



RESEARCH ARTICLE

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## Postural Orthostatic Tachycardia Syndrome (POTS). Follow – Up of 25 cases

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### ABSTRACT

**Background:** Postural orthostatic tachycardia syndrome (POTS) is a clinical syndrome diagnosed when orthostatic intolerance and tachycardia appear in the standing position. POTS significantly impairs patients' quality of life.

**Aim:** To report the symptoms, anamnestic and clinical elements, findings in the Tilt Test (HUT), evolution and treatment of POTS patients with a follow-up from 8 months to 28 years.

**Material and Methods:** We reviewed from march 1996 to june 2024, 1269 HUT exams in our laboratory. Those reports in which orthostatic postural tachycardia and symptoms compatible with POTS appeared, were selected for analysis.

**Results:** We identified 25 patients (2.6% of all positive Tilt test reports) with compatible signs and symptoms. Most patients complained of orthostatic intolerance, dizziness and frequent fainting. There was a delay of 8 -10 years between the onset of symptoms and the time of diagnosis. Orthostatic tachycardia and symptoms occurred on average after 3.5 and 5.2 minutes, respectively, when staying in the standing position.

Our patients had a high frequency of syncope or presyncope in their families (60% frequency) and hypermobility joint syndrome (64% prevalence). 40% of the patients reported relief of their symptoms after being treated (most of them with fludrocortisone). Most patients that reported little or no relief, did not use medications or were treated for a short period.

**Conclusions:** POTS is not common but significantly impairs the quality of life of those who suffer from it. We found a clear association with joint hypermobility syndrome, an excessive venous pooling during standing and a family history of syncope or lipothymia. Best treatment is with fludrocortisone alone or in combination with midodrine.

### ARTICLE HISTORY

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### KEYWORDS

Postural orthostatic tachycardia syndrome, POTS, Head –up Tilt-table test, Hypermobility joint syndrome.

### Introduction

Postural orthostatic tachycardia syndrome (POTS) is a type of dysautonomia clinically characterized by orthostatic intolerance and tachycardia within the first 10 minutes of standing, with a heart rate exceeding the rate by 30 beats the basal (lying down) or that exceeds 120 beats in total [1-3]. Orthostatic intolerance is defined as appearance of symptoms of cerebral hypoperfusion when standing, which are relieved when lying down. Patients often complain of extreme fatigue, exercise intolerance, dizziness, decreased concentration and syncope [4-8]. They do not usually consult the doctor for a long time or are misdiagnosed as depression, stress, chronic fatigue or panic disorder [4-8].

### Material and Methods

We review from march 996 to june 2024, 1269 HUT exams in our laboratory. Of these, 939 (74%) demonstrated to be positive

for dysautonomia. We found 25 cases (2.6 % of the positive tests) in which patients presented early postural orthostatic tachycardia and symptoms in the Tilt Test consistent with the definition of POTS [1-3].

Table 1 describes the demographic's characteristics of the patients at the time of diagnosis. We included 25 healthy controls, matched by sex and age with patients. In both groups the same HUT protocol was applied.

### Study prior to the Head – up tilt test

In order to rule out a cardiac cause of fainting, the patient undergoes an evaluation by a cardiologist and tests such as: electrocardiogram, holter of heart rhythm, echocardiogram, and sometimes an electrophysiological study. If this evaluation is negative, or doubtful or another cause is suspected, the patient is sent to us for neurological evaluation and a tilt test.

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**Table 1:** Sex and age at beginning of symptoms and at the time of diagnosis.

