

VILNIUS UNIVERSITY

Odeta Kinčinienė

**ETIOLOGY OF FAINT IN CHILDREN WITH RECURRENT SYNCOPE AND
SYNCOPE' HEMODYNAMIC PATTERNS**

Summary of doctoral dissertation
Biomedical sciences, medicine (07 B)

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Scientific supervisor:

Prof. Dr. Habil. Vytautas Usonis (Vilnius University, biomedical sciences, medicine – 07 B)

Dissertation is being defended at Medical Research Council of Vilnius University under equivalency

Chairman:

Assoc. Prof. Dr. Habil. Alicija Dranenkienė (Vilnius University, biomedical sciences, medicine – 07 B)

Members:

Assoc. Prof. Dr. Virginija Grabauskienė (Vilnius University, biomedical sciences, medicine – 07 B)

Dr. Birutė Skerlienė (Vilnius University, biomedical sciences, medicine – 07 B)

Assoc. Prof. Dr. Rimantas Kėvalas (Kaunas University of Medicine, biomedical sciences, medicine – 07 B)

Assoc. Prof. Dr. Jurgis Bojarskas (Kaunas University of Medicine, biomedical sciences, medicine – 07 B)

Opponents:

Prof. Dr. Habil. Dalia Bakšienė (Kaunas University of Medicine, biomedical sciences, medicine – 07 B)

Prof. Dr. Habil. Arūnas Valiulis (Vilnius University, biomedical sciences, medicine – 07 B)

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Odeta Kinčinienė

**DAŽNAI ALPSTANČIŲ VAIKŲ ALPIMO PRIEŽASTYS IR SINKOPĖS
HEMODINAMIKA**

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Disertacija ginama eksternu

Mokslinis konsultantas: prof. habil. dr. Vytautas Usonis

(Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

Disertacija ginama Vilniaus universiteto Medicinos mokslo krypties taryboje

Tarybos pirmininkas

Doc. habil. dr. Alicija Dranenkienė

(Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

Nariai:

Doc. dr. Virginija Grabauskienė

(Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

Dr. Birutė Skerlienė

(Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

Doc. dr. Rimantas Kėvalas

(Kauno medicinos universitetas, biomedicinos mokslai, medicina – 07 B)

Doc. dr. Jurgis Bojarskas

(Kauno medicinos universitetas, biomedicinos mokslai, medicina – 07 B)

Disertacijos oponentai:

Prof. habil. dr. Dalia Bakšienė

(Kauno medicinos universitetas, biomedicinos mokslai, medicina – 07 B)

Prof. habil. dr. Arūnas Valiulis

(Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

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SCIENTIFIC PROBLEM OF THE STUDY

Syncope – transitory loss of consciousness due to global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. Syncope is very common problem in children and adolescents. As many as 15-18% children experiencing at least one episode of syncope before adolescence. Although syncope in children and adolescents is almost always benign, in a few cases it may be a clue to the presence of an underlying cardiovascular disease and may predict a risk of sudden death. Syncope is also a major challenge for child, his parent and practicing physician. Consequently several guidelines for syncope diagnosing and managing have been developed in American Heart Association and European Society of Cardiology,- the last one in August 2009. However, the guidelines are mainly applicable to adults, not children or adolescents. Thus diagnostic protocols for children and adolescents suffering from syncope must be evaluated. Rationality and validity of tests in children after syncope is unclear: impact of anamnesis, physical examination is unquestioning. Laboratory testing – needs inquiring impact of glucose concentration, anemia in syncope's development. Electrocardiogram and ultrasound examination of heart is regularly most popular diagnostic methods in children with syncope. Ritters S. et al. after retrospective analysis of 480 children and adolescents with syncope came to the conclusion, that echocardiography is not effective method for syncope cause detection and is not necessary if anamnesis, objective examination and 12-lead electrocardiogram not revealed heart abnormality.

Orthostatic testing is supposed to be most informative method for syncope evaluation. There are many methodologies with different orthostasis time; different vertical position time and grade for perform this test. Many clinical studies estimated various rate of testing results. Chen Li et al. after examining 208 children with syncope in several hospitals in China detected that orthostatic test was positive in 155 children (28,8% had postural orthostatic tachycardia syndrome, 34,6% - vasovagal syncope with vasodepressor pattern, 2,4% - vasovagal syncope with cardioinhibitory pattern and 8,7% - vasovagal syncope with mixed pattern) 25,5% - demonstrated normal

neurocirculatory response. Zhang Q.Y. et al. testing 100 children after syncope detected 50% vasovagal syncope (31% - vasodepressor, 12% - mixed, 7% - cardioinhibitory pattern), 33 % postural orthostatic tachycardia syndrome, 2% orthostatic syncope and 15% unknown syncope. Some scientists and practical physicians doubt about rationality and validity of orthostatic testing in children. That's why we have found publications, where head up tilt testing is compared with active standing (s. Schellong') test. Matsushima R. et al. after examining 51 child with syncope and 51 – without syncope in anamnesis and after performing passive head up tilt and active standing testing in both groups came to conclusion that is no statistically significant differences in test's efficacy, sensitivity and specificity. Kulakowski P. et al. after examining 202 unselective patients with syncope came to the conclusion, that in patient with typical reflex anamnesis and multiple syncope, orthostatic testing's result can be predicted and such expensive, long and uncomfortable examination is not necessary. Otherwise many researchers are trying to predict results of tilt testing using anamnesis, clinical symptoms and hemodynamic changes. Kazemi B. et al. after careful anamnesis, physical examination and orthostatic testing of 640 adults made the conclusion that elder people statistically significant frequently demonstrated vasodepressor pattern of vasovagal syncope later, younger people developed vasovagal syncope with cardioinhibitory pattern earlier. Virag N. et al. in retrospective analysis of 1155 people orthostatic test's result, made the conclusion that systolic blood pressure and its changes during orthostatic test can statistically significant predict vasovagal syncope. Gielerak G. et al. after examination of 105 patients with syncope came to conclusion, that syncope's mechanism can be faithfully predicted by early changes in systolic blood pressure and peripheral vascular resistance.

AIM AND TASKS OF THE STUDY

Aim of study. To estimate common causes of children faint, to clear rationality and validity of tests diagnosing syncope, to research possibility of prediction orthostatic tests result in children.

Tasks of study:

1. To estimate causes of faint in children hospitalized for recurrent syncope.
2. To value rationality and validity of common performing tests diagnosing syncope in children.
3. To compare eligibility and informativity of two orthostatic tests (passive head up tilt test and active standing test) for syncope simulation and hemodynamic pattern's investigation.
4. To estimate rate of syncope mechanisms and early hemodynamic accents of each mechanism simulating syncope in children.
5. To determine optimal short and sufficient time of orthostatic testing in children for reliable forecast mechanism of syncope.

STUDY SCIENTIFIC ORIGINALITY AND PRACTICAL SIGNIFICANCE

1. There is no published studies in Lithuania where researched causes and mechanisms of children syncope.
2. There are no published studies in Lithuania about test's rationality and validity diagnosing syncope in children.
3. Trying to find published studies about pediatric syncope or orthostatic test's mechanism prediction was failed.

DEFENDED PROPOSITIONS

1. The common cause of faint in children is vasovagal syncope.
2. Active standing test is suitable for syncope provocation and hemodynamic pattern's investigation in children after syncope during orthostatic test.
3. Syncope hemodynamic pattern and orthostatic test result can be predicted until syncope develops with less negative emotions and discomfort for children and adolescents.

METHODOLOGY OF RESEARCH

Patients. I group (investigative) inclusion criteria: a) children and adolescents, b) ≥ 3 faint episode in anamnesis, c) hospitalization at Vilnius City University Hospital because of recurrent syncope. I group (investigative) exclusion criteria: a) neurologic disease diagnosed before present hospitalization, b) focal neurological symptomatic at hospitalization, c) epileptic disorder diagnosed before hospitalization or suspected during neurologic examination. I group – 214 children mean age $13,08 \pm 2,88$ years, 140 (65%) female and 74 (35%) male. II group (control) inclusion criteria: a) children and adolescents, b) no faint episode in anamnesis, c) absence of acute health disorder symptoms, d) absence of diagnosed chronic disease. II group (control) exclusion criteria: a) faint in anamnesis, b) any symptom of acute health disorder, c) diagnosed chronic disease. II group – facultative 92 children mean age $12,64 \pm 3,04$ year, 59 (63%) female and 33 (37%) male.

