Original Article

Nonpharmacologic Treatments Alone are Enough to Prevent the Neurally Mediated Syncope: A 3 Years Follow-up Study

Abstract

Background: Recurrences are common in neurally mediated syncope. The aim of this study is the evaluation of the effectiveness of nonpharmacologic treatments alone in preventing of syncope relapse. **Methods:** 70 patients (age 5–20 years) with neurally mediated syncope were enrolled. Thirty patients received pharmacologic therapies along with nonpharmacological methods, and 40 patients received just nonpharmacological treatments then followed them for 36 months. The incidences of different outcomes were analyzed with descriptive statistics using percentages. **Results:** The recurrence rate of syncope was significantly higher in pharmacological group than in nonpharmacological group in each period of the follow-up ($P < 0.001$). **Conclusions:** Nonpharmacologic treatment is very effective in the prevention of syncope relapses and can be a substitute for pharmacologic drugs in the initiation of treatment and if done correctly.

Keywords: *Neurally mediated syncope, nonpharmacological treatment, recurrence*

Bahar Dehghan, Mohammad Reza Sabri, Marjan Mansourian

Pediatric Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction

Neurally mediated syncope is a benign cause of syncope, but recurrences are common.[1-5] Management should be directed to the underlying cause.[1] They should avoid situations that may trigger syncope such as long-standing, any painful stimuli, watching, or experiencing medical procedures.[6-8]

Medical treatment options include vagolytic drugs, beta-blocking agents, fludrocortisones, serotonin reuptake inhibitors, alpha agonists, and midodrine.[9,10] With nonpharmacologic methods, the patients are trained to increase the daily water and salt intake and perform tilt training to improve venous return.[6]

The aim of this study is the evaluation of the effectiveness of nonpharmacologic treatment in preventing of syncope relapse.

Methods

The study was approved by our Local Ethics Committee, and all the subjects received written informed consent before any procedure was initiated.

We performed a cross-sectional study on 30 patients (13 males and 17 females) and 40 patient (18 males and 22 females), all with unexplained syncope which were matched in age, sex, and body mass index. Our patients in the first group received medical drugs along with nonpharmacologic methods and were named as pharmacologic group (Ph.G) and patients in second group received no pharmacologic drugs (NPh.G).

All patients with age 5–20 years referred to the outpatient clinic of cardiology hospital between August 2013 and 2014 for evaluation of syncope. After taking history and physical examinations, the presence of neurally mediated syncope in all patients was confirmed with head up tilt table test.

Patients with a history of seizure, abnormal physical examinations, abnormal electrocardiography, electroencephalography or echocardiography, and psychologic problems and whose tilt test was not positive or had any associated diseases which had influence on their diagnoses were excluded from the study.

All patients in Ph.G received both nonpharmacologic and pharmacological treatments according to their type and pathophysiology of neurally mediated syncope. In this group, 19 patients received atenolol (1 mg/kg/24 h), and

How to cite this article: Dehghan B, Sabri MR, Mansourian M. Nonpharmacologic treatments alone are enough to prevent the neurally mediated syncope: A 3 years follow-up study. Int J Prev Med 2019;10:69.

Address for correspondence:
Prof. Mohammad Reza Sabri, Pediatric Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: sabri@med.mui.ac.ir

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_386_17

Quick Response Code:

11 patients received fludrocortisone (0.1 mg/day) at first visit after positive tilt test. For those did not respond to these medications, their drugs changed to midodrine hydrochloride (5 mg twice daily). Another group (NPh.G) was considered for just nonpharmacologic methods include education and reassurance regarding the benign nature of the condition, awareness, and possible avoidance of triggers (e.g., hot, crowded environments, and volume depletion), having a suitable diet with added salt and water, early recognition of prodromal symptoms, and performing maneuvers to abort the episode (e.g., supine posture, physical counterpressure maneuvers), and tilt training.

Tilt training

For standing training at home, under the supervision and accompanied by at least one of the family members, the patients were instructed to stand with their feet 15 cm away from the wall and lean with the upper back against the wall. During the 1st week, the patient performed this exercise for 2 min daily without any motion, the test continued to 4 min standing daily for 2nd week, and it was increased 2 min every week until the patient could stand 15–20 min continuously and no symptom of syncope occurred.

