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Insulin resistance, parameters of carbohydrate metabolism, anthropometric parameters, interactions in diabetic patients

Diabetes mellitus type 2 is the most common form of diabetes. The number of patients with this disease has dramatically increased in the recent years. There are two main pathogenetic abnormalities in this type of diabetes: insulin resistance and beta cell dysfunction. The degree and proportions of these abnormalities can be a base for categorization of patients on this with predominantly insulin resistance and relative insulin deficiency or predominantly an insulin secretory defect with/without insulin resistance (14). The degree of insulin resistance and beta cell dysfunction in diabetic patients are not constant and usually we observed changes during the time of disease and after recommended therapy (8, 12). If insulin resistance and deficient beta cell function could be readily differentiated, it might be possible to predict an individual patient's response to diet, sulfonylurea or insulin therapy (7).

The methods used to assess these parameters: euglicaemic clamp, hyperglycaemic clamp, intravenous glucose tolerance test (IVGTT), continuous infusion of glucose with model assessment (CIGMA), homeostasis model assessment (HOMA), are rarely performed in practice because they are time-consuming, complex and costly. Especially first four of them are reserved only for science investigations.

The aim of the study was to assess the insulin resistance index and beta cell function in overweight and obese persons with diabetes mellitus type 2. We tried to investigate whether the insulin resistance index is associated with basic parameters of carbohydrate metabolism and anthropometrics values, which are cheap and simple to perform.

MATERIAL AND METHODS

We investigated patients with diabetes mellitus type 2 (n= 36) treated with oral hypogicemic agents, 19 of them with sulfonylureas and 17 with both sulfonylureas and Metformin. The known duration of diabetes ranged from 1 to 15 years with mean of 5.55 ± 3.7 years and mean age of 60 ± 10.14 years (ranging from 31 to 75 years). The control group represented patients with normal glucose tolerance (n= 37) with mean age of 60.65 ± 10.82 years (ranging from 43 to 80 years). There were no significant differences in age and gender structure between groups. The control group was completed with the similar body mass index (BMI) and waist to hip ratio (WHR) to the investigate group.

Table 1. Comparison of basic anthropometric parameters between groups

	Group				P value
	diabetic group		control group		
	mean	SD	mean	SD	
Weight (kg)	78.78	15.49	78.49	18.56	p = 0.94
Height (cm)	162.47	10.22	165.27	9.69	p = 0.23
Waist circumference (cm)	100.19	12.17	97.59	15.06	p = 0.42
Hip circumference (cm)	102.17	10.03	101.24	8.62	p = 0.67
BMI	29.72	4.41	28.46	4.69	p = 0.24
WHR	0.98	0.07	0.96	0.08	p = 0.26

In the diabetic group WHR value > 0.9 in men and > 0.8 in women was found in n= 35 (97.2%) cases. In the control group respectively in n= 34 (91.9%).

Body weight and height was measured with balance scale and height indicator. The body mass index (BMI) was calculated using the formula: BMI= weight/height^2 (kg/m^2) (4). Patients were categorized according to BMI (WHO classification) (1): normal 18.5–24.9, overweight 25.0–29.9, obese 30.0, very severely obese 40.0.

Waist circumference was measured at the level midway between the lower rib margin and iliac crest. Hip circumference was measured at the widest point between the hip and buttock. The circumferences were measured with the subjects standing using the measuring tape (9).

Waist to hip ratio was calculated according to the formula: WHR= waist circumference (cm)/hip circumference (cm). Central fat distribution was recognized when WHR exceed 0.9 in men and 0.8 in women. In all subjects we performed clinical examination (anamnesis, physical examination) and fasting blood sample was taken (10 ml). Fasting plasma glucose concentration was measured using enzymatic method. Normal range < 5.5 mmol/l (14). The percent of HbA_{1C} was measured in haemolyzed full blood sample

