

Modern Approach to Treat for Long-Lasting Salpingo-Oophoritis

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ABSTRACT

It has been determined that among maladies of genital system of women one of the leading parts (60,0-80,0%) is given to pelvic inflammatory diseases (PID) that are marked by recurrent course. The prominent clinical evidence of PID turns out to be disorders in menstrual function as it is irregular spotting or dysfunctional uterine bleeding (DUB). DUB during pelvic inflammatory diseases of women are primary since they are not connected with organic pathology of female genitals (specifically, oophorons), bearing of intrauterine contraceptive or administration of hormones with a view to contraceptive reason or other intention. Aetiopathogenesis of menstrual disorders when PID today still remains unknown and the major part in it is given to primary affection upon receptor of target-organs (neck of the womb), as well as follicular ovaries apparatus. It is an important point to be made that inflammatory reaction is a stress factor, therefore according to refference as to functioning of reproductive system, there arises hypothalamus activation, increasing its ability to produce gonadoliberin, adrenocorticotrophic hormone, releasing hormone, and other hypophysiotropic hormones. The effects of such a response of hypothalamus lie in stimuli of synthesis of cortisol, estrogen, and other steroid hormones. Together with it, secretion of endorphins and catecholamine increase.

KEYWORDS

Salpingo-oophoritis, hormonal disorders, recurrent course, treatment, approaches, medicines, women, age

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Introduction

Thematic justification

Early effective anti-inflammatory treatment, as well as correction of hormonal disorders, promotes resuming of normal cyclical processes and menstrual function. Whether inadequate treatment for menstrual function disorders may lead to pathomorphological alteration (prolonged anovulation, polycystic ovarian syndrome, hyperplasia, relapsing hyperplastic process of endometrium, leiomyoma, and other)

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(Auzan et al., 2004; Efendieva, Gusakova & Ondzhiu, 2007; Iarustovskaia et al., 2008; Razumov et al., 2002; Rymashevskii & Zaprudskaia, 1975; Tarnovskii et al., 2008; Kutashov & Kononov, 2015; Ayvazyan, Zaitsev & Yarustovskaya, 2004; Ayvazyan et al., 2007; Ayvazyan et al., 2012; Derevnina et al., 1998; Derevnina et al., 2008).

Most regrettably, up to date there have not been stated the advancement in prescription of combination therapy course of anti-inflammatory medication that would effective and secure effect on regulatory work of menstrual function. The efforts of some treaters to improve menstrual cycle by hormonal drugs are not always efficient; besides, there exist a certain part of women for whom such medication is contra-indicative. Among those we may consider, firstly, women having extragenital diseases (cardiovascular pathology, obesity, hepatic diseases) (Razumov et al., 2002; Bobkov et al., 2002; 2006; Kuznetsov et al., 1996; 2000). In addition to it, most of women negatively treat to prescription of hormonal medication having absolute and relative contradiction to administering (nearly 50 items) negatively affect upon body weight index (Ankirskaia et al., 1972; Ankirskaia, Savitskaia & Tokhiian, 1972; Orehova et al., 2004; Bondarev, 1997; Verspyck & Sergent, 2006).

The way out is to seek medication of non-hormone origin that safely and efficiently conditions menstrual cycle. That will promote efficiency of treatment of inflammation of inlying genitals, reactivation of normal menstrual cycle, as well as a prevention of long-term complications connected with pathomorphological alteration of receptive bodies of endometrium, and ovaries (Zaitsev et al., 2007).

Therefore we consider it actual to search optimal approach to PID-therapy and after-effects of inflammation. The possible option as to settle down the problem may be the use of remedies supplying medicinal effects directly upon the area of inflammation. Hence, the specific matter of concern arises as to vaginal or rectal administration of a medicinal product that would enable degrading a dose of medication, reduce occurrences of adverse reaction or allergic effects upon organism (Sahm, 1997; Snuth, Noble & Bensh, 1982; Tenover, 1991).

The above mentioned requirements would meet the medicinal product Distreptasa that compounds two components: streptokinase (15000 I.U.(ME)) and streptodornase (1250 I.U. ME) as in optimum dose for a maximum proteolytic and fibrinolytic effects.

