18 When do losses of maternal lymphocytes response to trophoblast antigen or alloantigen occur in women with a history of recurrent miscarriage ?

Bum Chae Choi, Ji Hong Song, Keun Jae Yoo, In Ok Song, Eun Chan Paik, Mi Kyoung Koong, Il Pyo Son, Jong Young Jun, Inn Soo Kang

Recurrent Pregnancy Loss Clinic, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Samsung Cheil Hospital & Women's Health Care Center, College of Medicine, Sung Kyun Kwan University

The maintenance of a viable pregnancy has long been viewed as an immunological paradox. The deveolping embryo and trophoblast are immunologically foreign to the maternal immune system due to their paternally inherited genes products and tissue-specific differentiation antigens. Therefore, speculation has arisen that spontaneous abortion may be caused by impaired maternal immune tolerance to the semiallogenic conceptus. Loss of recall antigen has been reported in immunosuppressed transplant recipients and is associated with graft survival. Progesterone(10^{-5}M) has immunosuppressive capabilities. Our previous study showed that fertile women, but not women with unexplained recurrent abortion (URA), lose their immune response to recall antigens when pregnant. Therefore, we hypothesized that immunosuppressive doses of progesterone may affect proliferative response of lymphocytes to trophoblast antigen and alloantigen.

Proliferative responses using ^{3}H-thymidine (^{3}H-TdR) incorporation of peripheral blood mononuclear cells (PBMCs) to the irradiated allogeneic peripheral blood mononuclear cells, trophoblast antigen and PHA were determined in 9 women who had experienced unexplained recurrent miscarriage. Progesterone vaginal suppositories (100 mg b.i.d) beginning 3 days after ovulation were given to 9 women with unexplained RSA who had prior evidence of Th1 immunity to trophoblast. We checked proliferative response to conception cycle before and after progesterone supplementation and then weekly through the first 7 weeks of pregnancy. A positive proliferative response that occured in the baseline phase were all patients of alloantigen, 4 in 9 patients (44.4%) of trophoblast antigen and all patients of PHA. Our data demonstrated that since in vivo progesterone treated PBMCs more suppressed T-lymphocyte activation and ^{3}H-TdR incorporation compare to PBMCs which are not influenced by progesterone. Only two (22%) repeat pregnancy losses occured in these 9 women, despite loss of antigen responsiveness (one chemical pregnancy loss and one loss at 8 weeks of growth which was karyotyped as a Trisomy 4). These finding suggested that pregnancy loss due to fetal aneuploidy is not associated with immunological phenomena. Furthermore, progesterone may play an important immunological role in regulating local immune response in the fetal-placental unit.