Increased Red Cell Volume in Impaired Glucose Tolerance: A Further Evidence of Hematologic Sequelae of Altered Glucose Metabolism

The occurrence of an increased mean red cell volume (MCV) in diabetes has been reported.[1] Moreover, we have suggested that metabolic control may influence MCV in diabetes.[2] Since the measurement of HbA_1 has been reported to be a quick, accurate, and simple screening test to reveal patients with impaired glucose tolerance,[3] we have evaluated plasma glucose, HbA_1, and MCV in 150 male blood donors (age 22–40 yr), who had no family history of diabetes.

Our normal range of HbA_1 is 5–7%.[4] All subjects had normal fasting plasma glucose (4.84 ± 0.44 mmol/L; mean ± SD).

When the subjects were divided according to their HbA_1 values, those with levels of HbA_1 about 7% (35 subjects) presented higher values of MCV (89.74 ± 4.21 femtoliters) than those subjects with HbA_1 below 7% (115 subjects) (MCV = 86.47 ± 3.44 femtoliters; $P < 0.001$). There was no correlation between HbA_1 and MCV values.

These data show that impaired glucose tolerance may be associated with increased MCV.[5–8]

FRANCESCO CURCIO, M.D.
PATRIZIA DELLO RUSSO
DARIO GIUGLIANO, M.D.
ANTONIO CERIELLO, M.D.

From the Laboratorio di Chimica, USL 38–Ospedale S. Paolo, Naples, Italy (F.C., P.D.R.); and the Istituto di Patologia Medica, I° Facolta di Medicina, Universita di Napoli, Naples, Italy (D.G., A.C.).

REFERENCES

[1] Davidson, R. J. L., Evan-Wong, L. A., and Stowers, J. M.: The mean red cell volume in diabetes mellitus. Diabetologia 1981; 20:583–84.

[2] Ceriello, A., Dello Russo, P., Curcio, F., Balsamo, C., and Pietrantuono, C.: Red blood cell volume and glycaemic control in diabetes. Diabetologia 1983; 24:397.

[3] Hall, P. M., Cook, J. G. H., Sheldon, J., Rutheford, S. M., and Gould, B. J.: Glycosylated hemoglobins and glycosylated plasma proteins in the diagnosis of diabetes mellitus and impaired glucose tolerance. Diabetes Care 1984; 7:147–50.

[4] Ceriello, A., Giugliano, D., Dello Russo, P., and Passariello, N.: Hypomagnesemia in relation to diabetic retinopathy. Diabetes Care 1982; 5:558–59.

[5] Graham, J. J., Ryall, R. G., and Wise, P. H.: Glycosylated haemoglobin and relative polycythaemia in diabetes mellitus. Diabetologia 1980; 18:205–207.

[6] Ceriello, A., Dello Russo, P., Sgambato, S., and Giugliano, D.: Glycosylated haemoglobin and reticulocyte count in diabetes. Diabetologia 1982; 22:223.

[7] Peterson, G. M., Jones, R. L., Koening, R. S., Helvin, E. T., and Lehrman, M. L.: Reversible hematologic sequelae of diabetes mellitus. Ann. Intern. Med. 1977; 86:425–28.

[8] Dello Russo, P., Ceriello, A., and Curcio, F.: Reticulocyte counts and haemoglobin glycosylation in diabetes. In press. Diabete Metab. 1984.

Hypertension and Diabetes

Like many of my colleagues, I am delighted to finally see the new and long-awaited report by the Joint National Committee on the detection, evaluation, and treatment of high blood pressure, which included a review of earlier recommendations. (Arch. Intern. Med. 1984; 144:1045–57.) Yet, like a number of physicians, especially diabetologists, I am concerned and rather disappointed by the failure of this report to specifically address the issue of hypertension in the diabetic patient, unequivocally, and in a more forthcoming and detailed fashion.