Medicinal or phylactic effects of Distreptasa are justified by pharmacodynamics of compounding its components. Prominent clinical efficiency and safety as to Distreptasa has been proved by a great amount of clinical and scientific research.

The aim to timely elimination of menstrual disorders during acute or subacute salpingo-oophritis we tried to achieve by means of applying anti-inflammatory treatment course compound product Dismenorm. We relied upon benefit with the account of pharmacodynamic properties either of compounds or sole effects of agents compounding the product.

Objectives

The aim of the research is to analyze efficiency in application of products Distreptasa and Dismenorm in combination treatment for salpingo-oophritis marked by menstrual cycle disorders.

Materials and methods

Under the clinical care there have been 150 female patients at the age of 18 up to 35 (the average age is $28,6 \pm 9,5$ years) that underwent salpingo-oophritis at acute or subacute condition within the latter 2-6 months, with one of the clinical aspects

menstrual cycle disorders. Depending on suggested treatment to all female patients have been divided into representative (taking age, obstetric-gynecologic, and physical background) groups. The main group consists of 100 sick women having salpingo-oophritis who underwent complex anti-inflammatory treatment course with administration of Distreptasa and Dismenorm. The experimental group constitutes 50 sick women having salpingo-oophritis who underwent complex anti-inflammatory treatment course and other phyto- and biocatalyst products.

There has been analyzed the social and economic condition, obstetric and gynecologic, and physical background, menstrual function behavior of all female patients.

The research was targeted on study of human-subjective data: patient complaints, survey of medical history, gynecologic history, evaluation of efficiency, and safety (physician/patient), evaluation of subjective perceptions of pain syndromes according to visual analogue scale (VAS) before and after treatment course.

The medical and gynecologic history survey has been carried out according to common methodology and formulae. While bimanual gynecologic examination there were determined size of a womb, annexa condition.

Female patients of both groups before and after treatment were examined throughout: analysis of vaginal flora, mediators of hemostasis factor, hormonal panel, USI and Doppler velocimetry of pelvic organs.

All the female patients took anti-inflammatory therapy course (worksheet No.582), to which there was included administration by the treatment group of Distreptasa as a rectal suppository according to the schedule – administration with dosage event 3 times per 24 hours during 3 days, or 2 times per 24 hours during 6 days, including complex treatment product Dismenorm – 2 pills 2 times per day sublingual during 3 months.

Results and Discussion

Specific features of gynecologic history of sick women having long-lasting salpingo-oophritis are PID (100,0%), ectopia and endocervicitis (70,0%), endometritis (every fourth), ectopic pregnancy (8,0%), ovarian apoplexy (5,0%). Among extragenic diseases that the female patients have the prevailing ones are of pathology of inflammatory nature (acute respiratory diseases, chronic bronchitis, tonsillitis, cholecystitis).

The outcome analysis of objective research indicated that there were 40 (40,0%) sick women at an acute condition before treatment. The main complaint from the beginning of the acute condition of inflammation the patients had pain, and it was evident as to all examined female patients (100,0%). The primary pain localized low at abdomen was observed at all patients; among them there were 68 (68,0%) sick women complaining of pain radiation to pelvic limb and inguen, less often to low back and straight intestine. The evident pain from female patients of both groups (17,0%) was either stationary and lasted during 24 hours, or periodic (with the increased pain at the evening time, on movement, at a certain body position). The acute pain was prevailing (76,0%), marked pain was distinguished by female patients as (54,0%) and moderate pain as of (46,0%), as to intenseness 16,0% female patients described it as tender pain.

The acute or subacute salpingo-oophritis was marked by quite marked pain, namely, from 6 up to 9 points ($7,1 \pm 0,2$ points) pain has been determined by 91,0% female patients.



While vaginal examination all female patients had enlarged ovaries, Tender, dragging pain in uterine tubes was defined at 50,0%, tenseness of vaginal fornix. More often the inflammatory process localized in area of both saplings, namely: two-side adnexities was evident at 65,0% female patients.