Methods. The study was prospective and included consecutive patients ≤ 18 -year old with suspected recurrent (third at least) syncope admitted to Vilnius City Hospital Clinic of Children Diseases from 1 January 2000 to 31 December 2007. Syncope was defined as transient loss of consciousness and vertical tone, passing without any reanimating manipulations. The first step. Detail anamnesis was taken in all patients focusing on typical reflex (prolonged standing/sitting, muggy environment, emotional stress, during eat, micturition, defecation etc.) and atypical (transient loss of consciousness occurred at sleep, in orthostatic position, during physical exercises) circumstances before supposed syncope. All patients underwent standardized physical examination including blood pressure and heart rate measuring, objective system' examination, basic laboratory evaluation, 12-lead electrocardiogram and ultrasound Doppler heart examination. The second step. Patients who after the first step of examination had no evidence for cardiac or neurologic pathology (205 patients) underwent orthostatic test. The test was performed in a quiet room with dimmed light, two-four ours after meal. Blood pressure and electrocardiogram during testing were measured and recorded by monitors DASH 2000 and Datascope Duo TM. Patients were hold in orthostasis for 10 minutes, in postural position - until syncope or presyncope develops with systolic and/or diastolic blood pressure and/or heart rate significant

change triggering at least two symptoms of: dizziness, nausea, aural and/or vision disturbances, palpitation, sweating. Results of hemodynamic measurement were qualified at the start of testing (rest) end of orthostasis (baseline), maximal changed after tilting (compensatory), at the first complaints (first complaint), at final test result (syncope) and 10 minutes resting when test was finished (recovery). Using statistic methods changes of hemodynamic data were calculated at every stage for possibility to predict orthostatic test's results and hemodynamic pattern of syncope at early stage of testing. According to technical and ethics possibilities and tasks of research there were performed 72 head up tilt and 133 active standing tests.

24 h electrocardiogram Holter examination was performed for 68 children with suspected arrhythmogenic syncope after the first step of study. Exercise testing was performed for 28 patients, in whom syncope was associated with physical activity.

Statistical analysis. Data were accumulated in Microsoft Excel 2000 or 2003 sheets. The feature rate was calculated by percentage, processed with Microsoft Excel 2003 and SPSS 17,0 demo statistical packets. Data were considered to be significant when $p < 0,05$. Comparison between two groups was made using Student's t-test, more than two groups – F (ANOVA)-test, percents - χ^2 test.

MAIN RESULTS

214 children of investigative group were examined after recurrent syncope. Diagnoses made after in methodology scheduled testing were divided thus: reflex vazovagal syncope – 103 (48,2%) children, reflex situational – 1 (0,5%), postural orthostatic tachycardia syndrome – 43 (20,1%), cardiogenic syncope – 9 (4,2%), psychogenic pseudosyncope – 3 (1,4%) and orthostatic syncope – 1 (0,4%). Syncope with unknown origin was diagnosed in 54 (25,2%) cases. 92 healthy children and adolescents were examined in control group. Groups haven't statistically significant differences in patients age distribution ($p = 0,23$; $t = 1,19$), sex distribution ($p = 0,71$; $\chi^2 = 0,13$) and physical development. Children of investigative group had mean height $158,21 \pm 16,35$ cm, children of control group – $155,70 \pm 19,31$ cm ($p = 0,20$; $t = 1,28$). Investigative group's weight was $47,03 \pm 13,69$ kg, control group's $49,62 \pm 20,80$ kg

($p = 0,24$; $t = 1,28$). During objective physical examination was established that investigative group's patients had statistically significant lower systolic and diastolic blood pressure at rest than comparable children from control group. Heart rate at rest in the first group was significantly rare in children with recurrent syncope too (table 1).

Compared	Sex	I group (n-214)	II group (n-92)	Statistical significance
Systolic blood pressure (mmHg)	Female	111,65 ± 11,25	117,41 ± 13,93	$p = 0,002$; $t = 3,11$
	Male	112,59 ± 11,70	119,56 ± 14,53	$p = 0,009$; $t = 2,65$
Diastolic blood pressure (mmHg)	Female	68,05 ± 9,29	71,47 ± 8,63	$p = 0,01$; $t = 2,40$
	Male	68,14 ± 9,50	73,38 ± 9,59	$p = 0,009$; $t = 2,66$
Heart rate (beat/min)	Female	79,02 ± 13,19	88,83 ± 17,73	$p = 0,000$; $t = 4,33$
	Male	79,39 ± 13,38	89,48 ± 16,21	$p = 0,001$; $t = 3,31$

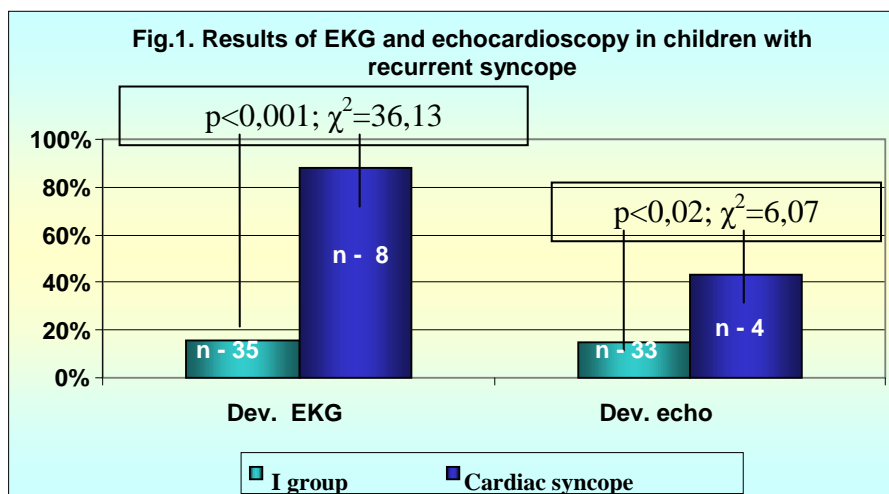
Table 1. Comparison of hemodynamic index's in investigative and control group.

Basic laboratory investigation showed no significant differences in hemoglobin concentration, peripheral blood saturation and glucose concentration between children with syncope and children without syncope in anamnesis.

Children included in control group had no diagnosed chronic disease or detected acute health disorder. Sustaining this impact of 12-derivation electrocardiogram and ultrasound heart examination diagnosing cause of syncope was analyzed only in investigative group. After 12-derivation electrocardiogram, performed to 214 children with recurrent syncope any deviation was detected in 35 cases (16,35%). The impact of EKG diagnosing cardiac syncope was 88,9%: 1 – hypertrophy of left ventricle caused by aortic stenosis, 2 – right atrial and ventricle hypertrophy, caused by atrial septal defect 1 – Long QT interval syndrome, 1 – atrial flutter, 1 – WPW syndrome, 2 – II degree atrioventricular block,- in one of them after rational testing was diagnosed acute myocarditis. Otherwise electrocardiogram sensitivity in children with noncardiac syncope was 13,2%: 6 – complete right branch block (without any abnormalities detected in ultrasound examination), 2 – I degree atrioventricular block in sleep, 4 – II degree sinoatrial block in sleep, 2 – short PQ interval phenomenon (1 developed

supraventricular tachycardia during tilt testing), 7 – significant sinus bradycardia, 2 – significant sinus tachycardia, 4 – pace maker’s migration.

Ultrasound Doppler heart examination was also performed to 214 children with recurrent syncope. Any abnormality was detected in 33 cases (15,42%). Despite electrocardiogram sensitive 4 congenital (aortic stenosis, atrial septal defects) and acquired (myocarditis) heart diseases were detected 22 mitral valve prolepses’ (10 of them with II degree valve insufficient), 5 – *foramen ovale apertum*, 2 – II degree insufficient of tricuspid valve. The impact of echocardiography diagnosing cardiac syncope 44,4%. But there was no cardiac syncope diagnosed only by ultrasound examination – all of them had abnormalities in physical examination and 12-derivation EKG performed before ultrasound. Sensitivity of echocardiography in children with noncardiac syncope was 14,1%.



