AJH 1993; 6:314–316

Red Blood Cell Na-Li Countertransport, Hypertensive Heredity, and Cardiovascular Risk in Young Adults

J.-M. Krzesinski, A. Saint-Remy, F. Du, and G. Rorive

The erythrocyte Na-Li countertransport (CT) has been considered as a marker of genetic propension to essential hypertension, but also to be linked to atherosclerosis risk factors. We have evaluated these relationships by measuring the Na-Li CT, blood pressure levels, the family predisposition to hypertension, body mass index, subscapular skinfold thickness, waist/hip ratio, and plasma lipids in 43 young adults (22 to 23 years; 13 with a positive family history of hypertension), followed since adolescence (± 10 years) to analyze the natural history of blood pressure in this period of life. The Na-Li CT was negatively correlated with the HDL cholesterol ($r = -0.37$) and the HDL cholesterol/total cholesterol ratio ($r = -0.44$). This transport system was positively correlated to family history of hypertension ($r = 0.38$), waist/hip ratio, and the diastolic blood pressure. When the family history of hypertension was present, Na-Li CT and diastolic blood pressure were higher ($P < .05$), but the HDL cholesterol was lower ($P < .01$). After separating people according to the blood pressure level during adolescence in two groups, one lower than the 75th percentile (P75), and one higher, we notice that the latter remains characterized by a higher systolic blood pressure. But neither the Na-Li CT nor family history of hypertension and plasma lipids could explain the difference in the blood pressure behavior during this period. Thus, an increase of RBC Na-Li CT activity in young adults would suggest a higher cardiovascular risk rather than to be a simple marker of a hypertensive risk. Am J Hypertens 1993;6:314–316

KEY WORDS: **Na-Li countertransport, family history of hypertension, plasma lipids, blood pressure, weight.**

A controversy subsists about the role played by an increase in the activity of the sodium-lithium countertransport (Na-Li CT): is it a marker of the hypertensive risk[1–3] or of more general cardiovascular risk?[4,5] This study evaluates the significance of Na-Li CT measurement as a predictor of essential hypertension and/or of atherosclerosis.

MATERIAL AND METHODS

We followed for 10 years, since adolescence, 43 patients (average age 23 ± 8 years), 13 of which had a family history of hypertension. We measured in this population, in fasting conditions and in the morning, blood pressure (BP), heart rate, weight, body mass index (BMI), subscapular skinfold (SSF) thickness, plasma lipids (total cholesterol, HDL cholesterol, and triglycerides), 24 h urinary sodium excretion (in mmol/g of creatinine, thus eliminating the problem of incomplete urine collection), red blood cell (RBC) sodium concentration

Received May 26, 1992. Accepted December 8, 1992.

From the University of Liege, Liege, Belgium.

This article is based on data presented at the American Society of Hypertension's annual meeting May 6 to 9, 1992.

Address correspondence and reprint requests to J.M. Krzesinski, Nephrology-Hypertension Unit, CHU Liege, B35, +6, 4000 Liege, Belgium.

0895-7061/93/$6.00

TABLE 1. CHARACTERISTICS OF THE POPULATION

Variables	Mean ± SD	Min–Max
SBP (mm Hg)	132 ± 10	110–151
DBP (mm Hg)	77 ± 10	54–93
Weight (kg)	74.7 ± 15	55–115
BMI (kg/m²)	24.2 ± 4	18–36
SSF thickness (mm)	13.7 ± 7	7–40
Waist/hip ratio	0.89 ± 0.06	0.78–1.04
Urinary Na/g Creatinine (mmol/g)	113 ± 65	25–268
Triglycerides (g/L)	1.1 ± 0.76	0.4–4.3
Total cholesterol (g/L)	1.9 ± 0.4	1.2–2.85
HDL cholesterol (g/L)	0.48 ± 0.1	0.33–0.69
HDL cholesterol/total cholesterol ratio	0.26 ± 0.08	0.12–0.44
RBC Na (mmol/L cell)	8.7 ± 1.2	4.9–11.5
Na-Li CT (μmol/L cell × h)	386 ± 110	185–681

(Na), and RBC Na-Li CT, according to the method described by Canessa et al.[6] The characteristics of the population are detailed in Table 1.

