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Arterial hypertension and prediabetes☆

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ABSTRACT

Background and objectives: The aim of this study was to assess the factors related to new diabetes in hypertensive.
Patients and methods: This prospective follow-up study involved 2588 non-diabetic, hypertensive patients. The total follow-up was 15,053 patient-years with a median of 3.4 years (interquartile interval 1.4–6.8).
Results: During the follow-up, 333 (13%) patients had new diabetes, with a conversion rate of 2.21 (95% confidence interval [CI], 1.98–2.46) 100/patients/year. In a Cox proportional hazard model including baseline characteristics and modifications during the follow-up the three components of metabolic syndrome (excluding blood pressure and glucose values) HR 1.69 (95% CI, 1.36–2.09), family history of diabetes HR 1.49 (95% CI, 1.20–1.85) and baseline blood glucose ≥110 mg/dl HR 7.84 (95% CI, 5.99–10.29) were the most important factors related to new diabetes. Weight variation during the follow-up, and statins, beta-blockers or diuretic treatment did not increase the risk of new diabetes, blood pressure control at the end of study reduce the risk HR 0.74 (95% CI, 0.61–0.91).
Conclusions: In hypertensive non-diabetic patients in primary prevention the factors related to new diabetes can easily identified at the beginning of follow-up. Being obese, with family history of diabetes, and glucose values ≥110 mg/dl dramatically increase the risk of developing new diabetes.

Hipertensión arterial y prediabetes

Palabras clave:
Hipertensión arterial
Estado prediabético
Síndrome metabólico

RESUMEN

Fundamento y objetivos: Valorar los factores que predisponen a la aparición de diabetes en hipertensos.
Pacientes y método: Estudio longitudinal prospectivo en 2.588 hipertensos no diabéticos sin enfermedad cardiovascular previa, con una mediana de seguimiento (mediana-intervalo intercuartílico) de 3,4 (1,4-6,8) años, con seguimiento total de 15.053 pacientes/año.
Resultados: Trescientos treinta y tres (13%) pacientes se convirtieron en diabéticos, con una tasa de conversión de 2,21 (intervalo de confianza del 95% [1,98-2,46]) 100/pacientes año. Se realizó un análisis de regresión de Cox con los factores que modificaban la aparición de diabetes. Al inicio del seguimiento los tres componentes del síndrome metabólico (excluyendo los valores de presión arterial y de glucemia) HR 1,69 (intervalo de confianza del 95%, 1,36-2,09), los antecedentes familiares de diabetes HR 1,49 (intervalo de confianza del 95%, 1,20-1,85) y especialmente la glucemia basal 110 mg/dl HR 7,84 (intervalo de confianza del 95%, 5,99-10,29) eran los factores mas importantes para la aparición de la diabetes. Ni las variaciones de peso ni el tratamiento con estatinas, betabloqueantes o diuréticos durante el seguimiento

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mostraron un incremento del riesgo, solo el buen control de la presión arterial al final del estudio redujo el riesgo de evolución a diabetes HR 0,74 (intervalo de confianza del 95%, 0,61-0,91).
Conclusiones: En hipertensos los factores que predisponen a la aparición de diabetes se pueden identificar fácilmente al inicio del seguimiento: ser obeso, tener antecedentes familiares de diabetes y una glucemia ≥ 110 mg/dl multiplican notablemente el riesgo de ser diabético en unos pocos años.

Introduction

Cardiovascular disease is the leading cause of overall mortality in our health environment, and high blood pressure (HBP) and diabetes mellitus (DM) are two of the main cardiovascular risk factors that promote atherosclerosis and its major complications such as stroke, ischemic heart disease and peripheral arterial disease.[1]

HBP and DM often coexist because they share common etiologic and pathogenetic factors.[2] In addition, HBP increases the risk of developing DM, and even prehypertension is associated with increased incidence of DM over time.[3]

The diagnosis of DM is made after detection of glucose values, while fasting or after an oral glucose tolerance test, or elevated HbA1C values, perfectly determined and established.[4] The same tests are used to establish the prediabetes concept, as an intermediate stage for glucose metabolism, which clearly predisposes to DM onset. The diagnosis of prediabetes has a great interest in the hypertensive population.[5] Changes in lifestyle, weight loss, or certain drugs used in antihypertensive or lipid-lowering therapy are common in hypertensive patients and can modify the onset of prediabetes or diabetes and consequently the global cardiovascular risk of these patients.[6]

The aim of this study is to assess the factors associated with the onset of DM in a hypertensive population and the impact that the usual treatment, changes in lifestyle and antihypertensive and lipid-lowering drugs could cause in its onset.