Resuming results showed in Figure 1: electrocardiogram is sensitive and with deep impact test diagnosing cardiac syncope in children, ultrasound examination is satisfactory diagnosing cardiac syncope in children having any suspicion of such after anamnesis, physical examination and 12-lead electrocardiogram.

According to methodology, all patients had not diagnosed cardiac syncope and diagnosed or reasonably suspected neurological disorder and after exclusion 1 patient with micturition recurrent syncope (205) underwent orthostatic testing. Passive and active tests distribution between groups is showed in table 2.

Orthostatic test in group	HUT	Active standing test	Statistical significance
<u>I gr. - investigative</u>			
Positive	52 (72,2%)	95 (71,4%)	p = 0,904
Negative	20 (27,8%)	38 (28,6%)	$\chi^2 = 0,015$
<u>II gr. – control</u>			
Positive	11 (27,5%)	12 (23,1%)	p = 0,627
Negative	29 (72,5%)	40 (76,9%)	$\chi^2 = 0,236$

Table 2. Distribution and results of active and passive orthostatic test in both groups.

According to results showed in table 2 we can't find significant difference between head up tilt and active orthostatic test in both groups. In generally orthostatic test is significant frequently positive in children with recurrent syncope than in children without syncope ($p=0,000$; $\chi^2=56,6$). I group (investigative): 205 underwent testing, - 147 (71,1%) had positive, 58 (28,3%) - negative result. II group (control): 92 underwent testing, - 23 (25%) demonstrated positive, 69 (75%) – negative results.

At first we tried to predict orthostatic test result using anamnesis data. We divided all patients of investigative group in two subgroups: 4-12 year old (children) and 13-17 year old (adolescents). After that data were calculated in female and male separately. Then investigative group was divided in two subgroups according typical-reflex and atypical circumstances before syncope (table 3.)

Compared		Positive	Negative	Statistical significance
Age	≤12 year	46 (73%)	17 (27%)	p=1,19
	≥13 year	105 (74%)	37 (26%)	$\chi^2=12,36$
Sex	Female	103 (76%)	33 (24%)	p=0,34
	Male	48 (70%)	21 (30%)	$\chi^2=0,89$
Circumstances	Reflex	127 (73%)	46 (27%)	p=0,31
	Atypical	20 (62,5%)	12 (37,5%)	$\chi^2=1,03$

Table 3. Impact of anamnesis for orthostatic test' result prediction.

Sustaining results of our study age or sex of patient with syncope can't predict orthostatic test results. Patients who had syncope in atypical situation rare demonstrated positive test' results, but difference is not statistically significant. Syncope frequency in anamnesis had no significant difference for orthostatic test result. Such conclusion was made due to dividing patient into three subgroups: ≤3 syncope, 4-5 syncope and ≥6 syncope ($p=0,17$; $\chi^2=3,55$) before hospitalization. But syncope atypical circumstances statistically significant commonly were detected in patients with cardiac syncope than

in patients with noncardiac syncope. 7 patients (77,8%) with cardiac syncope had atypical, 2 (22,2%) – typical reflex anamnesis; 172 patients (80,4%) with noncardiac syncope had typical, 33 (19,6%) – atypical circumstances before syncope developed ($p=0,000$; $\chi^2=28,96$).

Considering hemodynamic pattern of orthostatic test' results in our study seriated: 103 (51,5%) reflex-vasovagal syncope (47 with vasodepressive, 18 with cardioinhibitory and 38 - mixed pattern), 43 (21,5%) had developed postural orthostatic tachycardia syndrome, 1 (0,5%) – primary orthostatic syncope. In 58(28,3%) patients (54 - hemodynamic was compensated, 3 demonstrated psychogenic reaction without hemodynamic changes, 1 patient developed supraventricular paroxysmal tachycardia) orthostatic testing was negative. Because of trickle amount we had not calculated statistics of hemodynamic pattern' changes in psychogenic pseudosyncope, orthostatic syncope and paroxysmal tachycardia. Influence of anamnesis and physical development for syncope's hemodynamic pattern prediction in 200 patients is showed in table 4.

Compared		Vasodepressive (n-47)	Cardioinhibitory (n-18)	Mixed (n-38)	POTS (n-43)	Negative (n-54)	Statistical significance
Age (years)		12,64 ± 2,63	13,61 ± 2,87	12,78 ± 2,52	14,09 ± 2,19	12,94 ± 3,35	p=0,09; F=2,01
Weight (kg)		44,30 ± 13,99	48,63 ± 15,96	47,77 ± 12,01	51,34 ± 13,16	45,53 ± 13,28	p=0,10; F=1,91
Height (cm)		154,48 ± 17,93	162,61 ± 14,63	160,89 ± 14,08	160,90 ± 11,63	156,13 ± 16,71	p=0,12; F=1,84
Sex	Female (n-133)	26 (19,5 %)	11 (8,3 %)	29 (21,8 %)	34 (25,6 %)	33 (24,8 %)	p=0,14; $\chi^2=8,34$
	Male (n-67)	21 (31,3 %)	7 (10,4 %)	9 (13,4 %)	9 (13,4 %)	21 (31,3 %)	
Syncope frequency in anamnesis	≤ 3 episodes	26 (26 %)	5 (5 %)	16 (16 %)	20 (20 %)	34 (34 %)	p=0,38; $\chi^2=8,56$
	4-5 episodes	17 (25,0 %)	7 (10,3 %)	15 (22,0 %)	16 (23,5 %)	13 (19,1 %)	
	≥ 6 episodes	4 (12,5 %)	6 (18,7 %)	7 (21,8 %)	7 (21,8 %)	7 (21,8 %)	
Circumstances of syncope	Typical reflex	41 (24,1 %)	17 (10,0 %)	33 (19,4 %)	35 (20,5 %)	44 (25,9 %)	p=0,44; $\chi^2=4,74$
	Atypical	6 (20,0 %)	1 (3,3 %)	5 (16,6 %)	8 (26,6 %)	10 (33,3 %)	

Table 4. Influence of anamnesis and physical development for syncope's hemodynamic pattern's prediction.

Mean systolic BP (mmHg)	Vasodepressive (n-47)	Cardioinhibitory (n-18)	Mixed (n-38)	POTS (n-43)	Negative (n-54)	Statistical significance
At rest	108,29 ± 10,49	115,33 ± 13,50	112,86 ± 8,76	112,90 ± 13,09	112,64 ± 11,59	p=0,13; F=1,79
Basic	104,10 ± 8,02	106,41 ± 10,47	105,84 ± 7,62	104,81 ± 11,29	107,03 ± 9,22	p=0,56; F=0,74
Compensatory	128,78 ± 11,17	120,05 ± 13,45	127,34 ± 11,15	121,67 ± 11,41	124,33 ± 7,11	p=0,003; F=4,07
First complain	93,68 ± 5,80	109,35 ± 13,92	96,76 ± 10,33	110,51 ± 7,81	119,16 ± 6,17	p=0,000; F=74,49
Recovery	106,7 ± 7,77	109,35 ± 10,17	107,82 ± 6,90	111,33 ± 7,55	Not compared	p=0,000; F=12,11

Table 5. Changes of systolic blood pressure at different stages of orthostatic testing in separate hemodynamic patterns of syncope.

Mean diastolic BP (mmHg)	Vasodepressive (n-47)	Cardioinhibitory (n-18)	Mixed (n-38)	POTS (n-43)	Negative (n-54)	Statistical significance
At rest	68,19 ± 10,16	71,66 ± 9,41	68,89 ± 7,94	67,74 ± 10,08	66,68 ± 8,76	p=0,38; F=1,05
Basic	60,76 ± 7,21	59,29 ± 6,00	62,65 ± 5,83	61,74 ± 6,30	62,13 ± 6,38	p=0,36; F=1,09
Compensatory	78,93 ± 8,62	69,52 ± 14,20	78,68 ± 11,23	72,79 ± 10,4	74,63 ± 8,75	p=0,001; F=4,61
First complain	53,76 ± 5,89	59,82 ± 12,44	57,76 ± 9,18	66,53 ± 9,15	70,66 ± 5,95	p=0,000; F=34,09
Recovery	64,17 ± 6,88	62,88 ± 4,89	64,87 ± 4,99	64,65 ± 5,81	Not compared	p=0,000; F=6,34

Table 6. Changes of diastolic blood pressure at different stages of orthostatic testing in separate hemodynamic patterns of syncope.

