

UDC: 616.12-008.318-066:616.333-008.6]-092:616-018.2-053.5/.67

DOI: 10.15587/2519-4798.2021.238132

UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA AS A PREDICTOR OF HEART RATE DISORDERS IN COMBINATION WITH GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN

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The aim: to improve the early diagnosis of arrhythmia in combination with gastroesophageal reflux disease (GERD) in children, by studying the risk of connective tissue dysplasia on the occurrence of this pathology.

Materials and methods. We examined 100 children aged 8 to 18 years, mean age 13.7 ± 2.7 years, of which 32 children with arrhythmias without combined pathology were group I, 36 children with concomitant GERD - group II and 32 children with GERD without concomitant arrhythmias - group III. Patients underwent clinical and instrumental studies (electrocardiography, Holter daily ECG monitoring, esophagogastroduodenoscopy and pH-metry) and evaluation of phenotypic signs of NDST according to the criteria of T. Milkovskaya-Dimitrova and A. Karkasho.

Results. A risk factor for the formation of combined pathology in children in the form of arrhythmia and GERD was identified, namely the next main phenotypic feature of NDST (undifferentiated connective tissue dysplasia) – dysplastic tooth growth.

Also, predictors of both an isolated variant of arrhythmia in children and arrhythmia in combination with GERD – high height and scoliotic posture were identified.

In this case, the risk factor for an isolated variant of arrhythmia in children, according to the results of the study is asthenic constitution.

The severity of NDST in the studied groups was determined. The analysis of the results revealed the absence of a statistically significant relationship between the severity of NDST and study groups, although it should be noted that in children of group III the first degree of NDST was not observed in general.

Conclusions. It was found that asthenic constitution, dysplastic tooth growth, tall stature and scoliotic posture are statistically significant risk factors for the development of the studied pathologies.

There were no statistically significant differences between the study groups regarding the severity of NDST, but there was a complete lack of detection in children of group III (children with isolated GERD without concomitant arrhythmia) of the first degree of NDST

Keywords: undifferentiated connective tissue dysplasia, gastroesophageal reflux disease, arrhythmias, children, predictor

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How to cite:

Herasymova, O., Filonova, T. (2021). Undifferentiated connective tissue dysplasia as a predictor of heart rate disorders in combination with gastroesophageal reflux disease in children. ScienceRise: Medical Science, 4 (43), 41–45. doi: <http://doi.org/10.15587/2519-4798.2021.238132>

1. Introduction

In Ukraine and around the world there is a tendency to increase diseases of the digestive system in children [1, 2]. In childhood, the most common disease of the digestive system is GERD [3, 4].

GERD has a large number of different clinical symptoms, which is the cause of late diagnosis of the disease and leads to increased complications [5, 6].

The prevalence of arrhythmias in children also tends to increase, which is a serious medical problem, because there are many variants of arrhythmias with a malignant course and a large number of life-threatening complications [7, 8].

Differential diagnosis between arrhythmias and GERD in children is complicated due to the similarity of the clinical picture of arrhythmias with the clinic of atyp-

ical cardiac manifestations of GERD. It is even more difficult to differentiate the isolated course of these pathologies with their course in the form of combined pathology [9, 10].

Scientific studies have found that in patients with NDST GERD was found 4–4.5 times more often than without it [11].

Researchers have also found that NDST is often a predictor of arrhythmias, which is associated with high mortality from cardiac arrhythmias (more than 2,000 people every hour) [12, 13].

The problem of detecting NDST in children with combined pathology in the form of arrhythmia with concomitant GERD has not been sufficiently studied. Therefore, determining the risk of developing this pathology in children with NDST will simplify the differential diagno-

sis between it and isolated variants of arrhythmias and GERD. There was also no comparative analysis of the phenotypic features of NDST, characteristic of arrhythmias with signs of GERD, which may facilitate the differential diagnosis between these pathologies in the early stages. This work is devoted to the study of these issues.

The aim of the research to improve the early diagnosis of arrhythmia in combination with GERD in children by studying the risk of connective tissue dysplasia on the occurrence of this pathology.

