

613.888

Influence the preparation of the new form of the combined hormonal oral contraception klayra the somatic and psychological status of women of reproductive age

Vertkin A.L., Nosova A.V.

Authors:

Vertkin A.L.- managing faculty of therapy pharmacotherapy with a rate of first aid Moscow

Nosova A.V.- assistant of faculty of therapy of pharmacotherapy with a rate of first aid of the Moscow

The resume of clause: In clause the problem influence of the new form of the combined hormonal oral contraceptive klayra on the psychological and somatic status of women of reproductive age reveals.

Contact: Vertkin A.L. kafedrakf@mail.ru

In Russia about two million abortions are made every day from which about one million – is iterant. The similar such practice has become traditional, and consequences being of great medical and social significances discased only among gynecologists. Meanwhile, artificial interruption of pregnancy have an influence on somatic and psychological status of woman [5], and these results in formation of neyroendocrine metabolic syndrome.

Besides two first years after abortion at 8 % of women have complications of inflammatory aerthology and in four years 20-25 % of women have violation of menstrual function begin failure of second phase of a cycle anovulation and relative hyperestrogenia [4]. These changes not only make worsen quality of a life of the women, but aggravate metabolic infringements, favouring early progress of atherosclerosis and occurrence of arterial hypertension [2].

The connection of abortion with psychological health is a problem discussed among wide circle of specialists[11]. Some authors demonstrate statistical correlation between abortion and stress, others mark out the term « postnatal syndrome » which includes itself the feeling of quilt, depression, emotional distance, aggression and thoughts of suicide [6].

So according to the results of statistics it is possible to prognostigate that the number of women of reproductive age subjected after abortion to the danger of somatic and psychological problems are increased (WHO, 2009).

In connection with this diminution of number of abortions with the help of modern methods such as contraception is the most effective prophylactic way of influence upon the organism of a woman on the whole and that is more some psychological problems of fertility aged woman is



explained by fear and unwillingness of pregnancy in unsuitable for work and career advance time.

Considerable role in psychological comfort of the woman is played the chosen way of contraception [7]. Safe method of contraception according to criterion of WHO (2009) are complex oral hormonal contraception. Besides contraceptive effect they have wide remedial profilactic influence improving prognosis and quality of women life [1]. So, contained in complex oral hormonal contraception estrogens stimulating the synthesis oxide nitrogen, promote relaxation smooth-muscular cells vascular endothelium enlarging density of a bone fabric [9,10], stabilize menstrual cycle, normalize duration and intensity of menstrual cycle that like bleeding which brings to liquidation of iron deficiency anemia [8].

At the same time, despite obvious preference complex oral hormonal contraception their wide use in the structure of other methods of contraception in Russia no more that 5-6 % [1]. We know that no only among patients but doctors too in that number, including physicians exist ungrounded opinion about side action complex oral hormonal contraception, that restricts their use in practice.

At the same time against a background really can appear side effects including headaches, intermenstruel bleeding, depressing and troubled disorder and also hardning of lactiferous, leg vein thrombosis weight enlargement. These phenomenon are connected with hyperestrogenia frequency of which can be decreased by the means of low ring in complex oral hormonal contraception contraception of estrogen component combining it with progestins and selection of contraceptive sexual hormones [3].

The object of investigation

Determine the influence new form complex hormonal oral contraception klayra on psychological and somatic status of reproductive aged women.

Materials and methods of investigation

Investigation was made in 3 stages. In the first part of the work we stated back-ward glance at somatic status, use pharmaco-therapy and obstatic-gynecologic antecedent 1218 women of reproductive age (average $36 \pm 4,1$ years) according to archives files of large-scale polyprofile hospital (n=741), of four polyclinics (n=361) and two women's dispensary (n=116). Board of direction of the Department of public health services SAO of the city of Moscow. Besides it on the basis of reports of autopsy has been analysed the structure and complications of a somatic

pathology of 164 women of reproductive age (average age $34 \pm 2,1$ years), having died in four hospitals of Moscow, Bryansk, Kazan in the course of the last three years (2009-2011).

Revealing of a morphological substratum of illnesses of these women average age of which was no more than 44 has promoted the formation of getting a idea about dangerous illnesses of the women of that age (see scheme 1).

