

The New Approach of Myoendometrial Pathology Diagnostics

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Summary The evaluation of structural features of morphological picture of endometrial secretion, as well as the showing of enzyme levels of antioxidant system of protein and lipid peroxide modification allow to reveal with the help of the given approach the forming tendencies of myoendometrial pathology at the preclinical stage. These results give the possibility to detect the contingent of women with increased risk of the formation of the given pathology with subsequent profound examination.

Purpose of the investigation: to elaborate the complex approach to the diagnostics of myoendometrial pathology by the method of determination of structural peculiarities of biological liquids: endometrial washes and menstrual discharges, the identification of second products of peroxide lipid oxidation.

Methods of the investigation: clinical, pathohistological, cytological, biochemical, wedge-shaped dehydration of biological liquids, transvaginal echography, statistical.

The offered approach allows to diagnose early myoendometrial pathology, to evaluate the possibility of tumor recurrence after conservative operations.

Key words: hormonodependent tumors of reproductive organs, leiomyoma, hyperplastic processes of endometrium, endometrial washes, menstrual discharges, peroxide lipid oxidation, malon dialdehyde, catalase index and catalase number, carbonil derivatives .

Introduction. In many countries of the world the recent decades are characterizes by the incidence rate of hormonodependent tumors of reproductive organs, such as leiomyoma, hyperplastic processes and endometrial cancer.

In spite of the sufficient number of detection methods of myoendometrial pathology, the necessity of new ones is retained. It is stipulated by inadequate susceptibility of the existing methods, their complicacy and high cost at the screening and monitoring stages. For our research of biological material the endometrial secret (endometrial washes) was chosen, because the usage of immunofluorescent and histochemical research methods of normal, hyperplastic and malignant endometrium tissue the ability of some enzymes and their isoforms to be accumulated in apical parts of glandular mucus was revealed (E.G. Shvarev, 1993). The biological peculiarity of endometrium is that this hormonosensitive tissue has the ability of cyclic renewal of cellular composition and is influenced by sexual hormones, peroxide lipid oxidation products and proteins.

No doubts that the development of various pathologic processes is associated with the so called "oxidant stress", which can be the direct cause of a disease or accompanies its development. The production of active oxygen forms increases, and the antioxidant system which regulates pro-

cesses of peroxide lipid oxidation and peroxide protein destruction is involved into the process. The oxidant stress development doesn't affect the isolated disturbance of lipids, proteins or nucleic acids because of their close interaction; thus, they are to be considered as a whole complex.

Material and methods of the investigation

420 women were examined; they were divided into following groups:

- 1) control group, including 64 (15,2 %) women without reproductive organs pathology;
- 2) 208 (49,5%) women with leiomyoma having normal structure of endometrium;
- 3) 84 (20,1%) women with leiomyoma and endometrial hyperplastic processes;
- 4) 13 (2,86%) women with leiomyoma with atypical endometrial hyperplasia;
- 5) 52 (12,4 %) women with leiomyoma and endometrial cancer in combination.

The offered approach allows to carry out biochemical, cytological and crystallographical research of endometrial secret (endometrial washes) simultaneously. Diagnostically it turned out to be more effective than the detection of markers in serum, where the received indexes were rather diverse.

In these groups the content of catalase was detected. Catalase is one of the enzymes of anti-oxidant protection, that is malon dialdehyde, which is the secondary product of peroxide lipid oxidation and carbonil groups of protein – markers of peroxide destruction.

The determination of peroxide protein destruction was carried out according to the technique of R.L. Levine et al. (1990) in modification of E.E. Dubinina et al. (1995). The showings were evaluated in peripheral blood as well as in endometrial secret; the most convincing data were received in endometrial secret. The results showed the evaluation of showings of peroxide protein destruction on the level of carbonil derivatives in endometrial secret to be one of the most sensitive showings of the oxidant stress.

For the investigation of endometrial secret (endometrial washes), its transition into solid phase with the method of cuneate dehydration was made. The analysis of structural elements of a dehydrated drop was made with the stereomicroscope Mz-12 (Leica) and digital camera «Pixera» (USA). We investigated the samples of dried drops, i.e. facii, as well as their enlarged photographs (from x10 to x160). The coefficients appropriate the endometrial pathology of different levels were calculated. Morphometrical showings of facii of endometrial secret were evaluated with the help of the programme Image Tool.

The results of the investigation

The meanings of catalase index and catalase number in endometrial secret in the control group were $3,09 \pm 0,18$ units and $0,8 \pm 0,08$ units. In women with leiomyoma having normal endometrium structure, the investigated parameters were $2,53 \pm 0,16$ units and $0,71 \pm 0,05$ units; in women with leiomyoma and endometrial hyperplasia the parameters were $1,8 \pm 0,33$ units and $0,44 \pm 0,09$ units.

The lowest meanings of the enzymes were registered in the group of women with leiomyoma in combination with atypical hyperplasia of endometrium and endometrial cancer – $0,68 \pm 0,2$ and $0,2 \pm 0,09$ units ($p < 0,05$).