WBC differential analysis of the sick having the acute salpingo-oophritis indicated that considerable as to haemogram ($p < 0,05$) comparing to healthy women were alterations typical for the inflammatory process of adnexa: leukocytosis, differential leukocyte count shifted left, lymph – and monocytopenia, ESR increase.

According to our research, the leading part of salpingitis ethiology is given to aerobian (*Staphylococcus aureus*, *Corinebacterium* species, *Echerichia coli*, *Candida albicans*) and anaerobic (*Gardnerella vaginalis* *Bacteroides* species, *Corinebacterium* species, *Bacteroides Melaninosenicus*, *Peptococcus* species) germ. More often are marked anaerobic trigger (up to 46,0% events) comparing to an aerobian one (up to 30,0% of the sick). In most cases (up to 56,0%) the inflammatory process is caused by facultative aerobe and to a greater extent by anaerobic microorganisms. Highly frequent detection of bacterial association points out to polygenic nature of salpingo-oophritis and by this justifies loss of specificity as to nosology. Significant role in eathiology of salpingitis is given to protozoaires (*Chlamidia tr.*, *Ureaplasma ur.*, *Trichamonas vag.*), since the frequency of occurrences varies from 16,0% up to 24,0%. Recrudescence for long-lasting salpingo-oophritis is favored by sharp decrease of agents of normal vaginal flora (*Lactobacillus* species, *Bifidobacterium* species) that become detected at less than the third of the sick women.

The leading position at pathogenesis as to adnexitis takes response on disorders index of haemostasis in the area of inflammation. The evidence of common symptoms of inflammation, namely – pain, toxipathy, inflammatory alteration in hemogram – gave the background to assume that local disorders in hemostatic system (in the area of inflammation) duly have their evidence at hemostatic quotient of the whole organism.

The research index of vascular-thrombocytic heamostasis of the sick women point out to accurate ($p < 0,05$) reduction in number of thrombocytes ($198,6 \pm 12,3 \times 10^3$ – in the experimental and $143,4 \pm 10,9 \times 10^3$ – in the main group) whereas a significant ($p < 0,05$) increase aggregation ability of thrombocytes (relevantly $29,3 \pm 3,7 \times 10^3$ and $40,7 \pm 4,5 \times 10^3$ in the experimental and the main group). The analysis of attained measurement as to vascular-thrombocytic hemostasis points out to prominent tension thrombocytic mediate of hemostasis of the sick having the acute salpingo-oophritis.

Blood coagulation system of the sick women having the acute salpingo-oophritis was at a quite compensated condition, however, accurate increase of antithrombin concentration at the sick women having long-lasting salpingo-oophritis at recrudescence reflect the increase thrombogenic possibility according to hemostasis of these patients.

The sick women having acute salpingo-oophritis the fibrinolytic mediate at hemostasis are abruptly suppressed. The evidence of accurate ($p < 0,05$) increase of plasmatic lysis measurement (correlated $160,5 \pm 8,9$ with $215,0 \pm 12,3$) including tendency to increase of concentration of free heparine, lowering of anti-thrombine III (AT-III) ($63,5 \pm 1,2\%$ and $57,3 \pm 3,1$) and, comparing to measurement as to healthy women, the increase of solvable fibrin three times from $0,8 \pm 0,4$ up to $2,9 \pm 0,3$ ($p < 0,05$).

Besides, we observed response as to ethanol gelation test at 100,0% the sick women having chronic salpingo-oophritis in acute condition.

The survey of measurement of blood flow in ovarian arteries of women having acute or subacute salpingo-oophritis on the 2-4-day at incursion of disease indicated

accurate ($p < 0,05$) alteration RI (resistance index), PR (prothrombine index) and ULR (ultra long range). ULR were more indicative ($p < 0,05$) than other parameters (RI or PR). There was recorded increase of diastolic component at a doppergram as well as lowering ULR in average up to $2,5 \pm 0,2$.

Rapid-speed measurements of blood circulation were exactly ($p < 0,05$) lowered at side of the inflammatory process comparing to the experimental group.

Ultrasound investigation data of the examined women were not at a great extent differ from those described in reference books. According to our findings, the increase of affected by inflammation adnexa may occur 100,0% cases. Cyst formation in ovaries were observed 25,0%, adhesive process in the uterine annexes were marked at 56,0% of the sick.