The value of somatic status of 1218 women (average age of $36 \pm 4,1$ years)

Hospital (GCB №50) 741 women (average age $35 \pm 2,7$ years)	Hospital (GCB № 159,GP №164,GPN№ 155,GPN№28 361 women (average age $37 \pm 3,2$ years)	Women's dispensary (WD №4, WD №5) 116 women (average age $29 \pm 3,8$ years)
--	--	---

Analysis and comparison of the structure of the basic illnesses and their complications which became the reason of applying to the medical aid

Analysis and comparison of medicinal therapy, with the intention of basic somatic disease

Analysis and comparison of frequency of revealing family antecedent availabilizing of permanent sexual partner, use of methods of contraception, obstetrician gynecologic antecedent

Study of cause of lethality, outcomes of 164 women (average age of $34 \pm 2,1$ years), died in 4 hospitals of Moscow, Bryansk and Kazan in 2009-2011 year

The scheme 1. Design of the first research part

The second part of research consisted in sociological questioning of 97 women of different age, among whom 22 (average age $36,6 \pm 4,1$ years) were physician-general practitioners (group A), and rest 75 (average age $33,1 \pm 4,5$ years) - patients (group B). Average age of call. The average age of women who were questioned make up $35,3 \pm 4,3$.

Picture 1. Age structure of women who were questioned

As we see from picture .1, most of women were of reproductive age.

Questionnaire was carried out with status and the level of their possession of information in the problem of efficiency and safety available methods of contraception.

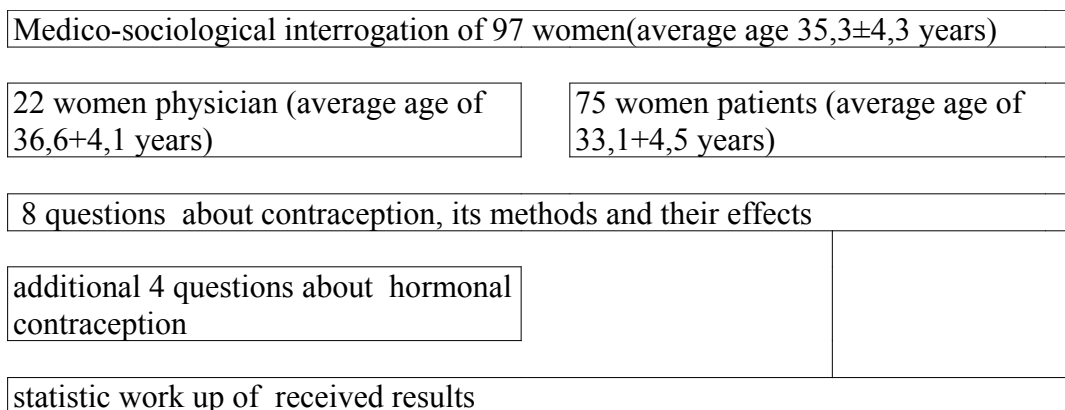
8 questions were put to all women including:

1. Do you now about connection between the quality of contraception and your health state?
2. What method of contraception is the most effective in your opinion?
3. What method of natural contraception is the most effective?
4. What of method of barrier contraception is the most effective?
5. What of method of chemical contraception the most effective?
6. What of method of hormone- containing contraception the most effective?
7. About what apprehension connected with talking hormones do you know?
8. What methods of contraception do you see ?

Besides interrogate no man from the group must have answered to additional questions, touching upon hormonal contraception to wit:

1. Do you now with what components of complex hormonal oral contraception tied the risk of development of undesirable phenomenon?
2. What do you think, what facts promote hyperestrogenemia ?
3. Do you know about distinction of composition and regime of dosage of different oral contraception's?
4. Must a therapeutic together with a gynecologist take part in prescription of hormonal contraception?

Design of the second stage of analysis is presented in scheme 2.