Mean HR (beat/min)	Vasodepressive (n-47)	Cardioinhibitory (n-18)	Mixed (n-38)	POTS (n-43)	Negative (n-54)	Statistical significance
At rest	82,08 ± 14,96	75,16 ± 12,02	78,10 ± 11,41	79,41 ± 13,76	78,72 ± 12,14	p=0,36; F=1,09
Basic	79,42 ± 11,05	74,41 ± 11,61	77,78 ± 8,57	74,95 ± 8,48	76,18 ± 10,16	p=0,18; F=1,59
Compensatory	108,80 ± 14,47	117,83 ± 12,67	112,89 ± 15,13	115,41 ± 16,48	103,42 ± 12,17	p=0,000; F=6,07
First complain	104,53 ± 13,71	94,29 ± 28,48	79,94 ± 16,42	123,53 ± 11,18	97, 57 ± 11,36	p=0,000; F=45,10
Recovery	79,62 ± 8,74	76,88 ± 7,38	76,39 ± 5,39	82,28 ± 8,89	Not compared	p=0,000; F=16,25

Table 7. Changes of heart rate at different stages of orthostatic testing in separate hemodynamic patterns of syncope

According to results showed in table 4, age, sex, physical development and syncope' anamnesis can't predict hemodynamic pattern of orthostatic testing and probably syncope. Trying to find occasion to predict hemodynamic pattern of syncope and orthostatic test we compared mean of systolic, diastolic blood pressure and mean of heart rate in separate orthostatic test's and syncope mechanism at any stage of testing (table 5, 6, 7). Considering the result we can say that our trying to detect differences between hemodynamic patterns of syncope at rest and after orthostasis failed. In our research we couldn't find statistical significant differences in systolic, diastolic blood pressure and heart rate among vasodepressor, cardioinhibitory and mixed pattern of vasovagal syncope, postural orthostatic tachycardia syndrome and normal neurocirculatory response at so early stages of testing. But at compensatory stage we detected differences in hemodynamic indexes among different pattern of syncope. Hemodynamic rate straight after syncope also can statistically significant predict mechanism of syncope. The lowest systolic BP recovering after syncope was detected in children suffering from vasodepressor and mixed vasovagal syncope. The highest systolic BP was detected in children after postural orthostatic tachycardia syndrome. The lowest diastolic BP straight after syncope specific for cardioinhibitory vasovagal syncope, the highest – postural orthostatic tachycardia syndrome. The most infrequent pulse was detected in mixed and cardioinhibitory pattern, the fastest – postural orthostatic tachycardia syndrome.

For more clear prediction changes of hemodynamic indexes were calculated in three period of orthostatic testing. I period – time from orthostatic test' start until finish of orthostasis between measuring hemodynamic indexes at rest and baseline, II period – time between baseline and compensatory, III period – time between compensatory and first complaint. Hemodynamic changes during the first period of orthostatic testing can't statistically significant predict mechanism of syncope (Fig. 2, 3, 4).

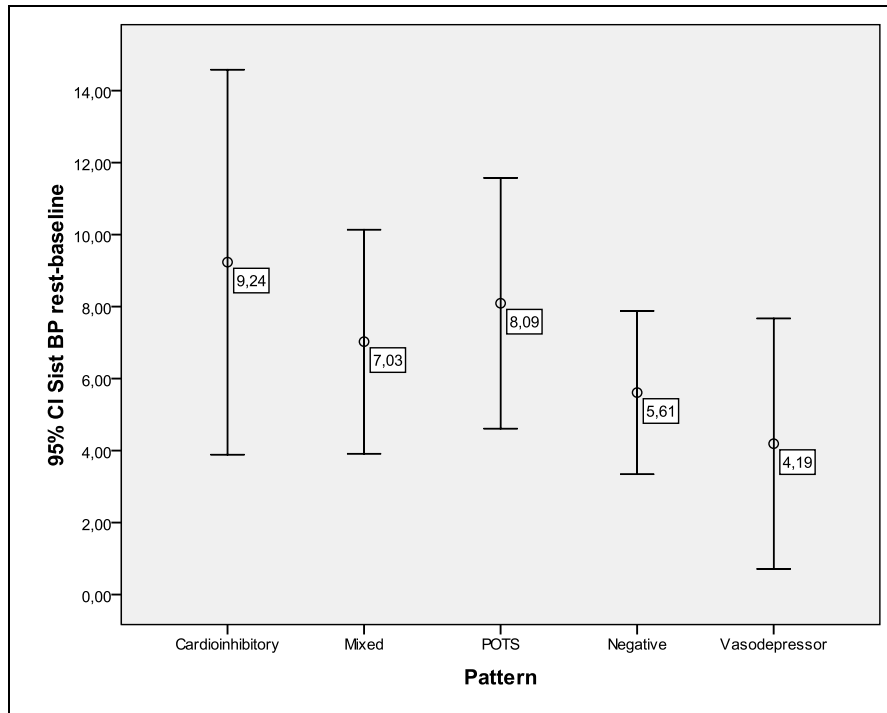


Figure 2. Changes of systolic blood pressure during orthostasis due to different hemodynamic patterns of syncope (p=0,28; F=1,27).

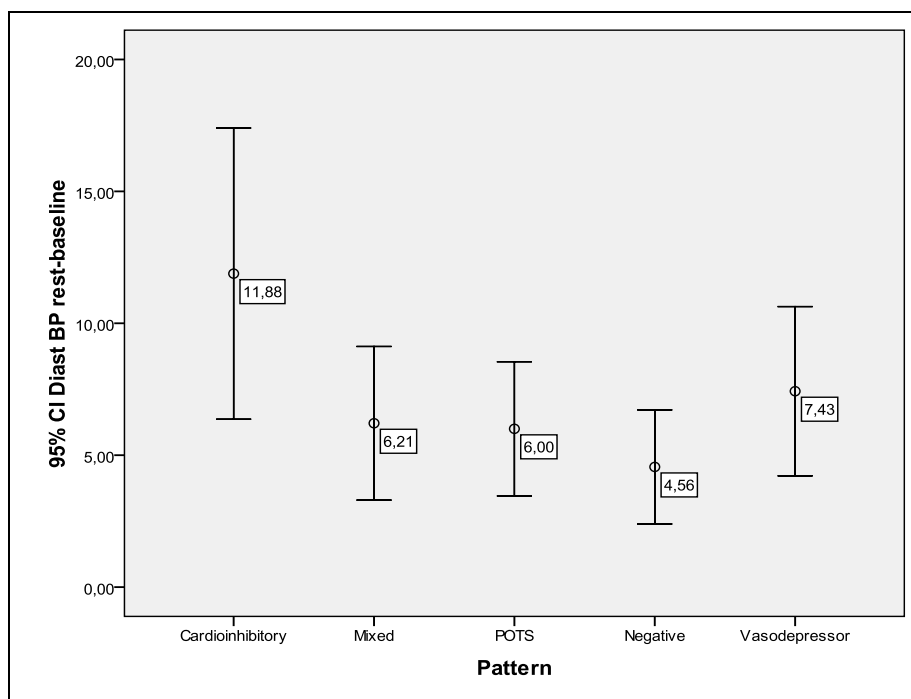


Figure 3. Changes of diastolic blood pressure during orthostasis due to different hemodynamic patterns of syncope (p=0,07; F=2,22).