	Female	Male	Age at beginning of symptoms	Age at time of diagnosis
Patients n: 25 cases Age:22,6 years Range: 9 - 43 years	16 cases	9 cases	14,07 years old Range: 7 – 40	22,6 years old Range: 9-43
Controls n: 25 Age:24,6 years Range: 10 – 50 years	16 controls	9 controls	-----	-----

**Head – up tilt test (HUT) conditions**

It is done between 8 and 12 o'clock. In a quiet room, with dim light at a temperature between 20 – 22 °C. A neurologist, a cardiologist and a medical technologist are present. Cardiology staff place continuous electrocardiographic monitoring. To rule out hypoglycemia, a hemoglucotest is performed prior to the examination. HUT is performed under cardiac monitoring, electrocardiogram, and continuous monitoring of blood pressure, heart rate, and medical and nursing surveillance. Drugs, intravenous lines, a defibrillator and equipment for cardiopulmonary resuscitation are available.

**Tilt test protocol**

A record of heart rate (HR) and blood pressure (BP) and symptoms reported by the patient are kept every 5 minutes or when is needed. The reason for interruption of the exam or any important incident is noted at any time. The protocol with sublingual nitroglycerin is based on Del Rosso [9].

Previous conversation with the patient (10 minutes) / Monitoring instalation (digital cuff to measure BP and continuous electrocardiogram) (15 minutes). Carotid massage is performed on all patients over 60 years of age\*. With previous ruling out murmur or carotid stenosis or stroke in the last 6 months (5 minutes per side) [10]. Basal HUT (horizontal) for 10 minutes / Passive HUT (standing at 70°) 45 minutes / Activated HUT with 0.3 mg of sublingual trinitrin (without lying the patient down) for 10 minutes. Total, approximate: 100 minutes. The test ends if a “positive HUT” is obtained: This is syncope (loss of consciousness) or presyncope (dizziness, nausea, paleness, etc. that announces that syncope is imminent). Associated with arterial hypotension (SBP < 70 mmHg) or arterial hypotension plus bradycardia. Or if intolerable discomfort occurs for the patient. If there are no symptoms, it is terminated due to the end of the protocol. Tilt Test equipment consists of: Digital monitor (Ohmeda 2300 Finapres BP Monitor USA). Digital cuff that is placed on the index or middle finger to measure BP and HR continuously. Electric tilt table (Magnetic Manumed USA) and electrocardiogram monitor (Quinton Q4500 USA). The patient is secured to the tilting table with two velcro bands, one on his knees and the other on his chest.

Our study has been approved by the Hospital ethics committee, and has been carried out in accordance with the ethical standards established of the International Committee of Medical Journal Editors (Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals) – Updated January 2024 and in the Declaration of Helsinki 1964. Patients and controls gave informed consent before inclusion. For statistical comparison, Anova and logistic

regression are used and, depending on the sample size, non-parametric tests are used.

**Results**

Consultation symptoms appear in Table 2.

**Table 2:** Consultation symptoms and their frequency in our sample.

Consultation symptoms	Patients	n (%)
Ortosthatic intolerance	10/25	40
Frequent lipothymia	8/25	32
Frequent syncope	7/25	28
Occasional syncope	6/25	24
Effort intolerance	5/25	20
Effort and syncope	2/25	8

**Family history of syncope or presyncope**

In first degree relatives (parents, siblings or children). Patients: 15/25 with family history of syncopes = 60%. Controls: 0/25 with that history.

**Joint hypermobility:** It is a described finding in patients with POTS and other types of dysautonomia [11-15].

According to Brighton’s criteria [14] 16 cases (64%) presented joint hypermobility and also their first degree relatives (parents and/or siblings). Only two controls had joint hypermobility (8%).

**Findings in HUT**

In table 3, we describe heart rate and blood pressure (averages) during resting and during passive HUT (70° of tilting).

**Table 3**

Hemodinamic parameters durign resting HUT		
	Patients n: 25	Controls n: 25
Blood pressure Average	105/60	107/60
Blood pressure range	82/60 – 120/68	92/60 – 120/62
Heart rate Average	75	78
Heart rate range	63 – 92	68 – 88
Hemodinamic parameters in passive standing HUT 70° of tilting		
	Patients n: 25	Controls n:25
Blood pressure average	115/72	122/80
Blood pressure range	108/60 – 122-85	108/62 – 128/88
Heart rate Average	114	84
Heart rate range	102-135	75 – 89

The HR in the passive HUT (Table 3) reaches a range 102-135 beats in patients, while in controls does not exceed 89 beats. The average heart rate in that phase (Table 3), makes a difference statistically significant between patients versus controls (114 vs 84 p ≤ 0.01).

