Original paper

The analysis of anamnesis and the hemodynamic response in tilting patients with recurrent syncope

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Abstract

Introduction: Vasovagal syncope (VVS) constitutes 70% of all unexplained syncope. In this group of patients (pts.) the head-up tilt test (HUTT) is a basic diagnostic method. The aim of the study was the analysis of anamnesis and of noninvasive hemodynamical parameters (heart rate and blood pressure) in tilting patients with recurrent syncope.

Material and methods: 170 patients (pts.) with history of recurrent syncope enrolled in the research. The control group comprised 19 healthy volunteers. In all the anamnesis with the specific data of syncope and HUTT in the Westminster protocol prolonged by nitroglycerin provocation were performed. All pts. were divided into the following groups according to the HUTT outcome: positive HUTT (I group) N=129; mean age 50.6±17.8 yrs, 0.37 males; and negative HUTT (II group) N=41; mean age 50.0±18.3 years, 0.56 males. In the multivariate approach the logistic regression analysis was used to identify from anamnesis and noninvasive hemodynamic parameters the most predictive factor of the positive HUTT.

Results: The HUTT explained vasovagal origin of syncope in 129 pts. (76%) of the study group. Group I noted a significant increase in: the number of syncopes, the prodromal symptoms ($p<0.05$) and typical vasovagal anamnesis ($p<0.00000$) in comparison to group II. The noninvasive analysis of blood pressure (RR) during the HUTT showed significant differences between the analyzed groups, especially in vasodepressor pts. A significantly lower heart rate was noted in pts. with the cardiodepressive reaction than in pts. with the vasodepressive reaction during the HUTT. In the multifactors analysis the highest sensitivity to positive outcome of the HUTT had the presence of typical vasovagal anamnesis (OR 5.85; 95%CI; 2.72-12.56, $p<0.00001$).

Conclusions: The only parameter, permitting to foresee the positive result of the HUTT was typical of vasovagal syncope anamnesis. Noninvasive estimation of hemodynamical parameters showed disturbances in response to the tilting and did not permit to univocally prognosticate the HUTT outcome.

Key words: vasovagal syncope, head-up tilt test, anamnesis, noninvasive evaluation in syncope.

Introduction

Syncope and transient loss of consciousness are the common clinical problems [1]. The patients with syncope are a heterogeneous group, and the paroxysmal character of the diseases causes that the diagnostic process is difficult and complicated. Anamnesis and physical examination with the rest ECG, blood pressure measurement in the supine and upright position are the basic elements of initial investigation. In patients

(pts.) with syncope the head-up tilt testing (HUTT) is the gold diagnostic standard in the elucidation of causes of symptomatic hypotension and bradycardia [2]. Since its introduction by Kenny in 1986 [3] in clinical practice many different protocols of the HUTT have been used [4-7]. The complicated structure of neurally mediated reflexes caused that only a complex analysis of anamnesis and hemodynamic responses to the tilting seems to be the most adequate in this group of pts.

The aim of the study was the analysis of anamnesis and of noninvasive hemodynamical parameters in tilting pts. with recurrent syncope of unexplained etiology.

Material and methods

170 pts with history of repeated syncope were involved in the research and divided into the following groups according to the HUTT outcome: positive HUTT (group I) N=129; mean age 50.6±17.8 years, 0.37 males; and negative HUTT (group II) N=41; mean age 50.0±18.3 years, 0.56 males.

The control group (group III) comprised 19 healthy volunteers; mean age 49.8±17.9 years, 0.37 males. In all patients, the history was taken, especially with the data about syncope, typical vasovagal anamnesis (Table I) and coexisting diseases (Table II). Besides the physical examinations with blood pressure measurement were performed. The HUTT with Westminster protocol [4] (supine phase +45 minutes of passive tilting, angle 60 degree) was made in the morning, with the patient fasting in a darkened room, using the mechanical tilt table SP-1 with a foot support and straps. If syncope did not occur in the passive phase of the HUTT, it was followed by a 20-min pharmacological phase after the administration of sublingual nitroglycerin 400 µg in aerosol. The results were considered positive in the case of syncope or presyncope associated with marked reduction of the blood pressure and/or heart rate, according to the type of VASIS (Vasovagal Syncope International Study) reaction [8]. There are three general types of response to the tilting:

- VASIS 1-type – mixed, cardiovascular with hypotension and bradycardia,
- VASIS 2-type – cardioinhibitory with significant bradycardia and/or asystole,
- VASIS 3-type – vasodepressor with hypotension without bradycardia.

