

Thyroid hormone in trophoblast invasion and early pregnancy maintenance

T Maruo (JP) [1]

[OBJECTIVE] : Hypothyroidism is one of the endocrine factors for habitual abortion syndrome. Actually, maternal serum levels of thyroid hormone at the clinical onset of threatened abortion were lower in patients who subsequently aborted compared to

those in patients who did not abort. To elucidate the molecular mechanism by which thyroid hormone takes a vital role in maintaining early pregnancy, effects of 3,5,3'-triiodothyronine (T3) on granulosa cell luteinization as well as villous and extravillous trophoblast function were investigated in vitro.

[METHODS and RESULTS] : Treatment with 10⁻⁸M T3 stimulated granulosa cell luteinization and trophoblast endocrine function. Treatment with either higher or lower concentrations of T3 gave attenuated effects. Adequate luteinization of granulosa cells accounts for normal corpus luteum formation, while increased production of hCG and P4 by villous trophoblasts rescues the corpus luteum in early pregnancy.

To determine if T3 affects apoptosis and invasive potential in early placental extravillous trophoblasts (EVTs), isolation of trophoblasts differentiating into EVT was performed by enzymatic digestion of anchoring chorionic villi with fibronectin (FN)-precoated dishes. The cells attached to FN-precoated dishes after 48-h subculture were immunostained for specific EVT markers. The EVTs expressed c-erbA1 transcript, indicating the presence of T3 receptor. The EVTs were cultured in the presence or absence of T3 for 72-h. In cultured EVTs, treatment with 10⁻⁸M T3 decreased apoptosis through inhibiting Fas/Fas ligand, caspase-3 and poly (ADP-ribose) polymerase expression. RT-PCR and Western blot analyses revealed that treatment with 10⁻⁸M T3 increased the expression of cell adhesion molecules including MMP-2, -3 and fetal FN and integrin α 5 β 1 as well as VEGF in cultured EVTs. Matrigel invasion assay revealed that treatment with 10⁻⁸M T3 increased the number of cell projections of EVTs compared to that in control cultures.

[CONCLUSION] : The optimal concentration of T3 promotes EVT invasion to the decidua by suppressing apoptosis and by up-regulating MMPs, integrin and VEGF expression in early placenta. This may explain in part the molecular mechanism for the vital role of thyroid hormone in early pregnancy maintenance.

[1] Kobe Children's Hospital, Kobe