CLINICAL STUDY

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

Stefikova K, Spustova V, Krivosikova Z, Dzurik R

Research Base of the Slovak Medical University, Institute of Preventive and Clinical Medicine, Department of Clinical and Experimental Pharmacotherapy, Bratislava, Slovakia. kornelia.stefikova@szu.sk

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 (Fiser 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 CheK Index (QUICKI) (Katz et al, 2000; Hrebiček 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

Research Base of the Slovak Medical University, Institute of Preventive and Clinical Medicine, Department of Clinical and Experimental Pharmacotherapy, Bratislava, Slovakia

Address for correspondence: K. Stefikova, MD, PhD, Slovak Medical University, Department of Clinical and Experimental Pharmacotherapy, Limbova 12, SK-833 03 Bratislava 37, Slovakia. Phone: +421.2.59369166, Fax: +421.2.59369906
evaluated. Patients with the nephrotic syndrome and/or dia-
etes 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; Hrebiček et al,
2002):

\[
\text{QUICKI} = \frac{1}{[\log \text{fasting insulin (uU/ml)} + \log \text{fasting glu-
cemia (mg/dL)}]}
\]

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 sensi-
tive (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 dis-
ease patients varies in the range of 30–100 % depending on se-

![Fig. 1. The relationship between QUICKI and body mass index (BMI).](image-url)

*SEM, **p<0.01, ***p<0.001
SBP — systolic blood pressure, DBP — diastolic blood pressure, Ccr — creatinine clearance, BMI — body mass index
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; Hrebiček 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.

References


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