The scheme 2. Design of the second part of research

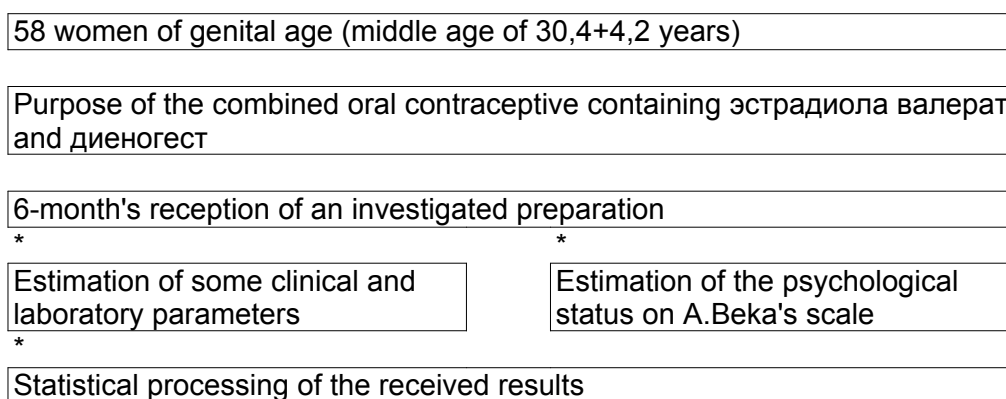
The third part of research was dedicate to the study of property of new KOK (preparation klayra, Bayer Shering Farma, Germany), containing in its composition valerat of estadiol and digionat, which are at most approached to estrogenus and progestins being uproduced organism of a woman.

Dynamic regime of dosage of preparation is characterised by lowering dosage of progestine for a period of 26 days of use of active pills. Estradiol of valerit after taking a medicine and during absorption in a mucous membrane of intestines it is quickly split up to valerian acids and estradiol, identical natural which absorption in mucous membrane of bowels splits and estradiol identical to natural concentration of which is supported on relatively stable level for the space of the whole cycle.

Dienogest is belonging to the to the progestagens of fourth generation as it does not contain in its structure etilic group, responsible for possible hepatotoxic effect, possesses high affinity to progesterone receptor calls forth its high selectivity.

58 women of genital age have been included in the given investigation phase (average age $30,4 \pm 4,2$ years), by which gynecologist in strict with the scheme of the therapy registered by the company-manufacturer the investigated preparation has been appointed. Duration of therapy has made for 6 months, and the period of supervision - 12.

Efficiency of spent therapy's analyzed by quantity of cases of the developed pregnancy, and safety - on dynamics of the psychological status of the women estimated by means of a scale of depression Becca, a level arterial pressure (AP), to a condition carbohydrate (definition basal maintenances of glucose and insulin of whey of blood with calculation of an index of sensitivity of fabrics to insulin an exchange of lipid and elecrolite, to change of an index of weight of a body, parameters coagulogram (activated partial tromboplastin time, fibrinogen, MNO) and an exchange of iron. The design of the third part of work is presented on the scheme 3.



The scheme 3. Design of the third part of research

Statistical processing of results carried out in programs « Microsoft Excel» and «Statistica» (Version 6.0). Used such statistical techniques, as: calculation of average value, calculation of a standard deviation, calculation of reliability and criterion Student, construction of diagrams and histograms. Distinctions between groups considered authentically significant at $p < 0,05$.



The received results and their discussion

In the first part of research it has been revealed, that from 741 women of genital age 476 (64,2 %) - have been hospitalized in gynecologic branch, 218 (29,4 %) - in surgical, and the others 47 (6,3 %) - in therapeutic clinic. From 476 patients hospitalized in gynecologic branch by an occasion for hospitalization at 309 (64,9 %) there was a threat noncarrying of pregnancy, at 52 (10,9 %) - ovarian apoplexy, at 48 (10,2 %)-disfunctional uterine bleeding, at 38 (7,9 %) - extrauterine pregnancy and at 29 (6,1 %>) – torsion legs ovarian . (fig. 2)

Figure 2. The reasons of hospitalization in gynecologic branch of women of reproductive age
Artificial interruption of pregnancy under medical indications has been made to 178 women (37,4 %) which middle age has made $29,0 \pm 6,1$ years, that below middle age of other women hospitalized in a hospital.