using 765 Glycomat (Ciba-Corning) with low pressure, ion exchange liquid chromatography method. Laboratory range for healthy subjects < 6%. Stressed fasting plasma insulin concentration was measured using Insulin-RIA-Prop code: MI-133 (radioimmune kit) produced by Research and Development Centre of Isotopes in Świerk. Normal range for healthy subjects 2–25 mU/l, sensitivity – 2.5 mU/l. Insulin resistance was predicted from stressed fasting plasma glucose concentration and stressed fasting plasma insulin concentration using a computer-solved model HOMA (homeostasis model assessment). The value of insulin resistance was calculated according to the formula: Insulin resistance= insulin/($22.5e^{-\ln \text{glucose}}$); insulin-stressed fasting plasma insulin concentration (mU/l); glucose-stressed fasting plasma glucose concentration (mmol/l).

Beta cell function was calculated according to the formula: Beta cell function (%)= 20 x insulin/(glucose – 3.5); insulin-stressed fasting plasma insulin concentration (mU/l); glucose-stressed fasting plasma glucose concentration (mmol/l). Subjects with plasma glucose concentration ≤ 3.5mmol/l were omitted, assuming that normal-weight, normal subject aged < 35 years have 100% beta cell function and an insulin resistance of 1 (11).

Statistical analyses. Standard methods were used to calculate mean values and standard deviations. Unpaired Student's t test and Chi^2 tests were used where appropriate for the comparison of clinical parameters between groups. Correlations were assessed by Person's correlation coefficient r. P value < 0.05 was considered significant.

RESULTS

Differences in stressed fasting plasma glucose concentrations were significant between the group with diabetes and control (mean 8.3±3.02 mmol/l vs. 4.6±0.54 mmol/l respectively, p< 0.0001). The mean value of HbA_{1C} level in the diabetic group was 7.6±1.99% and 5.49±0.33% in the control group, differences between the groups were significant (p< 0.0001). Stressed fasting plasma insulin concentration was similar in both groups with mean of 23.59±6.27 mU/l vs. 21.43±8.91 mU/l and p value 0.23. The mean value of insulin resistance was significant higher (p< 0.0001) in the diabetic group then in the control group (8.52±3.05 vs.4.51±2.02). The mean value of beta cell function (%) was significant lower (p< 0.0001) in the diabetic group then in the control group (157.22±140.73% vs. 380.94±149.9%).

The correlation between HOMA insulin resistance and stressed fasting plasma glucose concentration were in the diabetic group r= 0.67 (p< 0.0001) vs. r= 0.5 (p< 0.005) in the control group (Figs. 1 and 2).

The HOMA insulin resistance showed relationship with HbA_{1C} level r= 0.47 (p< 0.005) in the diabetic persons vs. r= 0.4 (p< 0.05) in the control group. We found significant (p< 0.01) negative correlation between insulin resistance and beta cell function r= –0.45 in the diabetic group. In the control group it was almost significant (p< 0.0067) but posi-

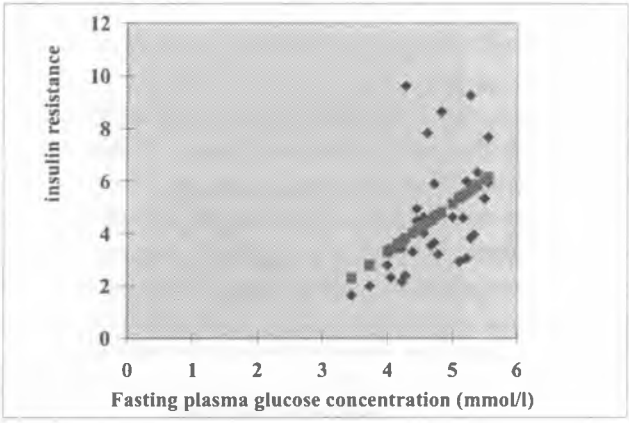

Fig. 1. Correlation between insulin resistance and fasting plasma glucose concentration in control group

