International Journal of Cardiology 153 (2011) 286–290

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Short-term metabolic changes achieved by weight loss in hypertensive patients

Alberto Cordero [a,*], Vicente Bertomeu-Martínez [a], Pilar Mazón [b], Diego Martín-Raymondi [c], Jose Luis Palma [d], Manuel Anguita [e], Iñaki Lekuona [f], Enrique Galve [g], José R. González-Juanatey [b]

[a] Hospital Universitario de San Juan, Alicante, Spain
[b] Hospital Universitario de Santiago, A Coruña, Spain
[c] Hospital Santos Reyes, Aranda de Duero, Burgos, Spain
[d] Hospital Ramón y Cajal, Madrid, Spain
[e] Hospital Reina Sofía, Córdoba, Spain
[f] Hospital Galdakao, Bilbao, Spain
[g] Hospital Valle Hebrón, Barcelona, Spain

ARTICLE INFO

Article history:
Received 5 April 2010
Received in revised form 13 July 2010
Accepted 17 August 2010
Available online 18 September 2010

Keywords:
Hypertension
Weight loss
Glucose metabolism
Diabetes
Fasting glucose

ABSTRACT

Introduction: Glucose and lipid metabolism abnormalities of hypertensive patients are highly relevant due to its increase in cardiovascular risk; moreover, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) have a high risk of new-onset diabetes mellitus (DM) development. The objective of the study was to describe glucose metabolism abnormalities and the impact of mid-term weight loss.
Methods: A six-month prospective, observational and multicentre study of patients with hypertension was conducted. Clinical antecedents, physical examination, blood test and treatments were collected in two separated visits; conventional advice was the only intervention planned.
Results: A total of 1957 patients were included, mean age 66.3 (10.9) years and 59.9% males. A previous diagnosis of glucose metabolism alteration was present in 43.9% (25.5% type-2 DM, 14.8% IFG, 1.6% IFG and IGT, 1.0% IGT and 1.0% type-1 DM). An increasing pattern of cardiovascular risk and target organ damage was observed according to the categories of fasting glucose. Oral glucose tolerance test (OGTT) was carried out in 234 patients (11.9%) patients and yielded the diagnosis of IGT in 44.7% or DM in 22.4% of patients with fasting glucose >100 mg/dl. Six months follow-up was achieved in 85.9% patients. A slight reduction in fasting glucose was observed in the whole cohort and patients who achieved ≥5% weight loss experienced the highest reduction in fasting glucose, LDL-c and triglycerides; moreover, 15.8% normalized their IFG.
Conclusions: Glucose and lipid metabolism abnormalities are highly prevalent in hypertensive patients and improve with 5% of weight lost at 6 months follow-up. OGTT is not currently extended in daily clinical practise.

1. Introduction

Patients with hypertension can often be diagnosed of several metabolic abnormalities, mainly related to glucose and lipid metabolism [1–3]. Glucose metabolism abnormalities involve a wide range of qualitative clinical settings that can globally be classified as impaired fasting glucose (IFG) when fasting glucose is >100 mg/dl, impaired glucose tolerance (IGT) if 2 h post-oral glucose tolerance test (OGTT) is 140–200 mg/dl and diabetes mellitus (DM) if fasting glucose is >126 mg/dl in two separate determinations or >200 mg after a OGTT [4]. Main clinical relevancy of IFG and IGT relies in two aspects: the high risk of mid-term new-onset DM [4,5] and the increased cardiovascular risk [6,7]. The accurate diagnosis of glucose metabolism and DM also has relevant clinical implications because the American Society of Diabetes recently recommended metformin initiation as soon as DM is diagnosed [8].

Abnormalities in lipid profile are also frequent in hypertensive patients and have a significant impact on cardiovascular risk [9]. Same as glucose metabolism, lipid abnormalities are closely related to obesity and insulin resistance [10,11]; consequently, lifestyle modification and weight loss are the primary recommendations for prevention and management of glucose and lipid metabolism [1,12] but the real impact of lifestyle modification and weight loss in high-risk patients has not been clearly reported [13]. Hypertension is the most prevalent risk factor in patients with established cardiovascular disease [14,15] and is responsible of approximately 50% of new coronary events in Spain [16]. Based on these antecedents the Hypertension Working Group of the Spanish Society of Cardiology designed and performed the EPYCAM–HTA study with three objectives: first, describing the prevalence of glucose and lipid abnormalities in hypertensive patients; second, identifying therapeutical

* Corresponding author. Cardiology Department, Hospital Universitario de San Juan, Carretera Valencia-Alicante sn, 03550, San Juan de Alicante, Alicante. Tel.: +34 965 938700; fax: +34 965 656268.
E-mail addresses: acordero@coma.es, acorderofort@gmail.com (A. Cordero).

