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ETIOPATHOLOGICAL JUSTIFICATION OF CO₂ LASER APPLICATION IN STRESS URINARY INCONTINENCE

Puchko M. S.

*Assistant at the Department of Obstetrics and Gynecology № 3
Bogomolets National Medical University*

Usevych I. A.

PhD,

*Associate professor at the Department of Obstetrics and Gynecology № 3
Bogomolets National Medical University*

Oleshko V. F.

PhD,

*Assistant at the Department of Obstetrics and Gynecology № 3
Bogomolets National Medical University*

Yarmak V. S.

*PhD Candidate at the Department of Obstetrics and Gynecology № 3
Bogomolets National Medical University*

Stasiuk V. M.

5th year Student

*Bogomolets National Medical University
Kyiv, Ukraine*

One of the most priority areas of the gynecological service is an improvement of the life quality of modern women. Regardless of age, problems may arise in a woman's life which lead to severe discomfort, cause isolation, and give rise to the development of complexes, and sometimes psychological disorders [1, 2, 4, 6].

Stress urinary incontinence (SUI) is one of the problems which a premenopausal woman faces. It manifests as an involuntary discharge of urine in response to physical exertion, coughing or sneezing [4, 7, 8]. One of the main reasons for its development is considered to be a weakening or stretching of the pelvic ligamentous apparatus, which forms the urogenital diaphragm, and occurs as a result of estrogen deficiency and a decrease in the formation of collagen and elastin in the tissues [7, 8].

That is why connective tissue pathology, namely dysplasia, is currently considered as one of the leading SUI's pathogenetic mechanisms [5, 6].

Various conservative and surgical methods are used in SUI treatment. The literature review indicates that the effectiveness of pharmacological agents in SUI treatment is approximately 40-50%, but it has a short-term effect in most cases and can be achieved mainly in its mild forms [2, 4]. At the same time, side effects and incompatibilities with a number of other drugs limit the possibility of their application [4]. Currently, for the correction and treatment of SUI, drugs containing estriol are widely used. The local estradiol drugs application helps to restore the physiology of the urogenital tract: vaginal epithelium, connective tissue elements of collagen and elastin.

The search for alternative treatment methods led to the development and implementation of the new technology for SUI correction which is based on the use of laser energy [5, 6, 7, 8].

It should be noted that currently more and more information about the prospects of using minimally invasive laser technologies in urogynecology is being accumulated. But the information about its clinical effectiveness and safety in the treatment of SUI in women are provided only in a few sources [4, 5, 6]. Structural mechanisms of the therapeutic effect of laser radiation on the morpho-functional state of the vaginal walls after treatment with laser technologies remain insufficiently studied. This determines the prospect of further studies in this area and the purpose of our research.

The purpose of the research: etiological and pathogenetical justification of CO₂-laser application in the complex treatment of stress urinary incontinence in perimenopausal period patients.

The materials and methods of the research. A prospective examination of 132 women at the age of 45-55 y.o. who were treated in the Gynecological Department No. 2 of the Kiev City Maternity Hospital No. 3 and in the Medical center “Academy of Your Health” with SUI manifestations was conducted. All women were divided into two groups depending on the prescribed therapy. The main group consisted of 56 premenopausal age women with SUI, who were offered the therapy with the CO₂-laser application in combination with local application of an estradiol-based cream once a day for the first month, followed by further dosage reduction to one application twice a week for 7 months. The comparison group was formed by 76 women with SUI manifestations, who were intended only for therapy with local estradiol application at the rate of one application of cream per day for a month, followed by further dosage reduction to one application twice a week for 7 months. The total duration of treatment for women in both groups was 8 months.

Taking into account the significance of the fibrous connective tissue condition in SUI etiopathogenesis we determined the level of synthesis (Total P₁NP, Total P₃NP) and resorption (deoxypyridinolin Pyriliks – D) connective tissue markers in blood serum of all patients before the treatment, 6 and 12 months after the treatment.