Thus, greater prevalence of diseases of the female reproductive system demanding stationary, frequently operative, treatment, high frequency of development of a pathology of the pregnancy dictating necessity of its interruption, and also younger age of this category of patients testifies to presence of lacks of questions of informing of women on planning pregnancy and a choice of a method of contraception.

Special attention in work gave a question of presence at surveyed women of the constant partner, which clinical physicians have specified only at 783 (64,3 %) from 1218 patients, including in a hospital at 62,6 % (n=464) and on

Outpatient reception hours in a polyclinic - at 56,8 %) (n=205). At the same time doctors of female consultations have reflected data of the family anamnesis in 98,3 % cases (n=114).

Thus, specification of presence of the constant sexual partner and the question of contraception naturally following it remains obscure in 35,7 % of cases.

The most informative medical documents containing rather developed data on applied ways of preventive maintenance of pregnancy, out-patient cards of the patients consisting on the dispensary account in female consultations were.

So, from 116 women whose archival documents were in female consultations, in 103 cases doctors paid attention of 88,8 % to a regularity of a sexual life of the patient, feature of an applied method of contraception or absence of those.

Return situation is observed in a hospital where the given parameter has made 32,4‰ (n=240), and on outpatient reception hours - only in 12,7 % of cases (n=46).

Thus, gathering of the anamnesis reflecting genital function of women, being at reproductive age and methods of preventive maintenance of pregnancy applied by them, is made extremely seldom (n=389), that makes 31,9‰ from all women with the kept genital function. Thus the

given questions are set in most cases (n=366) by advisers-gynecologists (94,1 %) while therapists pay attention to problems of female reproductive health and questions of contraception of the young patients in single instances - 5,9 %) (n=23).

From 1218 women of various age groups included in research of the obstetric -gynecologic anamnesis has been collected by clinical physicians only in 579 cases (47,5 %). So, from 579 patients in the anamnesis at 236 (40,8 %>) took place artificial interruption of undesirable pregnancy, and at 82 of them (14,2%) - abortions were repeated (*Table 1*).

Table 1. Influence of abortions on the somatic status of women (n=579)

Quantity of abortions in the anamnesis	Quantity of somatic diseases
0 (n=343)	1,2±0,1
1 (n=154)	1,2±0,1
2 (n=36)	1,4±0,2
3 (n=29)	2,6±0,2*
More than 3 (n=17)	3,1±0,3*

* corresponds meanings $p < 0,05$

As follows from tab. 1, together with the number of cases of artificial interruption of pregnancy the number of somatic diseases increases. So, at patients with three and more abortions in the anamnesis the somatic status is never heavier on 61,3 % in comparison with women resorted to abortion.

At the others 639 women (52,5 %) the information in section of the obstetric-gynecologic anamnesis in medical documents was absent.

At 893 (73,3 %) from 1218 women managed to be analysed a spectrum of medical products, which patients have been compelled to accept on a regular basis in connection with any somatic pathology. So, from 893 women fertile

age long medicinal therapy 349 patients (39,2 %) from whom 143 (40,9 %) - accepted anti-inflammatory preparations, 96 (received 27,5 %) - vitamins, 75 (21,5 %) – hypertensive preparations, 68 (19,5 %) - the medicines influencing bronchial passableness, 34 (9,7 %) - the medical products applied at diseases of bodies of digestion, 27 (7,7 %) - antimicrobial preparations, 14 (4,1 %) - system glucocorticosteroids and 11 (3,2 %) - other medicines (including sedative, корректирующие a metabolism, etc.). The information on long therapy of the others 325 (26,7 %) patients in medical cards was absent (fig. 3).

Figure 3. Medicamentous therapy of women of reproductive age

Thus, in case of occurrence of any possible pathology connected with infringement of reproductive function and demanding purpose of this or that hormonal preparation (including combined), its selection approximately at a quarter of women is complicated in a view of absence of the information on in parallel spent therapy and about potentially possible medicinal interaction.

