Metabolic monitoring in children during diabetic ketoacidosis via breath-analysis

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Introduction

Diabetic ketoacidosis (DKA) is a life-threatening and acute complication occurring in 30-50% of children with newly diagnosed type 1 diabetes (T1D). DKA is characterized by a severe catabolic state due to longstanding insulin deficiency with relevant weight loss, dehydration, and sighing (Kussmaul) respiration due to hyperglycemia-induced osmotic diuresis, ketone body formation, and consecutive metabolic acidosis. Insulin therapy reverts the catabolic state and results in normalization of body weight within 4-6 weeks. This study aims to describe the anabolic effect of insulin on metabolites captured in exhaled breath during acute diabetic ketoacidosis 1) and 2) during normalization of body weight in the weeks after diagnosis and onset of insulin therapy. These data will provide a deep insight into the metabolic switch induced by insulin therapy during the normalization of the severe catabolic situation.

Methods

Children and adolescents (age 4-18 years) with newly diagnosed type 1 diabetes and DKA were asked to provide breath samples in a custom-made Nalophan bag before the first administration of insulin (time point 0 = complete catabolic state) and several times per day throughout their hospitalization (multiple time points during anabolic state and weight normalization). Breath was analyzed by introducing the bag into the inlet of a secondary electrospray ionization coupled to a high-resolution mass spectrometer (SESI-HRMS) and was deflated. This instrumental configuration has to ability to ionize exhaled breath molecules and detect their mass over charge within 1-5 ppm mass accuracy. Hereafter, the data was preprocessed and analyzed using MATLAB. Briefly, raw files were converted to mzXML, peaks above 10^4 A.U. were considered for further analysis. The area under the curve was computed for each compound. A cluster analysis was followed to identify overall trends of the metabolic time profiles. Blood ketone levels (Beta-Hydroxybutyrate) were measured regularly until acidosis was resolved.

Results

Data acquired of the first patient included in the study (male, 14 y/o) presented with moderate DKA (pH 7.17, blood glucose 26 mmol/l, HbA1c 11.8%) and weight loss of 6.0 kg (12.2% of body weight). He regained 4.8 kg (9.7% of body weight) during the first 8 days after hospital admission. Blood ketones decreased sharply during the first 10 hours upon insulin administration. Decreasing blood glucose levels and resolution of acidosis was also captured by metabolic changes in exhaled breath following three different trajectories: As expected, breath acetone dropped consistently but at a much slower rate than blood ketones. A set of 25 compounds correlated (correlation coefficient > 0.9) with the acetone profile. In contrast, we found another cluster of 41 signals consistently (such as $[C_6H_{11}NO_3]^+$)increasing post-treatment. Another cluster of 36 exhaled metabolites (such as $[C_{12}H_{13}N]^+$) showed an increasing trend upon the treatment and then dropped about 80 hours after initiation of insulin treatment.

Conclusion

Near real-time exhaled breath analysis reveals intricate metabolic trajectories following treatment for DKA. The data indicates a potential to monitor patients non-invasively and to gain further insights at the metabolic level. Ongoing measurements will provide further evidence supporting this initial observation.