G-Suited for Prevention of Syncope in Patients with Vasovagal Syncope: A Pilot Study

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Background: *Vasovagal syncope (VVS) represents by far the most common cause of syncope as it is diagnosed in around 50% of all patients that come to an emergency department. Although VVS is not fatal, it can cause an injury. Even serious injuries are not common, but there are reports of serious injuries of up to 5%. There are no current studies that demonstrate the effectiveness of any treatment. Past studies found that an Anti-Gravity suit (G-suit) can increase blood pressure and has been reported to prevent orthostatic hypotension effectively in patients with diabetes. It is possible that the G-suit can prevent VVS.*

Objective: *In the present study, the authors assessed the efficacy of G-suit for vasovagal syncope prevention.*

Material and Method: *In this open-label, randomize controlled study, we used the Italian tilt protocol, namely 60° passive tilting followed by 0.4 mg nitroglycerin challenge when the passive phase fails to induce syncope. If test was positive, then patient was enrolled. Tilt table test was repeated to compare G-suited and no G-suited to assess efficacy of G-suit for vasovagal syncope prevention.*

Results: *10 patients were enrolled. There is no difference between the control group and an experimental group. In this study there is no cardio-inhibition vasovagal syncope. Positive tilt table test occurred in 50% of the patients receiving G-suited and 100% in control group (p 0.133).*

Conclusion: *G-suit is unable to prevent syncope in patients with positive tilt table test but the result is not statistically significant. However, the number of patients may be too small.*

Keywords: *G-suit, Vasovagal syncope, Tilt table test*

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Vasovagal syncope is a common condition. 50% of patients with syncope visit to the emergency room were diagnosed with this condition[1]. However, there are also many patients who have symptoms but do not visit a physician or hospital[2].

Although Vasovagal syncope is not fatal, injury is not uncommon. Generally, it is without serious injury but serious consequences have been reported in up to 5%[3]. In addition, the quality of life is also impaired from a fear of recurrence, leading to the patient being unable to work or live normally.

Mechanisms that cause unconsciousness of Vasovagal syncope is global transient cerebral ischemia caused by severe hypotension from an abnormal vasodilatation and can be related to bradycardia or ventricular pauses[4,5].

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Even with an understanding of the pathogenesis of the disease many treatments have been used in the treatment but all of them showed no benefit[6-12]. Even a pacemaker has been used in the prevention of Vasovagal syncope, but the results were negative[13]. Pharmacological treatment and a pacemaker are not effective and may even cause undesirable side effects. There have been evidences that counter-pressure maneuvers can prevent syncope based on the principle of increasing blood pressure and vascular resistance[14,15]. There is an anti-gravity suit (G-Suit) (Fig. 1) study that reported to increase blood pressure by increases in cardiac pre-load and cardiac output after inflation of the G suit[16]. It has been reported to prevent orthostatic hypotension effectively in patients with diabetes[17]. Therefore, it is possible that the anti-gravity can prevent the Vasovagal syncope.

Material and Method

G-suited for prevention of syncope in patients with vasovagal syncope was an open-label, randomized controlled study.

Fig. 1 G-suit (Anti-gravity suit)

Study patients

Patients who underwent a tilt table test at Siriraj hospital were eligible for enrollment if they were patients older than 18 years and had Vasovagal syncope diagnosed by Tilt table test (Italian tilt protocol)[18] based on the New VASIS (VAsovagal Syncope International Study) classification[19]. The exclusion criteria were a contraindication to the Tilt table test such as severe ischemic stroke or severe coronary artery disease, being unable to complete tilt table test protocol, having a negative tilt table test result, had other conditions that can cause loss of consciousness, pregnant or breast feeding, cancer or psychological problems, medical illness that investigators deem ineligible to participate in the present study.

Study design

The study purpose is to assess efficacy of G-suit for vasovagal syncope prevention by comparing with the group that did not wear G-suit if the first test is positive.