Ultra sound markers of hydrosalpinx (expanded lumen in tubes filled with liquid) nearly alike are shown from the right or left side. In particular, alterations as to fallopian tube on the right side were seen 38,0% women, alterations on the left side – 30,0% the sick. Most of female patients (94,0%) having acute chronic salpingo-oophritis behind the womb area a little amount of inflammatory exudate (up to 15-20 ml) was observed.

The survey of menstrual function of the sick having acute or subacute salpingo-oophritis indicated highly frequent disorders in menstrual cycle (100,0%). It is important to note that disorders arose at first time, and the women associated their evidence with the main disease, that is acute salpingo-oophritis. It was the reason for us to consider that causes of disorders of regulatory connection with pituitary - hypothalamus background turns to be the inflammatory injure of ovaries. Clinical aspects for disorders of menstrual cycle: algodismenorrhea – 78,0%, metrorrhagia – 56,0%, hyperpolymenorrhea – 42,0%. According to evaluation of functional diagnostics test (basal body temperature) it has been defined that most of (86,0%) the sick having salpingo-oophritis one-phase menstrual cycle is observed.

The survey of pituitary and ovaries function studies indicated that the sick having salpingo-oophritis there was high concentration of follicle-stimulating hormone (FSH) on 14-th and 21-st day of menstrual cycle (correlated $14,3 \pm 3,6$ mLU/ml to $12,8 \pm 1,7$ mLU/ml), lower level of luteinizing hormone (LH) (correspondingly $7,1 \pm 2,9$ mLU/ml to $8,5 \pm 2,8$ mLU/ml). Correlation luteinizing hormone/follicle stimulating hormone on 14-th day of cycle 7,5 times, and on 21-st day 4 times was less than healthy women have, what explicitly specify disorders in folliculogenesis processes anovulation. Concentration of prolactine (PRL) on 14-th and 21-st day of menstrual cycle were 1,5 times higher than relevant index rate healthy women have.

Levels of endoplasmic reticulum (Er) of the sick having salpingo-oophritis were on 14-th day of cycle 2 times higher ($p < 0,05$) than healthy women have (correspondingly $19,3 \pm 3,8$ pg/ml to $9,4 \pm 1,3$ pg/ml). On 21 -st day the levels of endoplasmic reticulum, that the sick women had, were almost 6 times higher than normal ones (correspondingly $18,1 \pm 4,7$ pg/ml to $3,1 \pm 1,1$ pg/ml). At this the level of prostaglandin (PG) on 21-st day of cycle was exactly lower ($p < 0,05$) this index rate than healthy women have (correspondingly $0,27 \pm 0,07$ pg/ml $0,49 \pm 0,01$ pg/ml), and correlation prostaglandin/endoplasmic reticulum (Er) was 10 times lower than healthy women have. All this points out to evidence of absolute and relevant deficit of progesterone as to the sick having salpingo-oophritis and menstrual function disorders.

In a fortnight after termination of anti-inflammatory treatment course for the sick having chronic salpingo-oophritis at recrudescence we observed normalization of hemostasis measures, being more prominent for the female patients of main group. To that points out vascular-thrombocytic hemostasis measure index. Comparing the sick



having chronic salpingo-oophritis at recrudescence, the female patients who administered Distreptasa (correspondingly $143,4 \pm 10,9 \times 10^3$ to $196,5 \pm 10,4 \times 10^3$), there normalized the amount of thrombocytes, and it did not differ ($p < 0,05$) from the amount of thrombocytes as to healthy women may have ($198,6 \pm 12,3 \times 10^3$). As for aggregation ability of thrombocytes the rate of their aggregation was evident ($29,9 \pm 5,1\%$), what did not differ from index of the experimental group ($29,3 \pm 3,7\%$).

The sick women who underwent a standard anti-inflammatory treatment course the amount of thrombocytes increased from $143,4 \pm 10,9 \times 10^3$ to $161,6 \pm 8,2 \times 10^3$, however, it was fairly littler ($p < 0,05$) than the healthy women $198,6 \pm 12,3 \times 10^3$ have (the experimental group). The aggregation ability as to thrombocytes did not achieve a standard index, and the difference between indices in groups (relevantly $29,9 \pm 5,1\%$ to $38,7 \pm 3,8\%$) was exact ($p < 0,05$).

