Efficacy of tilt training in patients with vasovagal syncope

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Abstract

Background: Besides pharmacological therapy and pacemaker implantation, tilt training is a promising method of treatment in patients with vasovagal syncope (VVS). Tilt training is usually offered to patients with malignant or recurrent VVS which impairs their quality of life and carries a risk of injury.

Aim: To assess the efficacy of tilt training in patients with VVS.

Methods: The study group consisted of 40 patients (29 females, 11 males, aged 36.6±14 years, range 18-57 years) who underwent tilt training using tilt table testing according to the Westminster protocol. The mean number of syncopal episodes prior to the initiation of tilt training was 6.5±4.9 (range 0-20); 3 patients had a history of very frequent faints. According to the VASIS classification, type I VVS (mixed) was diagnosed in 17 patients, type II (cardioinhibitory) in 22 subjects, and type III (vasodepressive) in one patient. Mean follow-up duration was 35.1±13.5 months. The control group, which did not undergo the tilt testing programme, consisted of 29 patients with VVS (25 females, 4 males, mean age 44.2±15.0 years) who had a mean of 3.3±3.2 (range 0-12) syncopal episodes in the past ($p < 0.05$ *vs* study group); 6 of these patients had only pre-syncopal episodes. Type I VVS was diagnosed in 23 controls and type II VVS in 6 control subjects (syncope occurred during the passive phase of tilt testing in 7 subjects, whereas the remaining 22 fainted during NTG infusion).

Results: Of the patients from the study group, 3 underwent pacemaker implantation at the time of the initiation of tilt training. At the end of follow-up, 31 (77.5%) patients remained free from syncope recurrences, 5 had syncopal episodes during the initial phase of tilt training, whereas the remaining 4 continued to suffer from syncopal episodes. Out of 3 patients with presyncope, 2 had no syncope recurrences whereas 1 patient continued to have presyncopal attacks. Out of 3 patients with pacemakers, 1 reported activation of pacing in the interventional mode. During the follow-up period, in 5 patients from the study group the diagnosis of VVS was not confirmed and another condition was diagnosed. In the control group, syncope recurrences occurred in 13 (44.5%) patients ($p < 0.05$ vs study group).

Conclusions: In patients with VVS, tilt training is effective in the majority of patients. Syncopal or presyncopal episodes and positive results of tilt testing take place more frequently in the early rather than in the late phase of training. Cessation of tilt training causes a recurrence of positive results of tilt testing in spite of the lack of spontaneous syncopal episodes. During long-term observation, a proper diagnosis, different from VVS, can be established in some patients.

Key words: vasovagal syncope, tilt training

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Introduction

Initiation of the vasovagal reflex is a physiological reaction to the augmented adrenergic activity when, for several reasons, fight or escape are not possible [1]. However, under specific conditions vasovagal syncope (VVS) may be induced in the majority of subjects who do not faint during their normal life [2]. In patients with VVS syncope may be triggered by stimuli which are well tolerated in the general population. Vasovagal syncope, especially recurrent, preceded by short-lasting prodromal symptoms and associated with injury, significantly diminishes the quality of life because it causes profound changes in lifestyle and occupation as

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well as psychological discomfort. Therapy is usually needed for patients with such a condition [3].

Among the therapeutic approaches to a patient with VVS, tilt training, together with pharmacological treatment and pacemaker implantation, is one of the most important methods [3]. Because of the lack of randomised studies, the efficacy of tilt training has not yet been well established [4-6]. However, it can be implemented with only minimal costs, although it is really useful only in highly-motivated individuals and requires the presence of another person [7-10].

The idea of tilt training is based on the observation that proper adaptation to an upright body position occurs only when the frequency and magnitude of the orthostatic stimulus are adequate, whereas it disappears due to long-term immobilisation in a bed or when there is lack of gravitation [11, 12]. Temporary exposure to gravitational forces may be sufficient to prevent changes induced by weightlessness [13]. Practices during which exposure to gravitational forces is enhanced due to lower limb decompression and reduction of postural muscle tension may improve orthostatic tolerance.

The aim of our study was to assess the efficacy of tilt training, combined with pharmacological therapy or pacemaker implantation, in patients with VVS.

