Hyperthyroidism Regulates Glucose Body Metabolism By Modulating Calcium Dynamics Of Mouse Islets Of Langerhans

Peçanha, F.L.M.[1,2], Stelmashenco, O.[2], Da Silva, W.S.[1], Berggren, P.O[2], Arrojo e Drigo, R.[2].

[1]Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro, Brazil

[2]Metabolic Disease Research Programme, Lee Kong Chian School of Medice, Nanyang Technological University, Singapore

Introduction: Calcium ion (Ca^{2+}) is a second messenger that regulates many processes in different cell types being crucial to insulin secretion by beta cells of islet of Langerhans. Triiodothyronine (T3) is able to modulate glucose metabolism, but there are few and controversial studies correlating the effect of T3 on islets of Langerhans. **Aim:** Investigate the effect of T3 on body glucose metabolism and calcium dynamics in islets of Langerhans. **Methods:** Hyperthyroidism was induced by daily intraperitoneal injection of 0.25ug T3/g body weight during 21 days. Calcium dynamics were performed in islets isolated by gradient centrifugation and loaded with Fura-2. **Results:** Hyperthyroid group gained more weight, but there were no differences in fat body content and growth. During hyperthyroidism induction, fed glycemia was unchanged, but hyperthyroid group showed lower fasting glycemia and glucose tolerance test curve. There was no difference in fasting insulinemia although glucose stimulated insulin secretion was increased in hyperthyroid group since day 3 of treatment. Islet structure, cell distribution and innervation were similar between groups, but hyperthyroid group showed a decreased alpha and beta cell number, islet area and an increased vessel diameter. Laminin, an inflammatory and fibrosis marker, staining was increased in hyperthyroid group. Moreover, no difference was observed in IBA1, a macrophage marker, staining. Cytoplasmic glucose induced calcium change was higher in hyperthyroid islets and no difference was observed in basal calcium and in KCl induced calcium change. Otherwise, the percentual of KCl response induced by glucose was greater in hyperthyroid islets. Gene expression of many protein related to calcium metabolism were analyzed (Serca2, Serca3, IP3R1, CaV1.2, CaV1.3 and NCX1) and we observed a decrease in CaV1.2 expression in hyperthyroid group. **Conclusion:** Results suggest that hyperthyroidism modulates glucose metabolism, islet size, insulin secretion and calcium dynamics.

Key words: hyperthyroidism, insulin, calcium