

**Research Article**

## **Primary Dysmenorrhea among Teenager Girls on the Background of Non-Differentiated Dysplasia of Connecting Tissue**

**Valentina S. Orlova, Oksana V. Motsnaya, Irina V. Kalashnikova,**

**Mikhail I. Churnosov and Evgeny V. Zhernakov**

Belgorod State University,  
85, Pobedy St., Belgorod, 308015, Russian Federation  
[orlova@bsu.edu.ru](mailto:orlova@bsu.edu.ru)

### **ABSTRACT**

**Objective of the study:** to identify the features of the primary dysmenorrhea clinic among adolescent girls with connective tissue dysplasia.

**Material and methods of the study.** 210 girls were examined at the age of 10-17 years with primary dysmenorrhea. Two groups were distinguished depending on the presence or the absence of connective tissue dysplasia: the main group is represented by 120 patients; the comparison group makes 90 patients. The severity of dysmenorrhea was assessed using three scales of McGill Pain Questionnaire. Psychological testing was carried out by anxiety self-assessment scale.

**Results.**  $90.9 \pm 2.6\%$  of patients in the main group had the debut of dysmenorrhea during the first 2 years after the menarche. The mean value of the rank index of pain in the main group is higher than in the comparison group. The emotional component prevailed in the inner picture of the perception of pain. Psycho-emotional status was distinguished by a high level of average score of reactive and personal anxiety.

**Summary.** Systemic pathology associated with connective tissue dysplasia increases the clinical course of primary dysmenorrhea among adolescents, which gives grounds to differentiate the treatment and diagnostic algorithm.

**Key words:** adolescent girls, primary dysmenorrhea, undifferentiated connective tissue dysplasia, menstrual pain syndrome.

### **INTRODUCTION.**

The study of conditions accompanied by pain syndrome remains the most important trend of medicine in the 21st century. In juvenile gynecology, pain accompanies many pathological conditions, one of which is primary dysmenorrhea - a cyclically arising syndrome, which aggravates the course of a female body physiological process [1, 2]. Clinically dysmenorrhea manifests itself during menstruation with an abdominal pain symptom and a complex of neurovegetative, metabolic-endocrine and psychoemotional disorders [3, 4]. In 1994, the International Association of Algologists (IASP) defined the definition of pain as "an unpleasant sensory sensation and emotional experience associated with a real or potential threat of tissue damage or described by the terms of such damage" [5, 6]. This means that the perception of pain

depends as on the intensity of pain so as on the emotional reaction of an individual.

Pain syndrome in the form of primary dysmenorrhea acquires a particular importance in adolescence, when a girl experiences the effect of two natural, but not simple processes: intensive socialization of a person and an active physiological restructuring of a body. In this regard, it is very important to take into account the combination of primary dysmenorrhea with undifferentiated connective tissue dysplasia (UCTS), which is currently widespread among adolescents. This pathology is characterized by a high level of functional disorders for a central and an autonomic nervous system, behavioral and emotional disorders [7, 8], which is supposed to aggravate the primary dysmenorrhea clinic.

At present they proved enough the pathogenesis of primary dysmenorrhea closely related to the

disruption of the synthesis or the exchange of arachidonic acid and its biologically active products - eicosanoids [9]. During the search for pathogenetic mechanisms of pain syndrome onset, the role of metabolic disorders of gender steroids, neurotransmitters, vasopressin, endothelial dysfunction, lipid peroxidation systems and antioxidant protection is considered [10]. One of the factors that have an adverse effect to some extent on virtually all listed pathogenetic links is magnesium deficiency. On the other hand, magnesium deficiency plays a key role in the pathogenesis of dysplasia, which refers to the systemic pathology of connective tissue [11].

**Purpose of the study.** To reveal the clinical features of primary dysmenorrhea among adolescent girls with the signs of undifferentiated connective tissue dysplasia.

**Materials and methods of the study.** 210 adolescent girls at the age of 10-17 years (mean age in years:  $15.1 \pm 1.4$ ) were examined, who applied for out-patient admission to the children's polyclinic because of menstrual pain. The diagnosis of primary dysmenorrhea was verified by the results of a gynecological examination by non-invasive methods, which made it possible to exclude the organic pathology of the reproductive system organs. The inclusion criterion was the diagnosis of primary dysmenorrhea, the criterion for exclusion is the organic pathology of the pelvic organs, indicating the secondary nature of the pathology.

