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OXIDATIVE SRARUS PECULIARITIES IN THE ADOLESCENTS WITH NON-DIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA OF DIFFERENT SEVERITY STAGE

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Summary: Total number of 225 adolescents with clinical features of non-differentiated connective tissue dysplasia (NDCTD) at the different stages and 60 healthy adolescents were examined. The hemiluminiscent method was used for the estimation of biogenesis of free radicals in blood serum. In the group of NDCTD patients the indexes, reflecting the processes of free radical lipid oxidation reliably increased and antioxidant defense system activity decreased. Gender and age related differences in the processes of free radical oxidation were revealed in minimal and severe stages of NDCTD.

Key words: adolescents, connective tissue dysplasia, free radical oxidation.

The disorder in the system “active oxygen metabolites generation (AOM) – AOM detoxication” is the early pre-clinical non-specific chain in the pathogenesis of chronic and autoimmune diseases. This fact permits to use the investigation of AOM biogenesis as the preliminary diagnostic criteria for the complex health status estimation [7, 8, 9]. Far-Easterners redox-status is characterized by decreased buffer capacity of AOM detoxication system as the result of unfavorable regional biogeochemical influences [5]. AOM hyper production permits the development of mitochondrial insufficiency - the base for connective tissue dysplasia formation, with collagen and elastin synthesis defects, resulting in different somatic pathology [6]. Non-differentiated connective tissue dysplasia (NCTD) considerably defines clinical features of the major disorder, permitting atypical and prolonged illness, low therapy effectiveness and early invalidization [4, 6]. We have not found the literature data about interconnections of redox-status and NCTD.

The aim of investigation: to examine the peculiarities of blood serum oxidative status in adolescents with the different stages of NCTD.

Materials and methods: 255 adolescents, 116 girls (51%) and 109 boys (49%) aged 10-17 years with the markers of NCTD were examined in the Mother and Child Care Institute Clinical Department. The criteria for including in this group were the following: NCTD features segregation in family history, outside dysplasia markers presence, visceral-locomotor markers detection by ultrasound examination, X-ray examination and endoscope gastrointestinal tract examination. The estimation of NCTD severity was performed according to the scale of clinical symptoms [4] in 131 of adolescents – 38 with minimal stage, 67 with moderate stage and 26 with severe stage. Control group was represented by 60 adolescents of the same age. All the patients were divided for gender (boys, girls) and age (prepubertal, pubertal) groups.

For the integral estimation of the free radical biogenesis processes in blood serum the method of chemiluminescence (CML) was used. CML registration was made by “Perkin Elmer” LS 50B spectrometer. Spontaneous and induced Fe^{2+} CML was detected by Vladimirov and et., [2] method: S-sp light-sum for 1 minute of spontaneous lighting, this index correlates with the intensity of free radical generation; Sind-1 – light sum for 2 minutes Fe^{2+} induced CML, which reflects the intensity of peroxide radicals accumulation; h1 – the amplitude of quick flash Fe^{2+} induced CML, reflecting the lipid’s hydroperoxid concentration. The kinetics of CML, induced by H_2O_2 with the presence of luminal [1], was analyzed for the following parameters: h2 – maximal flash amplitude, which is reversibly proportional for the peroxides substrate resistance; Sind-2 – light sum for 2 minutes H_2O_2 - induced CML, which is reversibly to antioxidant antiradical defense system. The intensity of CML detecting in mill volts calculated for 1 ml of blood serum and represented in depending units. Statistical analyze was performed by Statistika.6. program.

Results and discussion: Blood serum CML analyze revealed reliable increased active oxygen metabolite processing in both groups (in comparison with control levels) (S sp) in 3,0 – 3,5 times. The concentration of the primary stage lipid’s peroxidation products – hydroperoxides (h 1) was increased 3,0 – 3,2 times. The speed of peroxides radicals formation exceeds the similar indexes in control group in 2,7 – 3,1 times. The enforcement of active oxygen metabolites processing is accompanied by antioxidant defense system oppression. This fact submitted by 1,4-1,5 times increase of similar indexes (Sind 2). At the same time, the decrease of peroxide resistance (h2) in the examined substrates was 1,8-1,9 times (table 1).

The analyze of CML obtained data did not reveal any differences in common groups of examined adolescents, including control group. In the separation for age groups in coordination with the stage of sexual development, age-dependent and gender periods (prepubertal, pubertal) differences, reliable specific features were definitely revealed in the majority of cases. In the control group of adolescents (Picture 1) gender differences in the system “active oxygen metabolites generation (AOM) – AOM detoxication” have no reliable features, but the age-dependent indexes were significant. With the grow-up process all the indexes increase. This fact shows the increase of free oxygen metabolites concentration and the decrease of antioxidative defense system in healthy persons. It seems so, that this is non-specific organism's reaction at the pressing stress situations in this age and the increasing technogenic effect for the adolescent.

In the all clinical groups of both gender adolescents in the examined age periods, NCTD permits reliable increase of all detecting indexes, pointing the activation of free radical oxidation, at the base of antioxidant and antiradical defense systems depression. In the groups of adolescents with NCTD of different severity, especially with minimal and severe stages, the mostly considerable gender differences of all the indexes were obtained in the early age group. (Picture 1).

In all cases of NCTD in girls all the indexes, reflecting the AOM production had no definite age-dependent differences in comparison with control group. Some exception is the speed decrease of peroxide radicals formation in the pubertal period (Sind 1). Among the examined boys, in comparison with healthy persons, reliable decrease of the all indexes at the pubertal period, except hydroperoxid concentration, was revealed (h1). In case of severe NCTD at pubertal period gender differences revealed in the speed of peroxide radicals formation, hydroperoxid concentration and activity of antioxidant and antiradical defense system, more significant in boys.