0167-5273/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijcard.2010.08.051

changes induced by the newly diagnosed DM, and; third; describing short-term changes associated with weight loss achieved by the most commonly method used currently that is standard counselling.

2. Materials and methods

2.1. Study design

This study was an observational, prospective, multicentre and nationwide registry of patients with hypertension attended by cardiology specialists. The study was based on 2 visits: the inclusion visit that consisted in full clinical history of each patient and biochemical determinations; the second visit evaluated short-term changes in glucose metabolism, risk factors control and therapeutic modifications. Patients did not receive any specific or intensive recommendation regarding lifestyle changes or weight loss, just conventional advice about healthy habits and food patterns. Investigators were encouraged to perform OGTT in all patients with fasting glucose >100 mg/dl. The study protocol and the informed consent were approved by ethics committee of the Investigation Agency of the Spanish Society of Cardiology (study code *SEC-01/07*).

A random selection of 400 cardiologists were invited to participate in the study. Each investigator should include 10 consecutive patients through the first 15 days of January 2008 and scheduled a second visit 6 months later; investigators that did not make the follow-up of any patient were excluded. A total of 2093 patients were collected in the first visit by 285 investigators; 136 (6.5%) were excluded for missing data and the remaining 1957 were included in the follow-up, that was performed completely in 1682 (85.9% of total) patients.

Inclusion criteria were: age >18 years, previous diagnosis of hypertension and acceptance to participate in the study by signing the informed consent. Exclusion criteria were secondary hypertension, inclusion in a clinical trial or denial of informed consent.

2.2. Data collection

A specific data collection protocol by paper was designed by the investigator committee. Each patient and investigator received a code number to preserve anonymity and only one study coordinator could know the name of each investigator but none of patients' names. Demographical data, risk factors, physical examination, biochemical parameters and medical treatments were collected in the inclusion and follow-up visit.

2.3. Glucose metabolism

According to current recommendations [1,4], fasting glucose >100 mg/dl and <126 mg/dl was considered IFG; IGT if 2 h post-OGTT glucose was 140–200 mg/dl; and DM if fasting glucose was >126 in both determinations or >200 mg/dl 2 h post-OGTT. Fasting glucose had to be obtained after an overnight fasting of at least 8 h and OGTT was performed by the determination of serum glucose 2 h after the administration of 75 g of glucose dissolved in 250–300 ml of water (specifically commercialized) that had to be drunk in about 5 min and remain in complete repose until second blood determination.

2.4. Definitions

Patients were classified according to body mass index (BMI) as normal (<25 kg/m^2), overweight (25–30 kg/m^2) or obese (>30 kg/m^2). Abdominal obesity was registered if waist circumference was >102 cm in men or >88 cm in women [12]. The following target organ damages were collected [1]: proteinuria (microalbuminuria if albumin urinary excretion was 30–300 mg/24 h or macroalbuminuria if >300 mg/24 h), left ventricle hypertrophy (Cornell criteria in the electrocardiogram or left ventricular mass index >125 g/m^2 in men or >110 g/m^2 in women), glomerular filtration rate <60 ml/min/1.73 m² (assessed by the MDRD equation), atrial fibrillation, heart failure (diagnosis included in a medical report, any hospitalization with discharge diagnosis of heart failure or compatible signs and symptoms verified with an image technique) and coronary heart disease (defined as previous myocardial infarction, acute coronary syndromes, stable angina or any coronary revascularization procedure).

2.5. Statistical analysis

An independent company translated data collection protocols into digital format. Data were processed by statistical package SPSS 15.0 *(SPSS Inc, Chicago, IL)*. Comparisons of means were analyzed by Student's *t* tests; comparisons of the two visits means were performed by paired-samples ANOVA tests. Statistical significance was accepted at the value of $p \leq 0.05$.

