



Autonomic Profile of Patients with Primary Autonomic Failure

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Abstract: Primary autonomic failure (PAF) is an entity of dysautonomia characterized by the occurrence of severe orthostatic hypotension asympaticotonic often refractory to medical treatment, affecting quality of life. The aim of study is to describe the autonomic profile of patient with primary autonomic failure. It's a retrospective study including 125 patients admitted for primary autonomic failure at the diagnosis and treatment center for autonomic dysregulation in cardiology department A of Ibn Sina University Hospital in Rabat. All of them had clinical examination, electrocardiogram, biological exam and autonomic nervous system tests. The mean age of the population was 50.1 ± 14.4 years, with 64% women. The mean baseline HR was 66.6 ± 14.82 bpm. The mean baseline systolic BP (SBP) was 124.77 ± 21.62 mmHg and the average diastolic BP (DBP) was 72.26 ± 19 mmHg. The perturbation of the vagal response to DB is found in 70.4% of patients with deficiency in 40% of the cases. The perturbation of the vagal response to HG was found in 76.8% of patients with deficiency in 59% of the cases. The disruption of the peripheral sympathetic response alpha (alpha SP) to HG was found in 69.6% of patients with deficiency in 54.4% of patients. The disturbance of the central sympathetic response alpha (alpha SC) to MS was found in 71.2% of patients with deficiency in 62.88% of patients. The disturbance of the central sympathetic response beta (beta SC) to MS was found in 69.6% of patients with deficiency in 52% of the cases. The perturbation of the vagal response to tilt test is found in 82.4% of patients with deficiency in 70% of the cases without reflex tachycardia, confirming the neurogenic origin of orthostatic hypotension. Cardiovascular autonomic tests demonstrate the autonomic nervous system failure in this pathology whose major symptom is asympaticotonic orthostatic hypotension.

INTRODUCTION

The dysautonomia corresponds to a set of conditions leading to an ANS (Autonomic Nervous System) dysfunction. It may be the main clinical manifestation or integrate within symptoms of a characterized condition. The deficiency may be diffused or implicated in a specific function of the ANS.

Chronic forms of dysautonomia include primary autonomic failure. It is a pathology characterized by functional signs of dysautonomia, the occurrence of severe orthostatic hypotension (OH) of asympaticotonic type often refractory to medical treatment, thus affecting the quality of life.

The pathophysiology of this disease remains obscure and controversial [1].

Diseases categorized as primary autonomic failure usually include pure autonomic failure (PAF), Parkinson disease and multiple system atrophy.[2]

The last two pathologies are neurological disorders characterized by the attainment of autonomic centers.

It is however difficult to differentiate these three pathologies.

The objective of our study is to describe the autonomic profile of patients suffering from primary autonomic failure.

MATERIALS AND METHODS

This is a retrospective study that included 125 patients with primary autonomic failure in the ANS unit of the cardiology department "A" in Ibn Sina hospital of Rabat.

Cases included patients with pure autonomic failure (n = 114), Parkinson disease (n = 10), and multiple system atrophy (n = 1).

Inclusion criteria: All patients with asympaticotonic orthostatic hypotension defined by a sustained decrease in blood pressure of at least 20 mmHg of SBP



and / or at least 10 mmHg of DBP, with an increase in heart rate (HR) that remains less than 15 beats per minute during orthostatism.

These patients who have arrived in ANS unit exploration, usually have normal clinical and para-clinical examinations (biology, radiology and electroencephalogram).

Exclusion criteria: Patients with sympathicotonic HO, with an increase in HR of 15 beats per minute during orthostatism, and those with asympathicotonic HO with secondary autonomic insufficiency (diabetes, dysthyroidism, neoplasia, cardiopathy) were excluded from this study.

Description of the tests: The tests were done while all patients were fasting, and after cessation of any treatment for at least 48 hours.

The patient was initially placed in calm in supine position on a table of inclination. Monitoring of blood pressure (BP) was performed using a Dynamap (CRITIKON, 1846SXP) and heart rate (HR) by means of a display screen (LCD CS503 E; HELLIGE, EK 512 E). Basic BP and HR were measured at rest, every five minutes for at least 30 minutes. We have proceeded then to the different tests, interspersed with periods of rest, as described by Ewing [3;4], detailed by Phillip Low [5]

The Deep Breathing Test (DB): This test analyzes the vagal response. The result is expressed as a percentage: $(\text{Maximum RR} - \text{Minimum RR}) / \text{Min RR}$. The normal result varies between 25% and 50% depending on the age of the subject; it is generally higher with young people [6].