Based on literature review, Positive reproducibility of tilt table test in all three studies was 80% by Chen et al[20], 57% by Buitlier et al[21] and 92% by William et al[22]. In the present study, the investigators expected a positive reproducibility of Tilt table test at 80% and the efficiency of the anti-gravity suit to prevent a positive Tilt table test was 80%. With a power of 90% and a significance level of 0.05, a minimum of 13 patients in each group was required. Sample size was calculated as follows:

$$n = \frac{[Z_{\alpha/2}\sqrt{2P(1-P)} + Z_{\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)}]^2}{(p_1-p_2)^2}$$

$$\text{And } P = \frac{(p_1+p_2)}{2} = \frac{(0.20+0.80)}{2} = 0.5$$

$$n = \frac{[1.96\sqrt{2(0.5)(1-(0.5))} + 1.28\sqrt{0.2(1-0.2)+0.8(1-0.8)}]^2}{(0.2-0.8)^2}$$

$$n = 13$$

In patients who met the inclusion criteria, the Tilt table test (Italian tilt protocol) was performed. If the test was positive based on the Diagnostic criteria of VASIS, the second test will not be performed until blood pressure and heart rate return to baseline.

After the first test, patients were randomized to G-suited or control. In the G-suited group patient must put on G-suited during the second test and, if the result is negative, that means the G-suit is effective in preventing loss of consciousness from Vasovagal syncope (Fig. 2).

Data collection

All of the following data were recorded in all patients.

1) Baseline demographic data, such as age, sex, weight, heart rate, systolic and diastolic blood pressure values before, after and during the tilt table test.

2. Tilt table test results, before and after in G-suit group and control group.

Statistical analysis

Baseline demographic data were expressed as frequency and percentage for qualitative variables such as gender. The continuous data such as age were

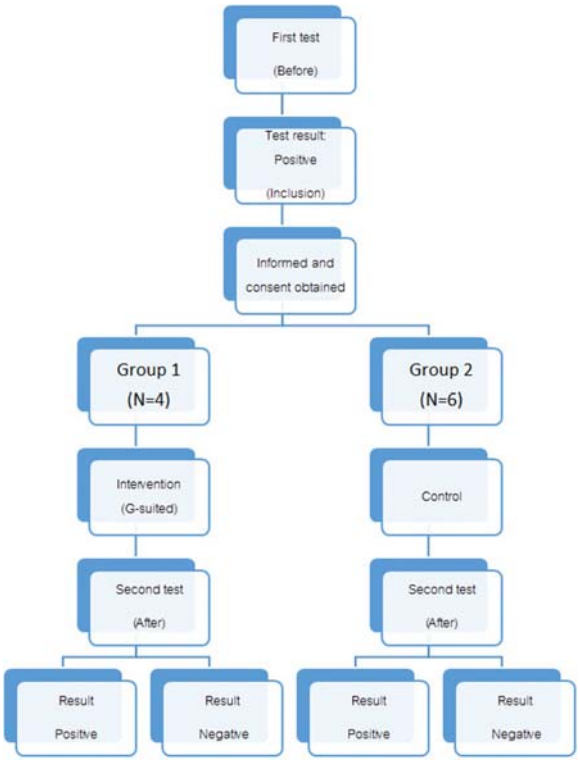

Fig. 2 Flow-chart of study protocol.

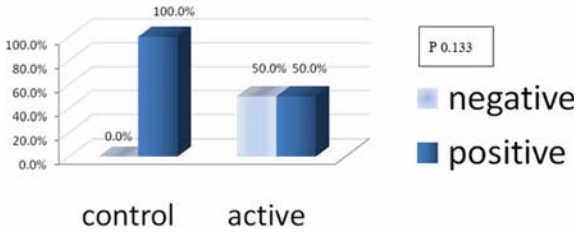

Fig. 3 Comparison of second test results in G-suited and control.

expressed as mean and standard deviation and compared among groups using a student t-test if the data have a normal distribution. If the data do not present a normal distribution, they were shown as median and in the interquartile range compared to groups using Mann-Whitney U test.

The difference between G-suit and control group was compared by using a Fisher's exact test for categorical data.

A p-value of <0.05 was considered statistically significant.

The present study was approved by the Ethics Committee of Siriraj Hospital, Mahidol University.

Results

Population

From September 2012 to March 2013, 10 patients were enrolled in the present study. 4 patients (40%) were randomized to the G-suited group and 6 patients (60%) placed in the control group. Baseline characteristic in each group were not statistically different, as shown in Table 1. There is no cardio-inhibitory vasovagal syncope in the present study.

