Реферати

МОДЕЛИРОВАНИЕ С ПОМОЩЬЮ РЕГРЕССИОННОГО АНАЛИЗА РАЗМЕРОВ СРЕДНЕЙ ЧЕРЕПНОЙ ЯМКИ У ЮНОШЕЙ И ДЕВУШЕК РАЗНЫХ КРАНИОТИПОВ

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SIMULATION У 82 практически здоровых городских юношей и 86 девушек Подольского региона Украины при разделении на разные краниотипы построены достоверные регрессионные модели компьютерно-томографических размеров средней черепной ямки в зависимости от антропометрических и соматотипологических показателей с коэффициетом детерминации (R2) большим 0,6. У юношей-мезоцефалов и брахицефалов из 6 возможных моделей построены все 6 (соответственно R2 равняется от 0,855 до 0,955 и от 0,611 до 0,802). У девушек-долихоцефалов и брахицефалов также построены все 6 моделей (соответственно R2 равняется от 0,705 до 0,900 и от 0,811 до 0,866); а у девушек-мезоцефалов лишь 3 модели (R2 равняется от 0,656 до 0,719). В построенные модели наиболее часто входят: у юношей-мезоцефалов – кефалометрические показатели (32,3 %), диаметры и обхватные размеры тела (по 19,4 %); у юношей-брахицефалов – кефалометрические показатели и обхватные размеры тела (по 25,7 %), а также толщина кожно-жировых складок (17,1 %); девушек-долихоцефалов – кефалометрические показатели и ширина дистальных эпифизов длинных трубчатых костей конечностей (по 22,9 %) и обхватные размеры тела (20,0 %); у девушек-мезоцефалов – кефалометрические показатели (42,9 %); у девушек-брахицефалов – обхватные размеры тела (28,0 %), кефалометрические показатели и толщина кожно-жировых складок (по 16,0 %).

Ключевые слова: средняя черепная ямка, компьютерная томография, антропометрия, краниотип, практически здоровые юнноши и девушки, регрессионный анализ.

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REGRESSION ANALYSIS IN MODELING OF DIMENSIONS OF MIDDLE CRANIAL FOSSA IN BOYS AND GIRLS OF VARIOUS CRANIOTYPES

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In 82 practically healthy urban boys and 86 girls Podillia region of Ukraine in the allocation on different craniotypes built significant regression models of computed tomographic size of the middle cranial fossa depending on anthropometric and somatic parameters with coefficient of determination (R2) greater than 0.6. In mesocephalic and brachycephalic males, of the 6 possible models build all 6 (correspondingly R2 is from 0.855 to 0.955 and from 0.611 to 0.802). In girls dolichocephalic and brachycephalic, all 6 models are also constructed (R2 is equal to from 0.705 to 0.900 and from 0.811 to 0.866, respectively); and in girls-mesocephalic only 3 models (R2 is from 0.665 to 0.719). The built models often include: in mesocephalic males - cephalometric indices (32.3%), diameters and girths of the body (by 19.4%); in brachycephalic youths - cephalometric indices and girths of the body (25.7%), as well as the thickness of skin and fat folds (17.1%); in dolichocephalic girls, the cephalometric indices and the width of distal epiphyses of long limb bones (22.9%) and the circumferential body size (20.0%); in girls-mesocephalic girls - cephalometric indices (42.9%); in brachycephalic girls - girths body size (28.0%), cephalometric parameters and thickness of skin and fat folds (by 16.0%).

Key words: middle cranial fossa, computed tomography, anthropometry, craniotype, virtually healthy young boys and girls, regression analysis.