The average severity of NCTD by activating “active oxygen metabolites generation (AOM) – AOM detoxication” for all represented indexes takes intermediate position. Gender and age differences in the detecting indexes are representing in the low degree. But the expression of AOM formation processes is high.

As the result, in all stages of dysplasia processes among adolescents of both genders, considerably increased the indexes, reflecting the processes of lipid's free radical oxidation and in the same time antioxidant defense system decreased. Hence, the adolescents with NCTD have the development of system oxidative stress. This may be the base for including of the medications with antioxidative and antiradical effects in the treatment and prophylactic approaches.

Literature

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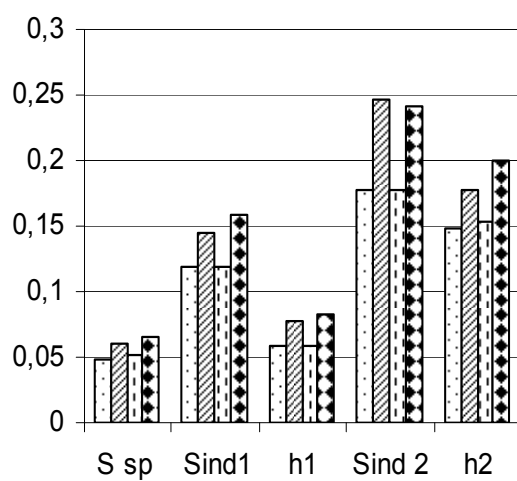
Table 1

The indexes of blood serum CML examination (relative units) in adolescents with NCTD of different severity (M±m)

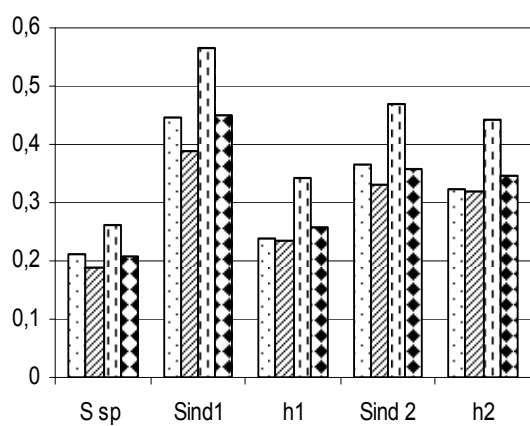
Group	S sp	Sind1	h1	Sind 2	h 2
Control	0.062±0.0028	0.146±0.0054	0.076±0.0034	0.225±0.006	0.178±0.0047
NCTD - minimal	0.212±0.001*	0.450±0.0019*	0.258±0.0012*	0.336±0.0018*	0.347±0.0016*
NCTD - average	0.214±0.0004** *	0.463±0.0008***	0.257±0.0006*	0.370±0.0008***	0.336±0.0007***
NCTD - high	0.197±0.001*** ***	0.431±0.0019***	0.264±0.0014*** ***	0.347±0.0018*** ***	0.327±0.0018*** ***

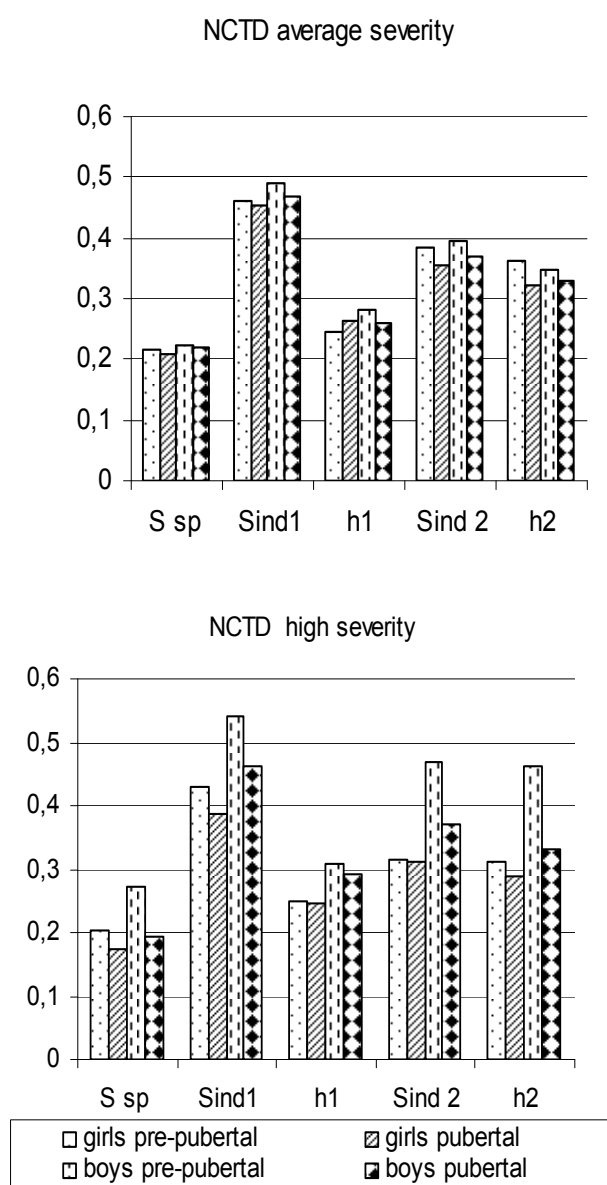
Annotation: * - $p < 0,05$ in comparison with control group; ** - $p < 0,05$ for the group of NCTD minimal severity; *** - $p < 0,05$ for the group of NCTD average severity

Healthy adolescents



NCTD of minimal severity





Picture 1. Adolescents with NCTD of different severity blood serum CML indexes