An alternative data mining oriented approach to the analysis of the long-term glucose counter-regulation to hypoglycemia in continuous glucose data

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Abstract and Objective

The hypothesis of a long-term glucose counter-regulation to hypoglycemia has gained recent interest using continuous glucose monitoring technologies, but long-term studies are lacking. The aim of the study was to evaluate the phenomenon in continuous glucose monitoring data, without the assumptions regarding hypoglycemia time of day and manifestation of the long-term glucose counter-regulation found in the study designs of previous studies. We compared continuous glucose data and insulin data from people with type 1 diabetes after spontaneous hypoglycemic events with matched hypoglycemia-free control periods. No significant difference in sensor glucose was seen, but the insulin intake was higher for 24 hours after hypoglycemia. As insulin has hypoglycemic effects, blood glucose after hypoglycemia would have been elevated with similar insulin intake. The results are thus consistent with the hypothesized long-term glucose counter-regulation to hypoglycemia.

Keywords:

Type 1 diabetes mellitus, Continuous glucose sensors, Hypoglycemia

Methods

The study is a retrospective quasi-experimental data mining oriented analysis of dietary data and blood glucose sensor data from type 1 and type 2 diabetic patients. Hypoglycemic events (≥15 minutes of sensor glucose ≤54 mg/dl) and near-hypoglycemic events (≥15 minutes of sensor glucose ≤72 mg/dl) and episodes of missing data (≥10 minutes of sensor glucose=0) were identified. Hypoglycemic events were included for analysis only if there were no subsequent or antecedent hypoglycemic events (within 15 hours) and if matching control and insulin data could be found. Control periods were found within-subject and included for analysis only if there were no antecedent or subsequent hypoglycemic or near-hypoglycemic events (within 15 hours). For each hypoglycemic event, sensor glucose difference between hypoglycemia day and control day was calculated as hypoglycemia day sensor glucose minus control day sensor glucose and analyzed for 24 hours following hypoglycemia.

Results

159 subjects (135 type 1 diabetic) were included. The type 1 diabetic subjects had 134 hypoglycemic events. 70 of these were excluded due to antecedent or subsequent hypoglycemic events, and 41 of the remaining were excluded due to lack of control periods. 14 of the remaining hypoglycemic episodes were excluded due to lack of insulin data, so 9 hypoglycemic episodes in 9 patients (5 female) were included.

Sensor glucose difference fluctuated between -20 and 40 mg/dl (non-significant). Mean total insulin intake was 37.0 IU after hypoglycemia and 30.0 IU in the control period ($p<0.05$).

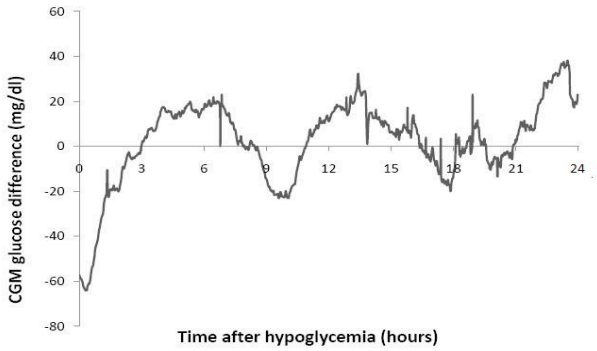

Figure 1 – mean sensor glucose difference

Conclusions

No difference in sensor glucose was seen, but with the hypoglycemic effects of insulin, blood glucose after hypoglycemia would have been elevated with similar insulin intake. The results can therefore be taken to be consistent with the hypothesis of a long-term glucose counter-regulation to hypoglycemia. Unrecognized, this phenomenon may initiate a vicious cycle of hypoglycemia, (relative) hyperglycemia and increased insulin doses that may worsen the initial hypoglycemia pattern.