Two groups were assigned to perform the task, depending on the presence or absence of UCTS signs: the main (Ist) group was represented by 120 patients (mean age made  $15.1 \pm 1.4$  years), the comparison group (II) - 90 patients (mean age in years:  $15.2 \pm 1.3$ ). The patients of both groups were the indigenous residents of the city, they studied in general schools and were comparable by age. At the time of the examination, they were all virgo intacta, had no history of hormonal therapy with gender steroids, had no inflammatory diseases or surgical interventions on the pelvic organs, and gave voluntary informed consent to participate in the study.

The manifestations of UCTS were diagnosed in accordance with the table of dysplastic markers T.I. Kadurina et al. (2008) [12] by phenotypic signs during the external examination and visceral

disorders, revealed during clinical and instrumental examination with the involvement of related experts. In order to evaluate the physical development as one of the phenotypic signs of UCTS, the mass-growth index Quetelet II ( $\text{kg}/\text{m}^2$ ) was calculated and its value was interpreted according to gender-age centile tables.

The Russian version of the McGill Pain Questionnaire (MPQ) was used for integrated assessment of menstrual pain. This questionnaire consisted of three scales - the evaluation, the sensory and the affective one [13, 14]. After an individual methodical instruction, the patients gave a self-evaluation of menstrual pain, choosing those descriptors that reflected their pain experiences most accurately. The analysis of the results was carried out by two indices separately for each scale and for the entire questionnaire as a whole: the rank index of pain (the sum of the selected word scores) and the index of descriptor number (the total number of selected words).

The state of psychoemotional status was studied by testing using Ch.D. Spielberger's scale of anxiety level self-assessment, adapted by Yu.A. Khanin (1976) [15]. The serum magnesium level was determined by a biochemical method with the interpretation of the results in accordance with WHO (2002) age criteria: the range of 0.74-1.15 mmol/l was regarded as norm magnesium, the level below 0.74 mmol/l was regarded as hypomagnesium [16].

The statistical processing of the study results was carried out using the software IBM® SPSS® Statistics Version 20. The probability of a fair null hypothesis (p) was taken at 5% significance level ( $p < 0.05$ ).

### Results of the study and their discussion

The patients of group I already had a phenotypic trait of UCTS even during the initial external examination. The dominant among them was the asthenic type of constitution in the form of a body disproportion with the predominance of longitudinal dimensions, an acute epigastric angle and the decrease in muscle tone, which occurred among 119 ( $99.2 \pm 2.4\%$ ) patients. The asthenic type of the constitution influenced their physical development: the average value of Quetelet II index was lower ( $16.0 \pm 0.1 \text{ kg}/\text{m}^2$ ) as compared to  $22.0 \pm 0.3 \text{ kg}/\text{m}^2$  in group II ( $p < 0.001$ ). Among the

overwhelming majority of the Ist group girls ( $92.5 \pm 2.4\%$ ), Quete II index went beyond the centile interval of 25-75, which indicated the disharmony of their physical development. In group II the proportion of such patients was significantly less -  $52.2 \pm 5.3\%$  ( $p < 0.001$ ). Besides, the disharmony of patients in the Ist group was associated with a body mass deficit in all cases, in group II  $95.7 \pm 2.9\%$  showed its excess.

Physical development determines the state of a body health, so the patients of group I are more burdened with functional disorders and/or chronic somatic pathology. Each girl from this group had 5.1 diseases on the average, while in Group II the amount of diseases made 2.8, which is explained by the generalized nature of the connective tissue defect at UCTS. This is confirmed by the structure of the revealed pathology among the patients of the 1st group: the diseases of the musculoskeletal (100.0%), nervous (100.0%), cardiovascular ( $56.7 \pm 4.5\%$ ), digestive ( $50.0 \pm 4.6\%$ ), respiratory ( $46.7 \pm 4.6\%$ ), urinary ( $45.8 \pm 4.5\%$ ), endocrine ( $30.0 \pm 4.2\%$ ) systems and the visual apparatus ( $46.7 \pm 4.6\%$ ).

