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THE RELATIONSHIP BETWEEN 1 HOUR GLYCEMIA, DURING ORAL GLUCOSE TOLERANCE TEST AND CARDIOMETABOLIC RISK

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Abstract

Background *Diabetes mellitus is a very common disease, worldwide there are currently over 366 million diabetics. It seems that people with normal glucose tolerance and blood glucose at 1 hour during OGTT ≥200mg% represent an intermediate phenotype of abnormal glucose metabolism, another disturbance of carbohydrate metabolism that is associated with increased cardiometabolic risk.* ***Objectives*** *Starting from these premises, we decided to analyze the subjects with glucose at 1 hour during OGTT ≥200mg%, but with normal values for fasting glucose and 2 hours glucose. In this subgroup of subjects some parameters of CMR were analyzed. We also performed a comparison of this subgroup of subjects with both normal glucose tolerance and 1-hour glucose <200mg%, and with those with abnormal glucose tolerance.* ***Results*** *According to currently used recommendations to diagnose diabetes mellitus, from the 778 people included in this study, 167 (21.5%) had disturbances of carbohydrate metabolism, being classified as patoglycemic and 611 persons (78.5%) had normal values of fasting glucose and 2 hours glucose during OGTT, being considered normoglycemic. From the 611 people who were classified as normal glucose tolerance, based on the currently used criteria for diagnosis of diabetes mellitus, a total of 44 persons (7.2%) had, however, the value of 1-hour glucose during OGTT ≥200mg%, which represents 5.6% of the entire group studied.* ***Conclusions*** *Patients with normal glucose tolerance and glucose ≥200mg% at 1 hour during OGTT represent a new subgroup of impaired glucose tolerance, which requires strict lifestyle advice and possibly pharmacological measures to prevent or delay progression to abnormal glucose tolerance.*

key words: *prevalence, cardiometabolic risk, carbohydrate metabolism disturbances*

Background

Diabetes mellitus (DM) is a very common disease, worldwide there are currently over 366 million diabetics. If in 1990 the number of people with DM worldwide was 125 million, in 2003 their number reached 194 million and is estimated to grow to 438 million in 2030 [1, 2].

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The continuous increase of the incidence and prevalence, the difficulty to achieve optimal glycemic control and association with other atherogenic risk factors will make the importance of this disease to further increase in the next years [3, 4].

A major requirement for epidemiological and clinical research and, of course, for the management of this disease, is its rigorous definition and classification [5].

Prediabetes, a term which has become more used in the last years, include pathological condition characterized by blood glucose levels (fasting and/or 2 hours during the oral glucose tolerance test - OGTT) over those considered normal, but under the values that are necessary for the diagnosis of DM [6, 7, 8]. Prediabetes includes:

1. Impaired fasting glucose (IFG) defined by fasting blood glucose of 110-125mg%. American Diabetes Association (ADA) proposed in 2003, to change the diagnostic criteria for IFG, to 100-125mg%, proposal which has not been adopted, yet, by the World Health Organization (WHO), but will probably be adopted soon [9].

2. Impaired glucose tolerance (IGT) is defined by a 2-hour glucose of 140-199mg% during OGTT. In this category, fasting plasma glucose and HbA1c are normal, hyperglycemia occurring only at 2 hours during OGTT. Recognition of this disorder of carbohydrate metabolism is important because these individuals have a risk for DM and complications, especially macroangiopathy [10, 11].

3. IFG and IGT can coexist (quite commonly) in the same patient, situation in which the cardiometabolic risk (CMR) increases significantly [12, 13], these intermediate states of carbohydrate metabolism being strongly associated with obesity (especially abdominal or visceral), atherogenic dyslipidaemia (increased triglycerides and/or low HDL-cholesterol) and hypertension (HTA) [14, 15, 16].

4. HbA1c is becoming more frequently used as a diagnostic criterion for DM. Individuals with values from 5.7% to 6.4% have an increased CMR and also a high rate of progression to DM [2].

To reduce the CMR of these people preventive measures are required as early as possible, represented primarily by lifestyle modification (diet and exercise) [17, 18].

