

Non-insulin dependent diabetes mellitus: the role of the family doctor

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Diabetes mellitus is a genetically determined disease resulting from a relative or absolute lack of insulin secretion from the β cells of the pancreas, caused, from a clinical-laboratory point of view, by hyperglycemia alterations in the metabolism of lipids, proteins and minerals of greater or lesser severity.

Given the heterogeneity of the clinical signs that may appear along with it, since 1875, this disease has been classified in various ways, in an attempt to highlight various types of the same nosological entity. However, in 1985, the World Health Organization proposed what is thought to be the most recent classification which, in my view, points out not only the cause but also suggests, with greater or lesser evidence, the treatment to follow and also the prognostic of its course (*Table I*).

Diabetes mellitus in general, and the non-insulin dependent type in particular, also called type II diabetes mellitus, continues to grow throughout the world, particularly in the developed countries of the West. The problem is that we are now seeing an outbreak of ever increasing numbers of cases in poor countries, and even in those considered to be "Third World" countries.

This means that the prevention, early detection and treatment of diabetics can only be successful with the collaboration of internists, endocrinologists, epidemiologists, preventive Medicine, and family

doctors, as well as all physicians who wish to be part of teams at regional or national levels, well trained and motivated to deal with this type of pathology, in which there should be no shortage of dieticians, nurses, sociologists and social workers.

All the professionals mentioned, and others, represent the qualifications needed to successfully provide support for individuals who are prone to or already have the disease, but as I have had occasion to say in other lectures, the set should be like a well-tuned orchestra, with the internist as the maestro, and the stringed instruments represented by the family doctors. But we should not leave out those who can introduce tones or sounds into the melody that are not always needed; those who contribute to the various musical compositions, in the way the oboe, harp, drums, clarinet, etc. do. The latter can be likened to the various medical specialists who are specially trained to provide important assistance in this field (endocrinologists, ophthalmologists, nephrologists, vascular surgeons, etc.); the bass drum and triangle, no less important (sociologists and other paramedic technicians) are, in turn, the mainstay on which the patients lean.

On writing this article, my firm proposal was to draw attention to the fact that diagnosing and prescribing the correct treatment to carriers of either insulin dependent diabetes mellitus (IDDM) or non-insulin dependent diabetes mellitus (NIDDM) is not difficult in current times; the worst thing is the regular follow-up of patients throughout their life, and early detection of the signs and symptoms that show the start of complications of microangiopathy or macroangiopathy, and in this case, the best placed professional to perform this task is, without doubt, the family doctor.

We have to admit that diabetologists are the specialists who best understand the molecular basis and pathophysiology of diabetes mellitus, but it is up to the family doctors to accompany the day-to-day evolution of the disease in their patients, while maintaining close contact with a specialist whenever some

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particular alteration occurs that jeopardizes the clinical evolution, because, as everybody knows, this is a disease that continues throughout the patient's life.

I often heard my dear, now departed Master and Professor Maurice Derot, one of the greatest internists/diabetologists of this century, say "God should only make the rich and the intelligent, diabetics". A profoundly Catholic man, aware of the social problems that diabetics face, warned diabetes mellitus patients that they need to spend more money on food and clothing than the general population; they also need have the minimum of intelligence to know and understand what the disease is, and how it evolves, as well as the ability to perceive the smallest alteration in their metabolism, so that they can immediately go to their family doctor, who will advise them on any appropriate dietary changes, or changes to their drug treatment, to correct the anomaly in good time. With this objective, it is up to the technicians to teach patients to be their own doctors, and the doctor's role should be merely to judge the attitudes taken by the diabetic patient.

The main focus of this article is to discuss the diagnosis and therapeutic aspects of diabetes mellitus with onset in early adulthood, scientifically designated non-insulin dependent diabetes mellitus or type II diabetes mellitus, but which at certain times may be insulin deficient (situation of serious pathological complications) or may, if severe serious micro- or macroangiopathy occur, become insulin-dependant.

Diagnosis

Compared with insulin dependent diabetes mellitus (IDDM), for which well-defined HLA genetic markers are already known, the same is not true of type of diabetes mellitus that is the focus of this article. In the latter case, insulin resistance is predominant, as well as pathological changes in the receptor cells for insulin or post-receptor metabolic changes. For this reason, the whole investigation has focused on the study of the gene that controls the insulin receptors.

