRACT

Non-insulin-dependent diabetes mellitus (NIDDM) is a common disorder, but less attention has been paid to its management over the years than to that of insulin-dependent diabetes mellitus (IDDM). Care is often in the hands of primary-care or general physicians or junior doctors in diabetes clinics. Morbidity and mortality are high. Recently there has been as increase in interest in NIDDM management; this has revealed wide variations between centres and countries. The USA tackled this problem by carrying out a nationwide education program and generating written guidelines for doctors. Many diabetologists in Europe felt that this was a good idea but that the guidelines were not entirely suitable for European practice.

INTRODUCTION

Diabetologists from 14 European countries [European NIDDM Policy Group (EUR-NIDDM PG)] met for several days in Amsterdam in late 1986 with the blessing of the Council of the European Region of the IDF to establish whether a consensus on the management of NIDDM could be reached. Surprisingly, after lengthy discussions a consensus view was reached. The first output was the policy statement that follows, which was discussed and amended at a major meeting of European diabetologists in Berlin. We hope this document will be helpful in its own right, but it is also intended to stimulate discussions, and we welcome constructive comments from all who read it. It has also been sent for information and comment to all member associations of the European Region. A practical desktop physicians guide and a more comprehensive monograph coauthored by the policy group are planned.

The EUR-NIDDM-PG was composed of cochairmen F.A. Gries (FR Germany) and K.G.M.M. Alberti (UK); members J.P. Assal (Geneva, Switzerland), H. Beck-Nielsen (Klampenborg, Denmark), M.Berger (Dusseldorf, FR Germany), G. Grepaldi (Padua, Italy), A. Czyzyk (Warsaw, Poland), L. Groop (Helsinki, Finland), J.Jervell (Oslo, Norway), H.M.J.Krans (Leiden, Netherlands), P.Lefebvre (Luttich, Belgium), J.E. Mann (Oxford, UK), A. Melander (Lund, Sweden), G. Panzram (Erfurt, German DR), K. Schoffling (Frankfurt, FR Germany), E. Standl (Munich, FR Germany), M.R. Taskinen (Helsinki, Finland), M. Toeller (Dusseldorf, FR Germany), W. Waldhausl (Vienna, Austria), and P. Watkins (London, England); and guest consultants D. Michaelis (Karlsberg, German DR), G.Pozza (Milan, Italy), M. Serrano-Rios (Madrid, Spain), and G. Slama (Paris, France).

Table 1
Impact of Non-insulin Dependent Diabetes Mellitus

Decreased quality of life
Excess mortality
Acute metabolic complications
Hyperosmolar coma
Ketosis with severe illness
Hyperlipidemia
Chronic complications
Macroangiopathy (peripheral vascular disease and ischemic heart disease)
Hypertension, stroke, cardiac failure
Neuropathy (diabetic “foot”, pain etc)
Amputations
Microangiopathy (as prevalent as in insulin dependent diabetes mellitus but less prolierative retinopathy and end-stage renal disease
Cataract