Numerous longitudinal studies have shown that 40% of patients with normal glucose tolerance (NGT) (at an initial evaluation) developed diabetes after 10 years.

During the OGTT there are individuals who present elevations of blood glucose at 1 hour as high (≥200mg%), as those with altered glucose tolerance (AGT). However, because of the adequate reduction of serum glucose within 2 hours, due to conserved late phase insulin secretion, these people can not be classified as having a disturbance of carbohydrate metabolism, according to current definitions used to diagnose DM.

It seems that people with NGT and blood glucose ≥200mg% at 1 hour, represent an intermediate phenotype of abnormal glucose metabolism, another disturbance of carbohydrate metabolism, that is associated with increased CMR [19].

Objectives

Starting from these premises, we decided to analyze the subjects with glucose at 1 hour during OGTT ≥200mg%, but with normal values for fasting glucose and 2 hours glucose. In this subgroup of subjects some parameters

of CMR were analyzed. We also performed a comparison of this subgroup of subjects with both NGT and 1-hour glucose < 200mg%, and with those with AGT.

Materials and methods

In the present study were included 778 subjects, 342 men (44%) and 436 women (56%), with average age of 47.7±13.1 (18-77) years, from Timis County. The only criterion for inclusion in the study was that none of the subjects shows any definite diagnosis of diabetes or other disturbance of carbohydrate metabolism.

Were measured height (m), weight (kg), abdominal circumference (cm) and blood pressure (mmHg). It was calculated the body mass index (BMI): $BMI=G/h^2$ (kg/m^2). Concerning the abdominal circumference (AC), the official recommendation is to maintain it <94cm in males and <80cm in women.

After at least 8 hours fasting, OGTT was performed, the measurement of three blood glucose (fasting, at 1 hour and 2 hour) from venous plasma, using an enzymatic method with glucoxidase.

Also the total cholesterol (TC), triglycerides (TG), HDLc have been dosed. LDLc has been calculated using Friedewald's formula: LDLc (mg/dL)=TC - HDLc-TG/5 or LDLc (mmol/l)=TC- HDLc-TG/2.2. When TG were higher than 400mg%, the above formula gives false results, so in this case, we calculated non HDL cholesterol, according to the formula: non HDLc= TC-HDLc.

This lot was organized into a database created in Microsoft Excel as a file that contains the following fields: reference number, age, sex, BMI, AC, fasting glucose, glucose at 1 hour, at 2 hours, serum TC, TG, HDLc, LDLc. The statistical analysis consisted in calculating the frequencies and percentages for qualitative variables, calculating the arithmetic mean and standard deviations for the quantitative variables, statistical comparison of average media of samples with unpaired Student t-tests (unpaired t-test), paired t-Student (paired t-test) for two samples and ANOVA (,,Analysis of Variance") for more samples. ANOVA is applied for testing an equality of mean value in two main variants: a). unifactorial analysis "one-way analysis" - to compare **n** independent series obtained by different groups (for example, comparing the mean fasting glucose in subjects with NGT, the IGT and DM), b). bifactorial analysis "two-way analysis" - to compare **n** dependent series, obtained on the same lot in **n** conditions.

Results and discussion

The main clinical and biological characteristics of persons included in the study are presented in Table 1.

According to currently used recommendations to diagnose DM, from the 778 people included in this study, 167 (21.5%) had disturbances of carbohydrate metabolism, being classified as patoglycemic and 611 persons (78.5%) had normal values of fasting glucose and 2 hours glucose during OGTT, being considered normoglycemic (Figure 1).

The prevalence of disturbances of carbohydrate metabolism in the included population in the study was 21.5%, as follows: 5.9% DM, 5.7% IGT, 4.9% IFG, and 5% IFG + IGT (Figure 1 and Table 2).

We also analyzed the prevalence of carbohydrate metabolism disturbances by sex in the studied group. The prevalence of DM was higher in men than women: 6.4% and

5.5%. Also, the prevalence of carbohydrate metabolism disturbances was higher in men than women: 22.2% versus 20.8% (Table 2).

