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Pulse pressure amplification, adiposity and metabolic syndrome in subjects under chronic antihypertensive therapy: The role of heart rate

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Abstract

Background: Body mass index (BMI) and waist circumference (WC) are increased in subjects chronically treated for hypertension. However, the relationships of BMI, WC and metabolic syndrome (MS) with central wave reflections and pulse pressure (PP) amplification have never been investigated.

Methods: A cohort of 517 treated hypertensives was studied cross-sectionally as function of BMI, WC and presence of MS, the latter used as index of insulin resistance. In men and women, carotid wave reflections were evaluated using pulse wave analysis and augmentation index measurement. PP amplification between brachial and carotid arteries was determined as a vascular factor contributing to protect against an increased afterload.

Results: When compared to their own controls, treated hypertensive subjects with increased BMI, WC or MS did not differ in terms of mean values of brachial and carotid blood pressure and augmentation index. However, they were characterized by increased heart rate (HR) and PP amplification. Such results were independent of age, drug treatment, and traditional cardiovascular risk factors. After HR adjustment, the increased PP amplification observed in subjects with high WC or MS became non-significant in men, but remained unmodified in women. The presence of beta-blockade did not modify the result.

Conclusion: In treated hypertensive subjects, adiposity and insulin sensitivity influence independently PP amplification. The finding is observed mainly in women.

Keywords: Adiposity; Metabolic syndrome; PP amplification; Augmentation index; Antihypertensive therapy; Central blood pressure

1. Introduction

Under antihypertensive drug therapy, the prevention of cardiovascular (CV) events has a maximal effectiveness for stroke and congestive heart failure but acts in a lesser extent when coronary risk is considered (see review in [1]). The Prime Study has shown that, at any given level of systolic blood pressure (SBP), coronary risk is higher in treated than in untreated hypertensive subjects, indicating that under treatment, a consistent residual coronary risk remains present [2].

In hypertensive subjects under chronic antihypertensive treatment, increased adiposity is frequently observed and, independently of blood pressure (BP) level, has several implications in CV risk [1–3]. First, overweight is frequently associated with increased waist circumference (WC), metabolic syndrome (MS) or type 2 diabetes, all factors predisposing to coronary ischemic disease [1]. Second, in the recent years, adiposity has been shown to be independently and consistently associated with increased aortic stiffness, a major factor predicting coronary ischemia and myocardial

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infarction [1,4,5]. Finally, adiposity is frequently linked to increased heart rate (HR), a parameter commonly involved in coronary ischemia and mostly in the development of SBP and PP amplification (see review in [1]).

Physiologically, whereas mean blood pressure (MBP) and diastolic blood pressure (DBP) are almost the same along the totality of the arterial tree, SBP and pulse pressure (PP = SBP − DBP) are significantly lower in central (thoracic aorta; carotid artery) than in peripheral (brachial artery) arteries [1]. This hemodynamic profile, called SBP and PP amplification, is the consequence of the propagation of pressure wave along vascular conduits, with a progressive reduction of diameter and increase in wall thickness and stiffness, together with resulting changes in timing and amplitude of wave reflections. Normally, the carotid–brachial SBP or PP amplification approximates 11–14 mmHg, both in normotensive and hypertensive subjects, thus contributing to protect the heart from an increased afterload [1]. Aging is associated with a consistent reduction of SBP and PP amplifications together with a resulting increase of CV risk [1,6]. Increased HR rather contributes to enhance amplification [1]. Reduction of HR, which is commonly observed under body weight reduction [1,5,7], may have a significant opposite effect on this process. However, the central hemodynamic profile of hypertensive subjects under chronic drug therapy has never been investigated in detail, particularly in subjects with increased adiposity and/or MS. Our working hypothesis is to show that, in treated hypertensive subjects, the interactions between obesity and autonomic nervous system will be shown more obviously using central (carotid) than peripheral (brachial) blood pressure measurements.

The purpose of the present study was, in a cross-sectional study of subjects chronically treated for hypertension, first, to determine the carotid (central) and brachial BP profile of subjects with or without increased adiposity and second, to determine which hemodynamic parameters, such as PP amplification, heart rate and pressure wave reflections, might characterize the CV risk of those who were or remained obese. A particular attention will be given to differences between males and females as regards insulin-resistance, clinically judged by the degree of abdominal adiposity and mostly the presence of MS.

2. Methods

2.1. Subjects

The cohort was composed of patients entered in day-hospitalization for a CV check-up ordered by their physician because of the presence of one or several CV risk factors involving normal or high BP, smoking, dyslipidemia, diabetes mellitus, obesity and/or family history of premature CV disease [8]. From the totality of this cohort, we selected all subjects receiving chronically antihypertensive drug treatment ($n = 517$) since at least 1 year were selected. The number of antihypertensive agents per day in each patient was 1.8 in men and 1.7 in women. The compounds involved calcium antagonists of dihydropyridine type (312 patients), beta-blockers (193 patients), diuretics (198 patients), angiotensin-converting enzyme inhibitors (161 patients), central-acting agents (105 patients), angiotensin II antagonists (36 patients), and alpha-blockers (18 patients), either alone or in combination. From the totality, 111 (21.5%) patients were medically treated for dyslipidemia (drugs including statins or fibrates) and 42 (8.1%) patients were medically treated for type 2 diabetes (drugs including sulfamides and/or biguanids). No patient was under dietary intervention or body weight reduction during the study. Patients with all forms of secondary hypertension, with cancer (other than basal cell carcinoma), insulin-dependent diabetes or severe renal insufficiency (plasma creatinine >300 μmol/l) were excluded from the study [8]. Each subject provided informed consent for the investigation, which was approved by our institutional review board.

2.2. Clinical evaluation of adiposity and/or insulin-resistance

In the total population, body mass index (BMI) was calculated as weight divided by height squared (kg/m^2) and waist circumference (WC) was measured in indoor clothing using an inelastic tape, as the circumference midway between the lower ribs and iliac crest in standing position. Global and regional adiposity cut-offs were defined according to international standards [9,10]. As all subjects are hypertensives, they were considered to have the MS if they had at least two of the four following characteristics [11]: (1) WC > 102 cm in men and >88 cm in women; (2) triglycerides ≥ 150 mg/dl (1.69 mmol/l); (3) HDL-cholesterol < 40 mg/dl (1.04 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in women and (4) fasting glucose ≥ 110 mg/dl (6.1 mmol/l). Participants using antidiabetic (oral agents or insulin) were classified as subjects having increased fasting blood. Finally, subjects were ordered according to their MS number of anomaly: 1–3 or more.

2.3. Brachial BP measurements and biological parameters

Information compiled from the questionnaire filled out at inclusion involved gender, age, smoking habits, previous CV diseases, use of medications including antihypertensive drugs, weight and height [8]. In all patients past CV complications were absent.

Measurements were performed in the morning after an overnight fast, each patient being in supine position. Brachial BP was determined with a mercury sphygmomanometer after 15 min rest. Phases I and V of the Korotkoff sounds were considered respectively, as SBP and DBP. Brachial pulse pressure (PP) was the difference between SBP and DBP. Five measurements 2 min apart were averaged. Hypertension was defined as SBP ≥ 140 and/or DBP ≥ 90 mmHg.