

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Role of T-Regulatory Cells in Preeclampsia: A Mini Review.

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ABSTRACT

The preeclampsia occurring in 5-8% of all pregnancies worldwide, is one of the pregnancy complications which is the major cause of perinatal and maternal morbidity and mortality. The exact molecular basis of preeclampsia is still unknown. In a Successful pregnancy, the semi-allogeneic fetus will not reject by maternal immune systems. The T regulatory cells (Tregs) controlled by the gene *FOXP3* seem to play a role in this maternal immune-tolerance. ICOS is one of the co-stimulatory molecules existing on surface Tregs. Previous studies have shown that blocking the co-stimulatory pathway ICOS-B7h could reduce the chance of fetal survival by reduction of regulatory cytokines like TGF-beta. In this brief review we are trying to show the roles of Tregs.

Keywords: preeclampsia, T regulatory cells, immune tolerance.

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INTRODUCTION

The preeclampsia occurring in 5-8% of all pregnancies worldwide, is one of the pregnancy complications which is the major cause of perinatal and maternal morbidity and mortality. The exact molecular basis of preeclampsia is still unknown [1-6]. Insufficient arterial remodeling of uterine spiral arteries results in inadequate blood supplying of the fetus and preeclampsia, and the controversies are mainly about involving immunological mechanisms. Because of this narrowness of uterine spiral arteries, blood pressure of the mother goes up [7-11]. In this brief review we are trying to show the roles of T regulatory cells (Tregs).

DISCUSSION

In a Successful pregnancy, the semi-allogeneic fetus will not reject by maternal immune systems. Tregs seem to play a role in this maternal immune-tolerance [12, 13]. Of course natural killer cells (NKs) has the most significant role in immune-tolerance [14, 15] and also in implantation and pregnancy based on previous studies [16-18]. It is worth noting that the size and function of these cells will be strengthened by the influence of male seminal fluid and ovarian steroid hormones in pre-implantation phase. IL-10 is another effective factor which can be pointed out. This inhibitory cytokine reduces apoptosis of Tregs [19]. Development and function of Tregs are controlled by the gene *FOXP3*. It has been observed that its allelic polymorphism is associated different outcomes the assisted ovarian stimulation [20] a technic used for treatment of infertility that of course because of its sequels is not recommended [21-26]. There are studies that show a relation between Tregs and vitamin D3 and the result was that Vitamin D3 deficiency in pregnant women can lead to damage Treg performance [27-33]. Two species of Tregs have been observed so far: 1) the nTregs which create in thymus and their task is to prevent systemic autoimmune and inflammatory diseases; 2) the iTregs which are produced by induction of exogenous antigens in the periphery. These roles can be listed for them: preventing fertility and pregnancy complications like infertility, recurrent spontaneous abortion and preeclampsia [34].

Inducible co-stimulator (ICOS) is one of the co-stimulatory molecules existing on surface Tregs. Previous studies have shown that blocking the co-stimulatory pathway ICOS-B7h could reduce the chance of fetal survival by reduction of regulatory cytokines like TGF-beta. In addition, disruption of this co-stimulatory system can be associated with preeclampsia and HELLP Syndrome [12, 13]. We should consider various Molecular aspects to identify the whys and therefore of infertility and reduce diagnostic medical errors. In the past even there was no belief to the role of human leukocyte antigen (HLA) typing in allograft organ transplantations let alone the semi-allograft pregnancies. But nowadays we should study HLA, immunoglobulin-like receptors (KIR), ICOS, CD94, NKG2a and other molecules and genes like *FOXP3* for genetic polymorphisms. Hence, it's upon us to setup and produce affordable polymerase chain reaction (PCR) [11], reverse transcriptase PCR [35, 36] or other genomic and proteomic-based [37] kits in knowledge-based companies across our countries.

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