Table 1. Mean values of the characteristics which are analyzed in the studied group.

Parameter	Mean ± Standard deviation
BMI (kg/m^2)	27,2 ± 4,8
AC (cm) M W	 94,8 ± 14,8 91,2 ± 13,2
Fasting plasma glucose (mg%)	93,9 ± 20,9
1-hour glycaemia (mg%)	158,2 ± 57,8
2 -hours glycaemia (mg%)	136,4 ± 44,7
TC (mg%)	201,2 ± 43,1
TG (mg%)	155,7 ± 46,5
HDLc (mg%)	46,6 ± 7,8
LDLc (mg%)	127,4 ± 46,3

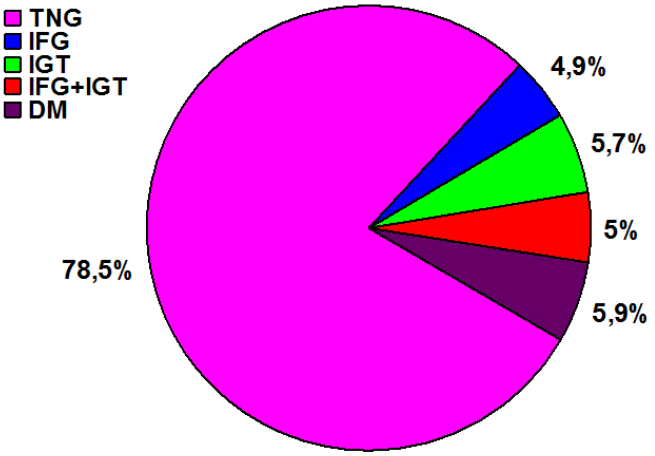

Figure 1. The prevalence of carbohydrate metabolism disturbances in the studied group.

Table 2. Distribution by sex of carbohydrate metabolism disturbances in the studied group.

Categories	Male		Women		Total	
	Number	Percent (%)	Number	Percent (%)	Number	Percent (%)
DM	22	6,4	24	5,5	46	5,9
IGT	17	5	27	6,2	44	5,7
IFG	16	4,7	22	5	38	4,9
IFG+IGT	21	6,1	18	4,1	39	5
NGT	266	77,8	345	79,2	611	78,5

From the 611 people who were classified as NGT, based on the currently used criteria for diagnosis of DM, a total of 44 persons (7.2%) had, however, the value of 1-hour glucose during OGTT ≥200mg%, which represents 5.6% of the entire group studied.

We analyzed this subgroup in terms of BMI, BP values, TC, TG, HDLc and LDLc, and the presence of MS.

Of these people, a number of 9 persons (20.4%) had a BMI <25kg/m^2, being considered of normal-weight, 12 people

(27.3%) had BMI between 25 to 29.9kg/m^2, being classified as overweight and 23 persons (52.3%) ≥30kg/m^2, these presenting obesity (Figure 2).

Hypertension was diagnosed in 39 persons (88.6%) of the ones with NGT and blood sugar ≥200mg% at 1 hour during OGTT.

In the present group we made a comparative study between the main characteristics of people with NGT and blood glucose ≥200mg% at 1 hour, and the ones both with the NGT and 1-hour glucose <200mg%, and also with the ones with AGT. For comparison we used the ANOVA test.

Comparing the three subgroups we observed a statistically significant difference: all the analyzed characteristics were higher both in persons with AGT and in those with NGT and blood glucose at 1 hour ≥ 200 mg%, as compared to NGT and 1-hour glucose <200mg% (p <0.001) (Table 3).