Methods

Patients

The study group, in which tilt training was implemented, consisted of 40 patients (29 females, 11 males, aged 36.6±14 years, range 18-57 years) with VVS (true syncopal episodes or frequent presyncopal spells), confirmed by tilt testing. The control group comprised 29 patients with VVS (25 females, 4 males, mean age 44.2±15.0 years) who did not undergo tilt training. A diagnostic tilt test was performed according to the Italian protocol with pharmacological provocation (400 µg of nitroglycerine) when the passive phase of the test was negative. Clinical characteristics of the studied patients are shown in Table I.

Tilt training

Tilt training was started in hospital in 80% of patients and was performed using repeated tilt testing according to the Westminster protocol (without pharmacological provocation). The sessions were interrupted in case of the occurrence of prodromal symptoms of syncope. Hospital training was followed by home sessions which consisted of the assumption of an upright position against the wall (distance between the back and wall ranging between 15 and 20 cm) for 30 minutes. Patients were instructed to perform training at a place where there was no risk of injury in case of syncope occurrence and to stop a session when prodromal symptoms occurred. The presence of another person, assisting the patient, was required.

In the remaining 20% of patients tilt training was started at home, initially as 15-minute sessions which were gradually extended to 30-minute sessions.

All patients, from both the study and the control groups, were instructed to avoid situations which might provoke syncope, to increase fluid intake and, in those without hypertension, to increase salt intake. The decisions to implement other treatment such as beta-blockers, fludrocortisone or pacemaker implantation, were left to the discretion of the attending physicians, both after first examination in the hospital and during follow-up.

Follow-up

The mean duration of follow-up was 35.1±13.5 months. An interim analysis of adherence to the tilt training protocol was also performed 18.0±6.8 months after the initiation of training.

During follow-up, patients were asked about syncope recurrences, adherence and continuation of tilt training, mean frequency of training, tolerance of training, pharmacological treatment and other significant changes in health condition. Some patients underwent repeated tilt testing according to the Westminster protocol. In the control group the syncope recurrence was determined after 18.0±4.3 months of follow-up.

Statistical analysis

The results are presented as mean ± one standard deviation or numbers and percentages. Qualitative variables were compared using χ^2 and quantitative variables using Student's t-test or U Mann-Whitney test, depending on data distribution. A p value <0.05 was considered significant.

Results

All patients were instructed how to avoid syncope. Other therapies during follow-up are listed in Table II.

During follow-up, nine patients from the study group reported at least one syncopal episode. Five patients experienced only one faint whereas the remaining four patients reported two, three, four and more than 10 syncopal episodes, respectively. Out of three patients with frequent presyncopal episodes at baseline, two remained free from symptoms during follow-up whereas one had recurrences. Out of three patients with a pacemaker implanted, one experienced a single episode of syncope.

Table I. Demographic and clinical characteristics of the studied and control groups

	Study group	Control group	p
Number of patients	40	29	(-)
Females/males	29/11	25/4	NS
Age (years)	36.6±14.0	44.2±15.0	>0.05
Number of syncopes in the past	6.5±4.9 (range 0-20)	3.3±3.2 (range 0-12)	>0.05
Presyncope only	3	6	NS
Tilt testing results:			
Syncope during passive phase	12	7	NS
Syncope during NTG	28	22	NS
Type of VVS (VASIS I/II/III)	17/22/1	23/6/0	<0.05

Abbreviations: NTG = nitroglycerine; VVS = vasovagal syncope

Propranolol was administered, permanently or temporarily, in seven patients. Syncope recurrences were significantly more frequent in patients receiving propranolol than in patients without pharmacological therapy (100 *vs* 6%, p<0.001). Demographic and clinical parameters of patients with or without syncope recurrences during follow-up are presented in Table III.

