

LETTER TO EDITOR

Early assessment of metabolic situation in young patients with hypertension may prevent subsequent adverse cardiovascular events

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Letter to the Editor

Hypertension is considered the main risk factor of cardiovascular mortality. Secular trends in highly developed countries have shown decrease in blood pressure in the young population, which has been associated with reduction in cardiovascular morbidity at later age of these individuals (1). In the Slovak population aged between 18 and 30 years, increased blood pressure is predominant in men compared to women (3:1) (2). Data on prevalence of hypertension in high school and college male students in Slovakia vary from 3 to 20 % (3, 4, 5).

According to current recommendations for diagnosis and treatment of hypertension (ESH/ECS 2003 (6)), evaluation of fasting glycaemia should be preferably included into the initial set of diagnostic tests. However, fasting glycaemia is normal when insulin resistance is compensated by increased insulin secretion. Moreover, it cannot detect also manifest impairment of postprandial glucose tolerance. DECODE study (7) has shown that 2-hour OGTT plasma glucose (2hPG) is a more reliable predictor of cardiovascular mortality than fasting plasma glucose.

While variability of different insulin assays and ethnic differences in insulin levels do not allow to set up standard criteria for insulin resistance, criteria for glucose intolerance, and thus increased risk for developing Type 2 diabetes and its macrovascular and microvascular complications, are clear and easily detectable (8). Our investigation in thirty young men with essential hypertension (age 20.8 ± 1.5 years, mean \pm S.E.) with normal body weight (BMI 22.4 ± 1.4 kg/m²) showed that 56 % had increased normal 2hPG levels (5.6–7.8 mmol/l) compared to 17 % matched subjects with normal blood pressure. Piché et al (9) has shown in 600 patients that increased normal 2hPG is an important risk factor of cardiovascular morbidity and Type 2 diabetes independently of obesity, gender or body fat distribution. Some experts therefore recommend measurement of haemoglobin A1c or real glucose tolerance test during initial examination for hypertension in offspring of subjects with cardiovascular diseases including hypertension, or with Type 2 diabetes (10).

Epidemiological studies have shown that hyperinsulinaemia is an independent risk factor of cardiovascular diseases (11, 12). Several studies confirmed insulin resistance in hypertensive subjects with obesity (13) and overweight (14). In our study, young men with essential hypertension and BMI well below 25 kg/m² had a two-fold increase of fasting plasma insulin levels compared to healthy controls (15). Hyperinsulinaemia has an adverse effect on lipid metabolism characterised by increased accumulation of fat in the abdominal area and dyslipidaemia, resulting in a vicious circle of events further promoting metabolic imbalance and potentiating the proatherogenic effect of high blood pressure (16). However, our analysis of results detected mild dyslipidaemia (lower HDL- or higher LDL- or total cholesterol) also in control individuals, which may be due to nutritional habits and composition of diet in this population.

Early atheromatous changes in vessels are characterised by endothelial dysfunction, which is frequently found already in children or adolescents (17). Subjects with hypertension in our study had increased plasma levels of an indirect marker of endothelial dysfunction, i.e. plasminogen activator inhibitor 1 (PAI-1, 37.3 ± 8.7 vs 12.5 ± 1.7 , $p=0.001$).

According to ATP NCMP 2003 criteria, 67 % of patients in our study displayed 3 to 4 traits of metabolic syndrome (MS), hypertension, dyslipidaemia, history of hypertension in parents, insulin resistance). Although WHO 1999 (18) criteria consider insulin resistance as the main characteristic of MS, the attention of experts is predominantly focused on obese individuals. Our

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results indicate that in order to successfully diagnose and treat MS, young males with hypertension appear to represent another important target population for longitudinal studies, such as Framingham study, evaluating the impact of early detection therapy of MS on future cardiovascular outcome.

Beta-adrenergic inhibitors represent the first-choice anti-hypertensive drugs in young patients with essential hypertension. It should be noted that chronic treatment with some of these agents is associated with worsening of insulin sensitivity and glucose homeostasis (19). Therefore, evaluation of metabolic status is required before onset of treatment in order to choose optimal agents with minimal or no negative effect on insulin sensitivity. In specific cases the use of antihypertensives from another class may be considered. Inhibitors of angiotensin converting enzyme (ACE) or of angiotensin receptor 1 (AT-1) possess some characteristics that may help to improve insulin sensitivity, dyslipidaemia and endothelial dysfunction (20, 21).