The mean age of menarche in the I group was  $12.2 \pm 1.1$  years, in the IInd group it made  $12.1 \pm 1.2$  years, this indicates the homogeneity of groups by gynecological age (years after the onset of the first menstruation). During the first 2 years the appearance of menstrual pain from menarche was indicated by  $90.8 \pm 2.6\%$  of adolescents in the 1st group,  $54.4 \pm 5.2\%$  ( $p < 0.001$ ) in the second group, also the dysmenorrhea debut coincided with the first menstrual period among  $24.2 \pm 3.9\%$  and  $20.0 \pm 4.2\%$ , respectively. After two full years (2 years 11 months 29 days) from the onset of menstrual function, the painful menstrual syndrome in groups appeared among  $90.8 \pm 2.6\%$  and  $54.4 \pm 2.2\%$  ( $p < 0.001$ ) from the start of menstrual function. Consequently, the patients with the presence of

**Table 1** : Distribution of adolescents with dysmenorrhea according to the scoring scale of the MPQ questionnaire

Subjective assessment of pain	Main group n=120		Group comparisons n=90	
	N.	%	N.	%
weak	0			
moderate	13	$10.8 \pm 2.8$	44	$48.9 \pm 5.3^*$
strong	42	$35.0 \pm 4.4$	27	$30.0 \pm 4.8$
the strongest	46	$38.3 \pm 4.4$	12	$13.3 \pm 3.6^*$
intolerable	19	$15.8 \pm 3.3$	7	$7.8 \pm 2.8$

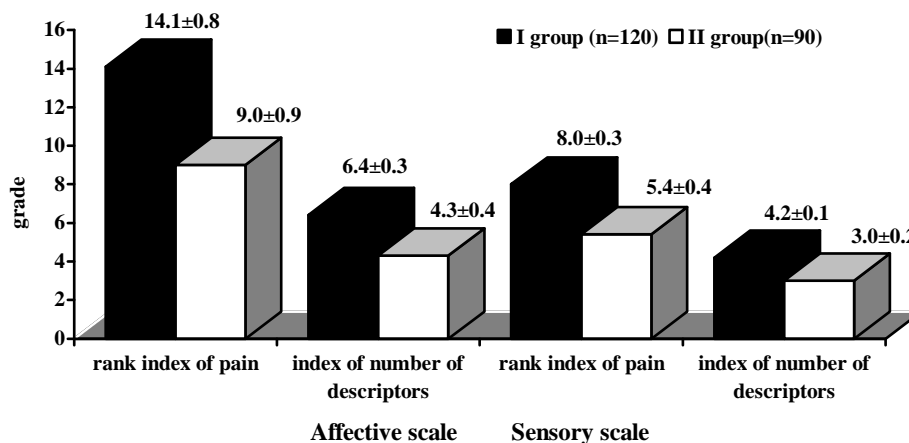
Note: \* –  $p < 0.001$  during the comparison with the indicators of the main group

background UCTS, have an earlier debut of dysmenorrhea and it occurs primarily during the first two years of the gynecological age. As is known the development of menstrual function, and the an ovulatory cycles prevail during this period.

Characterizing the pain syndrome, we were guided by modern ideas about the mechanisms of pain perception, which recommend to take into account equally subjective assessment of its intensity and individual affective reactions. The adolescents had neurovegetative and emotional manifestations, and not the intensity of pain sensations determine their influence on the quality of life most often [17]. Among the methods of such subjective phenomenon clinical evaluation as pain we chose the MPQ questionnaire. It expands the diagnostic possibilities, since it assumes a multifactorial self-assessment of pain sensations, taking into account not only the intensity, which is evaluated by all traditionally used verbal rank scales, but also sensory-emotional reactions.

In the evaluation scale of the questionnaire the intensity of pain is ranged from "weak" (1 point) to "unbearable" (5 points). As follows from Table 1, both groups did not have a single girl who considered her menstrual pain to be weak. The patients of the main group rated their pain as "strong" and "strongest" most often (73.3% in total). More than half of the girls with UCTS (54.1%) experienced "severe" or "unbearable" pain during menstruation, while in the comparison group almost every second considered her pain as "moderate" ( $48.9 \pm 5.3\%$ ), every third girl considered it a strong one ( $30.0 \pm 4.8\%$ ), the intensity of the pain syndrome was regarded as "intolerable" 2 times more often. Consequently, UCTS exacerbates the intensity of pain sensations.

Figure 1 gives an idea about the general results of the assessment by the affective scale, reflecting emotional responses to pain and by sensory scale, characterizing the sensory perception of pain. The figure demonstrates that the girls of both groups ( $p < 0.001$ ) used the terms of affective rather than the sensory scale more often. Besides, the values of average score indices in both scales are higher in the first group ( $p < 0.001$ ) than in the second group, that is, the patients of group I were choosing more descriptive terms and higher intensity grades. This makes it possible to assess the clinical course of dysmenorrhea among the girls with connective tissue dysplasia as more severe.