If the patient could not tolerate this training at every stage, the test continued with the last stage in which the patient was able to do and increment continued in slower rate.

Outpatient clinic visits were planned for both groups, 1 month after tilt test and then every 3 months for 1st year and then every 6 months for 2nd year and then yearly after the first visit. We followed our patients for 36 months both by visiting in clinic and telephone.

Statistical analysis

The incidences of different outcomes were analyzed with descriptive statistics using percentages. Statistical analysis was done with Chi-square test, and $P < 0.05$ was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 22.0 (IBM Co., Armonk, NY, USA).

Results

Table 1 summarizes baseline characteristics of the included subjects.

Of the 30 patients in Ph.G, 19 received atenolol. Fourteen patients could stop their therapy as did not have recurrent attacks of syncope in their follow-up period. Three patients had episodes of recurrent syncope on 1st year and presyncope during the 2nd years of follow-up and are still on atenolol. In two patients attacks of syncope did not controlled with atenolol, and the treatment changed to midodrine hydrochloride after the 1st year of therapy. Their syncope is now under control with continuation of midodrine. Among 11 patients who were taken fludrocortisone, two patients had episodes of syncope during the 1st year with presyncope during the 2nd year of follow-up and still continue their therapy, and in another 1 patient, the drug changed to midodrine after the 1st year of therapy. She is under control now and continues her therapy. Table 2 shows the rate of consideration of nonpharmacological recommendations in this group.

All patients in NPh.G received no medication. Of 40 patients, three patients did not follow their diet, and eight patients did not continue their home tilt training, on the first 3 months. All patients followed their diet after 6 months, but four subjects did not continue their home tilt training. At the end of our study, all of them follow their diet and tilt training. All of the patients are educated to continue their diet and tilt training for a long time [Table 3]. Table 4 shows the comparison of relapse of syncope in both groups during 3 years follow-up.

In our NPh.G, seven patients had episodes of syncope, and four had presyncope symptoms on the first 3 months of treatment. Of seven patients with syncope, five did not have performed the tilt training; two others had done it. Of four subjects who had presyncope, three did not have done tilt training, but one had done it. Patients, who did not follow their diet or tilt training, had more symptoms of vertigo, dizziness, and fatigue. After 6 months, one patient had 3 episodes of syncope whose attacks had triggered with stressful situations (university exams) and did not

Table 1: Baseline characteristics of case and control groups

	Pharmacologic group (*n*=30)	Nonpharmacologic group (*n*=40)	*P*
Age (year)	14.24±4.37	13.83±6.12	NS
Gender (male/female)	13/17	18/22	NS
BMI (kg/m^2)	21.32±5.24	20.93±6.86	NS

All variables reported as mean±SD. SD=Standard deviation, NS=Not significant, BMI=Body mass index

Table 2: The consideration rate of diet and tilt training in different periods of follow up by nonpharmacologic group

Period of time	Diet (%)	Tilt training (%)
First 3 months	87.5	82.50
3-6 months	100.0	87.50
6-12 months	100.0	90.00
2-3 years	100.0	95.00

Table 3: The consideration rate of diet and tilt training in different periods of follow-up by pharmacologic group

Period of time	Diet (%)	Tilt training (%)
First 3 months	76.7	36.7
3-6 months	83.3	76.6
6-12 months	80.0	66.7
2-3 years	96.7	63.3

follow his tilt training too. One patient had an episode of presyncope, and one had episodic vertigo although they had done their training and diet. At the end of our study, two little sisters had an episode of presyncope and syncope (each one of them) in school. They also had low tilt training and were encouraged to do it more regular and effective. Table 5 shows the comparison of the incidence of presyncope in both groups during 3 years follow-up.

Discussion

Our study showed that nonpharmacologic treatment alone is more effective than pharmacologic treatment in the prevention of syncope and can be substituted for medical treatments absolutely. Our results are comparable to those reported in the literature.