From 164 died women of reproductive age the reason of death of 102 patients (62,2 %) was malignant new growths, at 39 (23,7 %) - sharp alcohol- associate of a condition and alcoholic visceropathy, and at 23 (14,1 %) - infectious diseases and their complications. In structure of malignant new growths at 69 (67,4 %) were a cancer of female reproductive bodies, including at 37 (36,3 %) - cancer of a mammary gland. 17 (52,8 %) have been diagnosed ovary cancer, 11 (35,9 %) - a cancer of a body of a uterus, and 4 (11,3 %) - the diagnosis of neck a uterus cancer, at 22 (21,8 %) - cancer of a pancreas and in 11 (10,6 %) cases - cancer of other localizations (lungs, kidneys, a stomach, etc.) (рис.4) is established.

Figure 4. Structure of malignant new growths - the reasons of death of women of reproductive age

Thus, at women of reproductive age high prevalence of somatic diseases takes place, most adverse of which are malignant new growths of bodies of female reproductive system. In this connection pertinently to remind of value of estrogen in preventive maintenance of cancer of female reproductive bodies and a role the complex hormonal oral contraception as the aid donor of sexual hormones.

According to the lead questioning of 97 women existence of communication between frequency of artificial interruption of pregnancy and the somatic status is assumed only with 24,5 % of women (n=25), namely 16 of group " And " (72,7 %) and 6 - from group " In " (8,1 %) ($p < 0,05$).

Figure 5. An estimation of efficiency of contraception by respondents

Apparently from fig. 5, in opinion of 68,2 % of women of group " And " (n=15) and 44,1 % - groups " In " (n=33) the most effective method of contraception is the reception of hormonal contraceptive means. However natural a method of preventive maintenance of pregnancy of 9,1 % of women of group " And " (n=2) and consider as more successful 14,7 % - group " In " (n=11), and barrier - 22,7 % (n=5) and 37,3 % (n=28), accordingly. A chemical method of contraception consider as the best 4,1%o women-patients (n=3.) 40,9 % of women-doctors (n=9) and 41,3%o women-patients (n=31) as the most effective method of natural contraception consider the interrupted sexual certificate ($p > 0,05$). The temperature method is the most effective for 27,3% (n=6) and 16,1 % (n=12) ($p > 0,05$), calendar - for 18,2 % (n=4) and 32,1 % (n=24) ($p > 0,05$), and cervical- for 13,6 % (n=3) and 10,7 % (n=8) women ($p > 0,05$), accordingly. 59,1 % of women-doctors (n=13) and 77,3 % women-patients (n=58) consider as the most effective method of barrier contraception use of man's condoms ($p > 0,05$).

The application cervical hubcap is the most successful method in opinion of 13,7 % (n=3) and 13,3 %> (n=10) women ($> 0,05$), vaginal diaphragms - 9,1 % (n=2) and 8,1 % (n=6) (0,05), and female condoms - from the point of view of 18,2 % (n=4) and 1,3 % (n=1) women (0,05), accordingly.

68,2% women-doctors (n=15) and 44,1 % of women-patients (n=33) consider as the most effective method of chemical contraception use vaginal candles ($p < 0,05$). Application vaginal tampons is the most effective for 9,1 % (n=2) and 34,7 % (n=26) ($p < 0,05$), and vaginal cream-for 22,7 % (n=5) and 21,3 % (n=16) women ($> 0,05$), accordingly. 22,7% women-doctors (n=5) and 30,7 %> women-patients (n=23)

consider as the most effective method of hormonal contraception reception the complex hormonal oral contraception ($p < 0,05$). The reception not combined gestagens (mini-drink) is the most successful way of contraception in opinion of 18,2 % ($n=4$) and 16,1 % ($n=12$) women ($0,05$), and use postcoital hormonal contraception - 4,1 % ($n=3$) women-patients ($p < 0,05$). Besides the use of hormonal injections as much as possible effectively at a sight of 4,5 % and 4,1% ($n=3$) the interrogated women ($> 0,05$), hormonal hypodermic implant - 4,5% ($n=1$) and 2,7 % ($n=2$) ($0,05$), hormonal rings - 27,3 % ($n=6$) and 22,7% ($n=17$) ($0,05$), hormonal plasters - 4,5 % ($n=1$) and 5,3 % ($n=4$) ($> 0,05$), hormonal intrauterine spirals - 18,2 % ($n=4$) and 14,7 % ($n=11$) women ($p < 0,05$), accordingly.