During the HUTT a noninvasive estimation of the following hemodynamical parameters:

1) systolic (SBP) and diastolic blood pressure (DBP) using an automatic sphygmomanometer,
2) heart rate in R-R interval (msec.) was made.

All the patients and normal controls gave their written, informed consent to the investigation. The study was approved by the local Ethics Committee.

A descriptive statistical analysis using the T-student's test, F-Snedecor test, Chi-square test, Cochran Cox test, Shapiro-Wilk's test, Mann-Whitney's test in the univariate analysis and multivariate logistic regression analysis was made. Two-sided p value <0.05 was considered as statistically significant.

Results

The positive outcome of HUTT was observed in 129 pts. (f=0.759), including 37 pts. during the passive phase (f=0.287) and in 92 pts. after NTG provocation (f=0.713) and in 3 subjects from the control group (0.158). According to the VASIS classification: mixed reaction (VASIS 1) was observed in 74 pts., cardiodepressive (VASIS 2) in 27 pts. and vasodepressive one (VASIS 3) in 28 pts.

The statistical differences between the analyzed groups in the number of syncope, typical vasovagal history and presence of prodromal symptoms were observed (Table II). In group I syncope was most frequently preceded by the common weakness

Table I. Data from history in the initial evaluation

1) number of syncope
2) duration of syncopal history
3) typical vasovagal anamnesis [9]: • short-term syncope with self-limited loss of consciousness • syncope induced by prolonged up-right position, blood, intense stress or pain • presence of prodromal symptoms • prolonged duration of weakness in the recovery period
4) prolonged duration of warning symptoms (exceeding 5 seconds) according to Calkins et al. [9]: • common weakness • warmth • epigastric discomfort • nausea • cold diaphoresis
5) circumstances just prior to syncope

Table II. Characteristics of the study group

	Group I	Group II	Group III
Number of patients [n]	129	41	19
Mean age [years]	50,6±17,8	50.0±18.3	49.8±17.9
Female [f]	0.63*	0.44*	0.63
Age of female [years]	17-79	20-76	23-64
Mean age of female [years]	46.5±18.4	44.7±19.1	45.4±18.9
Male [f]	0.37*	0.56*	0.37
Age of male [years]	20-84	24-81	24-57
Mean age of male [years]	57.6±14.5	54.2±16.8	53.2±16.4
Coronary artery disease [f]	0.39	0.39	–
Hypertension [f]	0.21*	0.38*	–
Diabetes [f]	0.07	0.08	–
Depression [f]	0.04	0.10	–
Number of syncopes	3.3±3.4*	2.1±2.6*	–
Duration of syncopal history [years]	7±10.5	8±16	–
Typical history	0.81**	0.12**	–
Prodromal symptoms	0.74*	0.49*	–

*$p<0.05$
**$p<0.00000$

(f=0.74) and/or warmth (f=0.66), while in group II by palpitations (f=0.32) and vertigo (f=0.17). In 104 pts. of group I (f=0.81) syncope occurred in typical vasovagal circumstances, whereas in group II only in 5 pts. (f=0.12) (Table II). This difference has a high statistical significance (p<0.0000).

In the analyzed phases of the HUTT in group II, a superior mean value of blood pressure in comparison to the control group and group I of pts. was observed. Between group I and III, exactly like between the VASIS groups, there were no significant differences in the mean value of blood pressure during the HUTT (Table III). The analysis of the changing of the systolic blood pressure (SBP) between the rest, tilting and the first 5 minutes of tilting showed an insignificant rise of SBP, connected with tilting, in the control group and group II, instead in group I, where SBP reduction was noted (Figure 1a), especially in pts. with vasodepressor reaction (VASIS 3) (p<0.01) (Figure 1b). For diastolic blood pressure (DBP) a significant rise (p<0.005), caused by tilting was observed in all analyzed groups (Figure 2a), excluding the VASIS 3 group (Figure 2b), where no significant differences were noted (p>0.05).

