Prolactin Decreases Authopagy Markers Levels induced by Cytokines and ER Stressors in Beta-Cells

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Introduction: Autophagy is a conserved physiological system of intracellular degradation, it can be considered as a cytoprotective mechanism; however, autophagy is also able to promote cell death. It has also been proposed that deregulation of this process may have important roles in several diseases; its role in diabetes is still obscure, but recent observations suggest that autophagy may have important roles in the development and prevention of diabetes. Previous results showed a correlation between cytokines, known to have an important action in the development of DM1, and endoplasmic reticulum stressors, with autophagy induction in beta-cells. We also showed that prolactin promotes significant cytoprotection against cytokines and serum starvation induced beta-cells apoptosis. In order to analyze the cytoprotective capacity of prolactin (PRL) after other cell death-inducing mechanisms, we set out to investigate if the cotreatment with PRL would lead to a restauration of the expression of autophagy markers after different combinations of cytokines and ER stressors, as well as after serum starvation. **Material and Methods:** Viability was analyzed through immunofluorescence and autophagy markers expression and/or phosphorylation were accessed by Western Blotting in INS-1E beta-cell cultures or primary cultures of human islets treated under different conditions. **Results and Discussion:** rhPRL treatment was able to inhibit cell death in INS-1E cells after cytokines treatment, as expected. Additionally, the hormonal treatment restored p-mTOR levels after treatment with either different cytokines combination (IL-1β+IFN-γ, TNF-α+IFN-γ) or different ER stressors (Thapsigargin, Tunicamycin). Moreover, LC3-II/LC3-I ratio was also decreased in primary cultures of human islets treated with rhPRL after exposure to either cytokines (IFN-γ+IL-1β+TNF-α) or serum starvation. **Conclusion:** These findings support the hypothesis of ER stressors as inductors of beta-cell autophagy and provide a deeper characterization of the PRL prosurvival mechanisms in beta-cells.

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