The extraordinary impact that environmental factors and lifestyle represent in the appearance of NIDDM enables us to affirm that the older, more obese and sedentary the individual the greater the likelihood of their becoming diabetic. In reality the disturbance of energy balance as a result of excessive calorie consumption and reduced physical exercise, resulting in an increase in fatty acid deposits, especially in the

TABLE I

Classification of diabetes mellitus

Type 1 Diabetes mellitus
A – Immunologic
B – Idiopathic
Type 2 Diabetes mellitus
Other types of Diabetes mellitus
A – Genetic defects in b cell function
B – Genetic defects in the action of insulin
C – Exocrine diseases of the pancreas
D – Endocrine diseases
E – Iatrogenic diabetes
F – Diabetes secondary to infections
G – Uncommon forms of immunologic diabetes
H – Other genetic syndromes associated with diabetes
Gestational diabetes mellitus

visceral/abdominal adipose tissue, represents a consequence that favors the appearance of NIDDM. Under these circumstances, insulin resistance depends not only on changes in the metabolism of carbohydrates but also defects in lipid and protein metabolism. Of course, all these events have a genetic origin that so far, has not been completely identified.

What we can affirm with certainty, however, is that the maintenance of glucidic homeostasis depends on the good functioning of three biological processes: correct secretion of insulin; normal uptake of glucose through the peripheral tissues, and the corresponding suppression of glucose production by the liver.

Considering these basic phenomena, and so that we can all speak the same language, given that diabetes mellitus in general is a heterogeneous syndrome, I propose that we accept the classification of the International Diabetology Association, as well as its diagnostic criteria reviewed in 1993.¹

Once the diagnosis of type II or intolerance to glucose diabetes mellitus has been made, it is indispensable, in any situation, to apply appropriate therapy, which should be different from one individual to another, personalized, but with monitoring that should always include:

- Dietary treatment alone
- Dietary treatment + drug treatment
- Drug treatment

TABLE II

Diagnostic criteria for non-insulin-dependent diabetes

Diabetes mellitus

- Symptoms of polyuria, polydipsia, polyphagia and occasional glycaemia ≥ 200 mg/dL (11.1 mmol/L)
 - 8-hour fasting glycemia ≥ 126 mg/dL (7.0 mmol/L)
- Oral glucose tolerance testing (OGTT) with 75 g glucose
- Fasting glycaemia ≥ 126 mg/dL (7.0 mmol/L)
- Glycemia at 2 hours ≥ 200 mg/dL (11.1 mmol/L)

Glucose intolerance

- Fasting glycemia ≥ 110 and < 126 mg/dL
- Oral glucose tolerance testing (OGTT) with 75 g glucose
- Glycemia at 2 hours ≥ 140 mg/dL (7.8 mmol/L) and < 200 mg/dL (11.1 mmol/L)

- a - Glucosidase inhibitors
- Biguanides
- Sulphonylureas
- Insulin
- Miscellaneous drugs
- Adequate physical exercise in all of the above circumstances.

It is our opinion that the criteria for diagnosis are too permissive, therefore, for follow-up of patients aimed at preventing complications of micro or macroangiopathy we adopt the recommended criteria of the “EURONORM GROUP”, which are presented in the following chapter (*Table III*).

Therapy

Taking into account what has been said so far about the pathogenesis of type II diabetes, or NIDDM, what stands out in the diagnosis is that the patients are, in about 80% of cases, overweight due to an excess of adipose tissue, and reducing this excess weight is the initial immediate therapy to be imposed. Weight loss under these circumstances, achieved through diet and physical exercise, should aim not only to improve the esthetic appearance (although this psychological aspect should not be overlooked or even encouraged) but simultaneously, to produce an improvement in the metabolic changes that accompany the excess of adipose tissue, in particular, to improve glucose levels, reduce cardiovascular risk by reducing blood pressure, improve the low plasmatic insulin rate, nor-

malize or improve hypertriglyceridemia, and increase peripheral sensitivity to insulin.

The various types of therapy for type II diabetics aim to keep the patient in a state of homeostasis throughout their life, as this is the only way to prevent complications of micro or macroangiopathy. At my service (Medicine I – HUC (Hospital Universitário Coimbra) we follow the norms recommended by the “EURONORM GROUP” which are shown in *Table III*.²

Diet therapy

The normalization of weight in the “type II diabetic” or in the “glucose intolerant” type is imperative right from the start, as almost all of these patients are adipose type overweight. But how do we define obesity in these circumstances? It is useful to use three formulae, as of which offers important elements, not only for defining normal weight, but also providing other data that will help us to define the calorie intake and the type of obesity.

Assessment of body mass**Quetelet index or body mass index**

BMI = Weight / height²

Normal values

Men ≤ 25

Women ≤ 24

The value obtained using this formula tells us the weight the individual can bear per m² of body surface.