On the contrary, in systolic and diastolic BP no significant differences are found between patients and controls neither at rest or during the HUT. Orthostatic tachycardia (x: 114 beats, range 102 – 135) in patients. It is reached at an average of 3.5 minutes (range 1 – 10 minutes). The Standard Deviation is 1.2 minutes. In 15 cases (60%), this value is reached in the first 5 minutes of being in the upright position. Orthostatic symptoms in HUT (pre – collapse) are described in Table N° 4

**Table 4:** Orthostatic symptoms (pre – collapse).

Patient N°	Symptoms when standing	Time to reach symptoms
1	Dizziness + Orthostatic intolerance	1
2	Orthostatic intolerance	3
3	Orthostatic intolerance	8
4	Orthostatic intolerance	10
5	Orthostatic intolerance	5
6	Orthostatic intolerance + Dizziness	5
7	Dizziness + Orthostatic intolerance	10
8	Dizziness + Orthostatic intolerance	8
9	Dizziness + Orthostatic intolerance	6
10	Orthostatic intolerance + Presyncope	10
11	Orthostatic intolerance	10
12	Dizziness	5
13	Dizziness	1
14	Orthostatic intolerance	5
15	Dizziness + Orthostatic intolerance	5
16	Orthostatic intolerance	3
17	Dizziness + Orthostatic intolerance	3
18	Orthostatic intolerance	5
19	Orthostatic intolerance + Presyncope	3
20	Orthostatic intolerance	2
21	Dizziness + Orthostatic intolerance	4
22	Orthostatic intolerance	2
23	Orthostatic intolerance	6
24	Orthostatic intolerance + Presyncope	5
25	Orthostatic intolerance	4

Average 5,2 minutes Range: 1 – 10 minutes

On average, orthostatic symptoms come at 5.2 minutes (range 1 to 10 min).

In Table 5 we can see the type of final event in the exam

**Table 5:** Final event in HUT.

Final event in HUT	Patients n	%
Mixed presyncope	20	80
Severe orthostatic intolerance	5	20

The final event at HUT, was a severe discomfort due to orthostatic intolerance in five of the 25 patients, or a presyncope (lipothymia) in 20 of 25 cases. (\*Mixed presyncope means that both blood pressure and heart rate drop, causing symptoms of relative cerebral hypoperfusion).

**Treatments used**

All patients were instructed to increase their fluid and salt intake, to exercise moderately, and wear compression stockings. The difference between them was the pharmacological treatment chosen by each treating doctor for their specific patient [15,16].

**Tables 6 & 7: Response to treatment (june 2024)**

**Table 6:** Response to treatment patients 1 – 13 (june 2024).

Pat	Evol	* Init treatment	Current treatment	Relief	Current evolution
1	24 yrs	Florinef	Fnef **ocassional	Signif Relief	O I° Ocassional
2	14 yrs	Florinef	Fnef Permanent	Signif Relief	O I Ocassional
3	27 yrs	Florinef	Fnef Ocassional	Signif Relief	O I Ocassional
4	20 yrs	Nothing	No treatment	No relief	O I permanent
5	25 yrs	Florinef	Fnef Permanent	Little relief	O I Frequent
6	19 yrs	Atenolol	Midodrine last year	Little relief	O I Frequent
7	19 yrs	Midodrine	No treatment	Little relief	O I Ocassional
8	20 yrs	Propanolol	No treatment	Little relief	O I Frequent
9	15 yrs	Midodrine	Florinef	Signif Relief	O I Ocassional
10	19 yrs	Nothing	No treatment	No relief	O I Permanent
11	19 yrs	Midod & Fnef	Midodrine & Florinef	Signif Relief	O I Ocassional
12	18 yrs	Midod Ocass	No Treatment	No relief	O I permanent
13	17 yrs	Midod & Fnef	Midodrine & Florinef	Little relief	O I frequent