Evidence is now mounting that the use of diuretics is associated with potential cardiovascular risks; namely, hypokalemia, resulting in serious cardiac arrhythmia; hypertriglyceridemia; hypercholesterolemia; hyperuricemia; and decreased HDL, all of which contribute to the process of atherosclerosis in diabetic patients who already have compromised vascular status, let alone impairment of diabetes control, associated with these agents. Indeed, our European colleagues have long abandoned the use of diuretics as first-step agents, especially in the hypertensive diabetic population. And, although it could be argued by some that the dose of diuretics should not be pushed to the maximum to avoid possible hypokalemia and that the potassium level could be monitored in these patients, many studies indicate that abnormal glucose metabolism may occur without changes in the potassium level.[1–3] Furthermore, it can be argued that a limited rise in lipids is sufficient to increase the risk of atherosclerosis and coronary heart disease.[3,4] This is a fact that has also been recently suported by the results of the LRC study.[5] Add to this the economic impact caused by frequent office visits and lab tests to monitor potassium level, lipids, glucose, and uric acid in a patient whose blood pressure may remain uncontrolled, requiring the use of additional antihypertensive agents.[6]

The MRFIT Study,[7] the Morgan Study,[8] and the Oslo Study[9] provide us with at least some indirect evidence that the use of diuretic therapy in the treatment of hypertension has not helped reduce coronary morbidity and mortality, perhaps due to the above complications, which offset or negate the benefits derived from lowering the blood pressure through the use of such agents. Similarly, the problem of beta blockers causing a suppression of insulin release, a masking of hypoglycemic reaction with a blunted response or recovery, vasoconstriction, hyperlipidemia, and a reduction of HDL[10–12] in a population with already compromised vascular and lipid status has not been mentioned or seriously emphasized in the report. The use of Clonidine in the diabetic hypertensive patient, with its possible consequences of suppressed insulin

release from the pancreas in those who maintain at least some insulin reserve,[13,14] has not been discussed. Nor has it been emphasized that the centrally acting agents may indeed compound the problem of impotence, which already afflicts many diabetic patients.[15,16]

While it is understandable why the committee cannot discourage or advocate the use of specific antihypertensive agents in the diabetic population, I feel that, especially in treating the diabetic hypertensive patient, emphasis should be given to agents that have more favorable hemodynamic and metabolic profiles.[17–19]

I only wish to bring attention to a specific problem that may have been overshadowed by the general problem of hypertension in our population at large.

T. MERIDEN, M.D., F.A.C.P.

REFERENCES

[1] Sagild, U., Anderson, V., and Andraesen, P. B.: Glucose tolerance and insulin responsiveness in experimental potassium depletion. Acta Med. Scand. 1961; 169:243–51.

[2] Lewis, P. J., Petrie, A., Kohner, E. M., and Dollery, C. T.: Deterioration of glucose tolerance in hypertensive patients on prolonged diuretic therapy. Lancet 1976; 1:564–66.

[3] Ames, R. P.: Negative effects of diuretic drugs on metabolic risk factors for coronary heart disease, possible alternative drug therapies. Am. J. Cardiol. 1983; 51:632–38.

[4] Ames, R. P., and Hill, P.: Increase in serum lipids during treatment of hypertension with chlorthalidone. Lancet 1976; 1:721–23.

[5] The Lipid Research Clinics Coronary Primary Prevention Trial Results. JAMA 1984; 251:3.

[6] McCarron, D.: Diuretic therapy for mild hypertension: the real cost of therapy. The American Journal of Cardiology, Proceedings of a Symposium, First Line Therapy of Hypertension: Changing Directions. Am. J. Cardiol. January 27, 1984; 53:9–11A.

[7] Multiple Risk Factor Intervention Trial Research Group: Multiple risk factor intervention trial. JAMA 1982; 248:1465–77.

[8] Morgan, T.: Monotherapy in the treatment of hypertension. Chest 1983; 2(Suppl.):419–22.

[9] Helgeland, A.: Treatment of mild hypertension: a five-year controlled drug trial. The Oslo Study. Am. J. Med. 1980; 69:725–32.

[10] Leren, P., Foss, P. O., Helgeland, A., Hjermann, I., Holme, I., and Lund-Larsen, P. G.: Effect of propranolol and prazosin on blood lipids. The Oslo Study. Lancet 1980; 2:4–6.