The Isometric Contraction or Hand Grip Test (HG):

During three minutes the patient performs a manual pressure of 50% of the maximum with assistance of a dynamometer. The muscular contraction involves a rise in BP related to an increase of sympathetic nerve activity at the muscular level that is effort-dependent and time-dependent [7; 8]. The peripheral alpha sympathetic nerve response is given by the increase of the BP.

The Mental Stress Test (MS): The patient performs mental arithmetic calculations by removing the number 7 successively from 200. The result is an increase in BP and in HR by activation of the central sympathetic nerve [8].

In mental stress, the central sympathetic nerves activities “ α ” was evaluated by measuring the variations of BP as bellow [9;10]

The tilt test: It allows the study of the parameters (BP and HR) in orthostatism, for ten minutes, compared to the decubitus values. The curves of variations of these parameters corresponding to the normal values are borrowed from the works of Coghlan [7; 11]. A decrease in systolic BP of 20 mmHg and 10 mmHg diastolic BP below 94 mmHg, maintained for at least minus five minutes is considered hypotension orthostatic. The vagal response is also evaluated in the primary orthostatic 30 seconds. An increase of 10% than the basic HR is considered normal, above of 10%, we talk about vagal hyperactivity, below 10% is vagal disability [5,7].

Each autonomic test gives rise to a measurement response to stimulation in relation to the baseline state. Results are expressed as a percentage for all the stimuli both sympathetic and vagal. For sympathetic stimulations relating to the measurement of the variation in BP, only the systolic BP values were analyzed.

Statistical Analysis: Descriptive statistics include ranks, mean and standard deviation for quantitative variables and frequency and percentage for qualitative variables

All statistical analyzes were performed using the SPSS program (version 13.0, SPSS Inc, Chicago, IL, USA)

RESULTS

The mean age of the population was 50.1 ± 14.4 years (range 7 years to 85 years), with 64% of women.

The mean baseline HR was 66.6 ± 14.82 bpm. The mean baseline systolic BP (SBP) was 124.77 ± 21.62 mmHg and the average diastolic BP (DBP) was 72.26 ± 19 mmHg.

The disturbance of the vagal response to DB is found in 70.4% of patients with deficiency in 40% of patients and hyperactivity in 30.4% of patients.

The disturbance of the vagal response to HG was found in 76.8% of patients with deficiency in 59% of patients and hyperactivity in 17.6% of patients.

The disruption of the peripheral sympathetic response alpha (alpha SP) to HG was found in 69.6% of patients with deficiency in 54.4% of patients and hyperactivity in 15.2% of patients.

The disturbance of the central sympathetic response alpha (alpha SC) to MS was found in 71.68% of patients with deficiency in 62.88% of patients and hyperactivity in 8.8% of patients.

The disturbance of the central sympathetic response beta (beta SC) to MS was found in 69.6% of patients with deficiency in 52% of patients and hyperactivity in 17.6% of patients.

In tilt test, three groups of patients were identified:

- Patients with only systolic orthostatic hypotension: 47.6%
- Patients with only diastolic orthostatic hypotension: 21.4%
- Patient concomitantly presented with systolic and diastolic orthostatic hypotension: 30.2%

The receding pressure drop is considerable. The mean of this systolic blood pressure drop was 31.28 ± 20.05 with a maximum of 103 mmHg.

The perturbation of the vagal response to tilt test is found in 82.4% of patients with deficiency in 70% of patients and hyperactivity in 12.4% of patients.

In our series, all our patients have a sympathetic central and peripheral deficiency alpha and beta, and vagal deficiency with severe and asympathicotonic orthostatic hypotension.

The tilt test confirms the neurogenic origin of the orthostatic hypotension due to the absence of reflex tachycardia.

Table 1: Patient characteristics

Parameters	Value
Age (years)	50.1 ± 14.4
Sex	H 44 (35.2%) F 81 (64.8%)
IMC	25.63 ± 5.85
Baseline SBP (mmHg)	124.77 ± 21.62
Baseline DBP (mmHg)	72.26 ± 19
Arterial hypertension	19(15.2%)
Baseline HR (batts/min)	66.6 ± 14.82
AMI<1mois	5 (100%)