Lorenz formula

$$IW = H - 100 - \frac{H - 150}{M(4) W(2)}$$

IW = Ideal Weight

H = Height (cm)

M = Men

W = Women

Through this method we can find out what the desirable theoretical weight is for a certain individual, an important value for quantifying daily calorie intake.

Distribution of adipose tissue

Assessment of the type of distribution of adipose tissue is important because it is known that in type II diabetics, cardiovascular complications are more frequent in the case of abdominal-visceral obesity or android type obesity. In these cases, there is a predominance of

TABLE III

Monitoring of homeostasis in diabetics “Euronorm group” (2)

		Good	Acceptable	Poor
Glycemias				
- Fasting	mg/dL	80 – 120	≤ 140	> 140
	mmol/L	4.4 – 6.7	≤ 7.8	> 180
- Postprandial	mg/dL	80 – 160	≤ 180	> 180
	mmol/L	4.4 – 8.9	≤ 10	> 10
HbA1	%	< 8.5	8.5 – 9.5	> 8.5
HbA1C	%	< 7	7 – 8	> 8
Glycosuria	%	0	≤ 0.5	> 0.5
Total cholesterol	mg/dL	< 200	< 250	> 250
	mmol/L	< 5.2	< 6.5	> 6.5
HDL-cholesterol	mg/dL	> 42	> 35	< 35
	mmol/L	> 1.1	> 0.9	< 0.9
Fasting GT	mg/dL	< 150	< 200	> 200
	mmol/L	< 1.7	< 2.2	> 2.2
BMI	Kg/m ²	Men <25	< 27	> 27
		Women < 24	< 26	> 26
BP	mmHg	< 140/90	< 165/95	> 160/95
Microalbuminuria	mg/24h	< 30	30 – 300	≥ 300

adipose tissue in the upper half of the body.

This assessment of the type of obesity is provided by the value of the ratio between waist circumference and hip circumference.

The waist should be measured at the midpoint located on a vertical line between the circumference of the bottom of the rib cage and the circumference measured at the iliac crest. The hip circumference corresponds to a line that runs through the greater trochanters.

Android obesity is said to exist when:

- In men, the waist/hip ratio is higher than or equal to 1.0 (W/H³ 1.0)
- In women, the waist/hip ratio is higher than or equal to 0.85 (W/H³ 0.85).

Establishment of a diet

As mentioned above, each diabetic should have a personalized diet with the objective of reaching an ideal weight, as recommended by the “EURONORM

GROUP” recommend (and with which we are in agreement).

If the individual is obese, a low calorie diet should be established, readjusting the diet every 15 days until the weight ideal is reached. From this moment on, the quantity and quality of food allowed should not only maintain a stable weight, but also maintain a normal ratio between waist and hip circumference, for the reasons explained above.

It is always good to emphasize the fact that all this daily food control should be implemented alongside regular physical exercise, of which the most appropriate form is walking.

Basic rules for the establishment of a diet in type ii diabetes

1- Prohibiting the use of fast absorbing sugars.

2 – Determining the daily calorie intake in the maintenance phase by means of the Lorenz formula. We know that at normal weight, an individual’s daily calorie intake

should be around 30 kcal/kg per weight/day.

3 – Doing a quick diet survey, we see that the kind of daily calorie intake usually practiced. If the individual is obese, they should reduce the number of calories by 10% to 15% every 15 days, until the desired weight is reached.

4 – From this moment on, they should practice the rules suggested for a healthy diet, i.e.:

- 15% proteins with high biological value
- 55% medium slow or very slow absorption carbohydrates (starch and dietary fibers)
- 30% fats (7.5% saturated; 7.5% polyunsaturated; 15% monounsaturated)

5 – When establishing the diet, natural foods, which are economically affordable, should always be prescribed.

6 – Regarding alcohol consumption, provided there are no contra-indications and the prescribed calorie intake is not exceeded, 350 ml of red wine per day is acceptable.

7 – The number of meals should never be less than six per day.

Drug therapy

Most hypoglycemia treatments have been used for many years. It is known, for example, that since 1796, diets poor in carbohydrates have been used successfully in diabetics with adult onset of the disease. At that time, the designation non-insulin dependent diabetes was not known, and we can imagine the enormous controversy that existed in that era, over the differing results obtained with the same treatment, supposedly for the same disease, but which was in reality, not the same disease at all. This is because insulin-dependent diabetics inexorably evolved to ketosis, malnutrition and death, even when following the strictest of carbohydrate regimes. Nowadays, apart from the availability of human insulin, we have an arsenal of drugs for treating type II diabetes, which facilitates not only the lives of the patient but also the work of the medical team.