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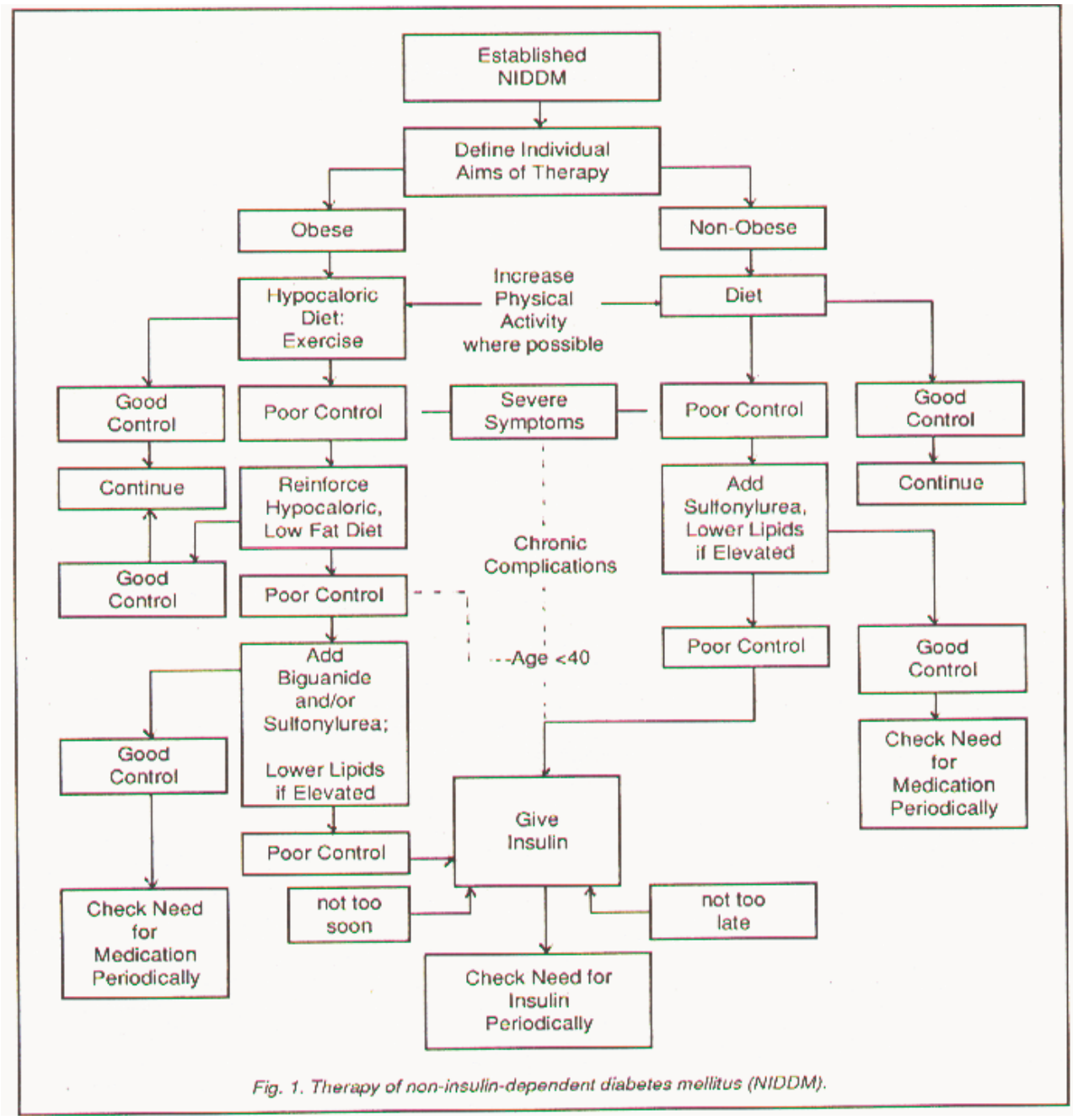

Fig. 1. Therapy of non-insulin-dependent diabetes mellitus (NIDDM).

EUR-NIDDM-PG CONSENSUS STATEMENT

In Europe, NIDDM is one of the most frequent metabolic disorders. As the WHO study group stated in 1985, "Its impact is often not fully acknowledged and should attract more attention from health care professionals and planners." Patients with this disease often do not receive optimal care, resulting in impaired quality of life, excess mortality, and enormous health-care costs. The EUR-NIDDM-PG was formed to improve this deplorable situation by focusing attention on the nature of the disease, the objectives and means of treatment, and strategies for the organization of care. The impact of NIDDM on the individual is shown in Table 1.

EPIDEMIOLOGY OF NIDDM

Exact prevalence data of NIDDM in many regions of Europe are lacking, but it is possible to make the fallowing statements. In most populations the prevalence of known NIDDM is > 1%. There is a striking increase of prevalence with age rising to 10% in those >65 yr. old. In most subjects NIDDM appears before the age of 65, and most patients are younger than 70 yr. There is a marked variations from country to country that may be explained partly by genetic and partly by environmental factors. The prevalence of NIDDM appears to be increasing. This may reflect increasing awareness of the disorder, better diagnosis, increasing longevity

of the general population, increasing affluence, and adverse life style.

The overall mortality rate of NIDDM is approximately twice as high as non-diabetic individuals. Those who acquire NIDDM before the age of 50 may expect a loss of 5-10 yr. of life. The average loss of longevity is greater in women than in men. It decreases markedly with age; is about 3 yr. in those who develop diabetes after the age of 70, and is negligible at age 75.

The main causes of death in NIDDM are cardiovascular and cerebrovascular diseases. The prevention of neuropathy and microangiopathy are closely related to duration and control of the metabolic disorder, as in IDDM, although varying in severity.

The prognosis of NIDDM is not solely dependent on the quality of control of glucose metabolism but also on the correction of frequently associated disorders, e.g. hypertension, obesity, lipid abnormalities, and adverse life-style, especially smoking. The costs of NIDDM are high and greater overall than for IDDM, although precise figures are lacking for Europe.