Table II. Treatment in the study and control groups

	Study group	Control group	p
Tilt training only	29	–	(–)
Propranolol	7	5	NS
Fludrocortisone	2	–	NS
Pacemaker	3	2	NS

Table III. Comparison of demographic and clinical data between patients from the study group with or without syncope recurrences during follow-up

	With syncope recurrence	No syncope recurrence
Age (years)	38.7±14.3	37.4±18.7
Females /males	6/3	24/7
Number of syncopal episodes in the past	9.0±5.6*	4.3±3.8
Time to the first syncope recurrence (months)	7.9±4.9 (range 1-18)	–

** p <0.05 vs patients without syncope recurrence*

In the control group, 13 (44.5%) patients experienced syncope recurrences (p <0.05 *vs* study group), including 12 patients with type I VVS and one patient with type II VVS. Out of the patients with a history of presyncopal episodes, syncope recurrences during follow-up occurred in two subjects. Out of two patients with a pacemaker implanted, one fainted during follow-up. Among five patients receiving propranolol, three had syncope recurrences. A comparison of the number of patients from the study and control groups who experienced syncope recurrence during follow-up is presented in Figure 1.

During follow-up, the diagnosis of VVS was not confirmed in five patients from the study group: two patients suffered from depression, one was diagnosed with disseminated sclerosis, one with epilepsy, and another one with psychogenic syncope. After 18.0±6.8 months of follow-up, tilt training was continued systematically by nine patients and sporadically by 10 subjects, 19 patients stopped tilt training and data on the remaining two patients were not available. Four

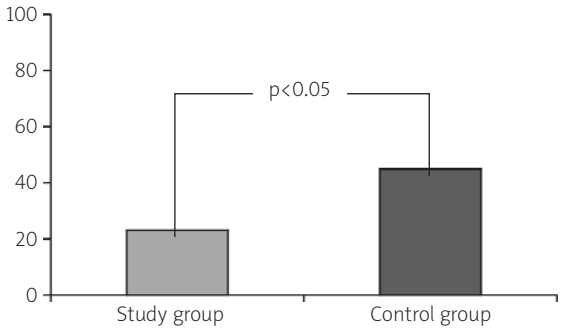

Figure 1. Comparison of the proportion of patients with syncope recurrences during follow-up between the study and control groups

patients reported weakness during tilt training sessions and in three of them repeated tilt testing revealed dysautonomic reaction. Analysis performed after exclusion of the patient with psychogenic syncope showed that out of eight patients with syncopal recurrences, only two (25%) continued tilt training on a regular basis compared with 7 (25%) of the remaining 31 patients (NS). During the further follow-up period (35.1±13.5 months) tilt training was systematically performed by six subjects, including one female who experienced four syncopal recurrences during follow-up. The most frequent reason for interrupting tilt training was the disappearance of syncopal episodes. Other causes, especially reported by patients with syncopal recurrences, included lack of time, lack of availability of another person assisting in tilt training, fatigue or bad feeling associated with training.

Discussion

To date, no effective method preventing syncope episodes in all patients with VVS has been established. The patient's reassurance about the benign nature of this condition, advice to avoid situations provoking syncope and to increase water and, in some patients, salt intake, as well as early recognition of prodromal symptoms, are effective in a significant proportion of patients [3]. Because of the physiological nature of the vasovagal reflex, it is difficult to identify a specific factor responsible for a temporary increase in syncopal spells in a given patient. This is the argument against the implementation of irreversible or difficult to reverse therapeutic procedures such as pacemaker implantation.

Tilt training, introduced by Ector et al., is currently the most promising prophylactic method in patients with VVS [4]. The physiological nature of tilt training has to be stressed - a patient is subjected to an orthostatic stress associated with a partial decrease in skeletal muscle tension which further diminishes venous return in the presence of gravitational forces. The patient's emotional adaptation to an upright posture and the psychological impact of training are also important because they diminish the adrenergic reaction to the orthostatic stress. Not all beneficial effects of training should however be attributed to psychotherapy, because the effects of tilt testing on activation of the renin-angiotensin-aldosterone system have also been documented [14].

Data from the literature suggest a high efficacy of tilt training, usually exceeding 75% [7-10, 15]. When analysing the efficacy of tilt training, characteristics of the studied patients have to be taken into account. The number of syncopal episodes in the past and the recurrence of spontaneous syncope following positive tilt testing are the strongest factors predicting syncope recurrences in the future [16, 17]. In our study, nine patients who experienced syncope recurrences during follow-up had a history of at least two syncopal spells. After acknowledging the fact that one subject probably had psychogenic syncope, syncope recurrences occurred in eight of 31 patients with at least two faints in the past, which accounts for 25% of the studied group. According to Sheldon et al., the probability of syncope recurrences during two years in this group of patients is 49% [17].