Thus, the awareness of women in questions of efficiency and safety of contraception is ambiguous, that, possibly, causes difficulties in a choice them of a contraceptive method. However if in questions of efficiency of natural, barrier and chemical contraception women have a certain clearness in a choice of the most effective hormonal method of contraception obvious difficulties are observed. Moreover, women-patients are assured of efficiency the complex hormonal oral contraception of the woman-doctors on 8 % less often. Ambiguity of the attitude to hormonal contraceptive means can be explained from positions of safety (fig. 6).

Figure 6. Knowledge of respondents of an opportunity undesirable effects of reception of hormonal contraceptives

Apparently from fig. 6, 7 % of women-doctors ($n=19$) and 70,7 % ($n=53$) women-patients are afraid of superfluous weight of a body ($> 0,05$). Superfluous growth of hair 22,7 % ($n=5$) and 33,3 % ($n=25$) women are afraid ($0,05$), occurrence of new growths - 63,7 % ($n=14$) and 24,1 % ($n=18$) ($p < 0,001$), depressive and disturbing frustration - 36,7 % ($n=8$) and 48,1 % ($n=36$) ($> 0,05$), thromboses-72,7 % ($n=16$) and 54,7 % ($n=41$) ($0,05$), and infringements of a menstrual cycle-18,2 % ($n=4$) and 64,1 % ($n=48$) women ($p < 0,05$), accordingly.

Thus, the basic arguments against hormonal contraception at the majority of women are the risk of adiposity, superfluous growth of hair, depressive and disturbing frustration and thrombosis complications. Moreover, women-doctors on 39,6 % more often than women-patients connect reception of hormonal contraceptive means with the development of new growths, including malignant. And on the contrary, women-patients on 45,9 % are afraid of infringements menstrual cycle on a background of reception of hormonal contraceptives is more often.

Doubts in safety of hormonal methods of contraception which overwhelming majority of women (68,2 % of women of group " And " ($n=15$) and 44,1 % women of group " In " ($n=33$)) admit to the most effective, at the same time lead to low frequency of reception of hormones (fig. 7).

Figure 7. The methods of contraception are used by investigated women

Apparently from fig. 7, prefer hormonal contraception of 38,1 % women (n=37). Thus the majority 42,3% (n=41) - chooses a barrier method of protection from undesirable pregnancy, and 7,2 % on a regular basis resort to natural and chemical methods of contraception (n=7) and 12,4 % (n=12) women, accordingly. Interrogation of 22 women-doctors the complex hormonal oral contraception has shown their lack of information in mechanisms of action and possible by-effects. So, the KOK of 40,9 % of doctors (n=9) connects the undesirable phenomena with estrogen and 27,3%o (n=6) with a gestagen component, 13,6 % (n=3) - with high doses of both hormones, a part the complex hormonal oral contraception, and 18,2% (n=4) - cannot answer on this question.

In opinion of 5 doctors (22,7%) hyperestrogenemia 3 doctors (13,6%) - adiposity, 4 doctors (18,2 %) promote hormone- modeless to a tumour, stress situations, and the others 10 clinical physicians (45,5 %) were at a loss to answer. Nicotinic and alcoholic dependences, and also associated with them any of clinical physicians to risk factors of development hyperestrogenemia has not carried a pathology. Any of the interrogated doctors-therapists have not answered a question on a chemical compound and a mode of batching of various hormonal contraceptive means, at the same time of expediency of purpose and a choice the complex hormonal oral contraception the joined decision of the gynecologist and the therapist had been convinced 19 interrogated women (86,4 %).

Thus, women of reproductive age, including being doctors of the general practice, have shown low awareness in the general questions of contraception, and also in aspect of efficiency and safety of a hormonal method of protection from undesirable

A background of 6-month's therapy the KOK of oppression of the psychological status of the women who have entered into research, it has not noted been. Moreover, during supervision the mean score of symptoms of depression has decreased with $12 \pm 1,1$ up to $9 \pm 0,7$ (for 41,7 %) ($p < 0,05$), and alarms - with $7 \pm 0,8$ up to $5 \pm 0,4$ (on 44,6 %) ($p < 0,05$).