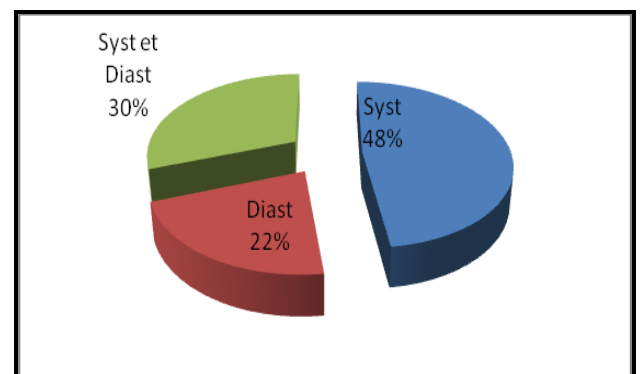


Figure 1: Distribution by type of hypotension

Table 2: Recapitulative table of the tests

Tests	Percentage of Disturbance
DB (Vagal Response)	70.4% Deficiency 40% Hyperactivity 30.4%
HG (Vagal Response)	76.8% D 59% H 17.6%
MS	Alpha 71.68% D 62.88% SC H 8.8% Beta 69.6% D 52% S C H 17.6%
Tilt Test (Vagal Response)	82.4% D 70% H 12.4%



DISCUSSION:

In this study, we evaluated the autonomic profile of 125 patients with primary autonomic failure by cardiovascular autonomic tests for both sympathetic and parasympathetic responses.

Cases included patients with pure autonomic failure (n = 114), Parkinson disease (n = 10), and multiple system atrophy (n = 1).

The average age was a 50.1 ± 14.4 year, with extremes ranging from 7 to 81 years. The majority of our patients were female (64.8%).

As for the epidemiology of these three pathologies in the literature, the age of prevalence of these neurodegenerative diseases is around sixty, especially for PAF. [12, 13]

In our study, a majority of women were found to be affected, with some studies showing that the mechanisms of orthostatic pressure regulation are less effective in women than in men [13]

Through the evaluation of the 125 patients in our series, we were able to identify certain abnormalities that may be the profile of patients with primary autonomic failure.

The mean baseline HR is 66.66 bpm, the baseline SBP is 124.77 mmHg and that of the PAD is 72.26 mmHg. 19.2% of the cases with a basic arterial hypertension.

A study by David S. et al of patients with primary autonomic failure showed that in these patients, decubitus hypertension is often associated with orthostatic hypotension, in the absence of any antihypertensive therapy, and be considered as part of the pathophysiology of PAF. [14]

Some authors explain the combination of orthostatic hypotension and decubitus arterial hypertension by baroreflex dysfunction with residual sympathetic response in subjects with central autonomic degeneration. [15]

Tests exploring the vagal response (DP-HG-Tilt test) determined vagal challenges in the majority of patients.

The MS helps to assess the responses for central sympathetic stimulation. A deficiency of the central alpha sympathetic response and the central beta sympathetic response was noted in the majority of patients.

The review of the literature showed that in these three forms, it is the deficiency of neurovascular sympathetic responses that is the cause of this fall in blood pressure.

When the increase in the sympathetic response is insufficient in orthostatism, there is no compensation for the decrease in venous return to the heart. Dozens of other studies done mainly on parkinsonian subjects showed that all patients with neurogenic orthostatic hypotension (OH), had a diffuse loss of sympathetic nerves in the left ventricle, but that a generalized loss of sympathetic norepinephric nerves can cause or at least contribute to the blood pressure drop. [16] [17]

However, recent studies of patients with multiple system atrophy have demonstrated in patients receiving fluorodopamine that their radioactive metabolites in the myocardium and cardiac release normal levels of noradrenalin thus confirming the presence of intact sympathetic termini at the heart. [18]

In the tilt test, three groups of patients were identified:

- Patients with only systolic OH: 47.6%
- Patients with only diastolic OH: 21.4%
- Patient with concomitant systolic and diastolic OH: 30.2%

The receding pressure drop is considerable. The mean of this systolic blood pressure drop was 31.28 ± 20.05 with a maximum of 103 mmHg.

Several authors note that a systolic blood pressure drop greater than 50 mmHg in patients with primary autonomic insufficiency is not uncommon. [19]

The tilt test confirms the neurogenic origin of the HO due to the absence of reflex tachycardia. [20]

CONCLUSION

Primary autonomic failure is a disabling pathology that is rarely encountered in routine practice and is essentially clinically diagnosed. Exploration of the autonomic nervous system revealed its major symptom, which is the asympathicotonic OH.

The failure of the autonomic nervous system objectified during the tests is obvious. In fact, the failure of the sympathetic and parasympathetic system reported by many authors is found in most of our patients.



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