Repeat tilt table test results

Positive tilt table test occurred in 2 (50%) patients receiving G-suited and 6 (100%) patients in control group (p 0.133). In G-suited group, all positive result patients have type 3 vasodepressor vasovagal syncope. In control group, 3 (50%) patients developed type 1 Mixed vasovagal syncope and 3 (50%) developed type 3 vasodepressor vasovagal syncope. Data are shown in Table 2.

Discussion

The study purpose is to evaluate an effectiveness of G-suit for vasovagal syncope. 50% of patients with G-suited yield negative tilt table test result compared with 100% in the control group; however, it did not reach statistical significance but the trend favored the G-suited group. It may be that the number of patients who enrolled in our study was too low. The present study population consisted of more females than males (70% vs. 30%). This reflects the higher prevalence of vasovagal syncope in female[2] and, in the present study, there is no type 2 cardio-inhibitory vasovagal syncope, which means this study cannot be applied to this population.

This is the first randomized controlled trial to assess the efficacy of anti-gravity suit (G-suit) for vasovagal syncope. G-suits are risk-free, easily put on and do not require any training to use. However, a limitation of the present study is that patients and investigator are not blinded to the outcome of the randomization. Additionally, while this study is ongoing and still incomplete, the results might be changed and, without the cardio-inhibitory vasovagal syncope used in the present study, results cannot be drawn from the present study.

From the concept of the Bezold-Jarisch reflex, transient vasodilation and/or bradycardia or ventricular pauses play an important role in pathophysiology of vasovagal syncope[4]. In previous studies, from patho-physiological knowledge many medications and interventions were unable to demonstrate efficacy in

Table 1. Personal and clinical characteristics of patients

Patients characteristics	G-suited (n = 4)	Control (n = 6)	p-value
Gender (% male)	50%	16.7%	0.5
Age, yrs (mean [SD])	50.5 (23.87)	53.67 (19.01)	0.23
Weight (mean [SD])	61 (14)	56 (3)	0.45
Height (mean [SD])	163.5 (8.5)	161.5 (7)	0.69
Duration form last syncope to tilt table test (median [quartiles])	578 (40-1,460)	14 (8-180)	0.18
Syncope frequency, month (median [quartiles])	1.25 (0.6-15.6)	1 (1-6)	0.9
Baseline SBP (mean [SD])	121 (17.3)	118 (8.4)	0.73
Baseline DBP (mean [SD])	78.5 (12.97)	68.3 (5.24)	0.22
Baseline HR (mean [SD])	73.75 (14.24)	61.33 (16.27)	0.25
Previous test results (%)			0.76
Type 1	0	66.7%	
Type 2	0	0	
Type 3	100%	33.3%	

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; SD = standard deviation

Table 2. Positive second test results

Test positive results	G-suited (n = 2)	Control (n = 6)
Type 1 (mixed)	0	50%
Type 2 (cardio-inhibition)	0	0
Type 3 (vasodepressor)	100%	50%

vasovagal prevention. Sheldon et al[8] studied effect of beta blockers for vasovagal prevention but the result was disappointing. Raj et al[11] used fludocortisone but the result is not impressive. Even though vasovagal syncope is benign disease, serious injuries are not uncommon; it can also impair quality of life. It is important to find an effective treatment for vasovagal syncope. In this study, we used the G-suit because it can prevent relative hypovolemia, the first cascade of vasovagal syncope by increasing venous return and can counteract transient vasodilation by increasing peripheral vascular resistance[16]; it is also easily put on and requires no training. But in the present study, G-suit cannot demonstrate the effectiveness in preventing tilt-table induced vasovagal syncope yet it does not disprove the Bezold-Jarisch reflex theory because our study population is too small, it is still incomplete so we need more data before we can draw any conclusions.

Previous studies have found that positive reproducibility of tilt table test ranges between 57-92%[20-22]. In the present study, positive reproducibility of the tilt table test using, Italian protocol was 100%. The difference between the present study and previous study is that we do a second test immediately after the first test, but once again study still incomplete.

From the knowledge that we have, there is no treatment that has proven beneficial in the prevention of vasovagal syncope. The G-suit cannot demonstrate effectiveness in vasovagal syncope prevention but there is a trend for G-suit benefit. However, study is still incomplete and the result cannot be finally concluded until the study is completed.

Conclusion

G-suit is unable to prevent syncope in patients with positive tilt table test. However, the number of patients was studied may be too small to make such a conclusion.