2. Materials and methods

We examined 100 children aged 8 to 18 years with an average age of 13.7 ± 2.7 years on the basis of the city cardiorheumatology department of “Children's Clinical Hospital № 24” of Kharkiv City Council and “City Children's Polyclinic № 23” of Kharkiv City Council in the period from September 2018 to July 2021, including 32 children with arrhythmias without concomitant pathology, who made up group I, 36 children with concomitant GERD – group II and 32 children with GERD without concomitant arrhythmia – group III.

The distribution by sex was homogeneous in groups II and III, and looked like this: in group II – (61.1 ± 8.1) % of boys and (38.9 ± 8.1) % of girls; and group III was represented by (50.00 ± 8.84) % boys and (50.0 ± 8.8) % girls. At the same time in group I the number of boys was statistically higher than the number of girls (98.7 ± 8.2) % of boys and (31.2 ± 8.2) % of girls, respectively. During the study, the principles of the Declaration of Helsinki, adopted by the General Assembly of the World Medical Association (1964±2000) and the protocol of the Bioethics Commission of the “Kharkiv Medical Academy of Postgraduate Education” № 1 dated 12.02.2021 were followed. Informed consent was obtained from all parents or guardians of children who participated in the study.

Inclusion criteria were:

- 1) the presence of arrhythmias or GERD in an isolated course or combined pathology,
- 2) the age of children from 8 to 18 years,
- 3) voluntary consent of parents to the participation of children in the study.

Clinical studies included a detailed survey of patients for the presence or absence of relevant complaints inherent in the studied pathologies; their nature, frequency, severity, duration and number.

Evaluation of phenotypic traits of NDST was performed according to the criteria of T. Milkovskaya-Dimitrova and A. Karkashov.

The first degree – the expressed symptoms of NDST, was appropriated in the presence of the subject of 5 main phenotypic signs of NDST and 3 secondary or more.

The second degree – moderate symptoms of NDST, was determined in the presence of a child 3–4 major and 1–2 secondary phenotypic traits.

For the third degree, which was a single symptom of NDST, was characterized by the presence of 2 main phenotypic traits.

The presence or absence of primary and secondary phenotypic traits of NDST was determined by examining and interviewing the patient.

The results of esophagogastroduodenoscopy and pH-metry were used to confirm the diagnosis of GERD according to the criteria of the Montreal Consensus (2006).

Verification of arrhythmias in children was performed on the basis of electrocardiographic examination and Holter daily ECG monitoring with the Poly-spectrum DM device (Ukraine).

Exclusion criteria included: congenital heart disease; acute inflammatory processes during the examination; condition after correction of congenital heart disease or radiofrequency catheter ablation; severe somatic pathology in a state of decompensation and refusal of parents of children to participate in the study.

Statistical processing of the results was performed using the spreadsheet MS Office Excel (Microsoft Corporation, USA) and the statistical online calculator epitools (epitools.ausvet.com.au, Austria). Quantitative traits (age) were assessed by determining the sample mean and its standard error. To describe the qualitative variables, the frequency of occurrence of the trait (P) was used and its standard error (Sp) was calculated. Differences in the relative frequencies of the indicators in the compared groups were determined using the Z-test, which is analogous to the Student's t-test for non-numeric variables.

3. Results

During the analysis of the results of the frequency of detection in the studied groups of the main phenotypic traits of NDST, certain features were identified, which are presented in Table 1.

There were statistically significant differences between the incidence of asthenic constitution, dysplastic tooth growth and tall stature.

The predominance of the frequency of high growth in groups I and II, compared with group III, can be explained by the fact that this indicator is a risk factor for the formation of arrhythmias in children without concomitant GERD and for combined pathology in the form of arrhythmia with concomitant GERD.

Dysplastic tooth growth was more common in children of groups II than in groups I and III, which may indicate that it is a risk factor for the formation of combined pathology in children in the form of arrhythmia and GERD.

