Prevalence of Primary Aldosteronism in Hypertensive Patients and Its Effect on the Heart

Pedro Morillas,[a] Jesús Castillo,[a] Juan Quiles,[a] Daniel Núñez,[a] Silvia Guillén,[a] Vicente Bertomeu-González,[a] Francisco Pomares,[b] and Vicente Bertomeu[a]

[a]Unidad de Hipertensión Arterial, Servicio de Cardiología, Hospital Universitario San Juan, San Juan de Alicante, Alicante, Spain
[b]Servicio de Endocrinología, Hospital Universitario San Juan, San Juan de Alicante, Alicante, Spain

Primary hyperaldosteronism (PHA) is thought to have a harmful effect on the cardiovascular system and, in recent years, the number of cases of hypertension due to PHA has been increasing. The aims of this study were to determine the prevalence of PHA and to assess cardiac damage associated with the condition in 183 consecutive hypertensive patients. A full secondary hypertension work-up was performed, and included ECG and echocardiography. In total, 11 (6%) patients were diagnosed with PHA. Compared with other hypertensives, those with PHA had higher systolic blood pressure, more frequently had evidence of left ventricular hypertrophy on ECG (45.5% vs 11.6%; *P*<.01), and had a larger left ventricular mass on echocardiography (145.5 g/m^2 vs 97.52 g/m^2; *P*<.0001). In conclusion, PHA is a significant contributor to the increasing prevalence of hypertension and its effect on the heart is greater than that of other causes of hypertension.

Key words: *Arterial hypertension. Left ventricular hypertrophy. Echocardiography.*

Prevalencia del hiperaldosterismo primario y afección cardiaca en el paciente hipertenso

El hiperaldosteronismo primario (HAP) es una causa creciente de hipertensión arterial (HTA) en los últimos años, y se lo ha asociado a un efecto deletéreo cardiovascular. Con el objetivo de conocer la prevalencia real de HAP en nuestro medio y sus alteraciones cardiacas, hemos estudiado a 183 pacientes hipertensos consecutivos. Se realizó un completo cribado de HTA secundaria, ECG y ecocardiografía. Se estableció el diagnóstico de HAP en 11 (6%) pacientes. Éstos presentaban mayores cifras de presión arterial sistólica, mayor prevalencia de hipertrofia ventricular izquierda en el ECG (el 45,5 frente al 11,6%; p < 0,01) y mayor masa ventricular izquierda (145,5 y 97,5 g/m^2; p < 0,0001) que el resto de los hipertensos. El HAP es una causa importante de elevación de las cifras de presión arterial y se asocia a una mayor afección cardiaca que otras causas de HTA.

Palabras clave: *Hipertensión arterial. Hipertrofia del ventrículo izquierdo. Ecocardiografía.*

INTRODUCTION

The examination of all patients with high blood pressure (HBP) should, among other things, try to identify any identifiable cause, which of course influences the therapy that should be followed.[1] The development of much more specific diagnostic tests in recent years has shown the frequency of secondary HBP to be much higher than once supposed, especially that caused by primary aldosteronism (PA). It is estimated that PA may affect 10% of all hypertensive patients, and up to 20% of patients with resistant HBP. Some authors believe PA to be the main cause of HBP.[2] It is important to identify patients with PA since an increase in plasma aldosterone is associated with negative cardiac and vascular effects and a greater risk of suffering a cardiovascular event.[3,4] Experimental studies have shown that aldosterone induces cardiac and vascular fibrosis, although the evidence linking aldosterone to left ventricular hypertrophy (LVH) is scarce and controversial.[5] The aims of the present study were to estimate the prevalence of PA as the cause of HBP in the specialist attention setting, and to analyze the cardiovascular repercussion of PA compared to other etiologies of HBP.

Correspondence: Dr. P.J. Morillas Blasco.
Sección de Cardiología. Hospital Universitario San Juan.
Ctra. N-332 Alicante-Valencia, s/n. 03550 San Juan de Alicante. Alicante. España.
E-mail: pedromorillas@teleline.es

Received June 30, 2007.
Accepted for publication September 24, 2007.