OBJECTIVES OF TREATMENT

The primary objectives of treatment are the same for all types of diabetes. These are relief of symptoms, improvement of the quality of life, prevention of acute and chronic complications, avoidance of excess mortality, and treatment of accompanying disorders.

Diabetes-specific symptoms can be relieved and diabetes-specific complications can be prevented by correction of the metabolic disorder. Therefore, early detection of diabetes and near-normal control of metabolism are desirable. However, NIDDM is often associated with additional disorders and disabilities or very limited life expectancy, so that the priority of aims must be tailored to the individual patient. Near normal control of metabolism may not be desirable if there is a major possibility of hypoglycemia or not justified with regard to prevention of long-term complications in the very aged. Control of hypertension lipid abnormalities, and smoking may be more important for the prevention of complications than blood glucose control and quality of life may be jeopardized by rigid therapeutic regimens.

TREATMENT OF THE METABOLIC DISORDER

It is axiomatic that treatment of the metabolic disorders of NIDDM include more than control of glycemia. The principal means for achieving this control are dietary adjustments, reduction of over weight in the obese, blood lipid-lowering therapy, adequate physical activity oral antidiabetic agents, and insulin.

Education

Education provides the basis for successful treatment. It can improve the safety of treatment, enhance the quality of metabolic control, increase social and psychological well-being, prevent complications, and reduce costs. Education should include patients, relatives and friends. The educational plan should cover diabetes and its management, nutritional requirements and meal planning for achieving and maintaining optimal body weight, the role of physical activity, self-monitoring, how to deal with changes in life-style, and how to cope with emergencies, particularly hypoglycemia in drug or insulin-treated patients.

In addition, patients should know about long-term complications, e.g, the diabetic and foot care, neuropathy, coronary heart disease, eye changes, nephropathy, and hypertension, and the role of treatment for which their active participation is crucial. It is irresponsible to withhold such a minimal teaching program for any NIDDM patient. For many patients, information on the genetics of NIDDM and the importance of normal body weight and physical activity for the prevention of NIDDM in their off-spring may be helpful.

Diet

Diet should focus us on total energy intake to avoid or correct overweight (the most important precipitating factor for NIDDM). A fall in blood glucose may be seen even before appreciable weight loss occurs. Weight loss is associated with a decrease in insulin resistance and hepatic glucose production.

Many patients will respond adequately to being offered lists indicating foods that can be eaten regularly, those that should be taken in moderation, and those that should be avoided and need not necessarily count to calories as such.

As a rule, carbohydrate intake should be higher and fat intake relatively lower than that of most Europeans. The proposed contribution to energy

intake should be 50-55% carbohydrate, 30-35% fat, and 15% protein. The composition of dietary fat should be saturated: monounsaturated: polyunsaturated 1:1:1. if this dietary intake is achieved, it is associated with an appreciable reduction of cholesterol, and further specific advice to reduce cholesterol, intake is usually unnecessary. Carbohydrates should preferably be complex, associated with low glycemic response, and high in dietary fiber.

If nutrients are fairly evenly spread throughout the major meals and snacks, carbohydrate exchange lists are unnecessary for NIDDM patients except those on insulin and some patients on sulfonylureas. Alcohol should be restricted, particularly in patients with hypertriglyceridemia and/or overweight. Artificial non-caloric sweeteners should be used instead of sugar wherever possible.

Exercise

Exercise has beneficial effects overall. It may, in particular, increase insulin sensitivity, thus helping improve glucose tolerance and lower hyperinsulinemia. It may also reduce total plasma cholesterol and triglycerides while increasing high density lipoprotein cholesterol. It can also help reduce body weight and hypertension. Limitations to exercise must, however, also be considered. This includes poor metabolic control with ketosis as and/or blood glucose > 300 mg/dl (16.7 mM), advanced retinal or renal disease, ischemia heart disease, decreased joint mobility (osteoarthritis) and other physical problems associated with ageing.

Oral Antidiabetic Agents

When diet fails to achieve adequate metabolic control the physician must decide whether insulin or oral agents should be given. The group recognizes that (except in emergency cases) if diet and exercise treatment fails, sulfonylureas are generally the first choice for additional treatment. This is because sulfonylureas may stimulate insulin secretion, lower blood glucose, and improve insulin sensitivity.

