Bulgarian Society for NDT
International Journal "NDT Days"
Volume 1, Issue 2, Year 2018 ISSN: 2603-4018

Increase of Parasympathetic Influences on Heart Rate Regulation as a Marker of Connective Tissue Dysplasia

Anna V. AKIMOVA

Ural State Medical University; Ekaterinburg, Russia
Phone: +7 90498 15684; e-mail: anna_v_akimova@mail.ru

Abstract
Connective tissue dysplasia (CTD), especially the undifferentiated form, is common among young people. External CTD signs and minor malformations are associated with somatic diseases and autonomic disfunction.
The aim of the study was to identify phenotypic manifestations and features of autonomic regulation in young people with undifferentiated connective tissue dysplasia (UCTD).
We examined 67 young people aged 18-25 years. Clinical signs and symptoms of CTD were evaluated using standard methods. Autonomic disorders were assessed using the Vein Questionnaire. The autonomic regulation was evaluated by heart rate variability (method of high resolution rythmocardiography). All participants were divided into 2 groups. The UCTD group included persons with 6 or more external signs. The control group composed of participants who had less than 6 signs of CTD.
The UCTD syndrome was identified in 64.2% (43 participants). The features of autonomic regulation of heart rate variability were found using the rhythmocardiography method. The predominance of the parasympathetic regulation of sinus rhythm was revealed in young people with UCTD.

Keywords: connective tissue disorders, autonomic regulation, heart rate variability.

1. Introduction

The name "connective tissue dysplasia" (CTD) covers a wide range of disorders. These disorders are caused by a weakness in the connective tissue including bone, ligaments, tendons, skin. CTD is a genetically determined condition that affect the normal metabolism of connective tissue and the disruption of the structure of fibers and ground substance. The uniqueness of the structure and function of connective tissue creates the conditions for the emergence of a large number of anomalies and diseases caused by chromosomal and gene defects in the embryonic and postnatal periods and having a certain type of inheritance [5].
Depending on the characteristics of the etiological factor, it is advisable to allocate the hereditary disorders of connective tissue (differentiated or monogenic diseases) and the connective tissue dysplasia (undifferentiated forms – UCTD). The prevalence of hereditary forms is small. Thus, the frequency of Marfan syndrome in the population is 1:10000-1:15000. In contrast, UCTD is widespread in Russia: about 8.5 % in the sample of 400 people.
According to the literature data, the prevalence of individual external signs is extremely high: single external signs are detected in 94% of persons of young age. The frequency of occurrence of UCTD among young people are contradictory, according to some scholars, they range from 13.0% to 85.4% [2,5].
There are the following clinical syndromes of UCTD: a syndrome of neurological disorders, asthenic, valve, thoraco diaphragmatic, vascular, arrhythmic, respiratory, visceral syndrome, immunological disorders, eye pathology, foot pathology, joints hypermobility, and mental sphere disorders [1,3].
Widespread UCTD with progressive nature of the disease and multiple organ destruction make it an important medical and social problem.
The aim of the study was to conduct a comprehensive evaluation of phenotypic characteristics and heart rate variability in persons with UCTD.

2. Methods

We studied 67 young adults aged from 18 to 25 years. The research was conducted in "5th Military Clinical Hospital of National Guard Troops of the Russian Federation" in Ekaterinburg.

The study based on voluntary participation and informed written consent. A total of 67 young people with a median age of 22 (20÷23) years were enrolled in this study. CTD symptoms were determined in accordance with the National Recommendations of the Russian Scientific Society of Internal Medicine, 2016 [5]. We considered the following UCTD symptoms: dolichostenomelia, arachnodactyly, Steinberg thumb sign and Walker-Murdoch wrist sign, protruding ears, "crumpled" ears, fused earlobe, high arched palate, dental crowding, diastema, lax joints, hyperextensibility of knees and elbows, hyperextensibility of thumbs and fingers, genu varus, genu valgus, flat foot, pes planovalgus, wide gap between the first and second toes, syndactyly of the second and third toes, short 1 toe, hallux valgus, alar chest, pectus excavatum or carinatum, scoliosis, winged scapula, straight back, hyperkyphosis, hyperlordosis, varicose veins, sclera blue, hypo/hypertelorism, hyperextensible skin, skin striae distensae, multiple moles, depigmentation. We diagnosed UCTD if there were 6 signs and more. The autonomic dysfunction symptoms ware determined on the Vein score (A.M. Vein, 2003). If the Vein score is 15 and more, we recorded an autonomic dysfunction.