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PATHOGENETIC ASPECTS OF STATINS' APPLICABILITY IN COMBINATION TREATMENT OF PATIENTS WITH UTERINE FIBROIDS AND EXTRAGENITAL PATHOLOGIES

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Hyperplastic processes of the uterus (HPPU) maintain leadership in the structure of gynecologic morbidity. As reported by the medical literature, hyperplasia of endometrium occurs in 50% , and uterine fibroids – in 20% of all gynecologic female patients of reproductive age [3, 11]. Hyperplastic processes of the uterus are one of the major causes of reproductive loss and performance decrement among women aged between 35-45 years [6, 10]. It has been established that the development of hyperplastic processes of the uterus increases significantly against the background of metabolic disorders [1], the implication of which in the stimulation of proliferative and neoplastic processes is not completely defined. However, obesity plays an important role in this process, as it is accompanied by the accumulation of estrogens in

edipose tissue leading to the increase of «estrogenic pool» in the body and thus stimulating the development of hyperplastic processes of endo- and myometrium.

Thus, the goal of our research was to give scientific credence and develop a system of comprehensive treatment of hyperplastic processes of the uterus involving the use of gonadotropin-releasing hormone (GnRH) analogues and atorvastatins in women of reproductive age with uterine fibroids and obesity.

Materials and methods. Group I (experimental) involved 60 female patients with HPPU and extragenital pathology. All women had class I-II obesity, and body mass index (BMI) was 36.31±1.82 kg/m2. Abdominal obesity was present in 56 patients. The experimental group was divided into 2 subgroups: 1a subgroup consisted of 40 patients with uterine fibroids and extragenital pathology (obesity and hypertensive disease), and were administered background therapy (GNRH agonists 3.6 mg 3 times every 28 days), hepatoprotectors (1capsule 3 times), sedatives (1capsule 3 times)) in combination with atorvastatin – 20 mg/day for a period of 6 months; 1b subgroup involved 20 patients with the same pathology receiving only the background therapy.

The control group involved 30 patients without gynecologic or somatic pathology at the moment of examination. The age of examined patients ranged from 30 to 45 years.

Examination and treatment of patients was carried out in gynecologic units of Ivano-Frankivsk city maternity hospital and in private clinic «Ekstramed».

Before and over the time of treatment all women underwent clinical examination, duration of menstrual bleedings. The size of the uterus was determined with the help of ultrasound scan using mathematical formula V = D x S x W x 0.521, where V – volume, D – length, S – width, W – antero-posterior dimension.

Blood cholesterol levels, β-lipoproteins of low density (LDL) and high density lipoproteins (HDL), as well as triglycerides were measured in all women by means of kinetic method using biochemical analyzer «Stat Fax 19-04». Blood levels of estradiol, follicle-stimulating hormone (FSH), progesterone, luteinizing hormone (LH), testosterone were measured with the help of radio-immunologic and immunoenzyme methods using standard sets of reagents"Immunotech" (France) and test-system "Alkor Bio" (Russia), Human GmbH, Wiefbaden (Germany) according to the provided instructions. All the indices were measured before and 6 months after the treatment. Computer data processing was carried out with the help of statistical package Stat.Soft.Inc; Tulsa, OK, USA; Statistica 6.

Results and discussion. At the moment of examination women from group I had coexisting diseases, namely: hypertensive disease – 9 patients (15%), chronic ischemic heart disease – 5patients (8.33%), vegetative-vascular dystonia – 22 patients (36.67%); every one in four patients was diagnosed with the disease of hepatobiliary system – 18 patients (30%), allergic reactions – 11patients (18.33%) and varicose veins – 8 patients (13.33%).

The average volume of the uterus was 186.4±5.48 sm3 in women from experimental group (control 71.01±2.68 sm3, $p<0.0002$). Predominantly in 65% of cases women were diagnosed with intramural nodes with centripetal growth, M-echo of which was deflected to the opposite side of the uterus. Pedunculated subserosal fibroids were diagnosed in 25% of cases, but it was rather complicated to differentiate them, since they were located behind the uterine contours. The average volume of nodes made up 31.48±2.06 sm3.

It is important to note that these metabolic disorders are an important link in the pathogenesis of hyperplastic processes of the uterus.