The meanings of malon dialdehyde in endometrial secret in the investigated groups, on the contrary, had the tendency to the increasing and were $0,37 \pm 0,1$ nmol; $0,49 \pm 0,06$ nmol; $1,68 \pm 0,23$ nmol and $3,01 \pm 0,85$ nmol. When evaluating the coefficient of correlation it was determined that there is a strong inverse connection between the investigated data ($p < 0,05$).

In women with leiomyoma and normal endometrium structure the level of carbonil derivatives in endometrial secret were $4,0 \pm 0,09$ nmol/mg, with leiomyoma and endometrial hyperplasia - $9,3 \pm 0,27$ nmol/mg, with leiomyoma in combination with atypical hyperplasia of endometrium and endometrial cancer - $26,9 \pm 1,77$ nmol/mg ($p < 0,05$).

The previous years in clinical medicine a new diagnostic technique was developed; it is based on the information of overmolecular level during the transition of biological liquids into the solid states (V.N. Shabalin, S.N. Shatokhina, 1999; 2001; 2009; 2011).

This information is contained in the structure of the so called facii, the microscopic investigation of which allows to receive the morphological decoding (V.N. Shabalin, S.N. Shatokhina, 2000).

The described phenomena allows the usage of the results of structural analysis of biological liquids in screening and monitoring of patients with hyperplastic processes of myoendometrium and endometrial cancer.

During the examination of endometrial secret of hormonodependent tumors we determined 3 types of facii: radial (it is found in 48,4% of patients having leiomyoma with the normal endometrial structure); mixed, which is found in patients with combination leiomyoma and endometrial hyperplasia; three-radial, which is found in patients with atypical endometrial hyperplasia and endometrial cancer.

In patients having leiomyoma with normal endometrial structure in the samples of facii large fissures prevailed, forming special separate parts, where only isolated three-radial fissures were met (pic. 1, 2). With the increasing of severity of endometrial pathology (glandular endometrial hyperplasia) the spread of three-radial fissures increased (pic. 3). In patients with atypical endometrial hyperplasia and endometrial cancer the structure of facii differed from that described above: in the investigated samples all over the area of facii the net of three-radial fissures was found (pic. 4, 5).

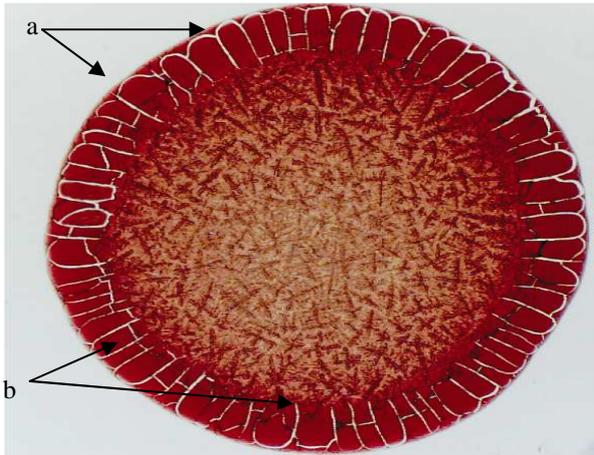
To determine the power on interaction between the showings S rad and S tr the tetrachorioidal coefficient of Pirson was calculated, which was increased with the severity of pathology of myoendometrium from 0,3 to 0,8.

The main structural elements of facii are given in the table №1.

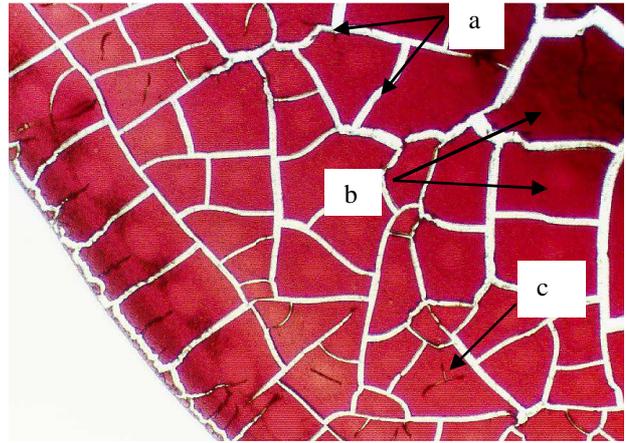
Table №1.

The main Characteristics of Endometrial Facii in endometrial secret of Patients with Myoendometrial Pathology.