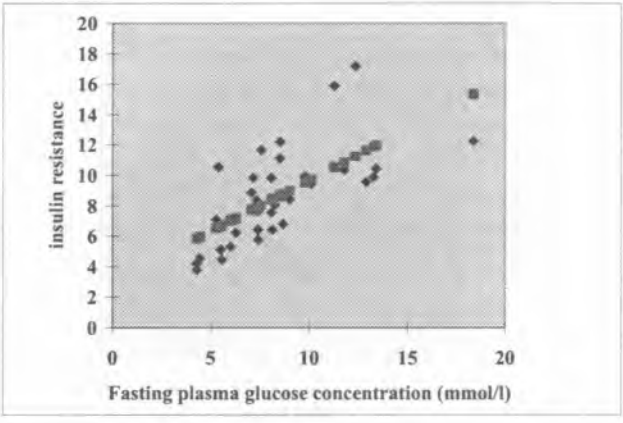

Fig. 2. Correlation between insulin resistance and fasting plasma glucose concentration in diabetic group

tive correlation r= 0.3. The relationships between stressed fasting insulin concentration and insulin resistance assessed by HOMA were significant in both groups respectively: r= 0.38 (p< 0.05) vs. r= 0.97 (p< 0.01).

In the group with normal glucose tolerance we showed significant correlations between insulin resistance and: waist circumference r= 0.52 (p< 0.001) (Fig. 3), BMI r= 0.48(p< 0.005) (Fig. 4), body weight r= 0.42 (p< 0.05), WHR r= 0.38 (p< 0.05). We did not find any significant relationships between HOMA insulin resistance and anthropometric parameters in diabetic group. Respectively, the correlation between insulin resistance and: BMI was r= 0.008 (p=0.6), waist circumference r= 0.24 (p= 0.15), body weight was r= 0.25 (p= 0.14), WHR r= 0.26 (p= 0.12) (Fig. 3, Fig. 4).

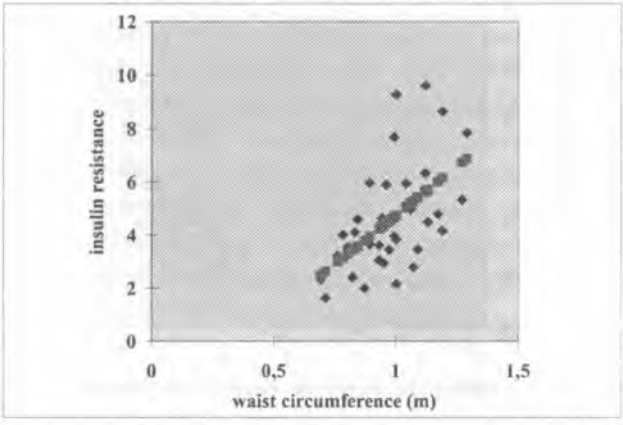

Fig. 3. Correlation between insulin resistance and waist circumference in control group

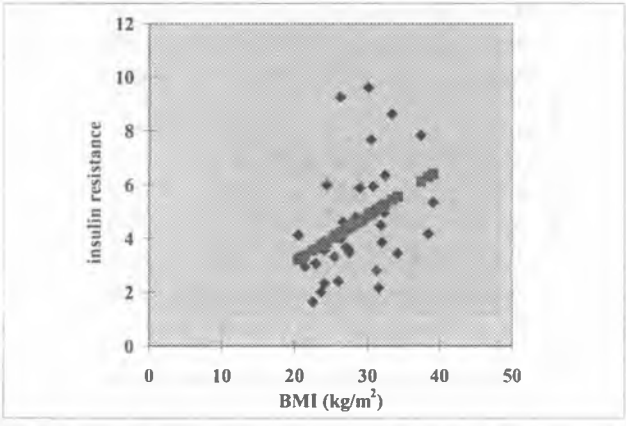

Fig. 4. Correlation between insulin resistance and BMI in control group

DISCUSSION

A mathematical model has been used to predict insulin resistance and beta cell function from fasting plasma glucose concentration and fasting plasma insulin concentration. The values of insulin resistance assessed by these method in authors' opinion correlate with values assessed by the euglicaemic clamp ($p< 0.0001$), hyperglycemic clamp ($p< 0.01$), fasting plasma insulin concentration ($p< 0.0001$) and continuous infusion of glucose with model assessment ($p< 0.0001$) – 11. HOMA provides a useful model to assess insulin resistance and beta cell function in epidemiological studies in which only fasting samples are available (5, 10). The beta cell function assessed by HOMA has a

strong correlation with other methods used to calculate this value (6,11). The usability of HOMA method was confirmed in subjects treated with oral hypoglycemic agents (2, 3, 8, 12).