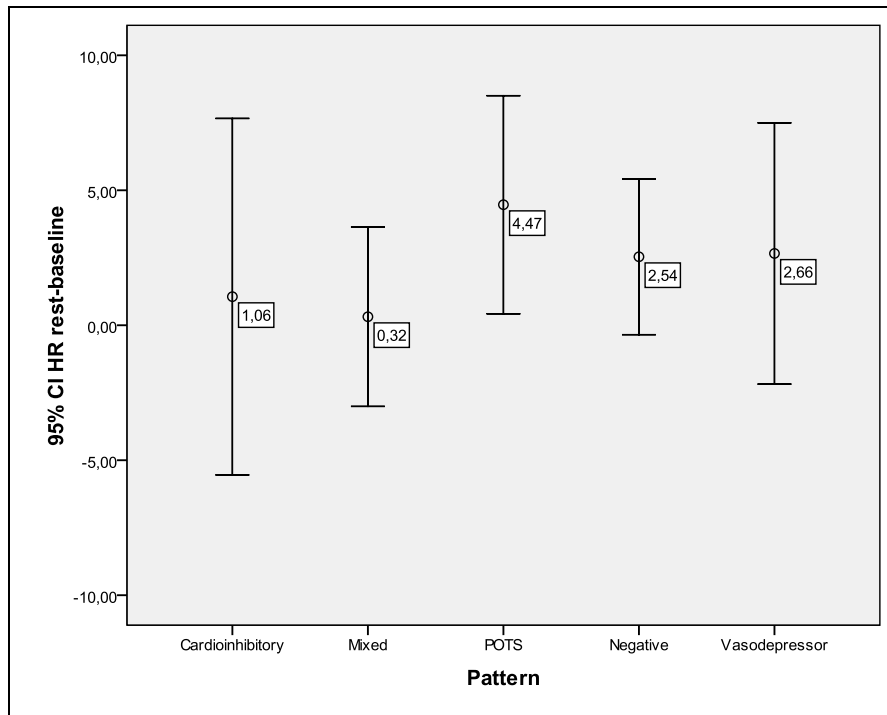


Figure 4. Heart rate changes during orthostasis due to different hemodynamic patterns of syncope (p=0,68; F=0,58).

Hemodynamic changes at II period of orthostatic testing can statistically significant predict the mechanism of syncope (Fig. 5,6,7).

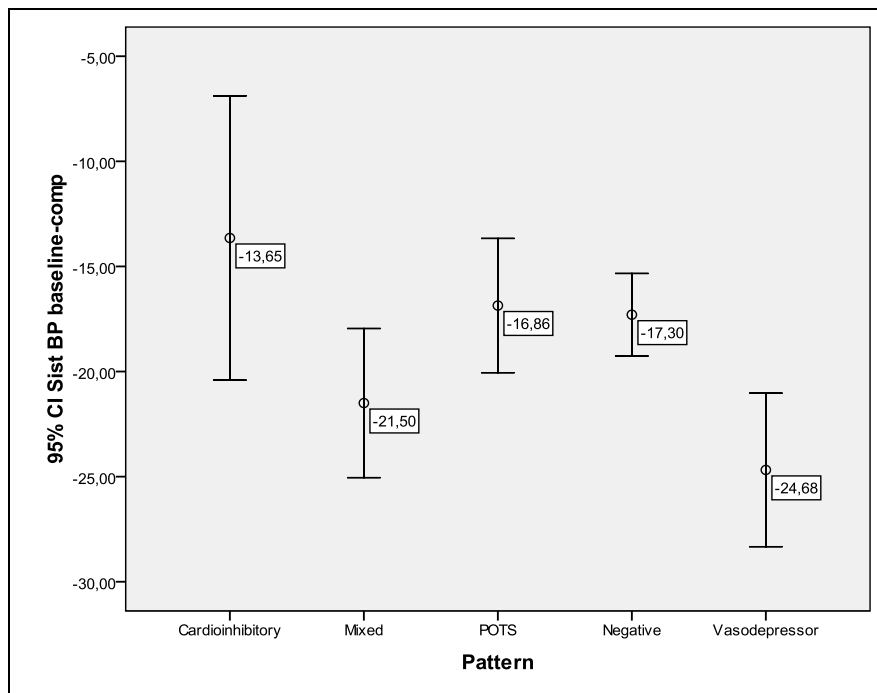


Figure 5. Changes of systolic blood pressure during II period of orthostatic testing due to different hemodynamic patterns of syncope (p=0,000; F=5,78).

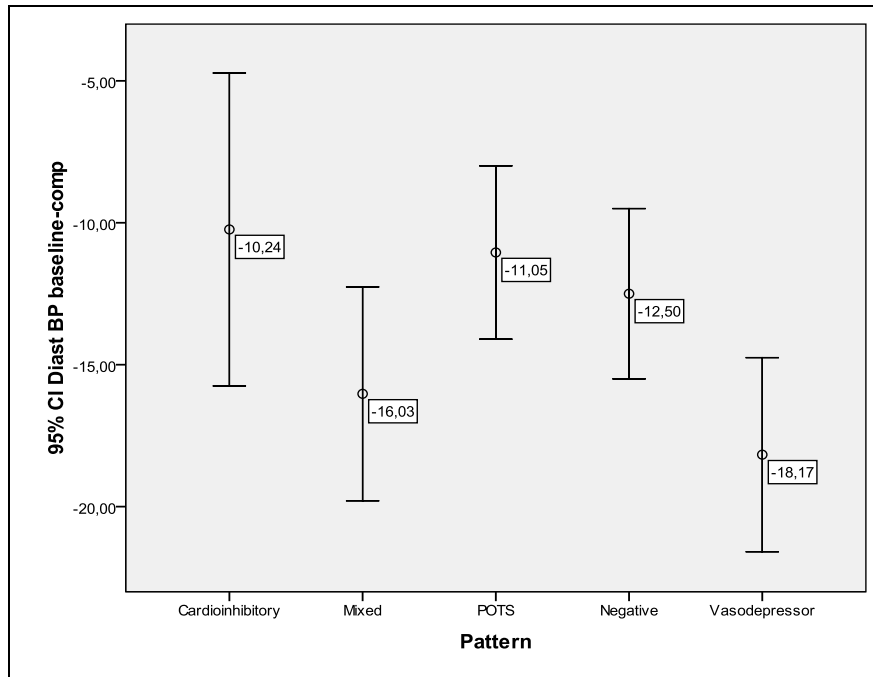


Figure 6. Changes of diastolic blood pressure during II period of orthostatic testing due to different hemodynamic patterns of syncope ($p=0,008$; $F=3,53$).

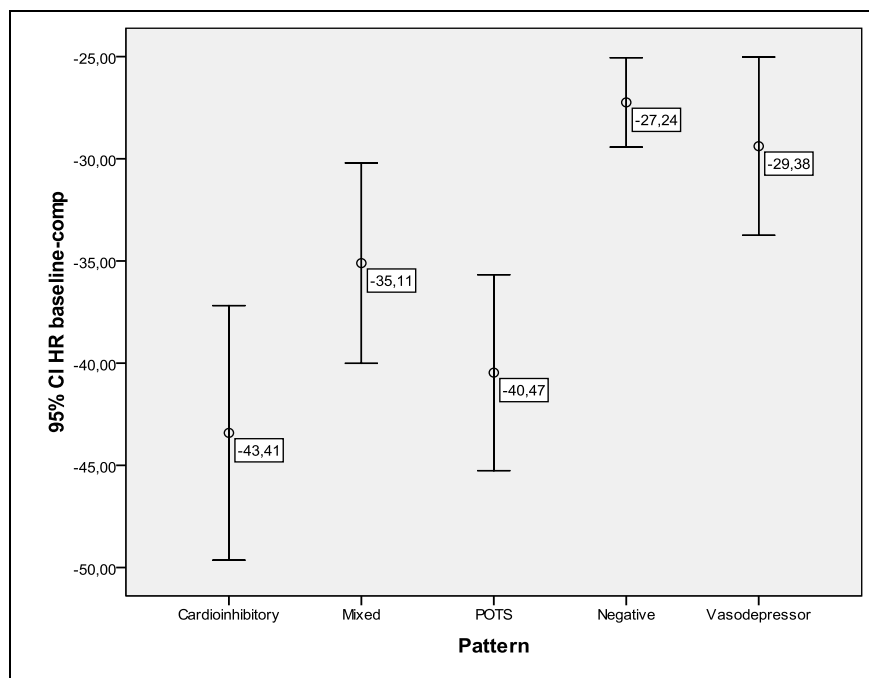


Figure 7. Heart rate changes in II period of orthostatic testing due to different hemodynamic patterns of syncope ($p=0,000$; $F=9,56$).