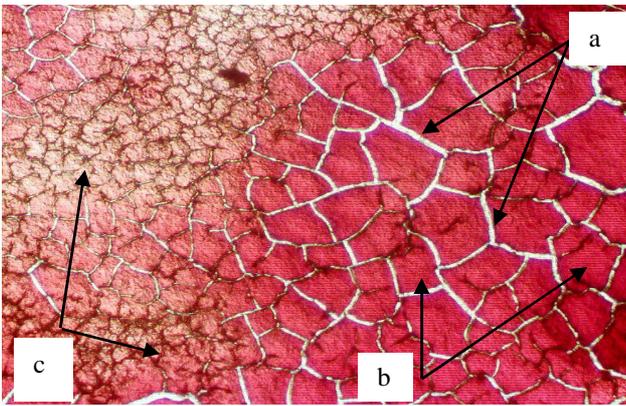
The investigated groups	The main structural elements of facii of uterus biological liquids	S rad (mm ²) (area of radiality)	S tr (mm ²) (area of 3-radial fissures)
Patients without tumor pathology of reproductive system (N=64)	siteness, radial fissures, separate parts are expressed, in 10% isolated three-radial fissures can be found.	6,8 ± 0,12	0,3-0,5± ± 0,06
Leiomyoma with normal endometrium (N=208)	siteness, radiality of fissures, separate parts, in 48,4% isolated three-radial fissures at any age are found.	5,1 ± 0,42	1,1 ± 0,08
Leiomyoma with endometrial hyperplasia (N=84)	siteness, radiality of fissures, increasing number of separate parts, three-radial fissures.	6,1 ± 0,46	2,1 ± 0,11
Leiomyoma with atypical endometrial hyperplasia (N=13)	clear siteness is being lost, in peripheral zone isolated radial fissures are kept, on the other part of surface there is a net of three-radial fissures.	2,23 ± 0,58	3,2 ± 0,58
Leiomyoma with endometrial cancer (N=52)	siteness is lost, in 88% of patients radial fissures are absent, three-radial fissures are the main structural elements.	0	6,7 ± 0,6



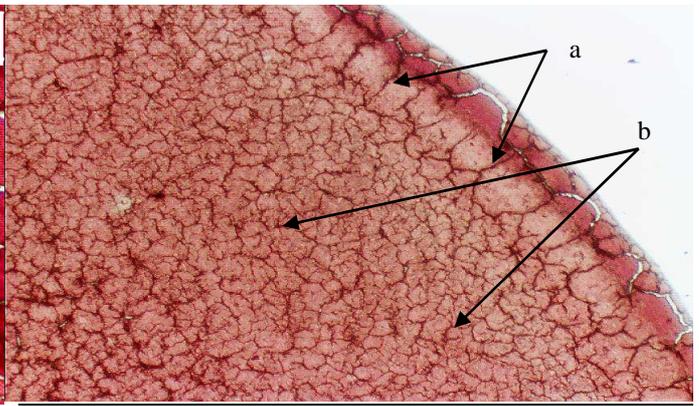
Picture 1. Facia of wash from the uterus cavity of the woman from control group with normal structure of endometrium: radial fissures {a}, separate parts {b} x25



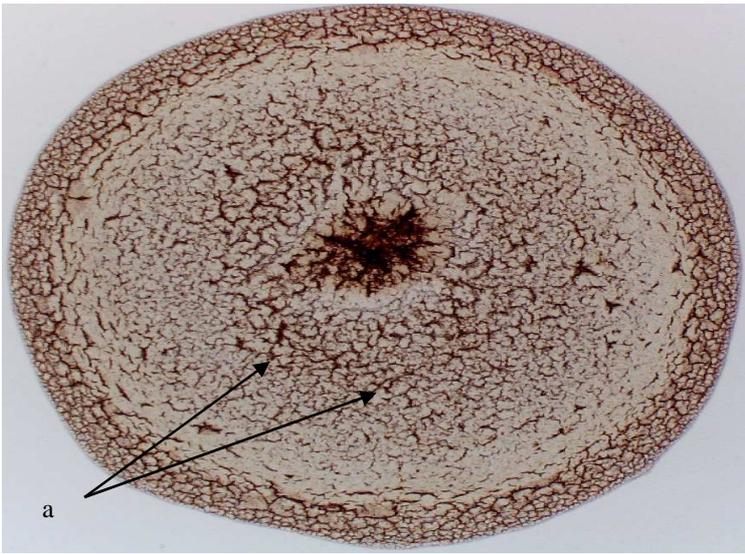
Picture 2. Fragment of facia of wash from the uterus cavity of the woman having leiomyoma with normal structure of endometrium: the presence of big fissures {a}, forming separate parts {b} and single three ray fissures {c}; x25.



Picture 3. Fragment of facia of wash from the uterus cavity of the woman having leiomyoma and hyperplastic processes of endometrium: the presence of big fissures {a}, separate parts {b} and a number of three ray fissures {c}; x25



Picture 4. Fragment of facia of endometrial wash of the woman having atypical hyperplasia of endometrium (a - single radial fissures, b - net of three ray fissures) x25.



Picture 5. Facia of endometrial wash in endometrium cancer (a – net of three ray fissures) x25.

Conclusions: thus, the evaluation of structural peculiarities of endometrial secret, some enzymes of antioxidant protection, secondary products of peroxide lipid oxidation and markers of peroxide protein destruction allows to reveal patients of high risk group with endometrial pathology at the pre-clinical period; it also allows to reveal forming pathologic processes of myoendometrium, preventing the development of precancer and cancer of this localization. Nontraumatic sampling of the material, the simplicity of its processing give us large possibilities of effective dispancerization of women with the investigated pathology.