**Table 7:** Response to treatment patients 14 – 25 (June 2024).

Pat	Evol	Init treatment	Current treatment	Relief	Current evolution
14	19 yrs	Midodrine	No Treatment	No relief	O I Frequent
15	17 yrs	Midodrine	No Treatment	No relief	O I Frequent
16	10 yrs	Midodrine	Pyrido# & Midodrine	Mod Relief	O I Monthly
17	12 yrs	Florinef	Midod*** & Florinef	Signif Relief	O I Ocassional
18	12 yrs	Florinef	Florinef permanent	Signif Relief	O I Ocassional
19	13 yrs	Propanolol	Florinef permanent	Signif Relief	O I Ocassional
20	9 yrs	Midodrine	Midod & Florinef	Signif Relief	O I Ocassional
21	8 yrs	Propanolol	Florinef	Mod Relief	O I Monthly
22	6 yrs	Midodrine	Midod & Florinef	Mod Relief	O I Monthly
23	5 yrs	Florinef	No treatment	No Relief	O I Frequent
24	2 yrs	Midodrine	Midodrine	Signif Relief	O I Ocassional
25	1 year	Florinef	Florinef permanent	Mod Relief	O I Monthly

**Note:** \*Init treatment: Initial treatment \*\* Fnef: Florinef (fludrocortisone) #Pyrido: Pyridostigmine \*\*\*Midod: Midodrine O I° orthostatic intolerance

1. No relief implies no improvement. Orthostatic intolerance every day. The patient cannot walk a block, without having symptoms.
2. Little relief: The patient perceives the discomfort of orthostatic intolerance or presyncope slightly better. Symptoms occur several times during a week
3. Moderate relief: Occasional orthostatic intolerance or presyncope: Up to one episode per month or less and the patient can walk a block, without symptoms. Intolerance
4. Significant relief is considered a symptomatic episode every 3 months or less.

### Observations

The onset of symptoms was on average at 14 years old (7-40 years). The evolution time and follow-up of our patients ranges from 8 months to 28 years.

The medications used at the time of diagnosis were: Fludrocortisone (8 cases), midodrine (8 cases), fludrocortisone & midodrine (combination) (3 cases) and propranolol or atenolol (4 cases). Two patients did not use treatment at the beginning of the condition.

The medications currently used are: fludrocortisone (9 cases), midodrine (2 cases), pyridostigmine & midodrine (1 case), and fludrocortisone & midodrine (5 cases). We have 8 (30%) patients who are not currently using drugs, six (24%) of them prefer to tolerate their permanent discomfort because they suffered many adverse reactions when taking drugs. Two (8%) never attended a medical check-up, after the diagnosis and initial prescription. The average time of drug use, in patients who achieved significant relief of symptoms (10 cases: 40%), ranges between 4 to 12 months. This relief was achieved using florinef (6 cases), in 1 case with midodrine and in 3 cases with midodrine & fludrocortisone.

### Discussion

In our study we found that POTS has a low frequency representing only the 2.6% of our positive HUT. Main symptoms of consultation of our patients were: Orthostatic intolerance (40%) and frequent lipothymias (32%). Orthostatic intolerance is the symptom most mentioned in the literature for POTS [2-7] which coincides with our observation.

### Predisposing Factors

#### Family history of syncope

It was common for us to find a family history of orthostatic symptoms 15/25 (60%) of our patients had first-degree relatives (mainly the mother and female siblings) with a history of orthostatic intolerance or presyncope. Even the cases 3, 4 and 5 correspond to a mother and her 2 children [17,18].