Asthenic constitution was observed more often in children of group I than in group III, which means that this indicator is mainly a predictor of isolated arrhythmias in children without concomitant GERD.

During the analysis of the results of the frequency of detection in the studied groups of secondary phenotypic traits of NDST, certain features were identified, which are presented in Table 2.

Table 1

Frequency of detection of the main phenotypic features of NDST in the studied groups, abs., P±Sp, %

The main phenotypic features of NSDT	Group I n=32	Group II n=36	Group III n=32
Asthenic constitution	10 (31.2±8.2) ³	8 (22.2±6.9)	2 (6.2±4.3)
Refraction anomalies	6 (18.7±6.9)	8 (22.2±6.9)	10 (31.2±8.2)
High palate	4 (12.5±5.8)	9 (25.0±7.2)	6 (18.7±6.9)
Dysplastic growth of teeth	18 (56.2±8.8) ¹	29 (80.6±6.6) ²	14 (43.7±8.8)
Curvature of the nasal membrane	2 (6.2±4.3)	3 (8.3±4.6)	4 (12.5±5.8)
Hernia	0 (0.0±3.1)	5 (13.9±5.7)	6 (18.7±6.9)
Keel-shaped chest	0 (0.0±3.1)	1 (2.8±2.7)	0 (0.0±3.1)
Funnel-shaped chest	2 (6.2±4.3)	2 (5.6±3.8)	0 (0.0±3.1)
Hypermobility of joints	22 (68.7±8.2)	22 (61.1±8.1)	22 (68.7±8.2)
X-shaped lower extremities	2 (6.2±4.3)	0 (0.0±3.3)	0 (0.0±3.1)
Scoliosis	0 (0.0±3.1)	5 (13.9±5.7)	0 (0.0±3.1)
Lordosis	0 (0.0±3.1)	1 (2.8±2.7)	0 (0.0±3.1)
Flat feet	6 (18.7±6.9)	6 (16.7±6.2)	4 (12.5±5.8)
Shortening of the toes	1 (3.1±3.1)	0 (0.0±3.3)	0 (0.0±3.1)
Tall	12 (37.5±8.6) ³	19 (52.8±8.3) ²	4 (12.5±5.8)
Polydactylism	0 (0.0±3.1)	0 (0.0±3.3)	1 (3.1±3.1)

Note: ¹ – significant difference between indicators I and II group ($p < 0.05$); ² – significant difference between indicators between groups II and III ($p < 0.05$); ³ – a significant difference between the I and III groups ($p < 0.05$)

Table 2

Frequency of detection of secondary phenotypic traits of NDST in the studied groups, abs., P±Sp, %

Secondary phenotypic traits of NSDT	Group I n=32	Group II n=36	Group III n=32
Extended bridge of nose	2 (6.2±4.3)	3 (8.3±4.6)	2 (6.2±4.3)
Abnormal shape of the auricles	8 (25.0±7.6)	10 (27.8±7.5)	10 (31.2±8.2)
Antimongoloid shape of the eyes	2 (6.2±4.3)	2 (5.6±3.8)	0 (0.0±3.1)
Short upper lip	14 (43.7±8.8)	16 (44.4±8.3)	20 (62.5±8.6)
Proboscis-shaped lips	0 (0.0±3.1)	1 (2.8±2.7)	0 (0.0±3.1)
Short bridle of the tongue	4 (12.5±5.8)	4 (11.1±5.2)	4 (12.5±5.8)
Short neck	2 (6.2±4.3)	2 (5.6±3.8)	2 (6.2±4.3)
Cryptorchidism	0 (0.0±3.1)	0 (0.0±3.3)	1 (3.1±3.1)
Joint pain	6 (18.7±6.9)	11 (30.6±7.7)	6 (18.7±6.9)
Scoliotic posture	26 (81.2±6.9) ³	26 (72.2±7.5) ²	8 (25.0±7.6)
Disproportionately long fingers	0 (0.0±3.1)	1 (2.8±2.7)	0 (0.0±3.1)
Expansion of the gaps between the toes	2 (6.2±4.3)	2 (5.6±3.8)	2 (6.2±4.3)
Dislocations and subdislocations of joints	3 (9.4±5.1)	4 (11.1±5.2)	4 (12.5±5.8)

