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Pharmaceutical Chemistry & Pathology Congress 2019: Cellular magnesium as a regulator of glucose homeostasis and insulinmediated signaling and cellular metabolism - Andrea M P Romani - Case Western Reserve University

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The last thirty years have registered a progressive and dramatic increase in the incidence of obesity and type 2 diabetes mellitus world-wide. Metabolic Syndrome, one of the most commonly conditions associated with obesity and insulin resistance, has also increased considerably.

The latest releases from the WHO estimate that approximately 1 billion people worldwide are obese, and more than 500 million are diabetic or pre- diabetic. Interestingly, increasing evidence suggest that our current western diet is hypercaloric but hyponutritive, as it is lacking essential micronutrients and minerals. Our laboratory has focused on the possible role of reduced cellular magnesium levels in the dysregulation of cellular and systemic glucose homeostasis.

Experimental data obtained in animal and cellular models, including cells of human origin support the conclusion that cellular magnesium regulates transmembrane glucose transport as well as its utilization, and neosynthesis in gluconeogenic tissues, by modulating the activity of specific cellular enzymes and insulin-mediated signaling. Regardless of the tissue considered, decreased cellular and serum magnesium levels impact the proper operation of Glut 4, and Glut 2 transporters, thus limiting the ability of tissues like heart, muscles, liver, and possibly beta-islets, to effectively transport glucose into the cell to support glycolysis, ATP production, and ultimately storage as glycogen.

As a consequence, gluconeo-genesis becomes erroneously activated, further enhancing the circulating levels of glucose and resulting in the dysregulation of fatty acids, cholesterol, and protein degradation, to support gluconeogenic activity through increased cortisol production and insulin resistance.

Also, decreased cellular magnesium levels appear to contribute directly to increased basal inflammation within tissues, further impairing insulin responsiveness and systemic metabolic homeostasis.

Altogether, our results argue for the necessity to better understand the role that micronutrients play in modulating both organ- specific and systemic metabolism and inflammation, to ultimately identifying more effective therapeutic and dietary approaches.

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