What is already known on this topic?

Vasovagal syncope is a common cause of syncope in patients without structural heart disease. The diagnosis was based on typical prodrome and symptoms and may require a tilt table test. No medication has been proven very effective in preventing

vasovagal syncope.

What this study adds?

This study is a preliminary study trying to explore a new way of preventing vasovagal syncope by the use of an anti-gravity suit (G-suit). The result indicated that the G-suit had a trended toward a benefit in the prevention of vasovagal syncope during the tilt table test.

Potential conflicts of interest

None.

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การป้องกันโรคหน้ามืดหมดสติจากเส้นเลือดขยายตัวด้วยชุดต้านแรงโน้มถ่วง: การศึกษานำร่อง

ประยุทธ รัศมีหิรัญ, รุ่งโรจน์ กฤตยพงษ์

ภูมิหลัง: *โรคหน้ามืดหมดสติจากเส้นเลือดขยายตัว (Vasovagal syncope) เป็นโรคที่พบได้บ่อยและมีความสำคัญ 50% ของผู้ป่วยหน้ามืดที่มาตรวจที่ห้องฉุกเฉินนั้นจะได้รับการวินิจฉัยเป็นโรคนี้ ถึงแม้ว่าโรค Vasovagal syncope จะไม่ทำให้เป็นอันตรายถึงชีวิตแต่ก็ทำให้เกิดการบาดเจ็บได้ ถึงแม้ว่าโดยทั่วไปการบาดเจ็บจะไม่รุนแรงแต่ก็มี รายงานถึงการบาดเจ็บที่รุนแรงได้ถึง 5% ในปัจจุบันยังไม่มีการศึกษาใดที่แสดงให้เห็นถึงประสิทธิภาพของยาที่นำมาใช้ มีการศึกษาที่นำชุดต้านแรงโน้มถ่วง (G-Suit) มาศึกษาพบว่าสามารถเพิ่มความดันโลหิต และได้มีรายงานถึงการนำมาใช้ป้องกันอาการเป็นลมแบบ Orthostatic hypotension อย่างได้ผลในผู้ป่วยเบาหวาน จึงมีความเป็นไปได้ว่าชุดต้านแรงโน้มถ่วงจะสามารถป้องกันการเกิด Vasovagal syncope ได้*

วัตถุประสงค์: *ศึกษาประสิทธิภาพของการสวมใส่ชุดต้านแรงโน้มถ่วง (G-suit) ในการป้องกันการหมดสติจากโรคหน้ามืดหมดสติจากเส้นเลือดขยายตัว (Vasovagal syncope)*

วัสดุและวิธีการ: *ในการวิจัยเชิงทดลองแบบสุ่มและมีกลุ่มควบคุม (Open-label randomize controlled study) นี้เราเลือกใช้ Italian tilt protocol คือปรับระดับเตียงไว้ที่ 60 ° หากผู้ป่วยไม่หมดสติก็จะให้ 0.4 mg nitroglycerin เป็นตัวกระตุ้น ถ้าผลตรวจให้ผลบวกก็จะทำการตรวจ Tilt table test อีกครั้งเพื่อเปรียบเทียบผลของการใส่ชุดต้านแรงโน้มถ่วงกับไม่ใส่เพื่อศึกษาประสิทธิภาพของชุดต้านแรงโน้มถ่วง*

ผลการศึกษา: *มีผู้ป่วย 10 รายเข้าร่วมการศึกษา ข้อมูลพื้นฐานของผู้เข้าร่วมการวิจัยทั้งสองกลุ่มไม่มีความแตกต่างกัน แต่ในการศึกษานี้นั้นไม่มีผู้ป่วย cardioinhibition vasovagal syncope รวมอยู่ด้วย 50% ของผู้ป่วยที่ใส่ชุดต้านแรงโน้มถ่วงเปรียบเทียบกับกลุ่มผู้ป่วยที่ไม่ได้ใส่ชุดมีผลการตรวจเป็นบวก100% (p 0.133)*

สรุป: *ชุดต้านแรงโน้มถ่วงนั้นไม่สามารถป้องกันอาการหมดสติ vasovagal syncope ได้ถึงแม้จะไม่เห็นความแตกต่าง อย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามจำนวนผู้ป่วยในการศึกษานั้นยังน้อยและการศึกษายังคงดำเนินต่อไป*