The study of lipid metabolism in women from experimental group showed statistically significant increase of the average levels of basic indices of blood lipids as compared to the control group. Specifically, the level of cholesterol was 6.29±0.89 mmol/L (control – 4.18±0.32 mmol/L) $p<0.0001$, triglycerides levels made up – 2.31 ±0.39 mmol/L (control 1.13±0.13 mmol/L) $p<0.001$, LDL – 4.03±0.88 mmol/L (control – 2.03±0.03 mmol/L) $p<0.0001$, HDL – 1.05±0.29 mmol/L (control – 1.68±0.11 mmol/L) $p<0.003$. The atherogenic index was 6.04±1.63 (control 1.5±0.03). High levels of the latter indicate high probability of atherosclerosis development, and as a result, diseases of the cardiovascular system which are observed in all women of the experimental group. That is why, the use of atorvastatin to correct the lipid metabolism is reasonable for patients of this group.

Study of data from different literature sources revealed no detailed analysis of the hormonal state of patients with hyperplastic processes of endo- and myometrium which develop against the background of extragenital pathology combined with obesity [2]. It is considered, that the development of diffuse forms of endometrial hyperplasia is promoted by the violation of the feedback mechanisms between the centers of reproductive system control and ovarian functioning; while the development of focal changes

in endometrium are associated with direct alterations of hormonal homeostasis that involves moderate decrease in gonadotropic hormones release by the pituitary gland and weakening of steroid ovarian function [9].

Our findings show statistically significant increase of estradiol and FSH levels in the first phase of menstrual cycle (Table 1) in women with uterine fibroids and obesity, as compared to control group of patients. Relative estrogen deficiency is noticed in the second phase of menstrual cycle, while the levels of progesterone and luteinizing hormone are statistically significantly higher than the control ones. Increase of prolactin levels in luteal phase of menstrual cycle also calls our attention. The above described hormonal changes lead to the failure of adaptive-compensatory reactions at the level of hypothalamus-pituitary-ovaries-uterus. High progesterone and prolactin levels influence proliferative processes in mammary glands promoting the development of connective tissue, causing dilatation of mammary ducts. The above mentioned changes result in mastopathy which is observed in 42 women of experimental group (70%). We have established strong positive correlation between LH and BMI ($rs=0.83$; $p<0.001$), testosterone and BMI ($rs=0.64$; $p<0.005$).

Statistically significant close correlation between the levels of estradiol/progesterone and FSH/LH is observed in patients with uterine fibroids and obesity in various phases of menstrual cycle: first phase – between estradiol and FSH $rs=0.93$; $p<0.0001$; between progesterone and LH $rs=0.83$; $p<0.0001$; in the second phase this correlation was $rs=0.85$; $p<0.0001$ and $rs=0.84$; $p<0.0001$, namely, the increase of steroid hormones causes the increase of tropic ones.

Table 1

Levels of gonadotropic steroid hormones in blood serum of patients with HPPU and obesity (X±SD)

Hormones	First phase of menstrual cycle		Second phase of menstrual cycle	
	Group I	Control group	Group I	Control group
Estradiol (pg/ml)	156.4±11.6*	114.99±8.54	85.2±9.3*	87.91±4.82
FSH (IU/l)	5.44±1.02*	3.78±0.03	2.53±1.02*	2.8±0.02
Progesterone (nmol/l)	2.88±0.76	2.75±0.02	30.89±2.2*	21.1±0.98
LH(IU/l)	4.66±1.71	4.4±0.08	14.11±1.35*	8.36±0.17
Prolactin (mIU/l)	559.72±21.32	557.61+7.4	715.45+34.1*	625.52±20.61
Testosterone (ng/ml)	1.96±0.08 *	0.68±0.05		

Note. * - $p<0.01$ as compared to the control group

We have established a statistically significant relation between the levels of estradiol and LDL that indicates direct involvement of the latter in the processes of estrogen formation, both in the adrenal cortex and ovaries, and, as a result, leads to hyperestrogenemia. Some researchers [4, 8] consider estradiol to be the hormone that accelerates the rate of protein synthesis in smooth muscle tumors, contributing to their growth. Steroid receptors that are found on these cells bind with estradiol and penetrate through the caryolemma into the nucleus where they bind with RNA and thus stimulating their synthesis. The formed complex affects cell division or inhibits its growth.