Changes of hemodynamic indexes during III period of orthostatic testing is statistically significant different in all hemodynamic patterns (Fig. 8,9,10).

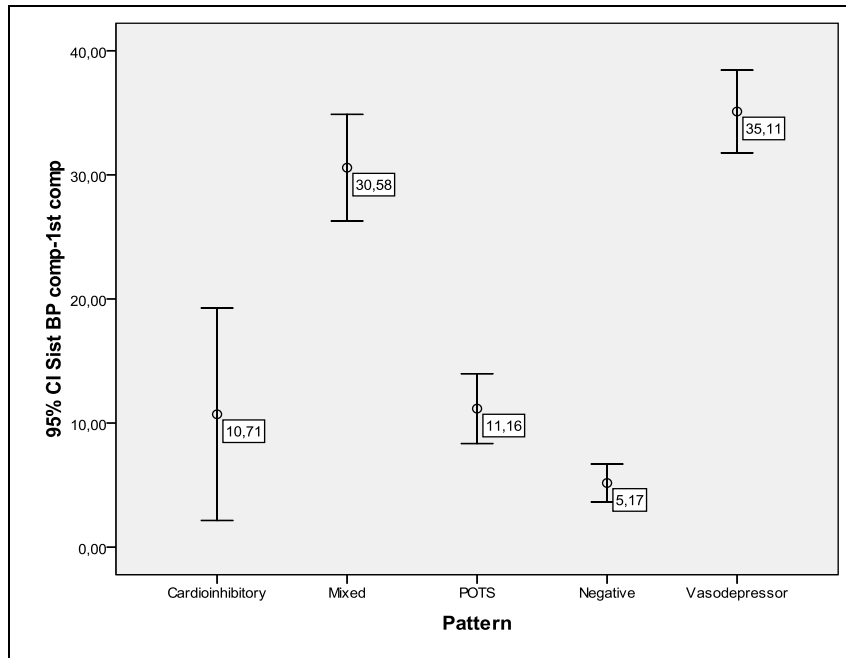


Figure 8. Changes of systolic blood pressure during III period of orthostatic testing due to different hemodynamic patterns of syncope (p=0,000; F=69,73).

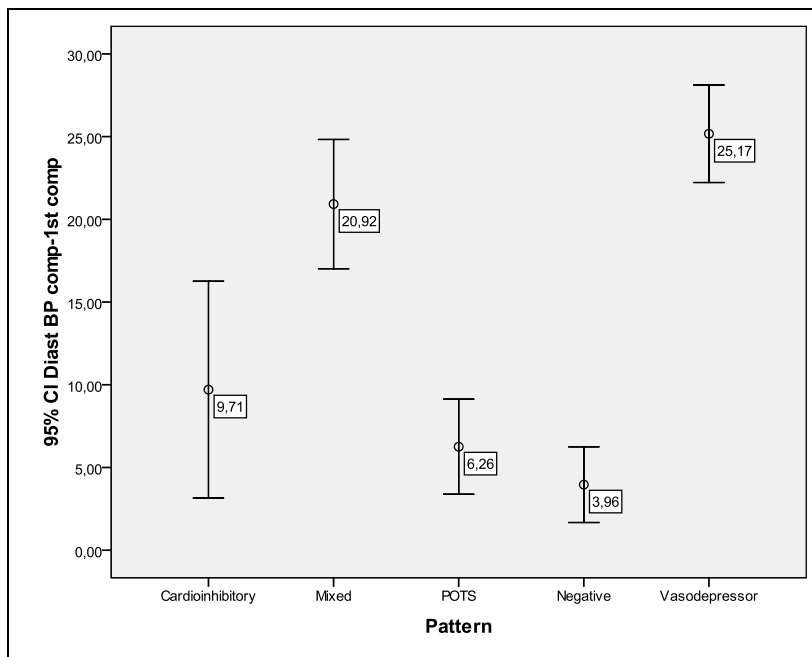


Figure 9. Changes of diastolic blood pressure during III period of orthostatic testing due to different hemodynamic patterns of syncope (p=0,000; F=38,84).

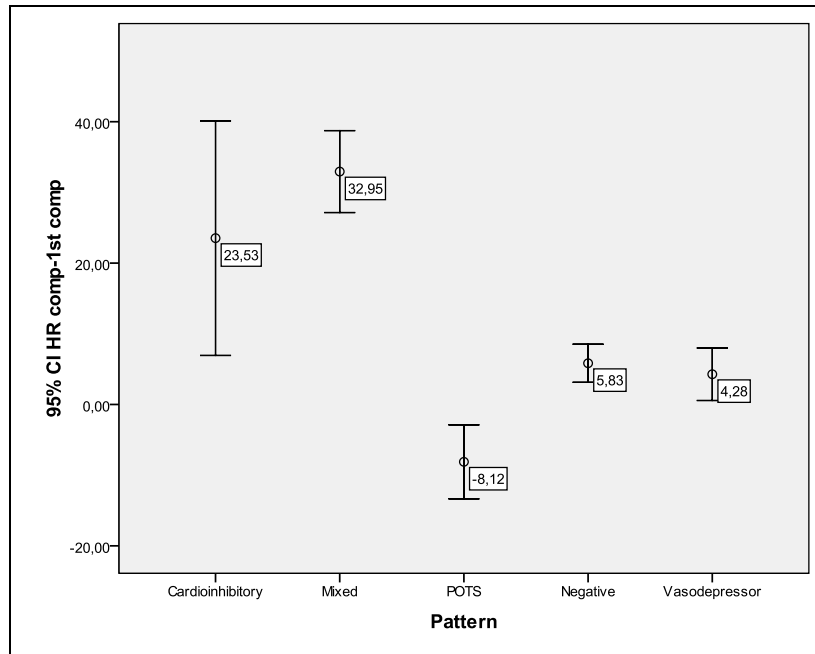


Figure 10. Heart rate changes in III period of orthostatic testing due to different hemodynamic patterns of syncope (p=0,000; F = 46,30).

In summary changes of hemodynamic indexes among different patterns can be described:

- ✓ Vasodepressor vasovagal reaction: slightly (~5%) decreasing systolic and diastolic blood pressure, heart rate stays unchanged during I period; then markedly increasing systolic and diastolic blood pressure (~25%) and less increasing heart rate ($\leq 20\%$) during II period; markedly decreasing blood pressure ($>30\%$) but heart rate stays unchanged.
- ✓ Cardioinhibitory vasovagal reaction: ~10% decreasing blood pressure and unchanged heart rate during orthostasis; dramatic (~40%) growth of heart rate and slight ($>10\%$) of blood pressure from baseline to compensation; dramatic decreasing of heart rate and only collateral decreasing of BP during III period of orthostatic testing.
- ✓ Mixed vasovagal reaction: I period – not actual changes of BP and HR; II period – markedly (~20%) increasing blood pressure and even more ($>30\%$) increasing heart rate; III period – markedly ($>30-40\%$) decreasing both hemodynamic indexes.
- ✓ Postural orthostatic tachycardia syndrome: I period – unchanging blood pressure and slightly ($>5\%$) decreasing heart rate; II period – unchanging

blood pressure and markedly (>40%) increasing heart rate; III period – unchanging blood pressure and slightly (~5%) increasing HR.

- ✓ Negative (normal neurocirculatory reaction): I period – unchanging hemodynamic indexes; II period – slightly increasing (~10%) BP and HR; III period – slightly ($\leq 5\%$) decreasing BP and HR without any complaints and reflex reactions.