The participants were divided into 2 groups: main group and control group. In case of determining 6 signs and more, the examined were assigned to the main UCTD-group (n=43); if the signs were less than 6, the persons were included in the control group (n=24).

We studied the heart rate variability (HRV) by rhythmocardiography (RCG). The examination was carried out on a computer diagnostic complex – CAP-RC-01-"Micor" (registration certificate № FS 02262005/2447). HRV indicates statistical analysis: median (25%÷75%) of the duration of RR-interval in seconds, standard deviation of all the waves from the mean RR (SDNN), standard deviation of each fluctuation: humoral-metabolic (σl), sympathetic (σm), parasympathetic (σs) effects divisions of the autonomic system, and the average amplitude of respiratory arrhythmia (ARA). The ratio of the factors of regulation in the sinus node after the expansion wave structure of the HRV frequency components 3 in the program "Micor" presents the percentages of influence on the pacemaker: humoral-metabolic effects – in a very low frequency (VLF%), sympathetic -in a low frequency (LF%) and parasympathetic in a high frequency (HF%); in the frequency ranges relative to the total spectrum, taken as 100%. Recording was performed in the supine position (initial background RCG record), modified Valsalva maneuver (Vm), Ashner-Dagnini test (Pa), active orthostasic test (Aop), loading test is a modified PWC120 test (Power Working Capaciti) [4].

Differences between the groups were assessed using nonparametric Mann-Whitney U-test, the differences in the frequency of symptom groups were assessed using χ^2 criterion, the significance of differences significant at $p<0.05$.

3. Results

Characteristics of the compared groups are shown in the Table 1.

Table 1. Characteristics of the compared groups (Me, 25%÷75%)

Signs	UCTD Group (n=43)	Control Group (n=24)	p
Age, years	22(20÷23)	22,5 (20÷25)	0,120
Vein score	25,5 (9,5÷37)	15 (3÷27)	0,148

UCTD signs were detected among 100% of patients in different quantities. The frequency of detecting 6 and more UCTD signs was 64.2% among young people. The results are shown in Table2.

Table 2. The frequency of connective tissue dysplasia signs among young people

Signs	Detection frequency (n=67)	UCTD Group (n=43)	Control Group (n=24)	χ^2	p
Fused earlobe	26 (38,8%)	16	10	0,09	0,760
Flat feet	**26** (38,8%)	**23**	3	8,49	**0,004**
Walker-Murdoch wrist sign	**24** (35,8%)	**23**	1	13,46	**0,000**
Scoliosis	23 (34,3%)	16	7	0,024	0,880
Alar chest	**22** (32,8%)	**19**	3	5,21	**0,022**
Malocclusions	20 (29,9%)	17	3	3,48	0,063*
Hyperextensibility of thumbs	**20** (29,9%)	**19**	1	9,30	**0,002**
Steinberg thumb sign	**19** (28,4%)	**17**	2	5,39	**0,020**
Hyperextensibility of elbows	**18** (26,9%)	**18**	0	11,80	**0,000**
Hyperextensibility of fingers	**17** (25,4%)	**16**	1	6,70	**0,010**

People with UCTD are significantly more likely to have the following characteristics: flat feet, Walker-Murdoch wrist sign, alar chest, hyperextensibility of thumbs, elbow joints and fingers, and Steinberg thumb sign ($p<0.05$). These signs can be considered the most important in the diagnosis of UCTD. We found the high incidence of fused earlobe and scoliosis. These symptoms are often comparable in both groups. There is a tendency towards a higher frequency of high arched palate, syndactyly of the second and third toes, malocclusion, knee joints hypermobility and multiple moles in the UCTD group.