Furthermore, according to some researches [7], type II hyperglycemia, which is involved in our investigation, leads to the decrease of endothelin -1 level and increase of epidermal growth factor, which, in its turn, binds with specific receptors causing DNA synthesis and mitotic activity of endometrial cells as well as their proliferation [5, 7].

6 months after the treatment statistically significant decrease of levels of total cholesterol to 3.69±0.24 mmol/L ($p<0.001$), triglycerides to 1.18±0.15 mmol/L ($p<0.001$), LDL to 2.09±0.31 mmol/L ($p<0.001$), atherogenic index to 1.48±0.51 ($p<0.001$), and increase of blood HDL levels to 1.75±0.22 mmol/L ($p<0.0001$) were observed in women from subgroup 1a, as compared to the indices before treatment. Findings in subgroup 1b women revealed high levels of total cholesterol 6.15±0.53 mmol/L ($p<0.001$), LDL 4.02±1.17 mmol/L ($p<0.001$), triglycerides (TG) – 1.99±0.71 mmol/L ($p<0.01$), atherogenic index 5.38±0.9 ($p<0.001$), low levels of HDL 1.07±0.26 mmol/L ($p<0,001$), as compared to the indices revealed in subgroup 1a women.

Statistically significant decrease of body mass index (BMI) to 29.31±2.64 kg/m2 ($p<0.04$) was noticed in patients of 1a subgroup 6 months after the treatment, as compared to the indices before treatment. In patients from 1b subgroup the BMI was 34.24±3.45 kg/m2 ($p>0.05$) and didn't significantly differ from the indices before treatment. We have established strong positive correlation between the triglycerides and BMI in subgroup 1b patients ($rs=0.71$; $p<0.03$), while this correlation was not revealed in1a subgroup patients at the same period of study.

Restoration of the levels and statistically significant correlation between gonadotropic and steroid hormones was revealed 6 months after the treatment in patients from subgroup 1a at various phases of

menstrual cycle. The estradiol and FSH levels were close to the control values and thus equaled: 116.32±8.14 pg/ml ($p<0.001$) and 3.98±0.48 IU/l ($p<0.001$) in follicular phase, 89.65±7.42 pg/ml ($p<0.001$) and 3.1±0.3 IU/l ($p<0.001$) in luteal phase, as compared to their levels before treatment. Such indices are within the control values. Speaking about the patients from subgroup 1b, the concentrations of these hormones have also decreased as compared to their levels before treatment: 132.32±11.44 pg/ml ($p<0.001$) and 4.51±0.58 IU/l ($p<0.001$) in follicular phase, 105.35±7.42 pg/ml ($p<0.001$) and 3.88±0.32 IU/l ($p<0.001$) in luteal phase, though statistically, they were significantly higher than the their levels in patients from 1a subgroup.

In experimental group women the levels of progesterone and LH in this period were significantly lower than their levels before treatment. They were close to control values in women from 1a subgroup and were lower than their levels before treatment: 2.77±0.42 nmol/l ($p>0.05$) and 4.56±0.34 IU/l ($p>0.05$) in follicular phase, 22.34±2.48 nmol/l ($p<0.01$) and 8.56±0.4 IU/l ($p<0.02$) in luteal phase. The blood levels of these hormones in 1b subgroup patients made up: 3.48±0.56 nmol/l ($p<0.01$) and 5.05±0.08 IU/l ($p<0.01$) in follicular phase, 23.95±3.01 nmol/l ($p<0.01$) and 9.86±0.5 IU/l ($p<0.01$) in luteal phase. Thus, the increase of progesterone and LH was revealed in 1b subgroup patients in follicular phase as compared to their levels before treatment, while their levels were significantly lower in luteal phase than before treatment, though statistically, they were significantly higher as compared to the levels in the control group.

