Combining Glucagon and Insulin Infusion with Glucose Sensing in Subcutaneous Adipose Tissue of Type 1 Diabetes Patients (CINFONY-01)

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Objective: The goal of this study was to ascertain in people with type 1 diabetes whether glucose sensing can be performed at the subcutaneous site of glucagon and insulin infusion.

Methods: A recently developed treatment device that enables glucose sensing and insulin delivery at a single subcutaneous tissue site (single-port device) has been adapted so that glucagon can also be delivered via this subcutaneous tissue site. Eight people with type 1 diabetes used the device for a nocturnal basal insulin replacement (~12 hours) and a 12-hour sequential glucagon and insulin delivery to raise and lower patients' blood glucose levels multiple times. To assess the quality of the glucose measurement at the site of subcutaneous insulin and glucagon administration, the readings of the single-port sensor were compared with plasma glucose measurements and the readings of a continuous glucose sensor additionally worn by the patients (control sensor). Agreement between sensor readings and plasma glucose concentrations was assessed by calculating the median absolute relative differences (ARD) for each subject and applying the Error Grid and Bland & Altman analysis.

Results: Thirteen people with type 1 diabetes (4 women and 9 men) were invited to take part in the study. Of these, 1 was excluded due to screening errors, and 3 dropped out of the study due to adverse events (nausea and vomiting after glucagon administration). The 8 subjects completing the study (8 men) had an average age of 35.8 ± 8.4 years (mean ± SD; range 22 – 47 years) and an average body mass index of 25.8 ± 2.5 kg/m^2, (range 22.6 – 29.8). Their mean duration of diabetes was 19.3 ± 8.9 years (range 9–33) and their percent HbA1C averaged 8.0 ± 0.7% (63.6± 7.3 mmol/mol) [range 7.3 – 9.4 % (56 – 79 mmol/mol)]. Glucagon and insulin delivery via the single-port device was successful in effectively increasing or decreasing the patient's blood glucose concentration. Furthermore, during the glucagon and insulin delivery periods, glucose readings of the single-port and control sensor agreed well with the observed plasma glucose concentrations. The average median ARD obtained for the single-port device (13.6 ± 1.4%; mean ± SEM) was found to be similar to that for the control sensor (vs. 13.9 ± 3.8%; p=0.925). In addition, error grid analysis indicated that the percentage number of the sensor readings that fall in the clinically acceptable range (zones A and B) is high for the single-port device (99.5%) and comparable to that obtained for the control sensor (99.0%). Furthermore, applying the Bland & Altman analysis, the 2SD values obtained for the single-port device were similar to those calculated for the control sensor (38.4 vs. 41.6%).

Conclusions: These data demonstrate the feasibility of performing glucose sensing, insulin delivery and glucagon delivery at the same subcutaneous tissue site. The study may build a firm foundation for the future development of a small-sized, autonomous treatment device that combines glucose sensing, insulin delivery and glucagon delivery at a single tissue site (bi-hormonal single-port artificial pancreas).