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DOI: 10.29256/v.03.01.2019.escbm55

## MOLECULAR-BIOLOGICAL MARKERS OF IMPLANTATION DISORDERS IN PATIENTS WITH INFERTILITY AND EXTERNAL GENITAL ENDOMETRIOSIS

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The effectiveness of the IVF program as one of the most effective methods of infertility treatment is 12.5% in case of external genital endometriosis (EGE) of the 1<sup>st</sup>-2<sup>nd</sup> stage, compared to 28.6-37.4% in case of tubal-peritoneal infertility factor (TPF). There is still no clear opinion on whether endometrial receptivity changes in patients with this disease and the expression of which morphological and molecular markers is impaired. The aim of this study was to study the molecular-biological peculiarities of endometrium in patients with infertility and stage 1-2 of the NEGP during the "implantation window".

**Materials and Methods.** A total of 72 infertile patients were studied: 23 with stage 1-2 of the NEG, 32 with tubal-peritoneal factor (TPF) and 17 with male infertility factor (MF). All patients underwent endometrial aspiration pipelle biopsy on the 6<sup>th</sup>-8<sup>th</sup> day after ovulation followed by histological and immunohistochemical examination. The number of pynopodia, the level of expression of estrogenic (EPa) and progesteronic (PR-A) receptors in the stroma and endometrial epithelium, the ratio of EP/EP in the stroma using mouse monoclonal antibodies to EPa (clone 1D5 RTU "DAKO", Denmark) and EP-A (clone 636 RTU "DAKO", Denmark) were determined.

**Results.** The average age of the patients of the main group was 34.17±0.69 years and did not statistically differ from the patients of the comparison group (32.63±0.72 years; p=0.138) and the control group (33.4±1.05 years; p=0.544). In the main group the expression of EPa in the endometrial stroma of the early and middle stages of secretion was low with a tendency to increase and averaged 50±12.25 and 62.27±19.45 points, respectively. In the endometrial epithelium of this group of patients, both early and middle stage of secretion, a moderate EPa expression with a tendency to decrease was noted and averaged 183.75±21.54 and 109.09±16.48 points, respectively. In the comparison group, the expression of ERa in the endometrial stroma of the middle stage of proliferation was moderate (140±20 points), and in the endometry of the early, middle and late stages of secretion, low expression was noted and averaged 40.56±12.68, 39.94±7.92 and 70 points, respectively. The expression of EPa in the epithelium of endometrium of the middle stage of proliferation and early stage of secretion was moderate (180±20 and 106.11±18.41 points, respectively), with a tendency to decrease, and in the endometrium of the middle and late stage of secretion there was a low expression of EPa in the epithelium and an average of 70.75±13.24 and 70.0 points, respectively. In the control group the expression of EPa in the endometrial stroma of both early and middle stages of secretion was low (50±20.0 and 60±17.61 points), in the endometrial epithelium the moderate expression of EPa in the early stage of secretion (105.0±35 points) and low (70±15.04 points) - in the middle stage of secretion. When comparing the nature of ERE expression in endometrium of patients with different types of infertility, a higher level of ERE expression in the endometrium of patients with NGE and its increase from early to middle stage of endometrial secretion (p=0.031) was revealed. Expression of ERa in epithelium significantly decreased depending on the phase of endometrial development in all groups (p=0.038), but the average ERa level in epithelium was statistically higher in patients with NGE (p=0.027).

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In the main group the level of expression of PR-A in the endometrial stroma of the early stage of secretion was high ( $202.5 \pm 14.36$  points) and decreased to moderate in the endometrial middle stage of secretion ( $143.64 \pm 17.54$  points). In the endometrial epithelium of patients with NSE both early and middle stage of secretion, a moderate expression of PR-A was noted with a tendency to decrease and averaged  $185 \pm 25$  and  $120.09 \pm 24.30$  points respectively. In the comparison group the level of expression of PR-A in the endometrial stromes of the middle stage of proliferation, early and middle stages of secretion was moderate and amounted to  $150 \pm 30$ ,  $161,11 \pm 17,98$  and  $156,25 \pm 8,56$  points, respectively, in the late stage of secretion - the level of PR-A in the stromes was high (210 points). The level of expression of PR-A in epithelium of endometrium of middle stage of proliferation, early and middle stage of secretion was moderate with a tendency to decrease and made  $190 \pm 10$ ,  $166,67 \pm 22,3$  and  $147,25 \pm 15,81$  points accordingly, in the late stage of secretion the expression of PR-A in epithelium was absent (1,0 points). In the control group, the expression of PR-A in the endometrial stromes of both early and middle stages of secretion was moderate and amounted to  $195 \pm 15.0$  and  $147.5 \pm 13.09$  points, respectively. The expression of PR-A was moderate in the endometrial epithelium of the early stage of secretion and low in the endometrium of the middle stage of secretion ( $180 \pm 0$  and  $58.25 \pm 20.14$  points). The level of expression of PR-A in epithelium and endometrial stroma of all groups decreased depending on the endometrial development phase ( $p=0.013$ ;  $p=0.032$ ), one of them did not differ statistically between the groups ( $p=0.186$ ;  $p=0.503$ ). We revealed that in patients with stage 1-2 NSE and TPF the ratio of PR-A/ER in the endometrium of the middle stage of secretion averaged  $5.964 \pm 2.5$  and  $9.481 \pm 3.57$ , respectively, and was statistically higher than the ratio of PR-A/ER in the endometrium of the middle stage of secretion in patients with MF ( $3.75 \pm 0.25$ ;  $p=0.043$ ).

**Conclusion.** Patients with infertility, combined with stage 1-2 NSE, have endometrial receptivity disorders during the "implantation window", which is manifested in the imbalance of hormonal receptors. The peculiarity of endometrial changes in the "window of implantation" in stage 1-2 of the NEGP is a significantly higher level of EPa in the epithelium and stroma. This may be one of the leading causes of infertility and lower efficiency of IVF program in patients with this disease.

DOI: 10.29256/v.03.01.2019.escbm56

## Fe, Mg CONCENTRATION IN RAT'S BRAIN UNDER INFLUENCE OF TRIGONELLA FOENUM-GRAECUM L. GRAIN EXTRACT

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Taking into consideration growing incidences of diabetes, cardiovascular diseases, severe chronic diseases of modern human, the search for alternative ways of their treatment and prevention is a priority in society. That is why it is perspective to create drugs based on plant components extracts enriched by vitamins and microelements. Their therapeutic effects have been proven by using historically thousands of years and scientifically motivated by preclinical and clinical results researches. The pharmacological activity of natural compounds is predetermined by their complex ability and change the activity of many regulatory proteins (Kovaliov, 2000). One of these is *Trigonella Foenium-Graecum L.* which have pharmacological, therapeutic and nutritional potential (Yadav UC, 2014; Abbas Mohammadi, 2016; Nagulapalli Venkata KC, 2017).

**Materials and Methods.** We used males Wistar line rats 140-230 g, which were on a standard diet of vivarium with free access to water and food. All procedures were