Statistically significant negative correlation between the levels of estradiol and FSH ($rs=-0.54$; $p<0.01$), progesterone and LH ($rs=-0.51$; $p<0.001$) was recorded in 1b subgroup women in follicular phase. Therefore, positive correlation was noticed between progesterone and LH ($rs=-0.74$; $p<0.001$) in luteal phase as it was before treatment, while these correlations between estradiol and FSH levels correspond to the ones in follicular phase. The prolactin level in various phases of menstrual cycle was: 1a subgroup patients – 544.32±10.45 mIU/l and 624.71±11.27 mIU/l; 1b subgroup patients – 552.68±9.52 mIU/l and 634.84±12.14 mIU/l. The level of testosterone decreased to 0.68±0.06 ng/ml ($p<0.01$) in 1a subgroup patients, and to 0.78±0.11 ng/ml ($p<0.04$) in 1b subgroup women. These indices are within the control values.

Hormonal balance restoration leads to the recovery of menstrual function in 38 (95%) women from 1a subgroup and 14 (70%) patients from 1b subgroup. However, the average duration of menstrual period was within the normal range.

6 months after the treatment the M-echo was characterized by smooth structure, except for the regions with fibromatous nodes. The volumes of the uterus and fibromatous nodes have significantly decreased in 1a subgroup women , as compared to the volumes before treatment, and made up respectively 114.34±5.12 sm3 and 10.82±0.08 sm3 ($p>0.05$ in all cases). On the other hand, the above mentioned volumes were statistically significantly higher in 1b subgroup patients as compared to those in 1a subgroup and made up 138.07±6.35 sm3 ($p<0.01$) and 19.42±0.62 sm3 ($p<0.01$).

Conclusion

1. Consequently, the use of comprehensive treatment leads to hormonal balance restoration and recovery of menstrual function 3 months after the last injection of GnRH analogue. However, the levels of estradiol and progesterone were significantly lower in 1a subgroup patients as compared to 1b subgroup ones. Positive attitude to the performed treatment and quality of life tended to increase among 1a subgroup patients that may be obviously attributed to lesser occurrence of «outbreak» syndrome, than in 1b subgroup, and associated with the use of atorvastatin as part of comprehensive treatment used in this group.
2. The use of comprehensive treatment results in: decrease of uterine volume in 1a subgroup patients to 40% and to 26% in 1b ones, decrease of fibromatous nodes to 66% and 38% respectively. Within the whole period of treatment the average sizes of uteri and fibromatous nodes were smaller in 1a subgroup patients than in 1b ones. We think that these differences in the sizes of uteri and fibromatous nodes in the studied groups of patients are associated with the use of atorvastatin, which leads to the loss of body mass and reduction of the amount of fat tissue, which is the depot for estrogen in the female body.

Prospects for further research. *Further investigations of hormonal and lipid metabolism, as well as, study of uterine volume in later periods after the treatment are prospective, as they will allow to timely diagnose and prevent disease recurrence.*

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Реферати

ПАТОГЕНЕТИЧНІ АСПЕКТИ ДОЦІЛЬНОСТІ ЗАСТОСУВАННЯ СТАТИНІВ У КОМПЛЕКСНОМУ ЛІКУВАННІ ХВОРИХ З ФІБРОМІОМОЮ МАТКИ І ЕСТРАГЕНІТАЛЬНОЮ ПАТОЛОГІЄЮ

Жураківський В. М.