The family doctor, as long as they are minimally informed and cultured, can and should regularly follow up on their diabetic patients until the moment when any special complication manifests that prompts the doctor to ask for the support of a specialist (internist, ophthalmologist, nephrologist, etc.).

It is good to keep in mind that whatever the pharmacological treatment used, this should always be accompanied by diet and physical exercise. There are even authors who defend that diet and physical exercise are the only correct treatment for type II diabetes.^{3,4} Nevertheless, various studies have shown that around 70% of patients diagnosed with type II diabetes do not manage to achieve homeostasis through diet and exercise alone.^{5,6}

Before discussing the various types of drugs used in NIDDM, it should be remembered that this disease is a complex plurimetabolic syndrome, and that the objectives that we seek to achieve with treatment are not reduced to obtaining a permanent state of euglycemia (normoglycemia), but should take into consideration other goals:

- Normalization of glycemia and glycosylated hemoglobin levels
- Balanced weight
- Physical and mental well-being
- Control of lipid metabolism
- Good hemorheologic state

- Absence of microangiopathy
- Absence of macroangiopathy
- Inexistence of iatrogenic effects

An ideal drug in the treatment of Type II diabetes should be one which, when associated with a balanced diet and moderate physical exercise, manages to obtain the above-mentioned goals.

The drug arsenal we have available to us nowadays, besides insulin, includes sulphonylureas, biguanides and α -glucosidase enzyme inhibitors, each of which can be used alone or with other drugs.

Sulphonylureas

Sulphonylureas were discovered by accident by Janbon and Loubatieres in 1942, on realizing their hypoglycemic effect, but only began to be used as a treatment for type II diabetes in 1954. The main effect of this substance is that it stimulates the secretion of insulin by the β cells in the pancreas,⁷ but it is only effective when there is a good pancreatic reserve.

Nevertheless, its action extends to the extra-pancreatic sector, promoting a reduction in hepatic glucose synthesis and increasing the efficacy of the insulin in the peripheral tissues.⁸

Indications for treatment with sulphonylureas

Candidates for treatment with sulphonylureas are type II diabetics who, despite presenting normal weight and following a correct diet along with regular physical exercise, continue to have hyperglycemia.

What type of sulphonylurea is used?

All sulphonylureas have the same action mechanism. Nonetheless, it is necessary to know their excretion mechanism, giving preference to those that are eliminated in the bile over those in which the kidneys are the main excretion organ for their catabolites. In this case, there is a danger of build-up, with the appearance of serious hyperglycemias, especially in individuals with renal pathology or those aged over 50 years old, in whom physiological renal failure is, in most cases, a real problem.

Metabolic interactions of sulphonylureas with other drugs

I think it has been made very clear throughout this article that sulphonylureas are used as treatment in non-insulin dependent diabetes as long as there is a good pancreatic reserve of β cells. Now, as this type

of diabetes is a plurimetabolic syndrome, individuals often use other drugs, which can interact negatively with sulphonylureas. We highlight the following:

- 1 – Alcohol and aspirin, giving rise to serious hypoglycemia.
- 2 – The b-blockers which, via the sympathetic system, reduce the sensitivity of awareness at the start of hypoglycemia.
- 3 – Anticoagulants that mutually enhance each other.
- 4 – Allopurinol and probenecid, which reduce the urinary excretion of sulphonylureas.
- 5 – Barbiturates, rifampicin, thiazide, etc.

Biguanides

Biguanides are substances derived from guanidine that inhibit the synthesis of hepatic glucose and have a positive effect on its metabolism in the peripheral tissues, especially the muscle. The difference between these and sulphonylureas is the fact that biguanides exert no effect on the secretion of pancreatic insulin.

There are various types of biguanides, namely: metformin, phenformin and buformin, as well as other chemical compounds in preparation, but not yet available on the market.

The only one that should be used is metformin, given the risk of lactic acidosis with phenformin and buformin.

Indication for treatment with biguanides

Based on its action mechanism, metformin should preferably be used in the early phases of NIDDM, since this is the phase in which patients often suffer from hyperinsulinism. This indication is particularly important in patients who are overweight.

Apart from its hypoglycemic effect, metformin lowers the plasmatic triglycerides, increases HDL cholesterol and reduces the plasminogen activator factor (PAF) (9).

Contraindications

- Advanced age
- Respiratory failure
- Coronary failure
- Hepatic diseases
- Kidney failure
- All situations that produce hypoxia.