If sulfonylurea treatment gives adequate glycemic control with a submaximal or single daily dose, the need for the drug should be tested by withdrawal. Sulfonylureas are not always effective in NIDDM (primary failures), and if they are effective, the duration of action is limited. Secondary failures occur at a rate of about 10%/yr.although the rate of side effects is low (with the exception of chlorpropamide and carbutamide, which should no longer be used) there is considerable risk of hypoglycemia, sometimes fatal,. This risk is apparently lower with short-acting than with longer acting agents such as chlorpropamide and glibenclamide (glyburide). It is therefore recommended that sulfonylurea therapy be commencd with shortacting agents in older patients.
The combination of sulfonylureas with insulin has recently been re-examined in some regions of Europe. Some experts propose that it should be tried in patients with endogenous insulin secretion, but it is not generally recommended.

Biguanides still have an important role in the treatment of the obese NIDDM patient. Their specific properties include an antihyperglycemic effect with simultaneous reduction of raised serum insulin levels, a lipid-lowering effect and the stimulation of fibrinolytic activity. Their main indication is NIDDM associated with obesity and/or hyperlipidemia. Administration as monotherapy is not unanimously recommended except in the very obese (body mass index > 30). Usually they are used in combination with sulfonylureas in situations where insulin therapy is not indicated. Biguanides should not be used in patients older than 65 yr.

The well-known risk of lactic acidosis can be avoided by strict observation of contraindications. Because the risk of adverse side effects is lowest with mtformin, this biguanide should be used preferentially if not exclusively.

Insulin

Insulin therapy should not be used in NIDDM patients if glycemia can be maintained within the individual target range by correction with diet, exercise, sulfonylureas, and/or biguanides. Insulin treatment is also irrational in a patient who achieves reasonable blood glucose control during hospitalization but is unwilling or unable to cope with therapeutic recommendations on an outpatient basis. Insulin treatment should, however be initiated in NIDDM patients once blood glucose values consistently remain above the target range despite strict adherence to appropriate treatment. Short-term insulintherapy may be necessary in some NIDDM patients during periods of illness.

In a considerable number of patients, one or two daily doses of intermediate acting insulin with or without added shortacting (regular) insulin results in improved metabolic control. If near normoglycemia is desirable and only achievable by intensified insulin treatment, such a regimen should be

Table 2
Examples of Self-Monitoring Regimens

Urine*
Test first postprandial urine daily or Check Fasting (first and/or second void) and Postevening meal urine 2 or 3 days/wk

Blood
Test 1 time/day at different times or Test before Insulin injection, postprandially, and bedtime 1 or 2 days/wk or Test fasting, before main meals, and at bedtime 2 days/wk

Self-measurement technique should be checked once or twice per year by the physician or appropriate health care professional

Extra tests should be performed with illness or life-style changes.

Regular weight measurement also essential.

Regular blood monitoring particularly useful in insulin-treated and young patients.

*Use only glucose-specific test strips.

instituted according to the rules for IDDM patients which include special training. Proper self-monitoring is essential in all insulin-treated NIDDM patients. Figure 1 depicts a decision tree showing a suggested scheme for the management of NIDDM patients.

MONITORING OF METABOLIC CONTROL

A major aim of treatment is the attainment and maintenance of near normoglycemia. This aim is relaxed in certain NIDDM patients where freedom from symptoms is the main goal. Nonetheless, blood glucose should be monitored, directly or indirectly, in virtually all NIDDM patients. In addition, blood lipids should be checked regularly. Urine ketones should be tested in poorly controlled or ill NIDDM patients.

Self-monitoring is the key element in the therapy of diabetes, because it improves both the quality and safety of treatment. This is usually achieved only if all test results are clearly documented in the patient's diary.

Table 3
Targets for Metabolic Control

	Good*	Acceptable	Poor
Blood glucose			
Fasting			
mg/dl	80-120	< 140	> 140
mM	4.4-6.7	< 7.8	> 7.8
Postprandial			
mg/dl	80-160	< 180	> 180
mM	4.4-8.9	< 10	> 10
HbA_1**	< Mean + 2 SD	< Mean + 4 SD	> Mean + 4SD
Urine glucose (%)	0	< 0.5	> 0.5
Total cholesterol***			
mg/dl	< 200	< 250	> 250
mM	< 5.2	< 6.5	> 6.5
HDL- cholesterol			
mg/dl	> 40	> 35	< 35
mM	> 1.1	> 0.9	< 0.9
Fasting triglycerides			
mg/dl	< 150	< 200	> 200
mM	< 1.7	< 2.2	> 2.2
Body mass index (kg/m^2)			
Men	< 25	< 27	> 27
Women	< 24	< 26	> 26

*This is the ideal and may be difficult, impossible or unnecessary to achieve in certain patients.
**Reference ranges for HbA_1 vary greatly, so targets expressed as mean + standard deviation.
***Lower targets may be desirable in younger patients.