Out of eight patients with VVS, who had positive tilt testing results, three (38%) continued to experience syncopal episodes during follow-up. Malik et al. showed that out of 46 patients with positive tilt testing with the use of isoprenaline, as many as 40 patients had symptom recurrence during a mean follow-up of 48±14 months [16]. Taking into account their results, our data suggest a high efficacy of tilt training in patients with VVS. It raises hopes that after a shorter or longer period of tilt training the majority of patients will resume normal daily activities without fear of fainting, provided that they follow the instructions on how to behave when prodromal symptoms occur. It should also be stressed that in case of syncope recurrence a patient will know that he or she may resume tilt training which will probably be effective.

A high recurrence rate of syncopal episodes in the control group may be explained by the lack of positive effects of tilt training, which was not implemented in this group. These patients had a lower number of syncopal episodes in the past than the study group patients, and thus the recurrence rate during follow-up was expected to be higher in controls. However, this was not the case in our study, which suggests that tilt training is effective in preventing syncope recurrences.

It should be stressed that the reduction of the syncope recurrence rate was not due to the beta blocker therapy, because all patients receiving propranolol continued to have syncopal episodes during follow-up. The number of patients who received a pacemaker or were treated with fludrocortisone is too small to draw any conclusions. Although some studies suggested that beta blockers are effective in patients with VVS, the majority of randomised studies have failed to confirm these initial findings [18]. Thus, the lack of effects of propranolol in patients with VVS undergoing tilt training documented in our study is not surprising, although the number of treated patients was small and the treatment was not randomised, which preclude proper analysis. It may be speculated that either the drug increased the risk of syncope recurrences or those treated with beta

blockers were the most susceptible to syncope recurrences and the drug was not effective [19].

The estimation of time from a positive tilt test to the first syncope recurrence has a significant clinical value because it allows further risk of syncopal episodes to be predicted. Out of nine of our patients who developed syncope following a positive diagnostic tilt test, in eight (including one with no true syncope) syncopal episodes occurred within 12 months after the diagnostic tilt test whereas only one patient fainted later - 18 months after inclusion in the study. According to Sheldon et al., the risk of syncope recurrence after two years in various groups, identified based on the number of faints in the past, was approximately 30% higher than during the first year [17]. In our study, the risk of syncope recurrence after two years was higher by 12% compared with the risk during the first year. The comparison of the time from a positive diagnostic tilt test to the first syncope recurrence between our and other studies is not always possible due to the lack of precise data in some reports or due to the fact that some authors presented only mean or median values. The mean time to the first syncope recurrence in the SYNPACE study in a subgroup of patients who did not undergo pacemaker implantation was 20 days during the mean follow-up duration of two years, with a minimum follow-up of four months [20].

The median time to the first recurrence of a syncopal episode in the study of Madrid et al. [18] was seven months (range 0-14.4 months). In the VPS study, this time was 54 days in patients not selected for pacing and 112 days in those who received a pacemaker [21]. In another study, Lafuente et al. found that the mean time from diagnostic tilt test to the first syncope recurrence was 4 months during a mean follow-up of 20 months [22]. The results of other studies as well as our findings suggest that, both in the study and in the control groups, the recurrence of syncope following positive tilt test takes place early rather than late during the follow-up period.

The motivation to continue tilt training mostly depends on the patient's attitude to this treatment. In our study, none of the patients who experienced syncope recurrence refused to continue training, whereas in the Foglia-Manzillo et al. study none of the patients who had syncope recurrence continued training [10].

The lack of difference in the rate of regular training between patients with or without syncope recurrence does not argue against tilt training efficacy, because these two groups significantly differed with respect to the number of syncopal episodes in the past. It shows rather what proportion of patients with VVS are willing to continue tilt training on a long-term basis. Such issues as the minimal duration of tilt training required to achieve therapeutic success and whether a patient should continue or stop tilt training in case of syncope recurrences have not yet been investigated.