Першу (дослідну) групу склали 60 хворих, які поділялись на 2 підгрупи: 1а підгрупа – 40 хворих з фіброміомою матки і екстрагенітальною патологією (ожиріння і гіпертонічна хвороба), отримували базову терапію (агоністи гонадотропін-релізінг гормону (3,6 мг х 3 рази через 28 днів), гепатопротектори (1к х 3 рази), седативні (1к х 3 рази)) в поєднанні з аторвастатином по 20 мг на добу впродовж 6 місяців; 1б підгрупа – 20 – хворих з тією ж патологією, які отримували тільки базову терапію. У таких хворих відмічається статистично значуще збільшення естрадіолу і фолікулостимулюючого гормону при відносній прогестероновій недостатності, а також достовірне підвищення в сироватці крові холестерину і атерогенної фракції ліпопротеїнів та зниження ліпопротеїнів високої щільності. Застосування комплексного лікування призводить до нормалізації гормонального обміну та менструальної функції через 3 місяці після останньої ін'єкції аналога Гн-РГ, проте слід зазначити, що рівень естрадіолу та прогестерону у жінок 1а підгрупи був достовірно менший, ніж у підгрупі 1б. Застосування комплексного лікування приводить до: зменшення об'ємів маток у підгрупі 1а на 40%, у підгрупі 1 б на 26% , фіброматозних вузлів відповідно на 66% та 38%. Упродовж всього періоду лікування в підгрупі 1а середні об'єми матки і фіброматозних вузлів були меншими, ніж у підгрупі 1б. Така різниця в об'ємах маток і фіброматозних вузлів у досліджуваних підгрупах пов'язана, на нашу думку, із застосуванням аторвастатину, який призводить до зменшення маси тіла та зниження кількості жирової тканини, яка є депо естрогенів в організмі жінки.

Ключові слова: гіперпластичні процеси матки, ліпідний обмін, статеві гормони, статини.

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ПАТОГЕНЕТИЧЕСКИЕ АСПЕКТЫ ЦЕЛЕСООБРАЗНОСТИ ПРИМЕНЕНИЯ СТАТИНОВ В КОМПЛЕКСНОМ ЛЕЧЕНИИ БОЛЬНЫХ С ФИБРОМИОМЫ МАТКИ И ЕСТРАГЕНИТАЛЬНОЙ ПАТОЛОГИЕЙ

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Первую (исследовательскую) группу составили 60 больных, которые делились на 2 подгруппы: 1а подгруппа включала 40 больных с фибромиомой матки и экстрагенитальной патологией (ожирение и гипертоническая болезнь) получали базовую терапию (агонисты гонадотропин-рилизинг гормона (3,6 мг х 3 раза через 28 дней), гепатопротекторы (1к х 3 раза), седативные (1к х 3 раза)) в сочетании с аторвастатином 20 мг в сутки в течение 6 месяцев; 1б подгруппа ¬ 20 больных с той же патологией, получали только базовую терапию. У таких больных отмечается статистически значимое увеличение эстрадиола и фолликулостимулирующего гормона при относительной прогестероновой недостаточности, а также достоверное повышение в сыворотке крови холестерина и атерогенной фракции липопротеинов и снижение липопротеинов высокой плотности. Применение комплексного лечения приводит к нормализации гормонального обмена и менструальной функции через 3 месяца после последней инъекции аналога Гн-РГ, однако следует отметить, что уровень эстрадиола и прогестерона у женщин 1а подгруппы был достоверно меньше, чем в подгруппе 1б. Применение комплексного лечения приводит к: уменьшению объемов маток в подгруппе 1а на 40%, в подгруппе 1 б на 26%, фиброматозных узлов соответственно на 66% и 38%. В течение всего периода лечения в подгруппе 1а средние объемы матки и фиброматозных узлов были меньше, чем в подгруппе 1б. Такая разница в объемах маток и фиброматозных узлов в исследуемых подгруппах связана, по нашему мнению, с применением аторвастатина, который приводит к уменьшению массы тела и снижению количества жировой ткани, которая является депо эстрогенов в организме женщины.

Ключевые слова: гиперпластические процессы матки, липидный обмен, половые гормоны, статины.

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