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THE DEPENDENCE OF THE RESISTANCE OF ESTRADIOL ON THE INFLUENCE OF THE MUTANT HENA OF THE ALLEL A WITH JUVENILE DYSMENORRHEA

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ABSTRACT

Girls were examined with YUD (n = 64) compared with the control group (n = 50). For the release of DNA, venous blood was served from the elbow vein, with the detection of estradiol-alpha receptor genes and serum estradiol (E2). The data obtained during genetic studies are consistent with the indicators obtained during the study of the level of estradiol, in the blood of girls with primary dysmenorrhea, depending on the presence of CTD criteria. It was revealed that the presence of a mutant allele A, as well as the G2014A genotype in the ESR1 G2014A genotype in women, can affect the level of estradiol levels in the blood, which was confirmed by genetic analysis, which revealed that the intelligence of the mutant allele of the estrogen receptor - alpha (one-deactive replacement of Guanin On adenine in RS2228480), 1.9 times higher in the group of girls with YUD with CTD than in the YUD group without CTD ($\chi 2$ = 4.515; p = 0.03).

KEYWORDS: *Juvenile Dysmenorrhea, Connective Tissue Dysplasia, Estradiol.*

INTRODUCTION

Around the world, one of the factors that worsen the quality of life of girls and teenage girls is considered painful syndrome accompanying the physiological process - menstruation. According to WHO, the prevalence of menstrual pain syndrome in the structure of teenage gynecological pathology is extremely high, while about 15% of them characterize menstrual pains as painful. Juvenile Dysmenorrhea (YUD) - painful menstruation in girls under 18, in the absence of pelvic pathology, are general and often depleting gynecological suffering regardless of age or nationality. Despite the high prevalence, the primary dysmenorrhea among girls is often poorly diagnosed and is even ignored by medical workers and the girls themselves and

their mothers who can take painful menstruation as a normal part of the menstrual cycle. If the pathological situation occurs in the body of the growing female body, the formation of pathological states of organs and tissues in the form of dysplastic manifestations from the connecting tissue is occurred. A large variety of clinical criteria for the severity of undifferentiated connective tissue dysplasia (CTD), but the features of the metabolism of the connective tissue are still unclear. To date, it has been established that human endometrium undergoes cyclic waves of proliferation, differentiation, apoptosis and regeneration, depending on the increase and decrease in the levels of estradiol synthesized in the ovaries and progesterone. The synthesis of specific proteins of estrogen alpha-receptors was determined by the ERα genome (ESR1). This gene is located on chromosome 6Q25. It consists of 8 exons, 7 intron and occupies more than 140 kilobes. Molecular mechanisms, thanks to which these polymorphisms affect the activity of receptors, remain intact. RFLP is found in the intron, i.e. The almost non-functional region of the gene, and since they are separated by 50 pairs of bases, are presumably in a strong linear clutch.

THE PURPOSE OF THE STUDY IS: to establish the role of molecular genetic mechanisms of violation of endometrial regulation on the basis of a survey of single polymorphisms of genuine receptor genes of genital steroids, regulation of angiogenesis, in patients with dysmenorrhea.

MATERIAL AND METHODS OF RESEARCH: We examined girls with YUD (n = 64) compared with the control group (n = 50). For the release of DNA, venous blood was served from the elbow vein, with the detection of estradiol-alpha receptor genes, polymerase chain reaction (PCR), which was carried out using specific primers (NPF Litech, Russia) in the automatic amplifier "Rotor Geene 6000". The concentration of serum and estradiol (E2) was determined by the IFA methods on the AT-858 analyzer (ShangheiAntaiDiagnosties CO, LTD) using the ELISA test system sets - Austria. The data obtained in the study was subjected to statistical processing on the Pentium-IV personal computer using the Microsoft Office Excel-2012 software package, including the use of built-in statistical functions.

THE RESULTS OBTAINED AND THEIR DISCUSSION.

Analysis of the distribution of allelic variants of the ESR1 G2014A gene, according to Table 1, showed that the frequency of occurrence of a mutant allele (a) in a group of patients with YUD, accompanied by CTD reliably higher compared to the control group of practically healthy persons ($\chi 2 = 3,999$, $p < 0.04$, $OR \geq 1.92$). A reliable increase in the homozygous genotype with the participation of risky alleles AA also met significantly more often compared to the control group, with the indicators $\chi 2 = 3.716$, $p = 0.053$. This gives grounds for assumption that YUD in girls with CTDs may have a genetically deterministic origin.

TABLE 1 DISTRIBUTION OF FREQUENCIES OF ALLELES AND GENOTYPES OF THE ESR1 G2014A GENE IN GIRLS WITH PRIMARY DYSMENORRHEAL WITH CTD COMPARED TO THE CONTROL GROUP OF PRACTICALLY HEALTHY FACES

Genetic type	YUD + CTDn=64	YUD + CTD %	Genetic type	control, n=68	control, %	OR	$\chi 2$	P
G	99	77,34	G	118	86,76	0,52	3,999	0,04
A	29	22,66	A	18	13,24	1,92		

GG	44	68,75	GG	53	77,94	0,62	1,429	0,23
GA	11	17,19	GA	12	17,65	0,97	0,005	1
AA	9	14,06	AA	3	4,41	3,54	3,716	0,053

In the study of the distribution of allele variants of the ESR1 G2014A gene in the group of patients with YUD, accompanied by CTD (n = 64) compared with a group of girls with YUD without CTD (N = 54), showed that the frequency of the mutant allele (a) in the patient group YUD with CTD is reliably higher compared to the control group of girls with YUD without CTD ($\chi 2 = 4.515$, $p < 0.033$, $OR \geq 2.14$). Homozygous risky genotype with the participation of alleles AA, also met significantly more often compared to a group of girls with YUD without CTD ($\chi 2 = 3.718$, $p = 0.05$, $OR \geq 4.25$) (TAB. 2).