The family histories of hypertension were very carefully researched by a survey on the causes of death in the families and by measuring the BP in all relatives still alive.

All the clinical data were determined by the same well-trained observer. The SSF thickness was measured under the tip of the shoulder blade by John Bull, Ltd. 0.2 mm graduated compasses. This biometric parameter could be considered as one of the most representative markers of central adiposity.

RESULTS

When the patients were divided into two groups according to family history of hypertension, either present (FH+), or absent (FH−), we were able to observe that the FH+ group was characterized by higher diastolic BP and Na-Li CT activity, and lower HDL cholesterol/total cholesterol ratio than the FH− group (Table 2). We also distributed these 43 patients according to the BP level through adolescence, either always above the 75th percentile (>P75, n = 15) or below this (<P75, n = 28). We noted that the RBC Na values or the Na-Li CT values could not predict who belonged to which of these groups: in the >P75 group, the RBC parameters were 8.7 ± 1.5 mmol/L cells for the Na concentration and 362 ± 118 μmol/L cells × h for the Na-Li CT, whereas in the <P75 group, the RBC values were 8.6 ± 0.9 mmol/L cells and 395 ± 105 μmol/L cells/h, respectively (P = NS). The systolic BP alone was significantly different between the two groups: 137 ± 11 mm Hg in the >P75 group and 129 ± 9 mm Hg in the <P75 group ($P < .01$).

Some significant correlations (Spearman coefficients) were noted between several of the parameters we tested: between SBP and BMI: r = 0.44, $P < .003$; between SBP and waist/hip ratio: r = 0.40, $P < .01$; between DBP and FH+: r = 0.38, $P < .01$; between DBP and SSF thickness: r = 0.30, $P < .05$; between RBC Na and FH+: r = 0.33, $P < .05$; between Na-Li CT and FH+: r = .38, $P < .01$; between Na-Li CT and waist/hip ratio: r = 0.29, $P = .06$; between Na-Li CT and HDL cholesterol/total cholesterol: r = −0.43, $P < .005$; and between Na-Li CT and HDL cholesterol: r = −0.37, $P < .02$.

By stepwise regression the best predictor for the RBC Na-Li value was given by Na-Li CT = 497 − 443 HDL/total cholesterol, $P = 0.057$, $R^2 = 10.5\%$.

DISCUSSION

In essential hypertensives, as well as in normotensive patients with a positive family history of hypertension,[6,7] the Na-Li CT was found to be increased in comparison to normotensives without such family history. In the literature, however, this RBC parameter is not specific for hypertension or for its predisposition. Indeed, the activity of this RBC transport system could be influenced by some clinical situations, such as pregnancy,[8] insulin-dependent diabetes with hyperfiltration[9] or microalbuminuria,[10] non–insulin-dependent diabetes prior to nephropathy,[11] hyperlipidemia,[12,13] treatment by oral contraceptives, or drug-induced hypokalemia.[14]

In this study, we confirmed the existence of an increase in the activity of the Na-Li CT in young normotensive adults with a positive family history of hyper-

TABLE 2. INFLUENCE OF HYPERTENSIVE HEREDITY ON CLINICAL AND BIOLOGICAL DATA IN 43 NORMOTENSIVE YOUNG ADULTS

	FH+ (n = 13)	FH− (n = 30)	P
SBP (mm Hg)	132 ± 11	132 ± 10	NS
DBP (mm Hg)	82.5 ± 8	74.5 ± 10	<.01
BMI (kg/m²)	24.6 ± 5.2	23.8 ± 3.0	NS
SSF thickness (mm)	15.4 ± 8.0	12.7 ± 6.6	NS
Waist/hip ratio	0.90 ± 0.07	0.88 ± 0.06	NS
Urinary Na/g creatinine (mmol/g)	106 ± 58	113 ± 68	NS
Triglycerides (g/L)	1.01 ± 0.4	1.14 ± 0.9	NS
HDL cholesterol (g/L)	0.47 ± 0.1	0.49 ± 0.1	NS
HDL cholesterol/total cholesterol	0.23 ± 0.1	0.28 ± 0.1	<.01
RBC Na (mmol/L cell)	9.1 ± 0.9	8.5 ± 1.2	=.09
Na-Li CT (μmol/L cell × h)	455 ± 142	353 ± 77	<.03

tension. However, the negative link between this RBC parameter and the HDL cholesterol or HDL cholesterol/total cholesterol ratio, and the absence of a significant difference in Na-Li CT between the two normotensive groups separated according to blood pressure level through adolescence, suggest that this transport system, more than being a marker of hypertensive risk, is the reflection of a bad lipid profile and also of a more central adiposity distribution (existence of a positive correlation between Na-Li CT and SSF thickness). This is in agreement with some authors.[4,15]

