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RESEARCH PAPER

New insights into orthostatic hypotension in multiple system atrophy: a European multicentre cohort study

A Pavy-Le Traon,[1,2] A Piedvache,[3] S Perez-Lloret,[4,5] G Calandra-Buonaura,[6,7] V Cochen-De Cock,[1,8] C Colosimo,[9] P Cortelli,[6,7] R Debs,[1] S Duerr,[10] A Fanciulli,[10] A Foubert-Samier,[11,12,13] A Gerdelat,[1] T Gurevich,[14] F Krismer,[10] W Poewe,[15] F Tison,[11,12,13] C Tranchant,[16] G Wenning,[10,15] O Rascol,[1,4] WG Meissner,[11,12,13] on behalf of the European MSA Study Group

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For numbered affiliations see end of article.

Correspondence to
Anne Pavy-Le Traon, MSA Reference Center, Department of Neurology, University Hospital of Toulouse, Hospital Pierre-Paul Riquet, Place du Dr Baylac, Toulouse 31900, France; pavy-letraon.a@chu-toulouse.fr

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ABSTRACT

Objectives Orthostatic hypotension (OH) is a key feature of multiple system atrophy (MSA), a fatal progressive neurodegenerative disorder associated with autonomic failure, parkinsonism and ataxia. This study aims (1) to determine the clinical spectrum of OH in a large European cohort of patients with MSA and (2) to investigate whether a prolonged postural challenge increases the sensitivity to detect OH in MSA.

Methods Assessment of OH during a 10 min orthostatic test in 349 patients with MSA from seven centres of the European MSA-Study Group (age: 63.6 ±8.8 years; disease duration: 4.2±2.6 years). Assessment of a possible relationship between OH and MSA subtype (P with predominant parkinsonism or C with predominant cerebellar ataxia), Unified MSA Rating Scale (UMSARS) scores and drug intake.

Results 187 patients (54%) had moderate (≥20 mm Hg (systolic blood pressure (SBP)) and/or ≥10 mm Hg (diastolic blood pressure (DBP)) or severe OH (≥30 mm Hg (SBP) and/or ≥15 mm Hg (DBP)) within 3 min and 250 patients (72%) within 10 min. OH magnitude was significantly associated with disease severity (UMSARS I, II and IV), orthostatic symptoms (UMSARS I) and supine hypertension. OH severity was not associated with MSA subtype. Drug intake did not differ according to OH magnitude except for antihypertensive drugs being less frequently, and antihypotensive drugs more frequently, prescribed in severe OH.

Conclusions This is the largest study of OH in patients with MSA. Our data suggest that the sensitivity to pick up OH increases substantially by a prolonged 10 min orthostatic challenge. These results will help to improve OH management and the design of future clinical trials.

INTRODUCTION

Multiple system atrophy (MSA) is a sporadic adult onset neurodegenerative disorder characterised by varying severity of parkinsonism, cerebellar ataxia, autonomic failure and corticospinal impairment.[1] Autonomic failure results in orthostatic hypotension (OH) and/or urogenital symptoms, key features of current diagnosis criteria. Autonomic failure is an independent predictive factor for rapid disease progression and shorter survival.[2] OH is defined by consensus as a drop of systolic blood pressure (SBP) ≥20 mm Hg and/or of diastolic BP (DBP) ≥10 mm Hg within 3 min in upright position.[3] A more pronounced drop (≥30 mm Hg for SBP and/or ≥15 mm Hg for DBP) is often reported in MSA and is one of the criteria for 'probable' MSA.[1] OH symptoms can cause significant disability for activities of daily living that require standing or walking. OH increases the risk of falls and associated morbidity.[4 5] Several studies have dealt with OH in patients with Parkinson's disease (PD) and atypical parkinsonian syndromes. These studies, which generally included a large number of patients with PD, showed that advancing age, disease severity and duration were related to OH in PD. In addition, non-specific predisposing factors may favour OH such as fluid depletion, medication intake, food ingestion, increased room temperature and physical deconditioning. However, none of these studies on the epidemiology and predisposing factors of OH focused on a large number of patients with MSA.

Jamnadas-Khoda *et al*[6] observed, in patients with PD, that OH frequently occurs after 3 min in upright position. Patients with PD and MSA can also remain asymptomatic despite large decreases in BP, and some orthostatic symptoms have low specificity.[4 5] These observations call for an optimisation of OH detection.

The study objectives were to analyse factors that may influence OH magnitude such as disease duration, disease severity, MSA phenotype (P with predominant parkinsonism or C with predominant cerebellar ataxia) and drug intake. We also evaluated the interest of a 10 min orthostatic test to detect delayed OH, and assessed the relation between OH and orthostatic symptoms in patients with MSA recruited into a large multicentre European cohort study.

METHODS

Patients

We studied 373 patients with 'possible' or 'probable' MSA from seven centres of the EMSA (European MSA)-Study Group (EMSA-SG); 349 patients with adequate BP measurements were included between 1995 and 2012 (Bologna

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