68 patients with suspected arrhythmogenic syncope after 1st step of investigation underwent 24 hours electrocardiogram monitoring. Sinus rhythm recorded in 56 patient, atrial rhythms - in 3 patients, pacemaker's migration – in 9 patients. Any electrocardiographic declinations detected in 33 (48,5%) patients. Arrhythmogenic cardiac syncope confirmed in 5 (100%) patients. It was 1 – atrial flutter, registred in 12-lead electrocardiogram before, 2 – 2nd degree atrioventricular block, 1 – supraventricular paroxysmal tachycardia, 1 – Long QT interval syndome. Asystolia lasting 13888 ms, 8888 ms, 8008 ms and 4005 ms) recorded in 4 patients with cardioinhibitory pattern vasovagal syncope provoked during orthostatic test. Almost everyone (61 – 89,7%) patient had benign premature supravetricular or ventricular beats, 10 patients (14,7%) had II-III⁰ sinoatrial, 3 – I-II⁰ atriovetricular block in sleep. Prolonged monitoring of electrocardiogram is effective method diagnosing arrhythmogenic syncope in patients with suspected such one after the first step examination.

Exercise testing was performed in 29 patient with physical activity suspected cause of syncope. Only 2 patients demonstrated systolic failure without any congenital or acquired anomalies in heart. Both of them revealed postural orthostatic tachycardia syndrome during orthostatic testing.

CONCLUSIONS

1. The most common cause of children faint according to our investigation is vasovagal syncope. In accordance with frequency causes are: vasovagal, unknown cause, postural orthostatic tachycardia syndrome, cardiac syncope and sporadic cases of orthostatic syncope and psychogenic pseudosyncope.
2. The most effective and rational examination for diagnosing syncope is anamnesis with point at syncope circumstances, physical examination, 12-lead

electrocardiogram and orthostatic testing. The least effectiveness and rationality showed echocardiography, prolonged EKG monitoring and exercise testing, - these tests are applicable for syncope diagnosis just after suspected cardiac pathology in the first step of examination.

3. In compare for syncope simulation and hemodynamic investigation we had not established statistically significant difference between head up tilt and active standing tests in children.
4. The most frequent result of orthostatic tests in children with recurrent syncope is vasovagal vasodepressor pattern. Mechanisms statistically significant differ with each other in hemodynamic separate patterns performing orthostatic test.
5. Orthostatic test's result can be statistically significant credibly predict at the end of compensatory period.

REZIUME

Mokslo problemos aktualumas

Sinkopė dažna vaikų ir paauglių problema, išgašdinanti ne tik patį alpstantįjį bet ir jo artimuosius. nepaisant šiuo metu pagausėjusių tyrimų, vaikų sinkopių priežastys, jų tyrimų vertingumas ir informatyvumas nėra aiškūs. Vaikai – tai riboto pakantumo ir tolerancijos skausmui visuomenės dalis,- jie demonstruoja nepasitenkinimą, kai skauda, nepatogu ar baisu, priešinasi visiems veiksniams, kurie gali sukelti minėtą diskomfortą. Kiekvienas vaikų gydytojas stengiasi pacientui sukelti kuo mažiau neigiamų emocijų, atlikti tai optimaliai greitai, racionaliai ir informatyviai. Literatūroje aptinkama tyrimų, kuriuose bandoma prognozuoti daug diskomforto sukeliančio suaugusiojo ortostatinio testo rezultatus, vertinant pacientų amžių, alpimo anamnezę, hemodinamikos rodiklius ramybėje, jų kitimą ortostatinio testo metu. Tyrimų, kuriuose bandoma prognozuoti alpusių vaikų ortostatinių testų rezultatai, aptikti nepavyko.

Darbo tikslas

Nustatyti dažniausias vaikų alpimo priežastis ir alpusiems vaikams atliekamų tyrimų diagnostinę ir prognostinę vertę bei ortostatinio testo rezultatų prognozavimo galimybes.

Darbo uždaviniai

1. Nustatyti dėl sinkopių hospitalizuojamų vaikų sąmonės netekimų priežastis.
2. Įvertinti dažniausiai vartojamų alpusio vaiko tyrimų diagnostinį ir prognostinį informatyvumą.
3. Palyginti sinkopės imitavimo testų – pasyvaus stalo pakėlimo mėginio ir aktyvaus gulėjimo-stovėjimo testo informatyvumą alpimui sukelti ir jo mechanizmui nagrinėti.
4. Nustatyti atskirų alpimo mechanizmų, sukeltant alpstančių vaikų sinkopės, dažnumą bei juos skiriančius ankstyvuosius hemodinamikos pokyčius.
5. Numatyti optimalų sinkopės imitavimo laiką, tinkamą ir pakankamą sinkopės mechanizmui prognozuoti

Darbo mokslinis naujumas ir praktinė vertė

Lietuvoje nepavyko aptikti darbų, kuriuose nagrinėtos vaikų alpimų priežastys, vertinti sinkopių mechanizmai ir ieškota efektyvių būdų alpusiems vaikams tirti. Užsienio medicinos mokslo spaudoje pavyko aptikti darbų, kuriuose bandyta prognozuoti suaugusiųjų alpimo klasę, vertinant anamnezę ir objektyvaus tyrimo duomenis bei ortostatinio testo rezultatus, vertinant amžių ir teigiamo atsako vystymosi greitį. Publikuotų darbų, kur bandoma prognozuoti vaikų sinkopių mechanizmą vertinant hemodinamikos pokyčius imitavimo testo metu, aptikti nepavyko.

Ginamieji teiginiai

1. Dažniausia vaikų alpimo priežastis yra refleksinė vazovagalinė sinkopė.
2. Aktyvus ortostatinis testas – tai efektyvus tyrimo būdas vaikų alpimui simuliuoti ir sinkopės hemodinamikai tyrinėti
3. Ortostatinio testo rezultata, o taip pat ir sinkopės mechanizmą galima patikimai prognozuoti dar vaikui nepraradus sąmonės.

Tyrimo metodika

Pacientai. I grupė (tiriamoji) – tai 214 ne mažiau nei tris kartus alpusių, židininė neurologijos simptomatikos ir diagnozuotų lėtinių nervų sistemos ligų neturinčių

ligonių: 140 (65 proc.) mergaičių ir 74 (35 proc.) berniukai, kurių amžiaus vidurkis $13,08 \pm 2,881$ metų. II grupė (kontrolinė) – tai 92 niekada nealpę, neturintys ūminės ligos simptomų ir diagnozuotų lėtinių ligų vaikai: 59 (63 proc.) mergaitės ir 33 (37 proc.) berniukai, kurių amžiaus vidurkis $12,64 \pm 3,044$ metų.

Alpimu laikyta trumpalaikis sąmonės netekimas su vertikalaus kūno tonuso praradimu, kuris horizontalioje padėtyje praėjo savaime netaikant jokių vaiko gaivinimo priemonių.

Tyrimas atliktas dviem etapais. I – detaliai surinkta anamnezė akcentuojant alpimo aplinkybes (tipinės refleksinės ir atipinės), įvertintas pacientų fizinis išsivystymas pagal procentiles, pacientui matuotas ir vertintas arterinis kraujospūdis, skaičiuotas ir vertintas širdies susitraukimų dažnis ramybėje, įvertintos organų sistemos objektyvaus tyrimo metu. Laboratoriniuose tyrimuose vertinta ir lyginta hemoglobino kiekis kraujyje, glikemija ir kraujo įsotinimas deguonimi. Kiekvienam pacientui atlikta ir įvertinta elektrokardiograma ir echokardioskopija. II – pirmojo etapo metu ekskludavus širdies ir nervų sistemos ligas, 205 pacientams atliktas ortostatinis mėginys, kurio metu registruota elektrokardiograma ir stebėtas arterinis kraujospūdis. Hemodinamikos rodikliai vertinti ramybėje, po ortostazės (bazinis), maksimaliai padidėję vertikaloje padėtyje (kompensacijos), atsiradus nusiskundimams (pirmųjų skundų), alpimo ir horizontalioje padėtyje atgavus sąmonę ir atsistačius hemodinamikai (atsistatymo).