TABLE 1. **Clinical Characteristics and Medical Background of Patients With and Without Primary Aldosteronism, and the Laboratory Tests to Which They Were Subjected**

	No PA (n=172)	PA (n=11)	*P*
Age, mean (SD), y	57.7 (13.65)	63.46 (11.51)	NS
Men	105 (61)	7 (63.6)	NS
Diabetes mellitus	16 (9.4)	3 (27.3)	.093
Smoker	36 (21.2)	2 (18.2)	NS
Dyslipemia	60 (35.1)	4 (36.4)	NS
Prior ischemic cardiomyopathy	6 (3.5)	3 (27.3)	.011
Heart failure	2 (1.2)	1 (9.1)	NS
Previous ACVA	8 (4.7)	0	NS
SBP, mean (SD), mm Hg	154.42 (21.27)	168.45 (31.92)	<.05
DBP, mean (SD), mm Hg	89.75 (12.85)	93.18 (15.38)	NS
BMI, mean (SD)	30.57 (4.9)	30.44 (5.1)	NS
LVH in ECG	20 (11.6)	5 (45.5)	<.01
Glucose, mean (SD), mg/dL	109.3 (23.5)	114.3 (19.6)	NS
Creatinine, mean (SD), mg/dL	1 (0.3)	1 (0.2)	NS
Potassium, mean (SD), mmol/L	4.3 (0.4)	3.8 (0.4)	.001
MAU, mean (SD), mg/24 h	52.9 (179.2)	172.9 (270.1)	.07
Plasma renin activity, mean (SD), ng/mL/h	2.3 (2.8)	0.3 (0.3)	<.001
Plasma aldosterone, mean (SD), ng/dL	20.6 (14.3)	36.7 (31.5)	<.01

ACVA indicates acute cerebrovascular accident; BMI, body mass index; DBP, diastolic blood pressure; LVH, left ventricular hypertrophy; MAU, microalbuminuria; NS, not significant; SBP, systolic blood pressure; SD, standard deviation.
Figures are numbers (percentages) except where indicated.

METHODS

The patients in this study (which was undertaken in a prospective manner) all suffered HBP, were all over 18 years of age, and all had been referred to an HBP unit linked to a cardiology department in 2005-2006. All patients were subjected to anamnesis and a complete physical examination, and specific laboratory tests were ordered to rule out different secondary causes of HBP. Samples for all laboratory tests were collected after a 12 h fast; analyses included a hemogram, standard biochemical tests, the determination of thyroid hormone levels, the determination of the plasma aldosterone/renin activity ratio (ALD/RA), urine catecholamines and cortisol, and microalbumin in 24 h urine. In addition, all patients were subjected to a baseline electrocardiogram (ECG) for the detection of LVH using the criteria of Sokolov and/or Cornell, as well as an echocardiogram to determine the diameters of the heart chambers and to calculate the left ventricular mass (LVM) using the Penn formula.

Primary aldosteronism was suspected when the ALD/RA ratio was >30 and plasma aldosterone levels were high (>20 ng/dL). This diagnosis was confirmed when intravenous transfusion of 2 L of isotonic saline solution for 4 h did not suppress plasma aldosterone (>10 ng/dL).

Statistical Analysis

Continuous variables were expressed as means (standard deviation). Qualitative variables were expressed as numbers and percentages. Quantitative variables were analyzed using the Student *t* test for independent samples, or the Mann-Whitney test when the distribution was not normal. The qualitative variables were analyzed using the χ^2 test or Fisher exact test. All calculations were made using SPSS v.12 software. A *P* value less than .05 was considered significant.

RESULTS

The study subjects were 183 patients with HBP (61.2% were men) with a mean age of 58 years (29-83). All had been referred for consultation due either to poor control of their blood pressure readings (65%), hypertensive crisis (16.1%), recently diagnosed HBP (14.4%), or suspicion of secondary HBP (4.6%). Table 1 shows the clinical characteristics of the population. Some 65% of the patients received treatment with diuretics, 61% with angiotensin II receptor antagonists (ARA-II), 47% with calcium antagonists, 35% with beta-blockers, and 27% with angiotensin converting enzyme inhibitors. The majority of patients were diagnosed with primary high blood pressure (88%). Among the secondary etiologies, PA was the most common, causing HBP in 11 patients (6%). Thyroid disease was the cause of a further 6 cases. The patients with PA showed a greater prevalence of diabetes mellitus and associated ischemic cardiomyopathy, a higher systolic blood pressure (168.5 compared to 154.4 mm Hg; *P*<.05), and a higher prevalence of LVH (as shown by their ECG; 45.5% compared to 11.6%; *P*<.01) than did patients with HBP of other etiology (Table 1).