In conclusion, our observations indicate that evaluation of glucose homeostasis, insulin sensitivity and endothelial function may represent an essential step in early diagnosis of hypertension in young individuals, which may lead to adequate lifestyle and pharmacological intervention decreasing the risk of atherosclerosis and its cardiovascular complications in later life.

References

1. **McCarron P, Smith GD, Okasha M.** Secular changes in blood pressure in childhood, adolescence and young adulthood: systemic review o trends from 1948 to 1998. *J Hum Hypertens* 2002; 10: 677–689.
2. **Čižmarová E.** Osobitosti a špecifiká hypertenzie v detskom a dorastovom veku. *Kardiológia* 2004; 5: 197–301.
3. **Egnerová A, Cagán S, Kamencová L, Červenka J.** Krvný tlak u vysokoškôľákov v Bratislave. *Bratisl lek Listy* 1981; 76: 173–181.
4. **Bakošová M.** Sledovanie krvného tlaku v období dospievania. Abstracta XX. Medzinárodného pediatrického kongresu. Bratislava 1979; 257.
5. **Mičieta V, Bahnova M, Lietava J.** Static physical exercise in adolescents is related to juvenile hypertension. *Journal of Hypertension* 2003; 21 (Suppl 4): S57.
6. **ESH/ECS 2003.** European Society of Hypertension- European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; 21: 1011–1053.
7. **DECODE Study Group** on behalf of the European Diabetes Epidemiology Study Group. Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases? *Diabet Care* 2003; 26: 688–696.
8. **American Diabetes Association:** Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabet Care* 2003; 26: S5–20.
9. **Piche ME, Lemieux S, Pérusse L, Weisnagel SJ.** High normal 2-hour plasma glucose is associated with insulin sensitivity and secretion that may predispose to type 2 diabetes. *Diabetologia* 2005; 48 (4): 732–740.
10. **National High Blood Pressure Education Program Working Group** on Blood pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004; 114 (Suppl 2): 555–576.
11. **Zavoroni I, Bonini L, Gasparini P et al.** Hyperinsulinemia in a normal population as a predictor of non-insulin-dependent diabetes mellitus, hypertension, and coronary heart disease: the Barilla factory revisited. *Metabolism* 1999; 48 (8): 989–994.
12. **Abbasi F, Brown BW Jr, Lamendola C, McLaughlin T, Reaven GM.** Relationship between obesity, insulin resistance, and coronary heart disease risk. *J Amer Coll Cardiol* 2002; 40 (5): 937–943.
13. **Modan M, Halkin H, Almog S et al.** Hyperinsulinemia. A link between hypertension obesity and glucose intolerance. *J Clin Invest* 1985; 75: 809–817.
14. **Ferrannini E, Buzzigoli G, Bonadonna R et al.** Insulin resistance in essential hypertension. *New Engl J Med* 1987; 317 (6): 350–357.
15. **Penesova A, Radikova Z, Kvetnansky R, Blazicek P, Koska J, Vigas M.** Insulin resistance in young males with early hypertension is not associated with aggravated neuroendocrine response. IV. European Meeting of Hypertension, Paris, France. *J Hypertens* 2004; 22 (Suppl 2): S226.
16. **Ginsberg HN, Huang LS.** The insulin resistance syndrome: impact on lipoprotein metabolism and atherothrombosis. *J Cardiovasc Risk* 2000; 7 (5): 325–331.
17. **Páll D, Settakis G, Katona E et al.** Increased common carotis arteria thickness in adolescent hypertension: results from the Debrecen Hypertension study. *Cerebrovasc Dis* 2003; 3: 167–172.
18. **WHO Consultation.** Definition, diagnosis and classification of diabetes mellitus and its complications. Geneva: World Health Organization, 1999: 31–33.
19. **Reneland R, Alvarez E, Andersson PE, Haenni A, Byberg L, Lithell H.** Induction of insulin resistance by beta-blockade but not ACE-inhibition: long-term treatment with atenolol or trandolapril. *J Hum Hypertens* 2000; 14: 175–180.
20. **Derosa G, Ragonesi PD, Mugellini A, Cicarelli L, Fogari R.** Effects of telmisartan compared with eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertensive, type 2 diabetic patients: a randomized, double-blind, placebo-controlled 12-month study. *Hypertens Res* 2004; 27 (7): 457–464.
21. **Vitale C, Mercurio G, Castiglioni C et al.** Metabolic effect of telmisartan and losartan in hypertensive patients with metabolic syndrome. *Cardiovasc Diabet* 2005; 15 (4): 6.

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