Changes in Basal Insulin Infusion Rates With Subcutaneous Insulin Infusion

Time until a change in metabolic effect is induced in patients with type 1 diabetes

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OBJECTIVE — Evaluation of the time required until a change in the basal insulin infusion rate with an insulin pump induces subsequent changes in the metabolic effect.

RESEARCH DESIGN AND METHODS — In this euglycemic glucose clamp study, 10 male subjects with type 1 diabetes received three different subcutaneous insulin infusion rates (0.5, 1.0, and 2.0 units/h; for 4 h each) of insulin lispro (IL) with insulin pumps.

RESULTS — An increase in insulinemia occurred within 15–30 min after changing the infusion rate. While the serum IL levels reached a steady state at the end of the infusion period, the respective change in serum insulin levels and the respective metabolic effect is achieved after a significant change in basal insulin infusion.

CONCLUSIONS — Several hours are required until a new steady state in the metabolic effect is achieved after a significant change in basal insulin infusion.

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units/h). Insulinemia reached a steady-state level in the last 120 min within the 0.5 and 1.0 units/h infusion period. No steady state was achieved with an infusion rate of 2.0 units/h, but there still was an increase after 4 h.

GIR showed no significant increase during the infusion of 0.5 units/h (from 0.1 ± 1.0 to 0.3 ± 2.5 mg · kg\(^{-1}\) · min\(^{-1}\); NS), however, with a doubling of the infusion rate to 1.0 units/h (to 1.7 ± 2.5 mg · kg\(^{-1}\) · min\(^{-1}\); \(P < 0.001\)) and again to 2.0 units/h (to 3.8 ± 3.5 mg · kg\(^{-1}\) · min\(^{-1}\); \(P < 0.02\)), such an increase was registered (Fig. 1D). This increase occurred within 30–60 min after switching the infusion rate. GIR reached a steady state in the last 120 min of the 0.5 and 1.0 units/h infusion period but not with the infusion rate of 2.0 units/h. FFA levels remained stable during the infusion period with 0.5 units/h (Fig. 1E). However, the further increase in insulinemia suppressed FFA levels by 65%.

**CONCLUSIONS** — This study indicates that it takes 2.5–4 h until a considerable change in basal infusion rate (0.5–1.0 units/h) leads to a new steady-state level in the induced metabolic effect even if a rapid-acting insulin analog is infused. Research on peak action of insulin boluses revealed that it takes 60 min until insulin and 100 min until GIR reach maximum levels (4). Similar changes of basal insulin infusion have also been evaluated employing cessation of insulin delivery. It has been disclosed that with IL, metabolic changes occurred within 1 h after termination of insulin infusion and were clearly demonstrated after 3 h (5–7).

In daily practice, the hourly basal rate pattern most often is not varied to this extent from hour to hour but is adjusted in smaller steps as shown for instance in children and adolescents (8). The different basal rates in this study were chosen to demonstrate substantial changes in insulinemia, glucose consumption, and FFA levels. However, a longer evaluation period of 5–6 h would have been more appropriate to demonstrate that new steady-state levels were reached.

Considering the observed delay after a significant change in the basal rate, the time gap before achieving a new stable metabolic effect should be taken into account when modifying the basal rate. There is a good body of clinical experience indicating that individual basal insulin adjustment via CSII is the best manner.

**Figure 1**—Means ± SE glycemia (A), serum human insulin (B), serum IL (C), GIRs (D; with baseline correction), and FFA levels (E) measured in 10 male subjects with type 1 diabetes with three different basal SC insulin infusion rates (0.5, 1.0, and 2.0 units/h), in addition to a baseline IV infusion of RHI (0.2 mU · kg\(^{-1}\) · min\(^{-1}\)).
to cover basal insulin requirements. The data presented here indicate that the options of modern insulin pumps need adequate coordination and fine-tuning with the metabolic effect. The observed delay also has to be considered when stopping the insulin infusion to avoid or to attenuate the development of a hypoglycemic event (5,7).

In summary, significant changes in basal insulin infusion rates with CSII might require several hours until a new stable metabolic effect level is reached. This topic should be systematically evaluated in greater detail within clinical trials.

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