Patients and method

Study

A prospective longitudinal follow-up study of a cohort of hypertensive patients treated at the Hypertension and Vascular Risk Unit (Internal Medicine) of the Sagunto Hospital (Conselleria de Sanidad, Valencia) with the diagnosis of hypertension was conducted.

Patients

All hypertensive patients seen consecutively from 01/01/2001 to 31/03/2013, who met the following inclusion criteria were included: (a) age > 18 and under 75; (b) have a clinical systolic blood pressure (SBP) ≥ 140 mmHg or clinical diastolic blood pressure (DBP) ≥ 90 mmHg in three successive measurements during one month of follow-up, or being on antihypertensive treatment in the initial assessment; (c) having at least one full year of follow-up in the study. The exclusion criteria were: (a) secondary hypertension of any kind; (b) neoplasm, systemic disease or liver or renal failure (glomerular filtration rate <30 ml/min/1.73 m^2 or clinical proteinuria); (c) heart failure (classes III and IV as per the *New York Heart Association*); (d) have a history of ischemic heart disease or a history of cerebrovascular disease or peripheral arterial disease; (e) taking hypoglycaemic drugs, or having been previously diagnosed or being diagnosed with diabetes at the initial visit. Epidemiological, clinical and laboratory data were collected in electronic format, in compliance with Law 15/1999 on confidentiality. The study was conducted in accordance with the standards of good clinical practice and was approved and monitored by the Clinical Research Ethics Committee of the Sagunto Hospital. All patients gave their informed consent at baseline.

Sample size: based on the hazard ratio obtained in previous studies with metabolic syndrome (MS)[7] with a relative risk of 1.5 for a proportion of patients exposed to the risk factor studied of 30%, with a significance level of 5% and 80% power and assuming a censoring proportion of 90%, the minimum sample size would be 2273 patients.[8]

Clinical examination and methods

At the start of follow-up all patients underwent a complete medical history and physical examination that included among others, body weight (kg), height (cm) and body mass index (BMI) (calculated as weight in kg divided by height in meters squared) and waist circumference measurement (cm).

Clinical blood pressure (BP) was measured with the patient seated after five minutes' rest following the directions of the British Hypertension Society.[9] A lab test determination was performed to all patients in the morning, after eight hours of fasting, which allowed to evaluate the main biochemical parameters. Fasting plasma glucose and HbA1c values were measured, among others. The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (MDRD) abbreviated formula.[10] These data were collected in a standardized way in a database to calculate their global cardiovascular risk (CVR) based on the calibrated Systematic Coronary Risk Evaluation (SCOREc) function[11] (in under 40-year-olds, the risk was calculated by projecting the age to 40 years, over 65-year-olds the risk was estimated as if the age was 65).

Patients who met the National Cholesterol Education Program-Adult Treatment Panel III[12] criteria were diagnosed with MS.

Follow-up and study design

After the initial evaluation, patients were monitored in the unit as outpatients once a month until clinical stabilization and, subsequently, in annual periods.

All patients were given written instructions advising about changes in their lifestyle, recommending increased exercise and a diet low in saturated fat and salt. Those who had a BMI ≥ 25 kg/m^2 were also given written instructions on following a low-calorie diet. These recommendations and instructions were repeated in each of the successive visits during follow-up.

When prescribing antihypertensive drugs (diuretics, beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors, receptor blockers and angiotensin vasodilators) the number, type and dose of drug were based on clinical data in order to obtain BP values <140/90 mmHg. In analysing the impact of different drugs on the onset of diabetes, it was required that a particular drug should be prescribed at least one full year for its evaluation.

The diagnosis of diabetes during follow-up was done when patients had: (a) values of fasting glucose ≥126 mg/dl repeated twice, (b) plasma glucose values 200 mg/dl with suggestive symptoms, (c) Hb A1C values ≥6.5% or when after going to one of the follow-up consultations they were receiving a new treatment with