CLINICAL STUDY

Insulin resistance in kidney disease patients with mild to moderate kidney disease

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Abstract

Background: **Insulin resistance is a very early sign of atherosclerosis and an increased risk of cardiovascular morbidity and mortality. Insulin resistance detection by the fasting plasma insulin and glucose determination enables early detection, follow-up, treatment and the search for accelerating factors in kidney disease patients threatened by atherosclerosis.**
Patients and methods: **Insulin resistance was evaluated by the Quantitative Insulin Sensitivity Check Index from fasting glucose and insulin plasma concentrations in 66 kidney disease patients with a mild to moderate decrease in kidney function.**
Results: **Forty patients were insulin sensitive and 26 suffered from insulin resistance. These groups of patients did not differ significantly in age, gender, clearance of creatinine and cholesterol concentrations. However, patients with insulin resistance suffered from increased BMI ($p<0.001$), fasting plasma glucose ($p<0.01$), insulin ($p<0.001$) and triglyceride ($p<0.01$) concentrations. Insulin resistance correlated with BMI ($r=-0.417$, $p<0.001$) and with plasma triglycerides concentration ($r=-0.307$, $p<0.01$). The absent relationship between insulin resistance and age ($r=-0.154$, NS) or creatinine clearance ($r=-0.061$, NS) suggests the need for screening of insulin resistance even in young patients with mild kidney function reduction.**
Conclusion: **A considerable number of renal patients in the early stages of kidney function reduction suffers from insulin resistance. They need to improve their life style and take medication (i.e. antihypertensive drugs) improving insulin sensitivity and to omit medications which harm it.** ***(Fig. 2, Tab. 1, Ref. 20.)***
Key words: insulin resistance, kidney disease, creatinine clearance, cholesterol, triglycerides, BMI, blood pressure.

Insulin resistance (IR) is a major risk factor for atherosclerosis and consequent cardiovascular, cerebrovascular or kidney disease morbidity and mortality (Rabasa-Lhoret and Laville, 2001). Its high prevalence was repeatedly documented in advanced renal failure or in dialysed patients (De Fronzo and Alvestrand, 1980; Ferrannini et al, 1987; Mak and De Fronzo, 1992) and also in a significant number of patients with mild to moderate kidney dysfunction evaluated by minimal model technique (Fliser et al, 1998; Kato et al, 2000). Unfortunately, the minimal model or clamp techniques are time consuming, invasive and costly. Thus, more accessible methods have been developed, which enable us to calculate IR according to the Homeostasis Model Assessment (HOMA) (Rabasa-Lhoret and Laville, 2001) or by QUantitative Insulin sensitivity ChecK Index (QUICKI) (Katz et al, 2000; Hrebíček et al, 2002) on the basis of fasting plasma glucose and insulin values. These formulas enable large scale investigations for clinical and epidemiological purposes.

Subjects, materials and methods

Sixty-six kidney disease patients with a mild to moderate decrease of renal function and no interfering treatment were

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Tab. 1. Pertinent data of the evaluated patients.

	Unit	All	IS QUICKI≥0.354	IR QUICKI<0.354	p
Number	n	66	40	26	
Gender	m/f	32/34	18/22	14/12	
Age	years	#51±2	52±2	50±3	
SBP	mmHg	142±3	141±4	145±4	
DBP	mmHg	87±1	86±2	89±2	
Ccr	ml/s	0.952±0.081	0.921±0.105	0.999±0.128	
BMI	kg/m^2	26.5±0.6	24.7±0.5	29.3±1.0	**
Triglycerides	mmol/l	2.19±0.20	1.79±0.14	2.80±0.44	*
Cholesterol	mmol/l	5.36±0.15	5.21±0.20	5.59±0.24	
Glucose	mmol/l	5.29±0.09	5.11±0.10	5.57±0.14	*
Insulin	mU/ml	10.73±1.03	6.59±1.071	7.10±1.28	**
QUICKI		0.353±0.006	0.380±0.007	0.313±0.003	***

x±SEM, * p<0.01, ** p<0.001, *** p<0.0001
SBP — systolic blood pressure, DBP — diastolic blood pressure, Ccr — creatinine clearance, BMI — body mass index

evaluated. Patients with the nephrotic syndrome and/or diabetes were excluded. The study was approved by the local Ethics Committee.

Samples of morning fasting venous blood were centrifuged at 4 °C and analysed immediately for plasma glucose, creatinine, cholesterol and triglyceride concentrations by analyser Vitros 250 (Johnson&Johnson, Rochester, NY, USA) or stored at -70 °C for the determination of insulin by immunoradiometric assay (IMMUNOTECH a.s., Prague, Czech Republik).

QUICKI was calculated according to standard formula (Katz et al, 2000; Rabasa-Lhoret and Laville, 2001; Hrebíček et al, 2002):

QUICKI = 1/[log fasting insulin (uIU/ml) + log fasting glycemia (mg/dL)]

The discrimination value of insulin sensitivity/resistance was 0.354. Statistical analysis was performed both by parametric and nonparametric methods with Statgraphics software (STSC).

