even greater in prepubertal children, who may have some difficulties in communicating their symptoms of hypoglycemia. The evaluation of blood glucose before the administration of lispro in children and adolescents may give useful information on assessing the optimal time for lispro injection to prevent hypoglycemic crisis. Lispro should probably be injected just before the meal if glycemia is in the range 80–180 mg/dl and 10–15 min before the meal if glycemia is >180 mg/dl; postprandial lispro administration could be a benefit if glycemia is <80 mg/dl.

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Response to Iafusco et al.

We would like to thank Iafusco et al. (1) for the valuable comment concerning the risk of early hypoglycemia relating to insulin lispro. In our crossover study comparing different injection times for regular insulin (40, 20, and 0 min before the meal) and insulin lispro (20 and 0 min before and 15 min after the start of the meal), we observed 13 hypoglycemic episodes (≤50 mg/dl) out of 108 visits, experienced by seven patients, of which seven occurred during treatment with regular insulin and six during treatment with insulin lispro. Early hypoglycemic episodes (within 60 min from the start of the meal) were mainly seen in the groups with regular insulin injected 40 min and insulin lispro injected 20 min before the meal, which was chosen as a comparison group for experimental reasons. No hypoglycemic episodes were seen in these 18 subjects with a tightly intensified regimen during 108 test meals when insulin lispro had been injected immediately before the meal.

We think, however, that it is absolutely justified to address the risk of early hypoglycemia. In both cases reported by Iafusco et al., early hypoglycemic episodes seem to have occurred before or during breakfast and in patients with good metabolic control. Because the patients did not measure their fasting blood glucose, it cannot be excluded that they already had biochemical hypoglycemia before injecting insulin lispro.

It is common knowledge that in cases of very high or low blood glucose levels before an intended meal, the time for the injection of the insulin bolus should be adapted accordingly. We, however, disagree that the postprandial injection of the bolus insulin is justified only in patients with blood glucose levels <80 mg/dl. Interim data from one of our ongoing randomized crossover trials in a larger number of patients (2), comparing the routine use of pre- versus postprandially injected insulin lispro, indicate no difference in terms of hypoglycemic episodes between both regimens. In contrast, the risk of early hypoglycemia appears to be reduced when injecting the lispro bolus after the meal, which, in addition to safety considerations, would offer more flexibility and precision in selecting the appropriate dose.

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Elevated Serum Tumor Necrosis Factor-α and Endothelin 1 Levels Correlate With Increased C-Peptide Concentration in Android Type Obesity

Endothelial cell dysfunction has been described by Enderle et al. (1) in NIDDM. We have also observed endothelial dysfunction in correlation with elevated basal and postprandial serum C-peptide levels and tumor necrosis factor (TNF)-α concentrations in android type obesity.

We have studied serum TNF-α, endothelin 1, and C-peptide levels in 15 patients with android type obesity (mean ± SEM; BMI 39.4 ± 2.1 kg/m^2, waist-to-hip ratio [WHR] 0.98 ± 0.05, age 44 ± 2 years, 6 men, 9 women) and in 15 lean healthy control subjects (BMI 22.3 ± 0.8 kg/m^2, WHR 0.78 ± 0.03, age 43 ± 4 years, 7 men, 8 women), all of whom had normal glucose tolerance and blood pressure. Blood samples were taken before and 1 h after the uptake of a standard meal containing 30 g of carbohydrates. TNF-α concentrations were measured by enzyme-linked immunosorbent assay (Sigma, St. Louis, MO), C-peptide (Biodata, Rome, Italy) and endothelin 1 levels (Sigma; Du Pont, Boston, MA) by radioimmunoassay. Significantly higher fasting TNF-α (8.92 ± 0.44 pg/ml, $P < 0.01$), endothelin 1 (5.38 ± 0.30 pg/ml, $P < 0.01$), and C-peptide levels (4.82 ± 0.71 ng/ml, $P < 0.01$) were found in the obese subjects with android type obesity (TNF-α 6.88 ± 0.26, endothelin 1 3.89 ± 0.43, C-peptide 1.46 ± 0.25). No change in TNF-α and endothelin 1 concentrations has been observed after food uptake, either in patients (TNF-α 8.71 ± 0.45, endothelin 1 5.20 ± 0.45) or in control subjects (TNF-α 6.52 ± 0.30, endothelin 1 4.01 ± 0.27). Significantly higher C-