Several studies have shown that the pharmacological treatment of syncope, based on medications such as beta blockers, fludrocortisone, and serotonin reuptake inhibitors, does not offer effective results in the vast majority of adult patients.[11-14] In addition, several authors have described the efficacy of tilt training to increase the tolerance in orthostatic position in patients with neurally mediated syncope.[15,16]

Takahagi *et al*.[17] studied 21 patients with a history of recurrent nonmotor symptoms (NMS) who were randomized into trained group and control group. The trained group received positive results from physical training (72.7% had a negative head-up tilt table test after intervention), with a significant increase in peak oxygen consumption. The control group did not show any statistically significant change during the follow-up period.

Romme *et al*.[18] showed that in patients with frequent recurrences of NMS, nonpharmacological treatment has a beneficial effect on both recurrence and quality of life. In their study, the recurrence rate was reduced in the 1st year of nonpharmacological treatment, but nearly half of their patients still experienced episodes of syncope. A higher rate of syncope before treatment was significantly associated with recurrence.

We learned that the effectiveness of nonpharmacologic prevention depends on its regular and proper implementation and also should continue for a long time. The episodes of syncope decreased more in those who had paid attention to our recommendations. In addition, the rate of success in preventing the syncope relapse was significantly higher in those who received just nonpharmacological treatments. It seems the association of nonpharmacologic and pharmacologic treatments in our Ph.G led to focus just on medications and did not pay attention to nonpharmacologic considerations properly.

In 2007, Gardenghi *et al*.[19] conducted a 4-month study about the impact of different therapeutic methods (moderate aerobic physical training, passive postural training, pharmacological treatment, and control) in patients with NMS and found that only aerobic physical training was effective in increasing arterial baroreflex sensitivity which improved vagal and sympathetic arterial baroreflex gain, but the other methods did not attain the same effects. In addition, they followed their patients weekly by telephone, and they understood that some patients may not point out all the reality in their reports. The authors also confess that a larger follow-up period should be considered.

Our study determined a recurrence rate of about 44% of syncope attacks in patients receiving medical therapies, but this rate was about 5% in non-Ph.G during 36-month follow-up.

In adults, in a long-term follow-up study by Kapoor *et al*.,[20] a recurrence rate of about 36%–43% has been reported during a 30-month follow up period. Similarly, a long-term follow-up study of children and adolescents with NMS by Kouakam *et al*.[21] has shown a recurrence rate of about 32% during a 46-month follow-up period. According to our knowledge, no similar study was done in children and adolescents to evaluate the syncope recurrence rate in patients received no medical treatments.

Limitations

We assessed syncope recurrence without pharmacologic therapy in 40 patients. It seems a larger study with more cases would be helpful.

Table 4: The comparison of relapse of syncope in different periods of follow up

Period of time	Nonpharmacologic group (%)	Pharmacologic group (%)	*P**
After first 3 months	12.5	66.6	<0.001
3-6 months	7.5	36.7	<0.001
6-12 months	5.0	53.3	<0.001
At the end of the 2nd year	0.0	50.0	<0.001
At the end of the 3rd year	0.0	16.0	<0.001

*P<0.05 sets as significant

Table 5: The comparison of incidence of presyncope in different periods of follow up

Period of time	Nonpharmacologic group (%)	Pharmacologic group (%)	*P**
After first 3 months	12.5	53.3	<0.001
3-6 months	7.5	70.0	<0.001
6-12 months	2.5	43.3	<0.001
At the end of the 2nd year	0.0	20.0	<0.001
At the end of the 3rd year	0.0	6.7	<0.001

*P<0.05 sets as significant

Conclusions

Our study showed that nonpharmacologic treatment is very effective in the prevention of syncope relapses and can be a substitute for pharmacologic drugs in the initiation of treatment and if done correctly.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Received: 01 Sep 17 **Accepted:** 13 Nov 17
Published: 17 May 19