TABLE 2. **Echocardiographic Variables for Patients With and Without Primary Aldosteronism**

	No PA (n=172)	PA (n=11)	*P*
LVEF, %	70.9 (8.75)	70.1 (10.3)	NS
TIS, mm	11.17 (2.06)	13.39 (1.93)	<.005
LVDD, mm	46.10 (5.42)	51.36 (3.58)	.001
LVPWT, mm	10.62 (1.77)	12.42 (2.15)	<.05
LVSD, mm	27.07 (5.90)	29.96 (5.70)	NS
LVM, g/m^2	97.52 (28.96)	145.54 (41.48)	<.0001
Left ventricle, mm	39.83 (6.34)	43.36 (5.22)	.05
Aorta, mm	32.14 (4.48)	39.66 (1.52)	<.005

LVDD indicates left ventricular diastolic diameter; LVSD, left ventricular systolic diameter; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; NS, not significant; LVPWT, left ventricular posterior wall thickness; TIS, thickness of the interventricular septum.
Data are means (standard deviation).

No significant differences were seen for the other variables analyzed, such as the severity of HBP, anti-hypertensive treatment, or the duration of HBP (171 [152] compared to 123 [146] months; *P*=.3).

The results of the echocardiographic study showed significantly thicker left ventricular walls and significantly larger left ventricular diastolic diameters among the patients with PA; the differences in the diameter of the left atrial wall were close to significant (Table 2). The patients with PA had a significantly greater mean ventricular mass than those with HBP of other etiology (145.54 compared to 97.52 g/m^2; *P*<.0001), independent of the systolic blood pressure.

DISCUSSION

These results show the importance of PA as a cause of increased blood pressure in the specialist care setting in Spain; 6% of the hypertensive patients studied were affected. The prevalence of PA among the present patients is similar to that reported recently by other authors—about 5% among patients with hypertension.[6] Others, however, report it to affect 16% of patients,[7,8] although these investigations generally based their diagnoses on the ALD/RA ratio alone; no confirmatory tests were undertaken unlike in the present work (Table 3). Not all the studies in this area analyze the same type of spectrum of patients; some have involved patients in the primary care setting,[9] while others,[7] including the present work, have investigated the problem in the specialist care setting. In addition, in the present work not only was PA the most common secondary etiology, its frequency was greater than all other secondary causes put together.

The diagnosis of PA, a potentially curable problem, is important since recent information suggests that patients with excess aldosterone are more likely to suffer premature cardiovascular events, cerebrovascular disease, cardiac fibrosis, and vascular inflammation.[10] Several studies have shown that aldosterone stimulates cellular growth and vascular remodelling,[11] which can lead to an increase in the mass of the left ventricle.[5] The present data confirm this to be more common among patients with PA than among other hypertensive patients; the mass of the left ventricle and the diameter of both this chamber, and the left atrium were greater in these patients. In addition, patients with PA showed a higher rate of prior ischemic cardiomyopathy, a problem some authors report leads to a greater risk of cardiovascular events, particularly ictus, myocardial infarction, and atrial fibrillation.[3] Nonetheless, there are authors who report similar frequencies of LVH in patients with primary HBP and in patients with PA.[12]

In conclusion, PA was the most common secondary cause of HBP in the investigated setting, and affected 6% of patients. These patients showed higher systolic blood pressure readings and a higher rate of heart problems: they more commonly showed a background of ischemic cardiomyopathy, had thicker chamber walls, and showed a larger left ventricular mass than patients whose HBP was due to other cuases.

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TABLE 3. **Frequency of Primary Aldosteronism Reported by Other Studies**

	Patients, No.	Screening Cut-off	Confirmation Test	Prevalence
Omura et al[6]	1020	ALD >12 ng/dL, RA <1 ng/mL/h	Yes	5.98%
Sabio et al[13]	1058	ALD/RA >50 ng/dL	No	5.1%
Fogari et al[14]	3000	ALD/RA >25 ng/dL	Yes	5.9%
Williams et al[7]	122	ALD/RA >750 pmol/L	No	16.39%
Mulatero et al[2] (Turin)	7343	ALD/RA >40 ng/dL	Yes	8%
Mulatero et al[2] (Singapore)	3850	ALD/RA >20 ng/dL	Yes	4.6%
Mulatero et al[2] (Chile)	914	ALD/RA >25 ng/dL	Yes	7.2%
Mulatero et al[2] (Minnesota)	1112	ALD/RA >20 ng/dL	Yes	10.8%

ALD indicates plasma aldosterone; RA, plasma renin activity

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