

In vitro Administration of Ubiquinol and Thiamine improve Cellular Oxygen Consumption in Patients with Diabetic Ketoacidosis

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Background

Diabetic Ketoacidosis (DKA) often requires significant hospital resources, is characterized by depletion of electrolytes, and may be associated with subclinical cellular injury with prolonged acidosis. Therefore, evaluating metabolic components (apart from insulin) that can more rapidly reverse DKA and protect cells may be beneficial. Thiamine and ubiquinol are essential for adequate aerobic metabolism. The objective of the current study was to investigate the effects of *in vitro* administration of ubiquinol and thiamine on cellular oxygen consumption in peripheral blood mononuclear cells (PBMCs) from patients with DKA.

Methods

We performed a prospective study of DKA patients and healthy controls presenting to the emergency department at an urban tertiary care center from November 2015 to June 2016. A single blood draw was performed and PMBCs were isolated from blood samples. Cells were randomly assigned to *in vitro* administration of 0.5 ug/mL thiamine, 1 µg/mL ubiquinol, or placebo treatment. The complete mitochondrial respiration profiles were measured using XF Cell Stress Mito Kit (Seahorse Bioscience) to reveal the key parameters of cellular oxygen consumption. One-way ANOVA was used to analyze differences in oxygen consumption rate between groups.

Results

10 DKA patients and 9 controls were included. Basal (7.0 ± 2.1 pmol/min/µg protein vs. 10.2 ± 2.4 , $p = 0.005$) and maximal oxygen consumption (16.6 ± 4.2 vs 28.3 ± 9.0 , $p = 0.05$) were significantly lower in PBMCs in DKA compared to controls. We found a significant increase in basal (10.3 ± 2.4 pmol/min/µg protein vs. 7.0 ± 2.1 , $p = 0.05$) and maximal (27.6 ± 5.2 vs. 16.6 ± 4.2 , $p = 0.04$) oxygen consumption between the ubiquinol and placebo group. Additionally, we found a significant increase in basal (9.3 ± 2.4 pmol/min/µg protein vs. 7.0 ± 2.1 , $p = 0.05$) and maximal (25.4 ± 5.0 vs. 16.6 ± 4.2 , $p = 0.05$) oxygen consumption between the thiamine and placebo group. Neither ubiquinol nor thiamine had a significant effect on basal and maximal oxygen consumption for controls.

Conclusions

DKA patients had overall lower oxygen consumption compared to healthy controls. *In vitro* administration of thiamine and ubiquinol independently increased oxygen consumption in DKA patients, but not in controls. These findings suggest thiamine and ubiquinol may have potential as mitochondrial resuscitators in DKA and potentially states with similar metabolic stress.