According to RCG, two groups were similar in the values RR-intervals ($p=0.92$). However, the UCTD-group showed higher values of ARA ($p=0.036$) and σs ($p=0.056$) after the Valsalva maneuver. A similar trend was registered after the Ashner-Dagnini test ($p=0.07$; $p=0.07$). According to the test with the physical loading of a person, the main group had a tendency towards higher values of σs ($p=0.073$) and showed a shorter recovery period ($p=0.001$).

Table 3. The parameters of heart rate variability in persons with undifferentiated connective tissue dysplasia (Me, 25%÷75%)

Tests	Signs	UCTD Group (n=38)	Control Group (n=20)	p
ph	RR	0.831(0.767÷0.995)	0.846 (0.799÷0.947)	0.92
	SDNN	0.046 (0.039÷0.06)	0.043 (0.03÷0.05)	0.28
	ARA	0.081 (0.056÷0.114)	0.061 (0.042÷0.093)	0.14
	σs	0.03 (0.021÷0.044)	0.023 (0.015÷0.036)	0.18
	HF%	43.9 (27.8÷64.4)	41.5 (22.7÷34.1)	0.47
Vm	**ARA**	**0.067 (0.054÷0.087)**	**0.049 (0.036÷0.08)**	**0.036**
	σs	0.025 (0.02÷0.034)	0.018 (0.013÷0.031)	0.056
	HF%	40.35 (27.3÷54.5)	29.6 (18.8÷41.3)	0.12
Pa	ARA	0.074 (0.049÷0.097)	0.048 (0.033÷0.071)	0.07

	σs	0.028 (0.019÷0.039)	0.02 (0.012÷0.028)	0.07
	HF%	41.6 (29.1÷55.0)	32.65 (18.1÷49.9)	0.21
	tr, s	16.01 (13.49÷25.07)	22.14 (16.26÷28.62)	0.068
PWC 120	ARA	0.092 (0.06÷0.132)	0.08 (0.049÷0.103)	0.23
	σs	0.036(0.023÷0.052)	0.027 (0.017÷0.039)	0.073
	HF%	60.6 (41.7÷74.0)	56.2 (20.9÷69.5)	0.26
	tr, int	**116.5 (97.5÷128.5)**	**162 (122.5÷189)**	**0.001**
	tr,s	**84.5 (70.26÷102.28)**	**124.07 (92.9÷146.8)**	**0.001**

Insights

1. UCTD was detected in 64.2 % in the study group.
2. The most important signs to diagnose UCTD are flat feet, Walker-Murdoch wrist sign, alar chest, hypermobility of thumbs, elbow joints, fingers, and Steinberg thumb sign.
3. Parasympathetic influence on the heart rate regulation is increased among persons with multiple UCTD signs and can be considered as a marker of connective tissue dysplasia.

References

1. Beighton P.H., R.Grahame, H.A. Bird. Hypermobility of Joints. Edn.3. London: Springer-Verlag, 1999, 218p.
2. Zemtsovsky E.V., E.G. Malev, S.V. Reeva etc. Diagnosis of inherited connective tissue disorders**.** Translational medicine, 2(5), 2015, pp.73-82.
3. Wheeler J. B., J.S. Ikonomidis, J.A. Jones. Connective tissue disorders and cardiovascular complications: the indomitable role of transforming growth factor-beta signalling. Adv. Exp. Med. Biol, Vol. 802, 2014, pp.107-127.
4. Mironov V.A., T.F. Mironova, O.Yu. Nohrina. Diagnostic noninvasive rhythmocardiography in clinical neurocardiology. XXXII International Conference "Defectoscopia'17", June, 12-17, 2017, Sozopol, Bulgaria, Book of abstracts, pp.66-71.
5. National Recommendations of the Russian Scientific Society of Internal Medicine for Diagnostics, Treatment and Rehabilitation of Patients with Connective Tissue Dysplasia. Medical News of North Caucasus, 11(1), 2016, 76p.