

ORIGINAL ARTICLE

Retinol-Binding Protein 4 and Insulin Resistance in Lean, Obese, and Diabetic Subjects

Timothy E. Graham, M.D., Qin Yang, M.D., Ph.D., Matthias Blüher, M.D.,
Ann Hammarstedt, Ph.D., Theodore P. Ciaraldi, Ph.D., Robert R. Henry, M.D.,
Christopher J. Wason, B.S., Andreas Oberbach, Ph.D., Per-Anders Jansson, M.D., Ph.D.,
Ulf Smith, M.D., Ph.D., and Barbara B. Kahn, M.D.

ABSTRACT

BACKGROUND

From the Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston (T.E.G., Q.Y., C.J.W., B.B.K.); the Department of Medicine, University of Leipzig Medical Center, Leipzig, Germany (M.B., A.O.); the Lundberg Laboratory for Diabetes Research, Department of Internal Medicine, Sahlgrenska University Hospital, Göteborg, Sweden (A.H., P.-A. J., U.S.); and the Veterans Affairs San Diego Healthcare System, San Diego, Calif., and the Department of Medicine, University of California, San Diego, La Jolla (T.P.C., R.R.H.). Address reprint requests to Dr. Kahn at the Division of Endocrinology, Diabetes, and Metabolism, Beth Israel Deaconess Medical Center, 99 Brookline Ave., Boston, MA 02215, or at bkahn@bidmc.harvard.edu.

Drs. Graham and Yang contributed equally to this article.

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Insulin resistance has a causal role in type 2 diabetes. Serum levels of retinol-binding protein 4 (RBP4), a protein secreted by adipocytes, are increased in insulin-resistant states. Experiments in mice suggest that elevated RBP4 levels cause insulin resistance. We sought to determine whether serum RBP4 levels correlate with insulin resistance and change after an intervention that improves insulin sensitivity. We also determined whether elevated serum RBP4 levels are associated with reduced expression of glucose transporter 4 (GLUT4) in adipocytes, an early pathological feature of insulin resistance.

METHODS

We measured serum RBP4, insulin resistance, and components of the metabolic syndrome in three groups of subjects. Measurements were repeated after exercise training in one group. GLUT4 protein was measured in isolated adipocytes.

RESULTS

Serum RBP4 levels correlated with the magnitude of insulin resistance in subjects with obesity, impaired glucose tolerance, or type 2 diabetes and in nonobese, nondiabetic subjects with a strong family history of type 2 diabetes. Elevated serum RBP4 was associated with components of the metabolic syndrome, including increased body-mass index, waist-to-hip ratio, serum triglyceride levels, and systolic blood pressure and decreased high-density lipoprotein cholesterol levels. Exercise training was associated with a reduction in serum RBP4 levels only in subjects in whom insulin resistance improved. Adipocyte GLUT4 protein and serum RBP4 levels were inversely correlated.

CONCLUSIONS

RBP4 is an adipocyte-secreted molecule that is elevated in the serum before the development of frank diabetes and appears to identify insulin resistance and associated cardiovascular risk factors in subjects with varied clinical presentations. These findings provide a rationale for antidiabetic therapies aimed at lowering serum RBP4 levels.