Urine Glucose Testing

Urine glucose testing is still an important method for the assessment of metabolic control. It is however, useful only in patients with a known normal renal threshold for glucose. It is used routinely for the detection of major hyperglycemic excursions is not required in whom near normoglycemia is not required or where blood glucose monitoring is impractical or refused by the patient. The aim should be to keep urine free of glucose. Examples of testing routines are shown in Table 2.

Blood Glucose Testing

Blood glucose testing is indispensable for insulin-treated NIDDM patients. Tests before insulin injection and postprandially 1 or 2 days/wk are sufficient and in patients with stable control (Table 3). More frequent measurement are necessary in patients with intensified insulin treatment if the patient is ill of if there are changes in life-style. Patients must provided with instructions on how to modify treatment according to blood glucose values.

Routine blood glucose self-measurements are also recommended in non-insulin treated patients with abnormally high-renal threshold and younger, compliant drug treated patients (fasting postprandially, and in the afternoon at least once a week).

Glycosylated Hemoglobin

Glycosylated (glycated) hemoglobin should be measured every 2-4 mo. Measurements of fructosamine and glycosylated serum proteins may also be used to assess overall glycemic control but reflect a shorter time span. Urine ketone testing is recommended if blood is persistently ≥ 360 mg/dl (20 mM), there is sever sustained glycosuria (≥2%), or the patient is vomiting or pyrexial.

Dislipoproteinemia

Is most countries, 50% of NIDDM patients have dyslipoproteinemias. In view of the importance of cholesterol and triglycerides as risk factors for macrovascular disease in NIDDM, it is strongly recommended that total cholesterol, high-density lipoprotein cholesterol, and triglycerides are checked annually. If results are abnormal and intervention is appropriate, values should be checked trimonthly.

CLINICAL MONITORING

The prognosis and quality of life of the NIDDM patient depends strongly on the chronic complications of the disorder, together with associated diseases. Particular attention should therefore be paid to precipitating factors and to early detection, monitoring and treatment of hypertension, smoking, cataract, retinopathy, neuropathy, foot lesions, and macrovascular disease. Regular review shown be available for all patient as shown on the clinical protocol in Table 4.

Table 4
Clinical Monitoring Protocol

At Initial visit
Complete examination
Weight, blood pressure
ECG
HbA_1 (or fructosamine)
Serum cholesterol if > 200 mg/dl (or > 5.2mM), also HDL-cholesterol), and triglycerides
Urine glucose, protein, ketones, infection, microscopy
Start teaching program
Teach self-monitoring
Search for neuropathy
Fundoscopy (dilated pupils)
Visual acuity
Plasma creatinine, electrolytes, glucose
Dietary advice

Once or twice a month*
Continue teaching program
Weight, blood pressur
Postprandial blood glucose

Trimonthly
HbA1
Lipids (if elevated)
Urine protein

Annually
Biochemical tests as for initial visit
Examine for complications, including macroangiopathy
Foot inspection
Fundoscopy (dilated pupils) and visual acuity
Urine glucose protein, ketones, microscopy culture
Reconsider therapy
Check self-monitoring technique

Transfer to specialist if progress is unsatisfactory

*Less frequently for stable, well-controlled patients.

SOCIOECONOMIC ASPECTS

Efforts to improve the care of the NIDDM patient should take into account the main reasons for failure. These differ according to the economic, social, political, cultural, and medical situation in each country.

Most frequently, however, the treatment of NIDDM fails because of factors related to medical services or to the patient, which are independent of regional differences. Insufficient knowledge, resources, and available treatment will often be a cause of failure despite the best intentions of the patients and physicians. Insufficient application of knowledge by the physicians and difficulties in communicating with the patient are other problems.

For some patients, there are so many problems of social or economic nature that diabetes management becomes just one of many problems and is not given high priority. Setting unrealistic goals of treatment or demanding unrealistic changes of life-style may block the willingness of the patient and his/her family to co-operate.

As a rule, the NIDDM patient should be managed by the practicing physician. At the initial visit a compete check-up is mandatory. At each routine visit, four questions should be asked, How is the patient? Is metabolic control satisfactory? How about complications? Any other matter? Actions should include advising and taking appropriate action based on answeres to the questions and fixing a time & date for the next visit. If facilities for education, monitoring, and appropriate treatment of diabetes and its complications are not available, referral to a specialist or a specialized clinic is mandatory.