There were no differences in the heart rate (HR) measured by R-R interval between groups I, II and

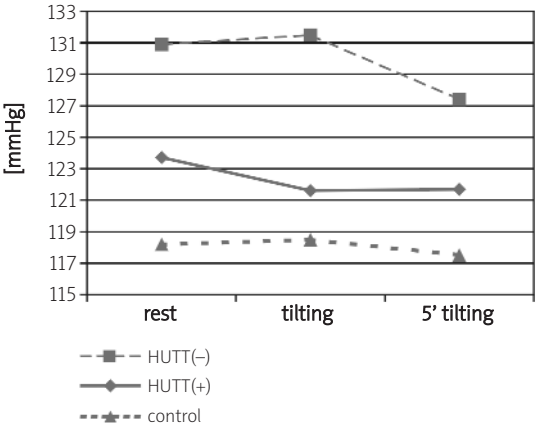

Figure 1a. The mean value of systolic blood pressure [mmHg] during the head-up tilt test

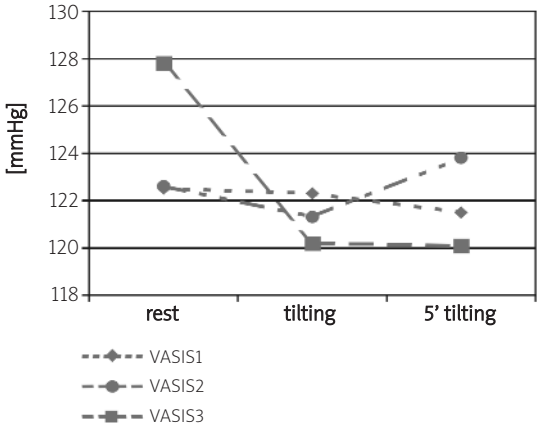

Figure 1b. The mean value of systolic blood pressure [mmHg] during the head-up tilt test

Table III. The mean value of systolic (SBP), diastolic (DBP) blood pressure and heart rate (R-R) during the following phases of the head-up tilt test (rest, tilting, 5' tilting)

	rest			tilting			5' tilting			
	SBP (mmHg)	DBP (mmHg)	R-R (msek.)	SBP (mmHg)	DBP (mmHg)	R-R (msek.)	SBP (mmHg)	DBP (mmHg)	R-R (msek.)	p
Group I	123.7±18.7	80.9±11.6	886.0±154.6	121.6±18.7	85.7±11.7	749.5±145.9	121.7±18.3	85.8±12.3	781.2±151.4	*
Group II	130.9±22.2	84.1±10.9	889.08±89.42	131.5±21.3	89.1±10.5	732.85±87.769	127.4±18.3	89.7±10.6	754.42±82.94	
GroupIII	118.2±5.9	78.1±4.3	889.1±89.4	118.5±9.5	82.1±4.6	732.9±87.8	117.5±5.1	82.2±5.2	756.7±81.4	***
p	*	*, **		**	*, **		*	*, **		
VASIS1	122.5±18.8	80.5±11.8	884.1±183	122.3±19.3	86.2±11.9	733.5±164.2	121.5±20.2	85.8±13.4	767.7±172.4	**
VASIS2	122.6±14.8	80.3±10.2	935.0±119.2	121.3±16.2	86.1±9.7	807.7±130.8	123.8±13.4	86.3±10.2	935.0±199.2	**
VASIS3	127.8±21.6	82.3±12.4	869.8±151.5	120.2±19.8	84.3±13.0	735.7±139.9	120.1±17.6	85.4±11.7	764.2±143.5	**
p			*		*		**			

SBP group I vs group II: *p<0.05 DBP group I vs group II: *p<0.05 R-R rest vs R-R tilting: *p<0.05 R-R VASIS2 vs VASIS3: *p<0.05
group II vs group III: **p<0.01 group II vs group III: **p<0.01 **p<0.001 **p<0.01
***p<0.005

Figure 2a. The mean value of diastolic blood pressure [mmHg] during the head-up tilt test

Figure 2b. The mean value of diastolic blood pressure [mmHg] during the head-up tilt test

III (Table III). During the HUTT a significantly lower value of HR was observed in the VASIS 2 group in comparison to the VASIS 3 and control group. The significant rise of HR related to the tilting was noted in all analyzed groups ($p<0.001$) (Figures 3a, 3b).

The multifactor analysis with the logistic regression method presented significant relations between the HUTT outcome and typical vasovagal anamnesis (OR 5.85, 95% CI; 2.72-12.56, $p<0.00001$). For these estimated values sensitivity of typical anamnesis amounted to 75%, specificity 66%, positive predictive value 87% and negative predictive value 54%. On the grounds of the data comparing the group of pts. with syncope and the control group sensitivity of the passive test amounted to 21.7%, specificity 94.7%, sensitivity of HUTT with NTG 75.8%, and specificity 84.2%. We also estimated the sensitivity and the specificity of HUTT in dependency of the presence of typical vasovagal anamnesis, obtaining respectively for the passive phase 67% and 75%, and for the active phase with NTG 83% and 54%.

