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Endometrial expression of adhesion proteins in idiopathic recurrent abortions

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Purpose: Analysis of endometrial function in patients with abortions, have raised controversial discussions about the relevance of the endometrium as an underlying cause of idiopathic recurrent abortions. Furthermore, even though endometrial adhesion proteins have been suggested to play an important role in the regulation of endometrial function, no research has been conducted before to study adhesion protein in idiopathic recurrent abortion. We therefore analyzed a set of adhesion proteins which have been found to be regulated in human endometrium with an up-regulation during the window of implantation. These adhesion proteins including Integrin- β 3, Galectin-1, Galectin-3, Galectin-9, Syndecan-1, and Syndecan-4 have been studied in human endometrium previously and have been considered to implicate in endometrial regulation and implantation. Thus the study was designed to analyze the role of adhesions proteins in endometrial dysregulation, as underlying cause of idiopathic recurrent abortions.

Methods & Material: Under ethical approval and informed consent from Heidelberg Protocol, biopsies were retrieved from 15 highly selected women suffering from at least three consecutive unexplained habitual abortions. To prevent any information bias, the documentation of the number of previous miscarriage was retrieved from hospital records or practitioner source. Meanwhile, biopsies of ten women attended our ART clinics with no history of habitual abortions were collected as control. Other purported causes of

recurrent abortion such as anatomical, endocrine, chromosomal abnormalities, coagulation and autoimmune disorders, which were found in 60% of abortion patients, were thoroughly excluded by hysteroscopy and blood analysis. All women had a regular cycle. Biopsies were taken on day LH +7/8 days.

Endometrium tissue was further analyzed using multiprobe RNA protection assays (RPA) simultaneously to minimize variability of the analysis.

Immunohistochemistry was performed to confirm RPA analysis of Integrin- β 3, Syndecan-1, -4 and Galectin -1,-3,-9.

Results: The average of women age in case groups is 35 years (Mean= 35.5; SD= 5.9), whereas women in control groups is on average 36 years (Mean= 36; SD= 4.619). No significant age different found between both groups (Mann-Whitney U test, $z= 0.222$, $p=0.824$). Thus, age can be excluded as potential confounder in our observation for its impact in recurrent spontaneous abortions. In this study, women suffering from recurrent miscarriage had lost their pregnancy within first-trimester (Mean= 10.1; SD= 3.8), and categorized as primary recurrent spontaneous abortions to which display the case severity in association to the clinical risk factors.

On the RNA level there was no difference detected for Integrin- β 3, Syndecan and Galectin members comparing idiopathic recurrent abortion patients with healthy controls. Using Immunohistochemistry we found endometrial protein expression as described in the literatures without any difference in the two groups examined, confirming the results of the RNA protection assay.

Conclusions: To our knowledge, this is the first systematic study looking at the expression of adhesion proteins, which have been suggested to be relevant during the menstrual cycle and in implantation, in women with idiopathic recurrent abortions compared to the healthy controls. Equal endometrial expression of adhesion proteins in both studied groups do not support the hypothesis that endometrial dysregulation is an underlying cause of idiopathic recurrent abortion.