[11] Tanaka, N.: Effects of chronic administration of propranolol on lipoprotein composition. Metabolism 1976; 25:1071–75.

[12] Waal-Manning, H. J.: Experience with B adrenoreceptor blockers in hypertension. Drugs 1976; 11(Suppl. 1):121.

[13] Metz, S. A., Halter, J. B., and Robertson, R. P.: Induction of defective insulin secretion and impaired glucose tolerance by Clonidine. Diabetes 1978; 23:554–67.

[14] Le Clercq-Meyers, V., Herchuelz, A., Valverde, I., Couturier, E., Marchand, J., and Malaisse, W. J.: Mode of action of Clonidine upon islet function. Diabetes 1980; 29:193–200.

[15] Lipson, L.: Treatment of hypertension in diabetic men: Problems with sexual dysfunction. Am. J. Cardiol. 1984; 53:46–50A.

[16] Lipson, L. G., Moor, D., Pope, A. M., Todd, F. J., and Avila, S. M.: Sexual dysfunction in diabetic men. J. Cardiovasc. Med. 1981; (Suppl.):30–37.

[17] Kaplan, N.: Therapy of mild hypertension, an overview. Am. J. Cardiol. 1984; 53:2–8A.

[18] Lowerstein, J.: Effects of prazosin on serum lipids in patients with essential hypertension. A review of the findings presented at the satellite symposium on coronary heart disease. Hypertension and other risk factors. Milan, 1983. Am. J. Cardiol. 1984; 53:21–23A.

[19] Inouye, I., Massie, B., Benowitz, N., Simpson, P., Log, D., and Topic, N.: Monotherapy in mild to moderate hypertension. Comparison of hydrochlorthiazide, propranolol and prazosin. Am. J. Cardiol. 1984; 53:24–28A.

Angioedematous Urticaria in a Diabetic Patient Successfully Treated with Nifedipine

Y. O., a female office worker, has had diabetes for the past 16 of her 22 yr. She presented to us for the first time on 5/26/84 for control of chronically elevated blood sugars and complained of nocturia, chronic fatigue, chronic constipation, and frequent nocturnal muscle spasms of her feet. She admitted to occasional cardiac "palpitations" associated with anxiety on running up stairs. She also admitted to chronically cold feet in winter, which do not rewarm readily when she returns indoors. She denied any allergic history, but noted that her father is allergic to penicillin and suffered an anaphylactic episode after a bee sting.

Daily medications consisted of beef-pork insulin (25 U NPH mixed with 3 U regular) each morning, a commercial vitamin mixture, and an "herbal laxative."

Physical examination disclosed the following positive findings. Background retinopathy, diplopia on lateral gaze, pustules on the left tonsil, a fine macular rash on the buttocks, reduced oscillometrics at both ankles, and a fungal infection of her toenails.

Laboratory findings included the following abnormalities: glycohemoglobin, 13.2% (normal 4.4–8.2%); ionized calcium, 3.62 meq/L (normal 2.25–2.95 meq/L) with a normal 24-h urine calcium; IgE, 161 U/ml (normal 0–150 U/ml); creatinine clearance, 80.5 ml/min. A throat culture yielded many non-group A beta hemolytic streptococci, sensitive to penicillin.

The patient was treated with 1% cicloperox olamine cream twice daily for her fungal toenails. She was asked to take Hydrocil (Rowell Laboratories, Inc., Baudette, Minnesota) (a high-fiber, sugar-free product) instead of the "herbal laxative." She was put on a very low carbohydrate diet, frequent self-monitoring of blood glucose (BG), and her insulin regimen was changed to 4 U of Monotard (lente) human insulin (Squibb-Novo, Princeton, New Jersey) in the morning and 4½ U at 11 p.m. In addition, she was asked to administer 3½–5½ U of Actrapid (regular) human insulin (Squibb-Novo) ½ h before each meal for a total of 21½ U of insulin daily.

On 5/30, we received the results of the throat culture and prescribed 500 mg oral potassium penicillin V every 6 h for 2 wk.

On 6/12, the patient phoned us complaining of swelling of her hands and itching all over her body. She admitted to having numerous insect bites and disclosed that a peacock