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Title: Influence of dairy protein breakfast on overall daily glycemia, weight loss, HbA1c and clock genes mRNA expression, in Type 2 Diabetes.

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Abstract

Background: In type 2 diabetes (T2D), the progressive decline in β-cell function and insulin resistance is associated with increased circadian glycemic excursions and overall postprandial glycemia (PPG) which are strongly linked to HbA1c and cardiovascular risk. Therefore, mitigating glycemic peaks, along with weight loss to improve insulin sensitivity, is main target in the management of T2D. Most of the metabolic pathways involved in obesity, postprandial and overall glycemia exhibit diurnal variations and are controlled by the endogenous circadian clock. However, the regulation by the circadian clock is bidirectional and is sensitive to food availability and food intake. We recently reported that a diet aligned with the circadian clock with high-energy, protein and carbohydrates breakfast, significantly upregulated clock gene expression and led to a more effective reduction of body weight, HbA1c and substantial reduction of overall glycemia and appetite as compared to the reverse schedule. However, it is currently unknown what the roll of the protein source in these findings. It was shown in acute studies that fluid milk or dairy beverages consumed before or within carbohydrates rich foods markedly reduces post-meal glycemia than the observed after the carbohydrate food alone.

Working hypothesis and aims: We hypothesize that a diet with high energy and protein breakfast consisting of milk and dairy proteins, by enhancing clock gene expression, will lead to improvement of overall glycemia compared to a diet with other (nondairy) proteins in the breakfast.

Methods: This study will be a randomized, open-label parallel cross-over clinical trial over a 1-month period in T2D subjects, comparing the effects of two isocaloric diets with the same meal timing and energy distribution (as the "breakfast diet" described in previous studies). While lunch and dinner in the 2 groups will be of similar composition, the breakfast will differ solely in the protein source, one group will be given high dairy breakfast and the other non-dairy breakfast. Type 2 diabetic overweight/obese patients (n=20) will be randomly assigned for one of the isocaloric diets for 2 weeks and will do the other diet after 2 weeks of washout. Daily glycemic excursions and clock genes expression in white blood cells will be measured before, and after each diet intervention.

Expected results: We expect that compared to non-dairy breakfast, high protein breakfast with dairy will lead to greater reduction of overall PPG, body weight, subjective appetite and HbA1c, and upregulation of

the circadian CG expression.
Probable implications to Medicine: If dairy breakfast would lead to upregulation of body CG, it will suggest that milk consumption is not only beneficial for glucose metabolism but for the whole-body homeostasis, preventing cardiovascular and other complications related to T2D.
Five Keywords: Milk, clock genes, overall glycemia, nutritional intervention, type 2 diabetes.

Publications associated with the project (PubMed Format): None