The Effects of Vitamin D on Pancreatic BETA-cells Under Glucotoxic Stress

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Pancreatic BETA-cells comprise the central regulatory tissue of the glucose homeostasis system. Glucotoxicity-associated loss of insulin producing BETA-cells is the most significant contributing pathogenic factor for hyperglycemia and Diabetes Mellitus (DM). Vitamin D3 deficiency is proposed to be linked with the pathogenesis of DM; however, a direct effect of vitamin D3 on BETA-cells remains to be elucidated. This research project aimed to evaluate the effect of vitamin D3 supplementation on the expression of key pro-function and survival marker genes in BETA-cells under glucotoxic stress. Briefly, INS-1 BETA-cells were cultured for 24-72 hr under: (i) 5 mmol/L of glucose (control), (ii) 20 mmol/L of glucose to simulate hyperglycemia, (iii) 5 mmol/L and (iv) 20 mmol/L glucose both in presence of 10 nM vitamin D3. Total RNA was isolated at 24-72 hr from n=3 samples under each experimental condition, followed by cDNA synthesis and real time polymerase chain reaction (PCR) using FAM-tagged primers for key BETA-cell genes: pdx1 and pparg (function and survival), gck (glucose sensing), glut2 (glucose transport). The gene expression results (n=3) show a progressive decline in gene expressions of pdx1, pparg, gck, glut2 under hyperglycemic conditions compared to normoglycemic conditions (5 mM glucose). Surprisingly, vitamin D3 supplementation failed to ameliorate the expression of these marker genes under hyperglycemic conditions. Expression of the Vitamin D receptor (VDR) was downregulated under hyperglycemia, raising an intriguing possibility that such susceptible populations or diabetic patients need higher than normal supplementation of Vitamin D3 to compensate for the depletion of VDR.

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