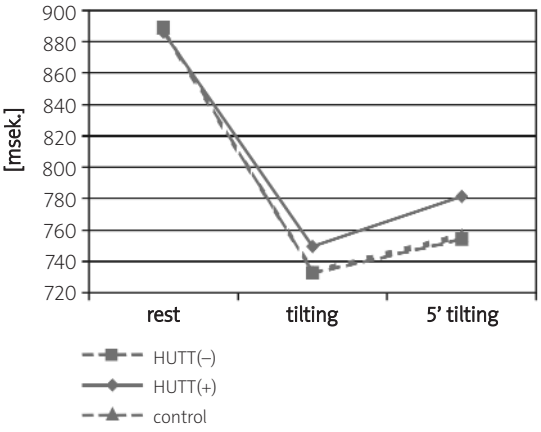

Figure 3a. The mean value of heart rate [msec.] during the head-up tilt test

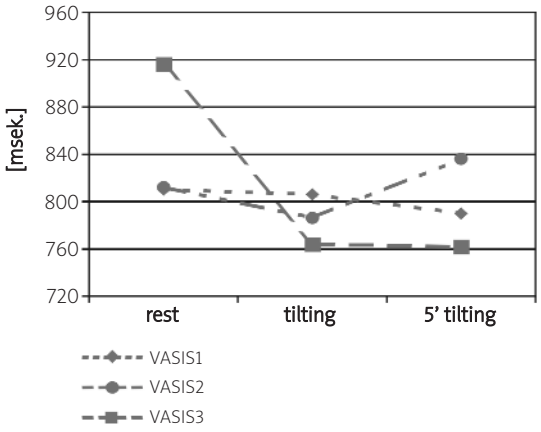

Figure 3b. The mean value of heart rate [msec.] during the head-up tilt test

Discussion

The difficulties of evaluation and comparison of patients with recurrent syncope result not only from their heterogenous structure, but also from the lack of the stricter definite diagnostic tests. However also in the instance of HUTT there are many controversial issues related with the angle of tilting, passive phase duration and using of pharmacological provocation [3-7]. Considering the best relation between sensitivity and specificity of the test, in our study we used, suggested by Fitzpatrick, the Westminster protocol [4], prolonged by pharmacological provocation with nitroglycerin [7].

In the research the relatively low sensitivity of the passive HUTT (22%) was obtained, but it was contained in the reported borders, however the total sensitivity of HUTT with NTG rose to 76%, which was similar to the data of Raviele et al. [7]. Specificity of the passive test was very high – 95%, and after the NTG use amounted to 84%. Reported differences could be related to the selection of the group.

Over the last few years special attention was paid to the value of history in evaluation of the patients with recurrent syncope with unexplained etiology [9-11]. Numerous publications caused that presence of the typical vasovagal anamnesis was included in the actual guidelines on management of syncope [12]. The pts. with the positive outcome of HUTT statistically more frequently registered typical circumstances and syndromes preceding the syncope in comparison to negative HUTT patients. On the grounds of the multifactor analysis with the logistic regression method, we documented that the presence of typical anamnesis augments 6 times the possibility of positive HUTT outcome.

Many authors analyzed the maintenance of the blood pressure and heart rate in reaction to the upright position during HUTT [13, 14]. On the basis of these observations it ascertained that tilting shows disturbances in the autonomic nervous system's homeostasis. No change or a limited reduction of the SBP and a progressive increase in DBP to tilting have been reported in normal subjects [15]. In this study the most expressive changes of blood pressure to the tilting in vasodepressor pts. were documented. Our study in connection to attainable data, confirms that series clinical and hemodynamical parameters do not permit to separate patients with vasovagal reaction from patients suffering from syncope. The presence of typical vasovagal anamnesis allows with high probability to foresee the positive head up tilt test outcome. The history evaluation is a cheap, rapid and noninvasive diagnostic method, as well in the older patients, especially with neurological history, performing the diagnosis on the basis of typical anamnesis, which allows to avoid complications connected with hypoperfusion of the central nervous system during provocation of syncope in HUTT. On the other hand, a substantial fraction of patients with negative results of all performed tests need extension of the diagnostic process, like implantable loop recorder ILR [16].

Conclusions

The only parameter, permitting to foresee the positive result of head-up tilt test was typical of vasovagal syncope anamnesis. Noninvasive estimation of hemodynamical parameters (heart rate and blood pressure) showed disturbances in response to the tilting and did not permit to univocally prognosticate of the tilt test outcome.

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