3. Results

Mean age of the 1957 hypertensive patients included was 66.3 (10.9) years and 59.9% were males. Mean years since the diagnosis of hypertension was 8.7 (7.0) years, median 8.0 (interquartile range 4.0–11.0). Previous diagnosis of glucose metabolism abnormality was present in 42.6% of the sample, type-2 DM being the most frequent diagnosis (34.3%), followed by IFG (5.0%), IFG and IGT (1.3%), IGT (1.1%) and type-1 DM (1.0%). General characteristics of the sample, according to fasting glucose, are presented in Table 1; an increasing pattern of cardiovascular risk and target organ damage was observed in the categories of normal fasting glucose, IFG and fasting glucose >126 mg/dl; as a consequence, the number of cardiovascular treatments, antiplatelets, lipid-lowering and glucose-lowering treatments were higher in each category of increasing fasting glucose (Table 2).

OGGT was performed in 234 patients (11.95% of total) without previous diagnosis DM; from these 5.5% had fasting glucose <100 mg/dl and 10.0% >100 mg/dl. As shown in Table 3, the diagnosis of IGT or DM according to OGTT result was much more frequent in patients with fasting glucose >100 mg/dl. No clinical difference was found between patients in whom OGTT was performed or not.

Mean follow-up time was 5.9 (1.5) months and was completely achieved in 1682 (85.9% of total) patients; clinical characteristics of these patients did not differ from the overall population. Mean weight lost was 0.70 (3.1) kg with the resulting reduction in mean BMI of 0.25 (1.2) kg/m^2; this was not equally distributed within the cohort because 14.9% patients achieved ≥5% weight lost, 4.4% increased ≥5% in their weight and 80.7% of the cohort did not modify their weight out of these thresholds. Compared to baseline, a significant reduction in fasting glucose was observed in the whole cohort (114.50 vs. 119.06; $p<0.01$). It is remarkable that the largest reduction in fasting glucose was observed in patients that lost ≥5% of their baseline weight, compared to those who did not modify significantly their weight or gained weight (Table 4); these changes translated into 2-fold higher normalization of fasting glucose in patients who achieved ≥5% of weight lost through follow-up, compared to the rest (Fig. 1).

According to fasting glucose and OGTT an increasing tendency of metformin initiation was observed, from 4.3% in patients with IFG to 9.6% in patients with final diagnosis of DM (Fig. 2); the percentage of patients in whom statins or antiplatelets was started very low.

Table 1
General characteristics of the sample according to fasting glucose.

	Total	Fasting glucose <100 mg/dl	Fasting glucose 100–125 mg/dl	Fasting glucose >126 mg/dl	*p*
n (%)	1,957	793 (40.5%)	588 (30.0%)	576 (29.4%)	
Age (years)	66.3 (10.8)	65.8 (11.4)	65.9 (10.9)	67.4 (9.8)	0.01
Males	59.7%	58.2%	62.1%	59.5%	0.25
Fasting glucose	119.6 (40.7)	89.5 (7.7)	110.3 (7.7)	167.9 (40.9)	<0.01
Body mass index	29.4 (7.3)	28.4 (6.3)	29.8 (10.0)	30.3 (5.2)	<0.01
Waist perimeter	100.4 (13.5)	97.9 (12.8)	101.5 (13.3)	102.4 (14.2)	<0.01
Current smokers	13.6%	13.7%	15.9%	11.2%	0.07
Dislipidemia	65.2%	58.4%	66.7%	72.8%	<0.01
Diabetes mellitus	35.3%	7.0%	28.7%	85.8%	<0.01
Heart failure	12.3%	10.0%	10.6%	17.1%	<0.01
Coronary heart disease	19.1%	15.2%	20.3%	24.9%	<0.01
GFR (mg/dl/min)	81.7 (80.1)	79.4 (45.6)	83.3 (101.3)	83.2 (92.3)	0.001
GFR <60 ml/min/1.73 m²	24.4%	20.9%	23.1%	30.1%	0.01
Proteinuria	3.3%	1.5%	2.3%	6.5%	0.01
Atrial fibrillation	15.4%	13.6%	14.8%	19.4%	0.05
LVH by ECG	27.4%	24.6%	29.1%	29.9%	<0.01
LVH by echocardiogram	48.4%	44.3%	52.6%	53.5%	<0.01
Target organ damage	74.0%	68.2%	76.7%	78.9%	<0.01
Diagnosis of glucose metabolism alteration	42.6%	8.8%	48.4%	89.0%	<0.01

GFR: glomerular filtration rate; LVH: left ventricle hypertrophy.