The results of the research and their discussion. The average age of patients in the examined groups was 47,3±2,4 years, but their structure was significantly dominated by women over 53 years old. Most of them had the presence of combined extragenital pathology, including those that had UDCTD phenotypic manifestations: cardiovascular diseases (the main group – 35 (62,5%); the comparison group – 37 (48,7%); p<0,05), gastrointestinal and hepatobiliary system (the main group – 27 (48,2%); the comparison group – 24 (31,6%); p<0,05), ophthalmological diseases (the main group – 14 (25,0%); the comparison group – 10 (13,1%); p<0,05) and diseases of the genitourinary system (the main group – 31 (55,4%); the comparison group – 30 (39,5%); p<0,05).

The gynecological anamnesis of women in both groups was marked by a predominance of inflammatory diseases of the female genital system (the main group – 48 (85,7%); the comparison group – 42 (55,3%); p<0,05), cervical diseases (the main group – 40 (71,4%); the comparison group – 39 (51,3%); p<0,05) and sexually transmitted infections (the main group – 23 (41,1%), the comparison group – 21 (27,6%); p<0,05).

Analyzing the childbirth parity, it has been found that only 4 (7,1%) of women in the main group and 6 (7,9%) of women in the comparison group did not have a childbirth history. However, the remaining women of both groups with a history of childbirth noted the presence of complications, such as perineal and vaginal ruptures of I-II degree (the main group – 21 (37,5%); the comparison group – 36 (47,4%); p>0,05), operative delivery (the main group – 15 (26,8%); the comparison group – 24 (31,6%); p>0,05), including vacuum extraction of the fetus with previous perineo-or episiotomy.

In order to determine the state of fibrous connective tissue, which plays a leading role in the performance of the pelvic floor support function and the obturation ability of the urinary-genital diaphragm sphincters, we studied the concentration of Total P₁NP and Total P₃NP, which indicate the activation of type I and III collagen synthesis in the blood serum of patients in both groups.

For women with SUI manifestations, the average value of the type I collagen synthesis marker was decreased by 58,5% (the main group) and by 65,2% (the comparison group) from the physiological norm (the main

group – $23,2 \pm 3,24$ ng/ml; the comparison group – $26,4 \pm 4,04$ ng/ml; the physiological norm – $30,9-57,6$ ng/ml) ($p < 0,05$). At the same time, the average value of the marker of III type collagen synthesis in women of the study groups was increased by 52,2% (the main group) and by 36,0% (the comparison group) from the physiological norm (the main group – $29,24 \pm 2,66$ ng/ml; the comparison group – $27,4 \pm 3,01$ ng/ml; the physiological norm – $0,6-19,9$ ng/ml) ($p < 0,05$).

The average value of the connective tissue resorption marker Pýriliks-D, which is a product of collagen degradation in women of the main and the comparison groups, did not differ significantly and was on the verge of exceeding the physiological norm by an average of 14,2% (the main group) and 10,4% (the comparison group) (the main group – $8,1 \pm 0,04$ nmol/l, the comparison group – $7,96 \pm 0,03$ nmol/l, the physiological norm – $3,0-7,4$ nmol/l).

After CO₂-laser application 18 (32,1%) women of the main group complained of stress urinary incontinence as a result of a strong urge to urinate (the main group before treatment – 38 (67,9%); the comparison group after treatment – 36 (47,4%); $p < 0,05$). Loss of urine droplets was observed in 4 (7,1%) women (the main group before treatment – 28 (50,0%); the comparison group after the treatment – 13 (17,1%); $p < 0,05$).

Determination of the average concentration of the collagen synthesis type I Total P₁NP marker in the dynamics of treatment after 6 months demonstrated a significant increase by 72,8% in women who received CO₂-laser therapy in combination with local estradiol treatment (the main group before treatment $23,2 \pm 3,24$ ng/ml; the main group 6 months after treatment – $40,1 \pm 4,28$ ng/ml; $p < 0,05$).