TABLE 2 DISTRIBUTION OF FREQUENCIES OF ALLELES AND GENOTYPES OF THE ESR1 G2014A GENEGIRLS WITH YUD WITH CTD COMPARED TO THE CONTROL GROUPAND FROM YUD WITHOUT CTD

Genetic type	YUD + CTD n=64	YUD + CTD, %	Genetic type	YUD +Without CTD, n=54	YUD +Without CTD, %	OR	$\chi 2$	P
G	99	77,34	G	95	87,96	0,47	4,515	0,033
A	29	22,66	A	13	12,04	2,14		
GG	44	68,75	GG	43	79,63	0,56	1,79	0,2
GA	11	17,19	GA	9	16,67	1,04	0,006	1
AA	9	14,06	AA	2	3,70	4,25	3,718	0,05

At the next stage, it was decided to analyze the distribution of frequencies of the occurrence of allele variants and ESR1 G2014A genotypes in the group of girls with YUD without CTD compared with almost healthy persons in population control.

TABLE 3 THE DISTRIBUTION OF THE FREQUENCIES OF ALLELES AND GENOTYPES OF THE ESR1 G2014A GENE IN GIRLS WITH YUD WITHOUT CTD COMPARED TO THE CONTROL GROUP OF PRACTICALLY HEALTHY FACES.

Genetic type	YUD +Without CTDn=54	YUD +Without CTD, %	Genetic type	controle, n=68	controle, %	OR	$\chi 2$	P
G	95	87,96	G	118	86,76	1,11	0,078	0,78
A	13	12,04	A	18	13,24	0,90		
GG	43	79,63	GG	53	77,94	1,11	0,051	0,8
GA	9	16,67	GA	12	17,65	0,93	0,02	0,8
AA	2	3,70	AA	3	4,41	0,83	0,038	0,8

As can be seen from Table 3 during the analysis of these groups, there were no reliable markers.

The indicators obtained during the study of the level of estradiol in the blood of girls with primary dismenoria, depending on the presence of CTD criteria are given in Table. four.

TABLE 4 ESTRADIOL CONTENT IN BLOOD SERUM (NMOL / L)

Group	estradiol
Practically healthy, n=25	0,9±0,12
YUD +Without	

CTD	
Light, n=10	0,85±0,06
Average, n=31	0,85±0,04
Heavy, n=15	0,85±0,04
YUD with CTD	
Light, n=24	0,56±0,16[a,б]
Average, n=100	0,52±0,06[a,б]
Heavy, n=50	0,47±0,12[a,б]

Note: A - Differences regarding these groups of healthy girls are significant, B - differences regarding these groups of girls with YUD without CTD meaning (P <0.05).

In the group of girls with a might of a light degree without the presence of criteria, the estradiol content in serum has only a tendency to reduce the values of practically healthy girls and amounted to 0.85 ± 0.06 nmol / l. These values corresponded to the norms of the norm in the 2nd phase of the cycle. In the group of girls with an average and heavy degree of dismenoria, the preservation of the regulatory quantities of estradiol was revealed. In girls with the presence of criteria for CTD, with a light severity of the severity, the separation of estradiol in serum was significantly reduced in 1.6 (p <0.001) times compared with the indicators of a group of practically healthy girls, in 1.51 (p <0.05) times Regarding the values of a group of girls with YUD without manifestation of CTD. As can be seen from the given data, the level of estradiol in the blood serum decreased more pronounced. As the pathological process progresses the content of estradiol even more decreased, especially with a severe degree of dismenoria. Thus, the level of estradiol in the blood serum of girls with an average degree of primary dismenoria decreased in 1.73 (p <0.001) and 1.63 (p <0.05) times, relative to the values of a group of girls with YUD without manifestation of CTD and practically healthy girls. That is, patients with CTD, at YUD, there was a hypooestroy.In the group of girls, the Estradiol in serum in the Signs of the CTD is 1.9 (p <0.001) and 1.8 (p <0.05) times, relative to the values of a group of girls with YUD without manifestation of CTD and practically healthy girls . A strong reverse correlation was noted between the severity of dysmenorrhea and the content of estradiol (R = -0.92 ± 0.1, p <0.01), and the presence of the manifestation of the Girls from the YUD is exacerbated by hypo ethroenemia.

It is interesting to note that the data obtained during genetic studies are consistent with the indicators obtained during the study of estradiol levels in the blood of girls with primary dysmenorrhea, depending on the presence of CTD criteria (Table 4).

Conclusions: 1. The presence of a mutant allele A, as well as a homozygous genotype AA in the ESR1 G2014A genotype in women, can affect the level of estradiol levels in the blood.

2. Genetic analysis revealed the intelligence of a mutant allele of the estrogen receptor gene - alpha (single-meter replacement of guanin on adenine in RS2228480) 1.9 times higher in the group of girls with YUD with CTD than in the YUD group without CTD ($\chi 2 = 4,515$; $p = 0\ 03$).

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