Alpha-glucosidase inhibitors

alpha- glucosidases are enzymes that are largely

present in plant and animal tissues, and in the small intestine, promote the release of glucose from the food consumed. The purpose of inhibiting these enzymes is to delay the digestion of carbohydrates which, in turn, reduces postprandial hyperglycemia by reducing the secretion of insulin from the pancreas after meals, and has a beneficial effect on type II diabetics.

There are currently two substances capable of inhibiting or reducing the activity of alpha- glucosidase: acarbose and miglitol. Only the first product is available on the market, and has been since 1994.

Less than 1% acarbose taken in appears in the blood stream; 70% is excreted in the feces and 14% in the urine.¹⁰

Action mechanism

Like metformin, acarbose has a primary anti-hyperglycemic effect. By inhibiting alpha-glucosidase, causing a considerable delay in the absorption of carbohydrates at the level of the small intestine, mimicking what happens in individuals who take in large quantities of dietary fiber or plantix. A beneficial consequence is the absence of postprandial hyperglycemia and, therefore, normal secretion of insulin from the pancreas, as well as an improvement in its effect in the peripheral tissues.

Indications for acarbose

Thanks to its action mechanism, acarbose will be the ideal drug for non-insulin dependent diabetics who have difficulty in controlling obesity, and in whom, for this reason, postprandial hyperinsulinism is constant.

It can and should be used in diabetic patients with hypertriglyceridemia, and also in those whose fasting glycemia concentrations are almost normal, but with significant postprandial hyperglycemia levels.

Contraindications

Acarbose should not be indicated for diabetics with intestinal diseases or those who already suffer from neuropathy.

Diabetics with the latter pathology may suffer from flatulence, excessive formation of intestinal gases, diarrhea, etc.

Insulin

As stated at the beginning of this article dedicated to non-insulin dependent diabetes, there are certain times when it is necessary to administer insulin. This

occurs in acute pathological complications, such as infectious diseases or in the case of surgery. It has also said that after some years, the reserve of b cells in the pancreas may run out, or changes in micro our macroangiopathy may arise, at which point it becomes necessary to introduce insulin treatment alone, or in combination with some of the drugs we have described above, for the rest of the patient's life.

Under these circumstances, the family doctor may, if he/she feels uneasy, meet with an internist or diabetologist to decide together what type of insulin to choose, as well as the number of daily injections that will best maintain glucidic homeostasis in the patient in question.

As stated at the beginning of this text, therapy for non-insulin dependent diabetics or those with type II diabetes who become insulin deficient will be addressed in another article, to be published shortly.

Conclusions

In writing this article, our aim is to call the attention of all physicians to the fact that due to the existence in Portugal of a large number of diabetic patients, the incidence of diabetes is increasing with the improvement in socioeconomic conditions nowadays, and the intention is that not only specialists in diabetology are responsible for their treatment.

On the other hand, although the fundamental cause is a total or partial lack of active insulin, diabetes is not only a disease of the pancreatic b cells. On the contrary, any one of the types of diabetes is, on its own, a disease of General Medicine, where the effects of poor glucidic metabolism will affect the whole organism, and which only the family doctor, knowing the patient very well as a whole and in their own environment, is capable of identifying in its early phase.

But nowadays, the maintenance of a blood glucose concentration in normal fasting is very easy, thanks to the drug arsenal available to us. What is difficult is keeping the diabetic individual in a state of homeostasis throughout his or her life, as the secondary effects of sporadic hyperglycemias over the twenty-four hours are insidious, occurring silently and chronically, with variable tropism from organ to organ. In these cases, the coefficient of intelligence and the socioeconomic and family conditions of people with the disease are of fundamental importance in the early detection of the appearance of the symptoms.

Which specialist other than the family doctor may be better informed of the sociofamiliar and economic conditions of his/her patient?

I would like it if the family doctors, who so often give me the pleasure of asking my opinion on this subject, educated themselves a little more in the area of diabetology, because I am certain that they would take pleasure of this education (the scientific material is beautiful, varied and easy to understand), and without even being aware of it, they would be providing an important services to thousands of Portuguese diabetics by detecting the signs of micro or macroangiopathy in good time, soon enough to cure the patient, or at least prevent its development.

I would like to end this article by making the following personal statements:

- 1) – Non-insulin dependent diabetes mellitus or type II diabetes mellitus is very frequent in our society.
- 2) – The treatment is easy.
- 3) – What is difficult is its primary prevention, early diagnosis and the detection of the first signs of micro or macroangiopathy in good time.
- 4) – The doctor best placed to follow-up on these patients is the patient's own family doctor.
- 5) – If I were forced to choose a disease, my preference would be: non-insulin dependent diabetes mellitus. ■

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