**Figure 1.** The average score of the indexes on the affective and sensory scales of the MPQ questionnaire

The comparison of the average rank indices for all three scales of the MPQ questionnaire revealed their predominance in the main group, i.e. the patients of the group I as compared with the girls from the group II rated their menstrual pain as more pronounced in intensity, sensory perception and emotional coloring. The average index of the scoring scale in the Ist group was  $3.5 \pm 0.1$ , in the IInd group it was  $2.8 \pm 0.1$  ( $p < 0.001$ ), sensory -  $8.0 \pm 0.3$  and  $4.3 \pm 0.4$ ; ( $p < 0.001$ ) and affective -  $14.1 \pm 0.8$  and  $6.4 \pm 0.3$  ( $p < 0.001$ ), respectively. Thus, the overall rank index of pain and the index of descriptor number showed that the patients in group I, in contrast to group II, chose a greater number of descriptive terms ( $11.5 \pm 0.4$  and  $8.4 \pm 0.5$ ,  $p < 0.001$ ) and their higher ranks ( $25.7 \pm 1.1$  and  $17.2 \pm 1.3$ , respectively) for the self-evaluation of their pain sensations. At the same time, the patients of both groups used the terms of the emotional category rather than the sensual one to describe menstrual pain, which is clearly demonstrated by the average indices of the number of descriptors for affective ( $6.4 \pm 0.3$  and  $4.2 \pm 0.1$ ,  $p < 0.001$ ) and sensory ( $4.3 \pm 0.4$  and  $3.0 \pm 0.2$ ,  $p < 0.001$ ) scales of the questionnaire. Consequently, all adolescents suffering from primary dysmenorrhea, had the predominance of the emotional component over the sensory component in the internal picture of pain perception.

The dominance of the emotional component in the perception of pain was the reason for an in-depth study of psychoemotional disorders by the scale of anxiety level self-assessment. The results of testing using Ch.D. Spielberger's scale in the modification by Yu.L. Khanin, which allows to differentiate reactive anxiety as a condition in a specific situation with personal anxiety as a character trait, supplemented the psychological "portrait" of patients (Table 2).

**Table 2:** Levels of anxiety among adolescent girls with primary dysmenorrhea

Level	Range (points)	I group		II group		Significance test	
		N	M±m%	N.	M±m%		
<b>Scale of reactive anxiety</b>							
1	low	≤30	5	4.2±1.8	31	34.4±5.0	$p_{I-II} < 0.001$
2	moderate	31-45	51	42.5±4.5	32	35.6±5.0	
3	high	≥46	63	52.5±4.6	27	30.0±4.8	$p_{I-II} < 0.01$

<b>p</b>		$p_{1-2;3}<0.001$					
average score (M±m)		45.3±0.9		36.3±1.4		$p_{I-II}<0.001$	
<b>Personal anxiety scale</b>							
<b>1</b>	low	≤30	1	0.8±0.8	13	14.4±3.7	$p_{I-II}<0.001$
<b>2</b>	moderate	31-45	27	22.5±3.8	37	41.1±5.2	$p_{I-II}<0.01$
<b>3</b>	high	≥46	92	76.7±3.9	40	44.4±5.2	$p_{I-II}<0.001$
<b>p</b>		$p_{1-2;3}<0.001$					
average score (M±m)		49.9±0.6		41.4±1.0		$p_{I-II}<0.001$	

More than half of the girls from the group I had a high level of reactive anxiety ( $52.5 \pm 4.6\%$ ) and only  $4.2 \pm 1.8\%$  had the indicators within the low range. They differed statistically significantly ( $p<0.001$ ) from the patients of the group II, where the distribution of reactive anxiety level was practically uniform.

The girls with a high level of personal anxiety as compared with the reactive anxiety in group I are even more -  $76.7 \pm 3.9\%$ , and the girls with moderate and low levels are less significantly ( $22.5 \pm 3.8\%$  and  $0.8 \pm 0.8\%$ ). In the II<sup>nd</sup> group, the proportion of patients with a high level of personal anxiety increased -  $44.4 \pm 5.2\%$ , but they were significantly less as compared to the main group. The patients of the I<sup>st</sup> group were characterized by a high level of both personal and reactive anxiety (mean score made  $49.9 \pm 0.6$  and  $45.3 \pm 0.9$ , respectively). On the contrary in group II the average level of anxiety on both scales corresponded to the moderate range ( $43.5 \pm 1.1$  and  $36.5 \pm 1.4$ , respectively). The differences between the average indices of anxiety levels of both scales in groups I and II are statistically significant ( $p<0.001$ ).