Results

Plasma glucose and insulin concentrations were in the normal range (Tab. 1). However, only 40 patients were insulin sensitive (IS); 26 patients were IR by the QUICKI evaluation. They suffered more from higher BMI, triglycerides and cholesterol plasma concentrations than IS ones. QUICKI correlated inversely with BMI (Fig. 1) and with triglycerides plasma concentrations (Fig. 2), while plasma cholesterol concentrations did not change significantly (r=0.006, not presented).

No significant differences were found between the IS and IR groups (Tab. 1) in gender, age, clearance of creatinine and blood pressure. Moreover, IR did not have a relationship with age (r=0.154) and with clearance of creatinine (r=-0.071).

Discussion

The prevalence of IR and glucose intolerance in kidney disease patients varies in the range of 30–100 % depending on se-

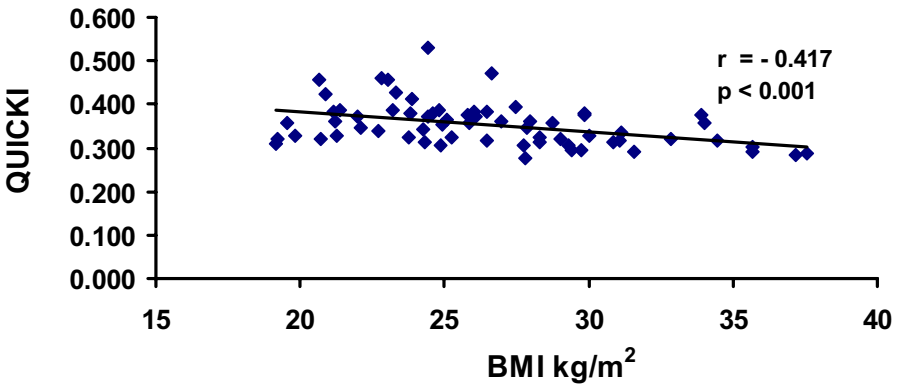

Fig. 1. The relationship between QUICKI and body mass index (BMI).

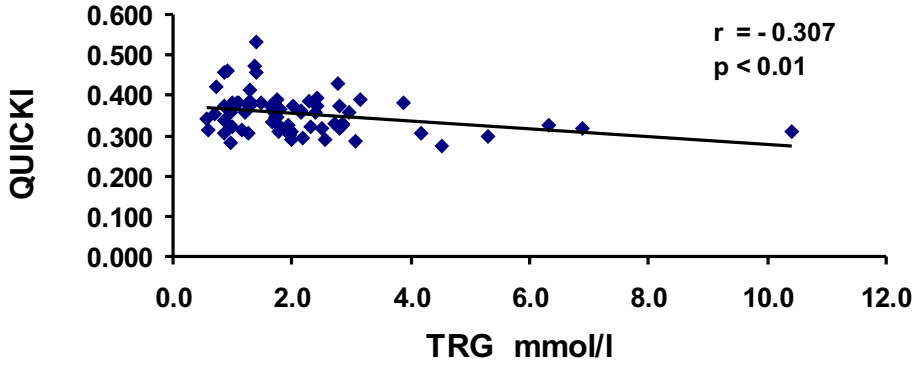

Fig. 2. The relationship between plasma concentration and QUICKI.

verity of kidney damage (De Fronzo and Alvestrand, 1980; Ferrannini et al, 1987; Mak and De Fronzo, 1992). It is present with lower prevalence even in the early stages of kidney function reduction (Katz et al, 2000; Hrebíček et al, 2002). It was nearly 40 % in the present study.

The decreasing kidney function evokes functional and metabolic alterations and the accumulation of "uremic toxins". Some of these interfere with carbohydrate metabolism. At least three of these compounds were identified, i.e. hippurate (Spustova et al, 1987; Spustová et al, 1989), pseudouridine (Dzúrik et al, 1993) and 5(OH)-indolacetic acid (Šebeková et al, 1996). These accumulated compounds increase IR further.

Moreover, metabolic acidosis also induces IR (Mak, 1998; Dzúrik a Spustová, 2003) and similar effects are caused by interferon-γ (Shiba et al, 1998), hydrochlorothiazide in diuretic but not in antihypertensive dosage (Neutel, 1996), nonselective β-blockers and many other drugs. On the other hand some drugs improve IR, i.e. α-blockers (Lehtonen, 1991), ACE inhibitors (Okša et al, 1994; Wu and Bao, 1998), vitamin D and calcitriol (Mak, 1998), etc. Therefore it could be expected that appropriate medication would improve IR. Unfortunately the effect of most drugs on IR is unknown.

In conclusion, the high prevalence of IR in kidney disease patients requires early diagnosis. The QUICKI formula present convenient method for large scale IR determination not only in renal patients. The detection, prevention and treatment of IR can decelerate atherosclerosis progression from participating significantly in the premature mortality and morbidity of kidney disease patients.

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