Statistinė analizė

Duomenys buvo kaupiami Microsoft Excel 2000 ir 2003 lentelėse. Požymių dažnis grupėse suskaičiuotas procentais. Vertinti ir lyginti hemodinamikos rodiklių vidurkiai su standartiniais nuokrypiais. Gauti duomenys apdoroti Microsoft Excel 2003 ir SPSS v.17 demo statistiniais paketais. Skirtumas laikytas reikšmingu, kai $p < 0,05$. Skirtumo tarp tolydžių požymių įvertinimui, kai lygintos dvi grupės, naudotas Stjudento kriterijus t , kai lygintos daugiau nei 2 grupės – F (ANOVA), procentai - χ^2 .

Pagrindiniai rezultatai

I tyrimo etape nustatyta kad alpstantys vaikai pagal fizinį išsivystymą statistiškai reikšmingai nesiskiria nuo nealpusių savo bendraamžių. Dažnai alpstantys vaikai turi patikimai žemesnį arterinį kraujospūdį ir mažesnį širdies susitraukimų dažnį nei kontrolinės grupės vaikai. Tyrimo metu nenustatyta žemesnio hemoglobino kiekio

kraujyje, kraujo glikemijos ir įsotinimo deguonimi įtakos alpimams. Atliekant 12 derivacijų paviršinę elektrokardiogramą patologijos aptikta 16,35 proc. tirtųjų. Šio tyrimo jautrumas diagnozuojant širdines vaikų sinkopes buvo labai aukštas ir siekė 88,9 proc. Ultragarsinio širdies tyrimo jautrumas diagnozuojant širdines vaikų sinkopes buvo 44,4 proc. Abu šie tyrimai statistiškai patikimai jautrūs vaikų širdinei sinkopei diagnozuoti: elektrokardiograma ($p < 0,001$; $\chi^2 = 36,13$), echokardioskopija ($p < 0,02$; $\chi^2 = 6,07$). Tačiau mūsų tiriamojoje grupėje nebuvo nei vieno paciento, kuriam širdinė sinkopės priežastis aptikta ir nustatyta atliekant ultragarsinį tyrimą, - visiems ligos pasireiškė objektyvaus tyrimo ir elektrokardiogramos metu.

II tyrimo etape, pacientams, kuriems I etape nebuvo nustatyta ar pagrįstai įtarta širdies ir nervų sistemos ligų (205) atlikti ortostatiniai testai. 72 pacientams atliktas pasyvus, 134 – aktyvus testas tiriamojoje grupėje, 40 pasyvus, 52 aktyvus – kontrolinėje grupėje. Pacientų pasiskirstymas pagal lytį, amžių bei ortostatinių testų dažnį abiejose grupėse statistiškai patikimai nesiskyrė. Ortostatinių testų rezultatyvumas tarp grupių statistiškai patikimai skyrėsi ($p = 0,000$; $\chi^2 = 56,6$), t.y. alpusiems jis statistiškai patikimai dažniau teigiamas nei sinkopių neptyrusiems. Ortostatinio testo tarp alpusių vaikų rezultatai: 147 teigiamos (103 vazovagalinės (47 – vazodepresinės, 18 – kardioinhibicinių, 38 – mišrios), 43 – būdingos posturalinės ortostatinės tachikardijos sindromui ir 1 – būdinga ortostatinei sinkopei) ir 58 neigiamos (54 – būdingos normaliai hemodinamai, išprovokuota 1 supraventrikulinė paroksizminė tachikardija, gautos 3 psichogeninės reakcijos be hemodinamikos pokyčių). Bandant prognozuoti ortostatinio testo rezultatus, skaičiavimus suskirstėme į dvi dalis. Pirmojoje pagal amžių, lytį, alpimo dažnį ir aplinkybes bandėme prognozuoti teigiamą ir neigiamą testo rezultatą. Vertinant gautus rezultatus galima teigti, kad anamnezės duomenys statistiškai patikimai nenulemia ortostatinio testo baigties. Tačiau tipinės refleksinės alpimo aplinkybės yra statistiškai patikimai dažniau aptinkamos neširdinių sinkopių, o netipinės – širdinių sinkopių patiriantiems vaikams ($p = 0,000$; $\chi^2 = 28,96$). Ortostatinio testo atsako mechanizmų taip pat nepavyko statistiškai patikimai prognozuoti vertinant paciento amžių, lytį, fizinį išsivystymą, alpimo anamnezės duomenis. Tačiau nustatėme, kad kiekvienam testo atsako, o tuo pačiu ir sinkopės mechanizmui jau ankstyvosiose stadijose būdinga savita hemodinamikos rodiklių kaita. Ortostazės metu šie pokyčiai atskiruose mechanizmuose skiriasi statistiškai nereikšmingai, tačiau sinkopės

mechanizmą galima patikimai prognozuoti dar pacientui nepasiskundus savijautos blogėjimu.

Išvados

1. Dažniausia vaikų alpimo priežastis yra refleksinė vazovagalinė sinkopė. Pagal dažnį alpimo priežastys išsidėstę taip: vazovagalinė sinkopė, nepatikslintos etiologijos sinkopė, posturalinės ortostatinės tachikardijos sindromas, kardiogeninė sinkopė ir pavieniai ortostatinės sinkopės ir psichogeninės pseudosinkopės atvejai.
2. Efektyviausi tyrimai vaiko sinkopės priežastiai nustatyti yra teisinga anamnezė, išskiriant alpimo aplinkybes, nuodugnus objektyvus ligonio tyrimas skaičiuojant ŠSD, matuojant AKS ir auskultuojant širdį, 12 derivacijų paviršinė elektrokardiograma ir ortostatinis testas. Mažiausiai efektyvūs – ultragarsinis širdies tyrimas, ilgalaikė elektrokardiogramos stebėseną ir veloergometrija, todėl juos tikslinga atlikti tik pagrįstai įtarus širdinę patologiją pirmame tyrimo etape.
3. Lyginant pasyvų stalo pakėlimo ir aktyvų ortostatinį testą, kaip tyrimo būdą sinkopei imituoti ir hemodinamikos pokyčiams jos metu nagrinėti, statistiškai reikšmingo jų skirtumo šio tyrimo metu nenustatyta.
4. Dažniausias alpstančių vaikų ir paauglių alpimo mechanizmas, sukeltas ortostatinio testo metu, – tai vazodepresinė vazovagalinė sinkopė. Mechanizmas tarpusavyje statistiškai patikimai skiria arterinio kraujospūdžio ir širdies susitraukimų dažnio pokyčiai ortostatinio testo eigoje.
5. Alpimo mechanizmui statistiškai patikimai prognozuoti pakanka įvertinti hemodinamikos rodiklių kaitą iki kompensacijos fazės pabaigos.

Trumpa disertanto biografija

Odeta Kinčiniienė gimė 1967 metų gruodžio 3 dieną Kauno rajone. 1993 metais baigė Vilniaus universiteto Medicinos fakulteto Pediatrijos programos studijas. 1996 metais baigė Vilniaus universiteto Podiplominių studijų Vaikų gydytojo rezidentūrą ir įgijo gydytojo-pediatro profesinę kvalifikaciją. 1998 metais baigė Vilniaus universiteto Medicinos fakulteto Podiplominių studijų Vaikų kardiologijos rezidentūrą ir įgijo gydytojo vaikų kardiologo profesinę kvalifikaciją. Nuo 1998 metų rugsėjo 15 dienos dirba Vilniaus universiteto Medicinos fakulteto Vaikų ligų klinikos asistente, nuo 2002 metų – Vilniaus miesto universitetinės ligoninės gydytoja vaikų kardiologe. Odeta Kinčiniienė ištekėjusi, augina sūnų.

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SHORT INFORMATION ABOUT DISSERTANT

Odeta Kinčiniene was born in Kaunas district, on 3 of December 1967. In 1993 she graduated Pediatric program in Vilnius University Medical Faculty. 1996 graduated residency studies in general pediatrics and was gained a Pediatrician's qualification. 1998 Odeta Kinčiniene graduated from residency in Pediatric Cardiology and was gained a Children cardiologist's qualification. Since 1998 she works as assistant in Vilnius University Medical Faculty Clinic of Children Diseases. Since 2002 she works as children cardiologist at Vilnius City University Hospital. Odeta Kinčiniene is married and has one child.