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ORIGINAL ARTICLE

Pharmacokinetics of Insulin Aspart and Glucagon in Type 1 Diabetes during Closed-Loop Operation

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Abstract

Background:

We assessed the pharmacokinetics of subcutaneous insulin aspart and glucagon during closed-loop operation and their relationship with body composition variables.

Methods:

We retrospectively analyzed data collected from closed-loop experiments in 15 type 1 diabetes patients (age 47.1 ± 12.3 years, body mass index 25.9 ± 4.6 kg/m^2, glycated hemoglobin 7.9% ± 0.7%). Patients received an evening meal accompanied with prandial insulin bolus and stayed in the clinical facility until the next morning. Glucose levels were regulated by dual-hormone closed-loop delivery. Insulin and glucagon were delivered using two subcutaneous infusion pumps installed on the abdominal wall. Plasma insulin and glucagon were measured every 10–30 min. Percentage of body fat, percentage of fat in the abdominal area, and mass of abdominal fat were measured by dual X-ray absorptiometry.

Results:

A pharmacokinetic model estimated time-to-peak plasma concentrations [t_{max} insulin 51 (19) min, t_{max} glucagon 19 (4) min, mean (standard deviation)], metabolic clearance rate [*MCR* insulin 0.019 (0.015–0.026) liter/kg/min, *MCR* glucagon 0.012 (0.010–0.014) liter/kg/min, median (interquartile range)], and the background plasma concentrations [I_b insulin 10.2 (6.3–15.2) mU/liter, I_b glucagon 50 (45–56) pg/ml, median (interquartile range)]. t_{max} correlated positively between insulin and glucagon (r = 0.7; p = .007) while *MCR* correlated negatively (r = -0.7; p = .015). In this small sample size, t_{max}, *MCR*, and I_b of insulin and glucagon did not correlate with percentage of body fat, percentage of fat in the abdominal area, or total mass of abdominal fat.

Conclusions:

Insulin and glucagon pharmacokinetics might be related during closed-loop operation. Our data suggest that slower absorption of insulin is associated with slower absorption of glucagon. Body composition does not seem to influence insulin and glucagon pharmacokinetics.

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