The obtained data confirm the opinion according to which the connective tissue dysplasia as a permanent stressogenic background influences the formation of personality characteristics, therefore these patients are included in the group of increased psychological risk [18, 19, 20]. Obviously, a certain level of anxiety is necessary for an individual's effective adaptation to the surrounding reality, but the long-existing elevated level of psychological stress leads to inadequate

emotional reactions and is considered as disadaptive.

Magnesium deficiency is considered as the factor of pathogenetic mechanisms for pain development, neuro-vegetative and psycho-emotional disorders with primary dysmenorrhea at the central and peripheral level. The prevalence of magnesium deficiency among the children with connective tissue dysplasia reaches 47.8%. At that the correlation with gender and age is noted. The most pronounced disorders are observed among 12-18 year old persons and more often ( $p<0.05$ ) among girls [21].

In our study, hypomagnesium was found among  $30.0 \pm 3.2\%$  of patients from all the examined subjects, but statistically significantly more often in the group with UCTS ( $36.7 \pm 4.4\%$  and  $21.1 \pm 4.3\%$ , respectively,  $p<0.05$ ).

It should be noted that in scientific publications the approach to the interpretation of the magnesium level is ambiguous. Some authors, in our opinion, believe reasonably that when you evaluate the magnesium balance, it is necessary to take into account the features of macroelement distribution in a body and the possibility of a normal level of blood serum in long-term maintenance due to the release of stocks from the depot (11, 22).

Obviously, this approach requires the differentiation between the concepts "hypomagnesium" and "magnesium deficiency". The proponents of this point of view suggest to consider the level of magnesium in the blood serum to 0.80 mmol/l as the sign indicating the deficiency of this macroelement in a body.

Based on this, we studied the frequency of different ranges of magnesium levels among the

patients with primary dysmenorrhea (Table 3).

**Table 3:** Distribution of adolescent girls with primary dysmenorrhea according to the level of magnesium

Level of a magniyemiya (mmol/litre)	I group n=120		II group n=90		Significance test
	N	M±m%	N	M±m%	
<0.59	5	4.2±1.8	1	1.1±1.1	
0.60-0.69	19	15.8±3.3	12	13.3±3.6	
0.70-0.79	55	45.8±4.5	24	26.7±4.7	$p_{I-II}<0.01$
0.80-0.89	29	24.2±3.9	29	32.2±4.9	
0.90-0.99	12	10.0±2.7	22	24.4±4.5	$p_{I-II}<0.01$
>1.00	0	0	2	2.2±1.6	

According to the table, the range below 0.80 mmol/l was detected in more than half of the patients ( $55.2 \pm 3.4\%$ ), regardless of connective tissue dysplasia presence or absence, but among the patients of the I group it was 1.6 times more common ( $65.8 \pm 4.3\%$  and  $41.1 \pm 5.2\%$ ;  $P < 0.001$ ). Therefore, even with a such approach to the evaluation of the norm level, the statistically significant differences between the groups persist.

#### SUMMARY.

The presence of UCTS clinical signs statistically significantly increases the severity of the integral indicator of menstrual pain perception (intensity, sensory and emotional reactions) by adolescent girls suffering from primary dysmenorrhea. Such patients also have the increase in the frequency and severity of neuro-vegetative and psycho-emotional disorders. A purposeful study of their magnesium level revealed a high frequency of a given macroelement deficit. The obtained data allow to consider the dysplasia of connective tissue and magnesium deficiency as the predictors of menstrual pain syndrome unfavorable course, which must be taken into account during the development of risk groups, as well as in the treatment-diagnostic algorithm of patient observation with primary dysmenorrhea during adolescence.

#### CONCLUSIONS

1. The vast majority of adolescent girls with primary dysmenorrhea, which developed against the background of UCTS signs, the disharmony of physical development caused in all cases by a body weight deficit is natural.

2. The dysplasia of connective tissue is associated with a high level of reactive and personal anxiety of patients suffering from primary dysmenorrhea, therefore they are the part of the group with an increased psychological risk.

3. The dysplasia of connective tissue and especially in combination with hypomagnesium aggravates the intensity of painful menstrual syndrome perception.

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