We observed higher insulin resistance and decrease beta cell function in the diabetic group relatively to the control group. These abnormalities are considered fundamental in pathogenesis of diabetes mellitus type 2 (14). The negative correlation between insulin resistance and beta cell function in the diabetic group may be caused by excessive insulin secretion primary due to persistent high insulin resistance observed in these subjects. The positive and almost significant correlation between these parameters in control group resulting from compensation of higher insulin resistance with increase in insulin secretion assures normal glucose metabolism control. Previous reports have demonstrated a significant correlation between fasting plasma insulin concentration and insulin resistance. The same observation was shown in our study (5, 10, 11, 13, 15).

Our results demonstrated significant relationships between insulin resistance and anthropometric parameters in normal glucose tolerance subjects. Particularly the waist circumference and BMI seems to be the most useful predictors of insulin resistance in this group. The degree of insulin resistance is not associated with anthropometric parameters in diabetic patients, so insulin resistance is not a simple function of obesity in this group. It is possible that the absence of relationships between insulin resistance and anthropometric parameters in the diabetic group resulted from treatment influence. All subjects with diabetes mellitus type 2 were treated with sulfonylureas or both sulfonylureas and Metformin. This kind of treatment significant modifies beta cell function and insulin resistance leads to a decline of correlations between insulin resistance and anthropometric parameters.

CONCLUSIONS

1. HOMA insulin resistance showed significant correlations with anthropometric parameters in normal glucose tolerance subjects.
2. The degree of insulin resistance is not associated with anthropometric parameters in the diabetic group.
3. In both diabetic and control group we found significant correlations between insulin resistance and stressed fasting plasma insulin concentration, stressed fasting glucose concentration, HbA_{1C} level.

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SUMMARY

The aim of the study was to investigate relationships between insulin resistance index and basic parameters of carbohydrate metabolism and anthropometric values. We investigated patients with diabetes mellitus t.2 (n= 36) treated with oral hypoglycemic agents. The control group represented patients with normal glucose tolerance (n= 37). Both, the group with diabetes and control had similar values of anthropometric parameters. The insulin resistance index showed significant correlations with fasting plasma insulin and glucose concentrations and HbA1C level in both groups. In the group with normal glucose tolerance we showed significant correlations between insulin resistance index and anthropometric parameters (waist circumference, BMI, body weight, WHR). We did not find any significant relationships between insulin resistance and anthropometric parameters in the diabetic group.

Wzajemne zależności pomiędzy insulinoopornością, wskaźnikami gospodarki węglowodanowej i parametrami antropometrycznymi u chorych z cukrzycą typu 2

Celem pracy było zbadanie zależności pomiędzy insulinoopornością a podstawowymi wskaźnikami gospodarki węglowodanowej i parametrami antropometrycznymi. Badaniem objęto 36 osób z cukrzycą typu 2 leczonych doustnymi lekami hipoglikemizującymi. Grupę kontrolną stanowiło 37 osób bez cukrzycy. Porównywane grupy nie różniły się w sposób istotny parametrami antropometrycznymi. Wykazano istotne zależności pomiędzy insulinoopornością a stężeniem insuliny i glukozy oznaczanym w surowicy krwi żylnej na czczo oraz pomiędzy insulinoopornością a poziomem HbA_{1C} w obydwu badanych grupach. W grupie osób bez cukrzycy stwierdzono istotne zależności pomiędzy insulinoopornością a parametrami antropometrycznymi (obwód brzucha, BMI, WHR). Jednocześnie nie stwierdzono takich zależności w grupie osób z cukrzycą typu 2.