Note: ² – significant difference between indicators between groups II and III ($p < 0.05$); ³ – significant difference between indicators I and III group ($p < 0.05$)

The study found that most often scoliotic posture was statistically more significant in groups I and II of children than in group III, which indicates that this parameter is a predictor of arrhythmia in children without

concomitant GERD pathology, and combined - in the form of arrhythmia with GERD. The severity of NDST in the study groups was also assessed during the study. The results presented in Table 3.

Table 3

The severity of NDST in the study groups

The severity of NDST	Group I n=32	Group II n=36	Group III n=32
The first degree - the expressed symptoms of NDST	3 (9.4±5.1)	5 (13.9±5.7)	0 (0±3.1)
The second degree - moderate symptoms of NDST	11 (34.4±8.4)	11 (30.6±7.7)	16 (50.0±8.8)
The third degree - single symptoms of NDST	18 (56.2±8.8)	20 (55.6±8.3)	16 (50.0±8.8)

The analysis of the results revealed the absence of a statistically significant relationship between the severity of NDST and study groups, although it should be noted that in children of group III the first degree of NDST was not observed in general.

4. Discussion of research results

According to the scientific literature for children and adults with GERD more typical musculoskeletal and musculoskeletal signs of NDST are such as: hypermobility of the joints, posture disorders, flat feet, arachnodactyly, dentition abnormalities and others; visceral manifestations of NDST – hernias, refraction anomalies, etc. were determined less often [14, 15].

Children and adults with arrhythmias were also most often characterized by musculoskeletal and musculoskeletal signs of NDST, namely: joint hypermobility, resolution disorders, dentition abnormalities, asthenic body constitution, tall stature; somewhat less often they showed such signs of NDST as: anomalies in the development of the auricles, nasal dilation, anomalies of the visual organs, etc. [16, 17].

No data on the signs of NDST observed in arrhythmias in children in combination with GERD were found.

The practical significance of the results of the study is to develop on their basis the criteria for early diagnosis and differential diagnosis of combined pathology in the form of arrhythmia with concomitant GERD and isolated variants of these pathologies in children. The use of these criteria will reduce the frequency of severe forms of these pathologies, their prevalence and duration, due to the beginning of treatment in the early stages, to the development of serious complications.

Study limitations: a small sample of patients participating in the study.

Prospects for further research: conducting research on a large sample of patients; study of information on the correspondence of the degrees of functional heart disorders in arrhythmias in children and morphological lesions of the esophagus in GERD - the frequency of

detection of phenotypic signs of NDST and the severity of it in patients.

5. Conclusions

1. Identified statistically significant phenotypic signs of NDST, which are risk factors for combined pathology in the form of arrhythmia with concomitant GERD; and predictors of the formation of isolated variants of these pathologies, namely: asthenic constitution, dysplastic tooth growth, tall stature and scoliotic posture. These indicators can be used in early and differential diagnosis of the studied pathological processes.

2. Asthenic constitution is a predictor of formation of exclusively isolated arrhythmia in children; and exclusively combined pathology in the form of arrhythmia and concomitant GERD - dysplastic growth of teeth.

3. Risk factors for the simultaneous formation of both isolated arrhythmia in children and combined with concomitant GERD: high growth and scoliotic resolution.

4. There were no statistically significant differences between the study groups regarding the severity of NDST, but there was a complete lack of detection in children of group III (children with isolated GERD without concomitant arrhythmia) of the first degree of NDST. This information can also be used in early and differential diagnosis of the studied pathological processes.

Conflict of interests

The authors declare that they have no conflicts of interest.

Financing

The study was performed without financial support.

Acknowledgments

We express our gratitude to the patients who took part in the study, as well as the specialists who contributed to the investigation.

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Received date 11.05.2021

Accepted date 15.06.2021

Published date 30.07.2021

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