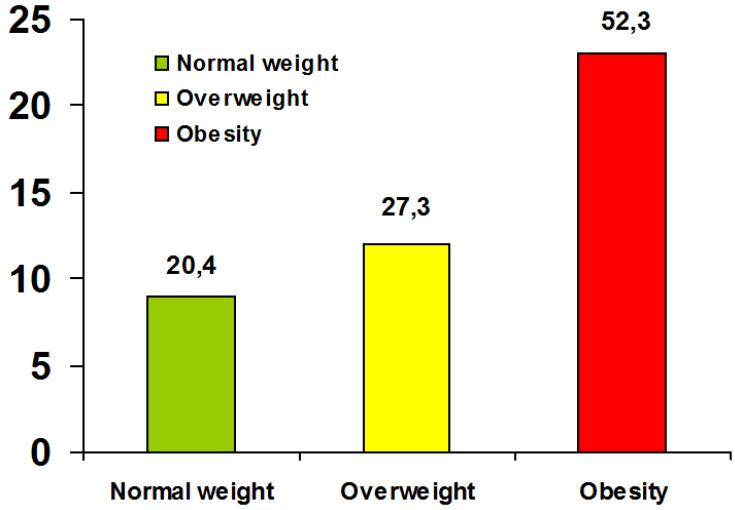

Figure 2. The distribution of people with NGT and 1-hour glucose ≥ 200 mg%, depending on weight status.

Table 3. Comparison of main characteristics of the three subgroups analyzed.

Parameter	NGT with 1 h glycaemia <200 mg%	NGT with 1 h glycaemia ≥200 mg%	AGT	p
BMI (kg/m^2)	23,8 ± 3,9	27,9 ± 4,4	29,7 ± 4,8	p<0,001
AC (cm)	85,7 ± 13,3	90,4 ± 14,5	93,2 ± 16,2	p<0,001
TC (mg%)	169,7 ± 38,6	212,1 ± 43,6	211,8 ± 42,1	p<0,001
TG (mg%)	97 ± 73,5	173,6 ± 81,2	196,5 ± 92,2	p<0,001
HDLc (mg%)	46,6 ± 6,8	43,2 ± 6,2	42,8 ± 6,1	p<0,001
LDLc (mg%)	112,4 ± 21,6	131 ± 23,2	138,9 ± 28,7	p<0,001

♦ Values are mean ± standard deviation

The prevalence of the MS was 54.5% in people with NGT and 1-hour glucose ≥200mg% during OGTT.

It is noted that the prevalence of the MS has been doubled in people who have blood sugar at 1 hour during OGTT ≥200mg% (fasting blood glucose ant at 2 hours in the normal range) as compared to those with NGT and 1-hour glucose <200mg %: 54.5% versus 21.7%, without significant differences from those with AGT: 54.5% and 58.7% (Figure 3).

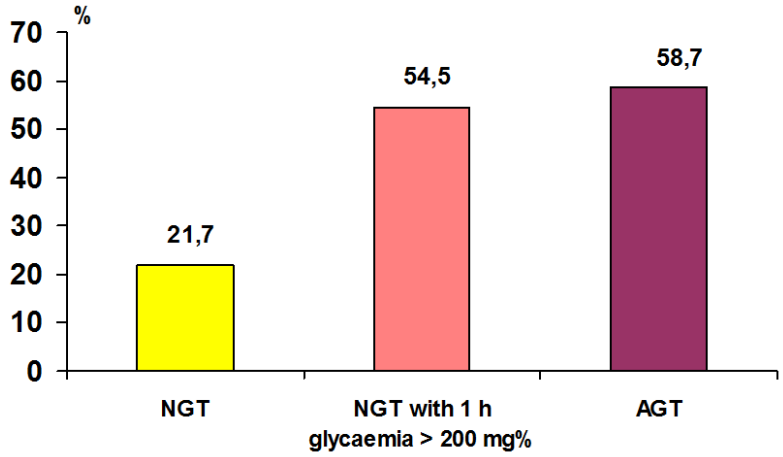

Figure 3. Prevalence of the MS in three categories of subjects.

Conclusions

The bigger values than 200mg% for the 1 hour glycaemia during OGTT test identifies an intermediate condition between the NGT and AGT, which is strongly associated with extremely high CMR.

Patients with NGT and glucose ≥ 200 mg% at 1 hour during OGTT represent a new subgroup of AGT, which requires strict lifestyle advice and possibly pharmacological measures to prevent or delay progression to AGT.

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