In women of the comparison group, a significant increase in this indicator by 46,2% (the comparison group before treatment – $29,2 \pm 2,66$ ng/ml; the comparison group 6 months after treatment – $42,7 \pm 3,16$ ng/ml; $p < 0,05$) was observed.

Determination of the Total P₁NP marker concentration after 12 months against the background of the proposed complex revealed that the women of the main group had a stable value of the indicator (the main group after 6 months of treatment – $40,1 \pm 4,28$ ng/ml; the main group after 12 months of treatment – $42,7 \pm 3,61$ ng/ml; $p > 0,05$). From our point of view, these changes were provided by the effect of laser radiation on the vaginal mucosa that led to activation of endogenous collagen production. However, in women of the comparison group, a significant decrease of this marker after 12 months against the background of local therapy (the comparison group

6 months after treatment – $42,7 \pm 3,16$ ng/ml; the comparison group 12 months after treatment – $34,7 \pm 3,79$ ng/ml; $p < 0,05$), was observed.

The average concentration of the collagen synthesis type III Total P₃NP marker in women who received CO₂-laser therapy in combination with local treatment significantly decreased compared to the base value by 62,4% (the main group – $29,2 \pm 2,66$ ng/ml; the main group 6 months after treatment – $18,2 \pm 0,41$ ng/ml; $p < 0,05$) (Tab. 3).

For women in the comparison group, a significant decrease for 58,4% was also observed against the background of local therapy (the comparison group before the treatment – $27,4 \pm 3,01$ ng/ml, the comparison group 12 months after the treatment – $16,0 \pm 0,29$ ng/ml; $p < 0,05$).

Determination of this indicator in 12 months in the dynamics of treatment in women of the main group, an insignificant tendency to increase of the average concentration, which exceeded the maximum permissible physiological norm by 15,7% (the main group 6 months after treatment – $18,2 \pm 0,41$ ng/ml; the main group 12 months after treatment – $21,6 \pm 0,21$ ng/ml; $p > 0,05$), was observed. At the same time, women in the comparison group showed a significant increase in the average value of the indicator by 37,7% (the comparison group 6 months after treatment – $16,0 \pm 0,29$ ng/ml, the comparison group 12 months after treatment – $25,7 \pm 3,08$ ng/ml; $p < 0,05$).

Against the background of CO₂-laser therapy in combination with local estradiol treatment in women of the main group and the comparison group, there was no significant difference in the indicators of the connective tissue resorption marker P_{yriliks}-D.

Conclusions. The positive therapeutic result of the CO₂-laser, from our point of view, occurs due to the effect on the etiopathogenetic mechanisms of the SUI complex – an age-related imbalance of markers of synthesis and resorption of connective tissue. In women who received laser treatment, a significant increase and stable plasma concentrations of the Total P₁NP marker (base value – $23,2 \pm 3,24$ ng/ml; 6 months after treatment – $40,1 \pm 4,28$ ng/ml ($p < 0,05$); 12 months after treatment – $42,7 \pm 3,61$ ($p > 0,05$), was observed. An increase in the concentration of I type collagen synthesis marker contributed to a synergistic decrease in the concentration of III type Total P₃NP marker in women of the main group and stabilization of its value in the dynamics of treatment (base value – $29,2 \pm 2,66$ ng/ml; after 6 months – $18,2 \pm 0,41$ ng/ml ($p < 0,05$), after 12 months – $21,6 \pm 0,21$ ($p > 0,05$)). There was no significant difference in the concentration of the connective tissue resorption marker P_{yriliks}-D in women of the studied groups, depending on the chosen treatment.

From our point of view, a study of the hormonal status of women with stress urinary incontinence to improve the tactics of etiotropic treatment and prevention of relapse, offers the greatest promise.

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