Apparently from tab. 2, on a background of therapy by the combined hormonal oral contraceptive containing estradioli valerat and dienogest a level systolic and diastolic the arterial pressure ($> 0,05$), carbohydrate ($> 0,05$), lipid ($> 0,05$) and hydrous an exchange ($> 0,05$), an index of weight of a body ($0,05$), parameters coagulagramm ($> 0,05$) and an exchange of iron ($> 0,05$) have not undergone changes. Besides on a background of its application at one of patients pregnancy has not come.

Table 2. Dynamics of clinic-laboratory parameters on a background of therapy KOK

Parameter	Before therapy	After therapy
IWB, kg/m ²	$28,7 \pm 4,3$	$27,8 \pm 3,9$
Index QUICKY, point	$0,365 \pm 0,012$	$0,371 \pm 0,011$
systolic arterial pressure, mm.hg.	128 ± 7	127 ± 6
diastolic arterial pressure, mm.hg.	78 ± 3	79 ± 4
PTT, sec.	$32 \pm 1,8$	$34 \pm 1,4$
fibrinogen, g/l	$2,5 \pm 0,2$	$2,4 \pm 0,2$
INR	$0,9 \pm 0,05$	$0,8 \pm 0,05$
hemoglobin, g/l	$121,4 \pm 2,7$	$123,3 \pm 1,9$
serum iron, micromoll/l	$24,4 \pm 0,8$	$24,9 \pm 0,9$



general cholesterol, mmol/l	3,8±0,3	3,7±0,2
glucose of blood, mmol/l	4,1±0,2	4,0±0,4
kalium of blood, mmol/l	3,9±0,9	4,1±0,6
sodium of blood, mmol/l	137,6±2,2	139,2±2,4

* corresponds meanings $p < 0,05$

Conclusion:

The findings reflect the high efficiency and safety of the known KOK, allow you to use it as a hormonal contraceptive drug in a wide range of women of reproductive age, not affecting the oppression of mental status, and has no influence on hemodynamic parameters and parameters of carbohydrate, lipid, water-salt exchange.

Literature:

- Adamyan, L.V. Genetic aspects of gynecologic diseases // L.V. Adamyan, V.A. Spitsin, V.N. Andreeva-M.; Medicina, 2008. - 240p.
- Kulakov, V.I. Treatment of female and male's barrenness // V.I. Kulakov, B.V. Leonov, L.N. Kuzmichev-M.; Medicina, 2005 - 592p.
- Podzolkova, N.M. Differential diagnostics in gynecology // N.M. Podzolkova, O.L. Glazkova-M.; Medicina, 2003. - 129p.
- Saveleva, G.M. Obstetrics. // G.M. Saveleva, V.I. Kulakov, A.N. Strishakov-M.; Medicina, 2000 - 262p.
- Hlomov, K.D. The influence psychoemotional and individual- characteristic on current of pregnancy at women with threat of interruption. // K.D. Hlomov, S.N. Enicolopov / Prenatal psychology and perental psychology. - 2007. - №3. - P. 38-49.
- Adler, N.E. Psychological factors in abortion // N.E. Adler, H.P. David, B. Major / American Psychologist. - 2007. - № 47. - P. 1194-1204.
- Coleman, P.K. Abortion and mental health: quantitative synthesis and analysis of research published 1995–2009. // P.K. Coleman / The British Journal of Psychiatry. 2007. - 199 (3). P. 180-186.
- Graser, T. Climodien (estradiol valerate 2 mg plus dienogest 2 mg) is safe and effective in the treatment of postmenopausal complaints. // T. Graser / Climacteric. 2001. - № 4. - P. 332-342.
- Katsuki, Y. Effects of dienogest (a synthetic steroid) on coagulation, fibrinolysis, and platelet aggregation in female monkeys. // Y. Katsuki, H. Nobukata, T. Ishikawa / Toxicol Letters. 1998. - (98). P. 105-113.

- Muck, A.O. Effects of estradiol and dienogest on potential markers of vascular function in postmenopausal women // A.O.Muck/ Jenapharm Company Documentation 1998.-21p.
- Pope, L. M. Postabortion psychological adjustment: Are minors at increased risk? // L. M. Pope, N. E.Adler, J. M. Tschann /Journal of Adolescent Health.2008.-№ 29.P. 2-11.