In 12% of patients the initial diagnosis of VVS was not confirmed during follow-up and a new diagnosis of a neuro-psychiatric disorder was established. Similar findings have been reported by others [23]. These findings show that there is a need for careful follow-up in patients with syncope of unknown origin, because a diagnostic positive tilt test may be in fact a false positive result and proper diagnosis can be established during further observation.

One of the limitations of our study is that the control group was historical; however, treatment modalities, except tilt training, were similar in the study and in the control groups.

In conclusion, our study showed that tilt training is effective in a significant proportion of patients with VVS. Syncope recurs early rather than late during follow-up. In some patients, long-term observation is needed to establish proper diagnosis.

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Trening pionizacyjny w leczeniu chorych z omdleniami wazowagalnymi

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Streszczenie

U chorych na omdlenia wazowagalne (*vaso-vagal syncope*, VVS) trening pionizacyjny, obok farmakoterapii i implantacji układu stymulującego, stanowi podstawową metodę leczenia. Kwalifikowani są do niego chorzy z omdleniami o charakterze złośliwym i nawracającym, pogarszającymi jakość życia i stwarzającymi zagrożenie urazami.

Cel: Ocena skuteczności leczenia chorych z VVS programem ćwiczeń pionizacyjnych, łącznie z farmakoterapią i/lub wszczepieniem sztucznego stymulatora serca.

Metodyka: Grupę badaną stanowiło 40 chorych (29 kobiet i 11 mężczyzn) w wieku od 18 do 57 lat (średnio 36,6±14,0 lat), u których wdrożono program treningu pionizacyjnego. Średnia liczba omdleń przed testem diagnostycznym wynosiła 6,5±4,9 (zakres 0–20). U 3 chorych w wywiadzie występowały bardzo liczne zasłabnięcia. W badanej grupie typ I VVS wg klasyfikacji VASIS występował u 17 chorych, typ II u 22 chorych, typ III u 1 chorego. Czas obserwacji wynosił średnio 35,1±13,5 mies. Grupę kontrolną, w której nie stosowano treningu pionizacyjnego, stanowiło 29 chorych z VVS (25 kobiet i 4 mężczyzn) w wieku 44,2±15,0 lat. W wywiadzie chorzy podawali średnio 3,3±3,2 omdlenia ($p < 0,05$ *vs* grupa badana, zakres 0–12). U 6 chorych występowały jedynie zasłabnięcia. W trakcie testu pochyleniowego w grupie tej 7 osób zemdlało w fazie biernej, a 22 osoby po prowokacji NTG. U 23 z nich stwierdzono mieszany typ reakcji, a u 6 typ kardiodepresyjny.

Wyniki: W grupie badanej w czasie ćwiczeń stosowano test pochyleniowy (HUT) wg Protokołu Westminsterskiego. Trzem osobom wszczepiono stymulator serca i jednocześnie rozpoczęto leczenie treningiem pozycyjnym. Obecnie nie mdleje 31 (77,5%) chorych, 5 miewało omdlenia w początkowym okresie ćwiczeń, zaś u 4 chorych w dalszym ciągu utrzymują się utraty przytomności. Wśród 3 osób ze stanami przedomdleniowymi, u 2 dolegliwości ustąpiły całkowicie, u 1 występują nadal. Z 3 chorych ze wszczepionym stymulatorem serca, 1 podawała jego włączanie się w trybie interwencyjnym. W obserwacji odległej u 5 chorych z postawionym pierwotnie rozpoznaniem VVS rozpoznano inne schorzenia. W grupie kontrolnej wystąpienie omdlenia stwierdzono u 13 (44,5%) chorych ($p<0,05$ vs grupa badana).

Wnioski: U osób z VVS lub licznymi zasłabnięciami leczenie programem ćwiczeń pionizacyjnych w dłuższym okresie obserwacji wykazuje dużą skuteczność. W początkowym okresie leczenia częściej występują omdlenia, stany przedomdleniowe i dodatnie wyniki kontrolnych HUT niż w okresie późniejszym. Przerwanie programu ćwiczeń prowadzi do ponownego występowania dodatnich HUT pomimo utrzymywania się dobrego efektu klinicznego. Długotrwała obserwacja chorych pozwala na postawienie pełniejszego rozpoznania.

Słowa kluczowe: omdlenia wazowagalne trening pionizacyjny.

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