Progesterone induces apoptotic pancreatic ß-cell death

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Gestational diabetes (GD) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy. The disease onset rises on the second trimester of pregnancy when progesterone levels are elevated. The progesterone diabetogenic effects have been related to the increasing in insulin resistance, but since progesterone receptors are expressed in pancreatic ß-cells, it has been suggested that it could exert a direct effect upon these cells. This hypothesis is corroborated by the fact that progesterone high levels are associated to ß-cell mass involution after birth. However, little is known about the involvement of progesterone in GD pathogenesis. This work aimed to investigate if progesterone is able to induce ß-cell death and to characterize some molecular events involved in the process, using a simplified cell culture system. RINm5F ß-cells were cultured in RPMI-1640 containing 10% fetal calf serum. Cells were incubated with different progesterone concentrations (1 to 100µM) for 24 or 48h. After that, cells were collected and cellular membrane integrity and DNA fragmentation were analyzed by flow cytometry using propidium iodide. Staurosporin was used as positive control. Incubation of ß-cells with different progesterone concentrations for 24 or 48h resulted in the loss of membrane integrity and DNA fragmentation, in a concentration and time-dependent manner. After 24h, about 70% of cells treated with 100µM progesterone lost their membrane integrity and DNA fragmentation was verified in 50% of them. Treatment with 25µM progesterone for 48h, however, was efficient to induce DNA fragmentation in 20% of cells. Our results showed that progesterone is able to induce ß-cell death and that the apoptotic pathway is triggered. (This work was supported by FAPESP and CNPq)