References

1. Syncope (Fainting). American Heart Association; 9 June, 2017.
2. Benditt DG, Fahy GJ, Lurie KG, Sakaguchi S, Fabian W, Samniah N, *et al.* Pharmacotherapy of neurally mediated syncope. Circulation 1999;100:1242-8.
3. Gardenghi G, Hachul DS, Negrão CE, Sosa E. Neurocardiogenic syncope and exercise. Reblampa 2004;17:3-10.
4. Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, Benjamin EJ, *et al.* Incidence and prognosis of syncope. N Engl J Med 2002;347:878-85.
5. Bastos S, Scanavacca M, Darrieux F, Ludovice AC, Sosa E, Hachul DT. Clinical evolution of patients with neurocardiogenic syncope following discontinuation of specific therapy. Arq Bras Cardiol 2006;86:256-60.
6. Task Force for the Diagnosis and Management of Syncope, European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA), Heart Rhythm Society (HRS), Moya A, *et al.* Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J 2009;30:2631-71.
7. Brignole M. Diagnosis and treatment of syncope. Heart 2007;93:130-6.
8. Allen HD, Driscoll DJ, Shaddy RE. Feltes TF. Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adults. 7th ed. Philadelphia, PA 19103 USA: Lippincott Williams & Wilkins; 2008. p. 269-73.
9. Martin K, Bates G, Whitehouse WP. Transient loss of consciousness and syncope in children and young people: What you need to know. Arch Dis Child Educ Pract Ed 2010;95:66-72.
10. Sra J, Maglio C, Biehl M, Dhala A, Blanck Z, Deshpande S, *et al.* Efficacy of midodrine hydrochloride in neurocardiogenic syncope refractory to standard therapy. J Cardiovasc Electrophysiol 1997;8:42-6.
11. Madrid AH, Ortega J, Rebollo JG, Manzano JG, Segovia JG, Sánchez A, *et al.* Lack of efficacy of atenolol for the prevention of neurally mediated syncope in a highly symptomatic population: A prospective, double-blind, randomized and placebo-controlled study. J Am Coll Cardiol 2001;37:554-9.
12. Raj SR, Rose S, Ritchie D, Sheldon RS, POST II Investigators. The second prevention of syncope trial (POST II) – A randomized clinical trial of fludrocortisone for the prevention of neurally mediated syncope: Rationale and study design. Am Heart J 2006;151:1186.e11-7.
13. Lippman N, Stein KM, Lerman BB. Comparison of methods for removal of ectopy in measurement of heart rate variability. Am J Physiol 1994;267:H411-8.
14. Sheldon R, Connolly S, Rose S, Klingenheben T, Krahn A, Morillo C, *et al.* Prevention of syncope trial (POST): A randomized, placebo-controlled study of metoprolol in the prevention of vasovagal syncope. Circulation 2006;113:1164-70.
15. Numata T, Abe H, Nagatomo T, Sonoda S, Kohshi K, Nakashima Y, *et al.* Successful treatment of malignant neurocardiogenic syncope with repeated tilt training program. Jpn Circ J 2000;64:406-9.
16. Reybrouck T, Heidbüchel H, Van de Werf F, Ector H. Tilt training: A treatment for malignant and recurrent neurocardiogenic syncope. Pacing Clin Electrophysiol 2000;23:493-8.
17. Takahagi VC, Costa DC, Crescêncio JC, Gallo Junior L. Physical training as non-pharmacological treatment of neurocardiogenic syncope. Arq Bras Cardiol 2014;102:288-94.
18. Romme JJ, Reitsma JB, Go-Schön IK, Harms MP, Ruiter JH, Luitse JS, *et al.* Prospective evaluation of non-pharmacological treatment in vasovagal syncope. Europace 2010;12:567-73.
19. Gardenghi G, Rondon MU, Braga AM, Scanavacca MI, Negrão CE, Sosa E, *et al.* The effects of exercise training on arterial baroreflex sensitivity in neurally mediated syncope patients. Eur Heart J 2007;28:2749-55.
20. Kapoor WN, Peterson J, Wieand HS, Karpf M. Diagnostic and prognostic implications of recurrences in patients with syncope. Am J Med 1987;83:700-8.
21. Kouakam C, Vaksmann G, Pachy E, Lacroix D, Rey C, Kacet S, *et al.* Long-term follow-up of children and adolescents with syncope; predictor of syncope recurrence. Eur Heart J 2001;22:1618-25.