Efficacy of a Continuous GLP-1 Infusion Compared With a Structured Insulin Infusion Protocol to Reach Normoglycemia in Nonfasted Type 2 Diabetic Patients: A Clinical Pilot Trial

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OBJECTIVE — Continuously administered insulin is limited by the need for frequent blood glucose measurements, dose adjustments, and risk of hypoglycemia. Regimens based on glucagon-like peptide 1 (GLP-1) could represent a less complicated treatment alternative. This alternative might be advantageous in hyperglycemic patients hospitalized for acute critical illnesses, who benefit from near normoglycemic control.

RESEARCH DESIGN AND METHODS — In a prospective open randomized crossover trial, we investigated eight clinically stable type 2 diabetic patients during intravenous insulin or GLP-1 regimens to normalize blood glucose after a standardized breakfast.

RESULTS — The time to reach a plasma glucose below 115 mg/dl was significantly shorter during GLP-1 administration (252 ± 51 vs. 321 ± 43 min, \(P < 0.01\)). Maximum glycemia (312 ± 51 vs. 254 ± 48 mg/dl, \(P < 0.01\)) and glycemia after 2 h (271 ± 51 vs. 168 ± 48 mg/dl, \(P = 0.012\)) and after 4 h (155 ± 51 vs. 116 ± 27 mg/dl, \(P = 0.02\)) were significantly lower during GLP-1 administration.

CONCLUSIONS — GLP-1 infusion is superior to an established insulin infusion regimen with regard to effectiveness and practicability.

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measurements or paired Student’s t-test.

The primary outcome was the time taken to reach a plasma glucose level below 115 mg/dl, and the secondary outcome parameters were plasma glucose after 2 and 4 h, as well as maximum glycemia and the number of hypoglycemic episodes. Differences of study variables were tested by using ANOVA for repeated measurements or paired Student’s t-test.

RESULTS — We investigated eight patients (five male) with a mean age of 58.2 ± 2.3 years, a BMI of 24.4 ± 1.0 kg/m², and an HbA1C of 7.3 ± 0.7%. Glucose levels at the start of infusion therapy were comparable on both days of investigation (insulin 252 ± 42 mg/dl, GLP-1 244 ± 24 mg/dl).

The primary end point (the time to reach plasma glucose below 115 mg/dl) was significantly shorter during GLP-1 administration (252 ± 51 vs. 321 ± 43 min, P < 0.01) (Fig. 1). Maximum glycemia (312 ± 51 vs. 254 ± 48 mg/dl, P < 0.01) occurred after 2 h (271 ± 51 vs. 168 ± 48 mg/dl, P = 0.012), and glycemia after 4 h (155 ± 51 vs. 116 ± 27 mg/dl, P = 0.02) were significantly higher during insulin administration in comparison with GLP-1. Glycemia after 8 h — at the end of the intervention — was comparable between both regimens (insulin 110 ± 24 mg/dl, GLP-1 103 ± 22 mg/dl, P = NS). Serum insulin levels were generally lower during GLP-1 treatment (data not shown). One symptomatic hypoglycemia occurred during insulin infusion (48 mg/dl), whereas no hypoglycemia was noted in the GLP-1 regimen. Nausea was observed in one patient during GLP-1 infusion.

CONCLUSIONS — Our study compared for the first time an established insulin infusion regimen with a GLP-1–infusion regimen in nonfasted type 2 diabetic patients regarding the efficacy to normalize hyperglycemia.

We clearly showed that glucose targets could be achieved faster with the GLP-1–based regimen in comparison with the insulin regimen, and that maximal glycemic excursions were markedly reduced. Beside the advantage in time course of lowering hyperglycemia, there is no need for frequent blood glucose measurements and subsequent dose adaptations as is required when using intravenous insulin. Our pilot study, thus, indicates that GLP-1–based regimens should be further tested in acute clinical settings (e.g., in hyperglycemic patients with acute myocardial infarction or undergoing vascular surgery where hyperglycemia was shown to predict a worse outcome) (1–6).

Until now, blood glucose lowering in this setting was performed by variable insulin infusion protocols that may cause hypoglycemia. High rates of hypoglycemia, in turn, were discussed as a possible explanation for the worse outcome of the intensive control arm (6.8 vs. 0.5% in the conventional arm) in the NICE trial (8). In addition, Kosiborod et al. (7) recently showed that the relation between mean in-hospital blood glucose and mortality rate is J-shaped, indicating that a low mean blood glucose or recurring hyperglycemic episodes are associated with a worse outcome. In that regard, a GLP-1 regimen has the clear advantage not to cause hypoglycemia.

Preserved capacity of insulin secretion is important for adequate GLP-1 action, thus type 1 diabetic subjects as well as insulin-treated type 2 diabetic patients might not respond sufficiently to GLP-1 infusion. Since postprandial hyperglycemia is the main target for GLP-1 due to additional inhibitory effects on gastrointestinal motility, our study might overestimate the therapeutic potential (11). Previous studies, however, could also demonstrate a clear beneficial effect of GLP-1 on fasting glycemia (12).

In summary, the results of our pilot trial indicate that for hyperglycemic clinically stable type 2 diabetic patients, a GLP-1–based infusion regimen is superior to an insulin-based regimen in effectiveness and practicability for reaching normoglycemia. We suggest that GLP-1–based treatment strategies should be further tested in hyperglycemic patients under conditions of acute illness with regard to effectiveness as well as clinical end points.

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