Comparative analysis of coagulation system in a fortnight after termination of treatment pointed out to absence of accurate differential between indices in the experimental and the main group of female patients. Herewith, Index analysis revealed prominent tendency to clinical benefits of auto-coagulation test, thrombine time and prothrombine index in patients group, to whom we prescribed Distreptasa. Concentration of antithrombine these female patients have reduced from $4,8 \pm 0,2$ g/l to $4,2 \pm 0,3$ g/l, that practically did not differ from measures healthy women had ($4,0 \pm 0,2$ g/l). Female patients after standard treatment course had concentration of antithrombine practically did not decrease ($4,7 \pm 0,1$ g/l) and remained exactly ($p < 0,05$) more than healthy women have ($4,0 \pm 0,2$ g/l).

Difference between indices of fibrinolysis the sick and the treated female patients have (complex treatment including Distreptasa) attain exact values ($p < 0,05$) in plasmic lysis (correspondingly $215,0 \pm 12,3$ mg/ min-l to $168,6 \pm 9,9$ mg/min-l) and concentrations anti-thrombine III ($57,3 \pm 3,1$ mg/min-l to $63,8 \pm 0,7$ mg/min-l). The women that recovered after the standard treatment course the relevant indices approached to those the healthy women have, and their absolute values essentially differed from that ones the healthy women have.

The outcomes of discussion on achieved by us the data of hemostasis condition in 2 weeks after cessation of anti-inflammatory treatment course, in our analysis, witnesses about high efficiency of suggested treatment and necessity to introduce a complex therapy based on antithrombine product Distreptasa.

Comparative analysis as to dynamics of revealing of aerobic and anaerobian causative agents in 2 weeks after termination of either standard or suggested therapy noted the advantages in treatment by means of anti-thrombine products. It is evident as lowering (2,0-2,5 times) of frequency of arising of aerobic or anaerobian infectious organisms, as well as by increase (6,0-14,0%) of lacto – and bifid bacteria detecting.

We also came to the conclusion that anti-inflammatory treatment with the involvement of Distreptasa appears to be the most efficient and enables in 100,0% of events eliminate the causative agents STD. After treatment course taken by the experimental group there were found Chlamidia tr. (2 sick) and Ureaplasma ur. (4 women).

The outcomes of blood circulation in ovarian arteries indicated that upon discharge from the hospital when we terminate anti-inflammatory treatment the complete and accurate ($p > 0,05$) circulation management in these arteries does not occur. Hence, in the 1-st group of patients (treatment course including Distreptasa) incremental recovery of blood flow comparing to healthy women was observed in 58,0% (29 female patients) events, however, in the II-nd group (standard treatment course) – was evident as to 17 sick women (34,0%). The rest of the I-st and the II-nd

groups (correspondingly 42,0% to 66,0%) speed of blood flow in ovarian artery remained abnormal. Such a fact points out to subclinical prolongation of the inflammatory process effecting upon reconvalescence period, menstrual cycle, potential ability to impregnation and "ovarial reserve».

The analysis of blood circulation in ovarian arteries revealed that essential advancement in doppermetric indices on blood circulation in 1 month after discharge from the hospital occur with patients who at a complex of anti-inflammatory treatment, as well as outpatiently during a week administered antithrombotic product Distreptasa. Exact ($p<0,05$) response primarily concerned SDS ($2,5\pm0,2$ – in main group, up to $3,6\pm0,4$ – female patients who admimistered Distreptasa) and indices of speed of blood circulation: MSSK and SSK in correlation to $10,3\pm1,5$ and $6,6\pm1,2$ $15,4\pm1,2$ and $11,8\pm1,2$ before and after suggested by us treatment course.

Blood circulation in ovarian arteries indices of group of female patients who took the treatment course, improved in a way, however, were not appropriate to those the healthy women have. An only sign that reflected accurate response was SSK ($6,6\pm1,2$ at the sick condition up to $8,9\pm1,2$ after standard treatment course).