#### Joint hypermobility

We observed it (>5 Brighton criteria) in 16 cases (64%) of our patients [14]. All of them had first degree relatives also affected by syncopes and by joint hypermobility but of lesser intensity than the patients. We believe that this is due to the high frequency and heritage in Chile of the type III Ehlers -Danlos syndrome [11,12,19,20].

### Excessive venous pooling

The hyperlaxity of the connective tissue causes great venous hyperdistensibility, which favors a decrease in venous return to the heart and therefore orthostatic symptoms. [11-13,15,21,22].

In our patients we observed, during the passive phase of the Tilt Test, a progressive venous congestion in the feet. Which we measure using a colorimetric (visual) method, in degrees from minimal congestion (grade 1) to grade 5 (very severe venous congestion). Grade 5 was observed in 20 of the patients (80%). In healthy volunteers, grade 1 (minimal congestion) to grade 3 (moderate congestion) was observed: 8 controls (3.1%).

### Viral Infections

Our patients generally do not give us a history of viral infection prior to the appearance of symptoms, a fact totally different from other publications [2,3,5]. Only one (4%) patient mentions (19-year-old woman) having suffered from COVID-19, about 10 months before symptoms started [23,24]. The majority of our patients (Table 1) begin their symptoms in childhood or adolescence (average 14 years) and mention a family history of orthostatic intolerance and/or syncope (60%) and ligamentous hypermobility in 64%.

### Medication

23 patients were treated with drugs at some point during their evolution. Then there were changes and in the end there were only 17 patients using drugs. The drugs used were fludrocortisone, atenolol, pyridostigmine, midodrine and propranolol. Other medications mentioned in the literature such as Clonidine, Droxidopa or Ivabradine were not used in our patients [16,25,26]. Because they are not available in our country or because there is little experience in its management.

### Treatment Results

We notice an important trend in the sample to abandon treatment or not attend to control with doctor. Thus, 6/25 (24%) of the cases decided not to use treatment (because of adverse reactions), plus the 2 cases (8%) that abandoned the follow – up, constitute 32% of our sample. This makes us think about the great need to inform and educate patients and doctors about the current treatments and that is possible to reduce discomfort.

Patients who achieved very significant relief constituted 40% and patients with little or no relief also constituted 40%. The best medication to find some relief was fludrocortisone alone or combined with midodrine (9 cases, 36%). Only one (4%) of the patients reported that under treatment was almost completely relieved of his symptoms. On the other hand (6/25) 24% of cases have never found relief from their complaints.

Patients 1, 2, 3, 9, 11, 17, 18, 19, 20 and 24 are those who had a better evolution, with greater relief with treatment. They considered that their symptoms occurred very occasionally. with an episode of lipothymia every 3 months or less (4 times or less in a year). To see treatments according to their effectiveness. Please see tables 6 and 7.

## Final Comments

POTS is a type of dysautonomia that is not very common, but it significantly affects the daily lives of those who suffer from it, since produces orthostatic symptoms that are very difficult to relieve. Our data show that the onset of symptoms is approximately 8 years before the diagnosis is made, indicating that the diagnosis is late and complex.

It is common for our patients to spend years with diagnoses such as depression, anxiety or panic disorder. In fact, all of our patients at some point in their evolution were sent for psychiatric treatment or psychological support. We believe that this occurs due to the limited diffusion that this condition has in the medical community and in the general public, where symptoms such as orthostatic intolerance or syncope are almost always attributed to emotional stress or depression.

In our cases, the POTS variant related to joint hypermobility and loose connective tissue predominates (Ehlers Danlos (EDS) syndrome type III) with excessive venous pooling during standing [19,22]. In which there is a strong hereditary factor. Inheritance that manifests with different penetration among the relatives of the patients. [17-20]. Being our cases more related to the variant linked to hypermobility and EDS, the best response is to the treatment with fludrocortisone alone or in combination with midodrine and sometimes midodrine alone.

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