Glucose-Induced Insulin Secretion in Uremia: Role of Anemia

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Dear Sir,

Impaired glucose metabolism in uremic patients has long been recognized [1]. However, until recently, little has been known about the pathogenetic mechanisms responsible for the disturbance in glucose metabolism [1]. Recently Kokot et al. [2] have found that erythro-poietin treatment improves insulin response and glucose tolerance after a test meal in maintenance hemodialysis (MH) patients, and concluded that anemia plays a major role in the derangement of glucose metabolism in uremia. Vasile et al. [3], using the intravenous glucose tolerance test (IVGTT), have not confirmed this report. Also studies in animals [4] have demonstrated that red blood cells actively participate in glucose homeostasis by regulating glucose transport to peripheral tissues.

To clear the role of anemia in the pathogenesis of insulin response and glucose tolerance abnormalities in uremia, we studied glucose metabolism, by IVGTT, in nondialyzed and dialyzed uremic patients with different hemoglobin (Hb) levels. 54 patients with endstage chronic renal failure (ESRF) and 119 patients on MH were studied. Their body weights varied between 90 and 110% of ideal body weight; none showed severe hyperkalemia. Abnormalities of acid-base balance in ESRF patients, if present, were corrected by oral bicarbonate therapy before the test. For MH patients dialysis schedule was as follows: 3.5-4.5 h $\times$ 3/week, plate or hollow fiber dialyzer with cuprophan membrane of 1-1.5 m² surface and 8 μ m thickness, blood flow 250-350 ml/min, dialysate flow 500 ml/min. IVGTT was performed 2-6 months after start of MH in the morning after the second weekly hemodialysis treatment, 39 patients were examined both in the phase of ESRF and after start of MH.

Both ESRF and MH patients were divided into groups according to their Hb levels (A Hb $\leq$ 6 g/dl, B $6 < \text{Hb} \leq 8$ g/dl, C $8 < \text{Hb} \leq 10$ g/dl, D Hb > 10 g/dl). Four MH patients of group A were examined even after blood transfusions. For each test we measured plasma levels of glucose (G), immunoreactive insulin (IRI) and C-peptide (C-p) at -30, 0, 2, 5, 15, 30, 45, 60 min and we calculated glucose constant decay (K), IRI and C-p areas of response (IRI area, C-p area), insulinogenic index (IGI) and insulin resistance index (RI). The technique was described in detail in a previous investigation [5].

Results are summarized in table 1. No differences were found in the various glucose metabolism parameters among the groups both in ESRF and MH patients. The 39 patients examined before

and after the onset of MH showed after hemodialysis an increase of insulin response and glucose tolerance although there were no significant changes in Hb levels. In the 4 MH patients examined after blood transfusions we noticed no changes in glucose metabolism parameters despite an increment in Hb levels from 5.3 ± 0.4 (mean $\pm$ SE) to 7.8 ± 0.6 g/dl). From these data we may infer that anemia does not play an important role in the pathogenesis of glucose metabolism abnormalities in uremia. The improvement of insulin response and glucose tolerance found by Kokot et al. [2] or the decrement of RI found by our group [3] after 3 months of erythropoietin treatment in MH patients may be due to a direct action of erythropoietin on pancreatic β -cells or other endocrine glands [2], or to erythropoietin-induced changes in physical activity, food intake, nutritional status and muscular mass [6-8], not to increment of Hb levels.

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Table 1. Glucose metabolism parameters, during IVGTT, in ESRF and MH patients with different Hb levels (mean $\pm$ SE)

Cases K IRI area, mU/ml IGI C-p area, ng/ml RI

*p < 0.01 vs. ESRF All. Statistical analysis was performed by ANOVA table and Tukey's test.

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Erratum

In the article by Yokozawa et al. (Vol. 61, 1992, pp. 236-237), entitled, 'Increase in Kidney 8-Hydroxyguanosine Level with the Progression of Renal Failure', the second author should read Koji Fujioka instead of Koji Jujoka as erroneously printed.