We assume that insufficient normalization as to blood circulation in fallopian tubes for the women who took the treatment course supplies the anatomic background for chronization of the inflammatory process with a sequential adnation, menstrual function disorders, agenesis, and other.

In 3 months after course of treatment we defined dynamic change in pituitary and steroid hormones background of blood plasma as to our female patients.

Comparative analysis of resulting data bear evidence of significant advantages of complex anti-inflammatory therapy course, to which there were included Distreptasa and Dismenorm (as for the main group), preceding the standard approach to cure of an acute salpingo-oophritis (as for the experimental group). It can be justified by an accurate ($p<0,05$) lowering of production of follicle-stimulating hormone upon 3 months after cure the sick of the main group having $14,3\pm3,6$ MIU/ml and $12,8\pm1,7$ MIU/ml up to $4,0\pm1,8$ MIU/ml and $2,3\pm0,8$ MIU/ml (correspondingly on 14-th and 21-st day).

The female patients who had not administered Dismenorm and Distreptasa complete normalization of follicle-stimulating hormone did not flow, as well as the hormone background indices were higher than those that have been evident as to the female patients of the main group or healthy women. The benefits of the suggested treatment course are also evident in dynamics of lactation hormone level that had become in 3 months accurately ($p<0,05$) lower comparing to the indices taken before the treatment course.

The resulting data of research on dynamics of steroid hormones levels of the patients having acute salpingo-oophritis pointed out to response at dynamics of steroid hormones in 3 months after application of both methods of curing salpingo-oophritis. There was observed the discrepancy in change evidence that had been recorded, since the standard treatment course (as to the experimental group) has only impact upon tendency to shifting indices to positive aspect. Positive values ($p<0,05$) at positive change become evident only in group of women to which we applied Distreptasa and Dismenorm (as for the main group). Hence, as for significant changes having a direct impact upon menstrual cycle the foremost aspect is considered lowering of endoplasmic reticulum from ng/ml on 14 th day and $18,1\pm4,7$ ng/ml on 21-st day preceding the treatment course up to $10,2\pm1,2$ ng/ml and $6,1\pm2,1$ ng/ml at the same time in 3 months after treatment course. Reinitiation of full-value 2-nd phase as to



female patients of the main group is also evident through normal level of progesterone on 14-th and 21-st day of cycle.

Evaluation of menstrual cycle background in 3 months after treatment course indicated differential as to elimination of disorders for the women who were cured by applying of Distreptasa and Dismenorm (as to the main group) and the standard anti-inflammatory treatment course (as to the experimental group).

The survey of obtained data points out to significant benefit of complex anti-inflammatory treatment course that constitutes Distreptasa and Dismenorm against common strategies when curing an acute or subacute salpingitis. Together with the anti-inflammatory treatment course the prescription of the above mentioned medication enabled to eliminate function disorders of hypothalamo-pituitary-ovarian system for more than 90,0% female patients having acute or subacute salpingo-oophritis that attended with menstrual cycle disorders. While application of standard treatment course normalization of menstrual cycle occurred as to 40,0% of the sick who had undergone the cure.

Obtained resulting data allow us to assume, that explicit effect of complex anti-inflammatory treatment course including Distreptasa and Dismenorm, is bound not only with thrombolytic and therapeutic activity of Distreptasa but with potential impact of mellific Apis, that constitutes compound of Dismenorm and stimulates anti-inflammatory effects.

The hospital treatment term for the main group was $9,45 \pm 2,1$ days, whereas for the experimental group - $14,2 \pm 2,1$, that was 5 days less. The more frequent reason of stay at a hospital was the evidence of stabile pain syndrome.

Conclusion

The remote result of cure (6-9 months from the begging of treatment course) on our assessment (pain syndrome dynamics according to Visual analogue scale, the data on general and pelvic examination, blood picture, bacterioscopy of meatus and vagina, USI of pelvic organs, normalization of menstrual function, complications, duration of the treatment course, side effects as sequela) – treatment efficiency as to female patients from the main group constituted 96,0%. The efficiency of applied standard treatment course as to the experimental group's sick women was shown in 78,0%.

Disclosure statement

No potential conflict of interest was reported by the authors.

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