These characteristics are prominent features of people with insulin resistance who are prone to hypertension and cardiovascular disease.[16] Moreover, recently it has been shown that insulin resistance is linked to a higher Na-Li CT activity,[17] strengthening the importance of this transport system's activity as a marker for the risk of atherosclerosis. In conclusion, these results indicate that the evaluation of this transport system can be an important diagnostic tool in the prevention of cardiovascular diseases.

REFERENCES

1. Laurenzi M, Trevisan M: Sodium-lithium countertransport and blood pressure: the Gubbio population study. Hypertension 1989;13:408–415.
2. Turner S, Michels V: Sodium-lithium countertransport and hypertension in Rochester, Minnesota. Hypertension 1991;18:183–190.
3. Weder A, Schork N, Krause L, Julius S: Red blood cell lithium-sodium countertransport in the Tecumseh blood pressure study. Hypertension 1991;17:652–660.
4. Yap L, Arrazola A, Soria F, Diez J: Is there increased cardiovascular risk in essential hypertensive patients with abnormal kinetics of red blood cell sodium-lithium countertransport? J Hypertens 1989;7:667–673.
5. Carr S, Thomas T, Laker M, Wilkinson R: Elevated sodium-lithium countertransport: a familial marker of hyperlipidaemia and hypertension? J Hypertens 1990; 8:139–146.
6. Canessa M, Adragna N, Solomon H, et al: Increased sodium-lithium countertransport in red cells of patients with essential hypertension. N Engl J Med 1980;302: 772–776.
7. Woods J, Falk R, Pittman A, et al: Increased red-cell sodium-lithium countertransport in normotensive sons of hypertensive parents. N Engl J Med 1982;306:593–595.
8. Worley R, Hentschel W, Cormier C, et al: Increased sodium-lithium countertransport in erythrocytes of pregnant women. N Engl J Med 1982;307:412–416.
9. Carr S, Mbanya JC, Thomas T, et al: Increase in glomerular filtration rate in patients with insulin-dependent diabetes and elevated erythrocyte sodium-lithium countertransport. N Engl J Med 1990;322:500–505.
10. Jones S, Trevisan R, Tariq T, et al: Sodium-Lithium countertransport in microalbuminuric insulin-dependent diabetic patients. Hypertension 1990;15:570–575.
11. Gall M-A, Rossing P, Jensen J, et al: Red cell Na^+/Li^+ countertransport in non–insulin-dependent diabetics with diabetic nephropathy. Kidney Int 1991;39:135–140.
12. Corrocher R, Steinmayr M, Ruzzenente O, et al: Elevation of red cell sodium-lithium countertransport in hyperlipidemia. Life Sci 1985;36:649–655.
13. Hunt S, Williams R, Smith J, Ash K: Associations of three erythrocyte cation transport systems with plasma lipids in Utah subjects. Hypertension 1986;8:30–36.
14. Beuckelmann D, Erdmann E: Exogenous factors influencing the human erythrocyte sodium-lithium countertransport system. Eur J Clin Invest 1984;14:392–397.
15. Nosadini R, Semplicini A, Fioretto P, et al: Sodium-lithium countertransport and cardiorenal abnormalities in essential hypertension. Hypertension 1991;18:191–198.
16. Ferrannini E, Natali A: Essential hypertension, metabolic disorders, and insulin resistance. Am Heart J 1991; 121:1274–1282.
17. Doria A, Fioretto P, Avogaro A, et al: Insulin resistance is associated with high sodium-lithium countertransport in essential hypertension. Am J Physiol 1991;261:E684–E691.