European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences | 2006; 10: 75-78

Body fluid compartments in hypertension

R. CIANCI*[§], F. CITRO[§], A. MIGNECO*[§], F. BALDONI[1], M.C. MINISCI[§], N. DI DANIELE[1], A. DE LORENZO[§]

[§]Division of Human Nutrition and [1]Internal Medicine, University of Rome "Tor Vergata" – Rome (Italy)
*Institute of Internal Medicine, Catholic University – Rome (Italy)

Abstract. – ***Background and Objectives:*** **There is a correlation between the fluid and ionic homeostasis and blood pressure but it is not known if these body fluid changes represent the cause or rather the effect of the blood pressure rise. We have estimated the compartmental distribution of body fluids by means of the Bioimpedance Spectroscopy (BIS) analysis in a hypertensive cohort compared to control subjects.**

Material and Methods: **We have enrolled 28 hypertensive patients (14 females, 14 males, mean age 47 ± 5) and a sex- and age-matched control group of 37 healthy subjects (17 females and 20 males, mean age 45 ± 8). They underwent anthropometric measurements, then extracellular (ECW) and intracellular water (ICW) were assessed using BIS.**

Results: **Both mean weight and BMI of hypertensive patients resulted significantly higher than of the control group ($p < 0.05$). We found higher ICW values in hypertensive compared to normotensive subjects. This difference was proportional to the difference of mean blood pressure values, reaching significance only as regards the stage II hypertensive subgroup ($p < 0.03$).**

Discussion: **Our data confirm that the blood pressure increases are associated to TBW, and caused mainly by ICW increases. The BIS, a simple, reliable, non invasive and cost effective methodical approach, estimating the distribution of body fluids, offers new possibility of the management of the hypertensive disease, to establish a more appropriate antihypertensive treatment. Moreover, the BIS, estimating the volume restoration of the different body compartments, may be helpful in evaluating the effectiveness of the pharmacological treatment.**

Key Words:

Bioimpedance spectroscopy (BIS), Arterial hypertension, Compartimental fluid distribution, Extracellular water (ECW), Intracellular water (ICW).

Introduction

It is well known that hypertensive patients have an up to seven time higher risk of developing cerebrovascular and cardiovascular affections than normotensive subjects[1]. Despite declines in recent years, heart disease and stroke remain the first and third leading causes of death in the United States, respectively. Of all US deaths in 2001, heart disease accounted for 29.0% and stroke for 6.8%. The major risk factors for both conditions are high blood pressure, high cholesterol, diabetes, smoking, and obesity, all of which have been targeted by national prevention programs[1]. These data explain the great number of scientific papers focusing on the pathogenesis of hypertension in the last years. Aim of all these studies is the development of an effective preventive therapy. The 95% of hypertensive subjects are classified as essential hypertensives, meaning that no clear cause can be found underlying such disease. The role of the renin-angiotensin system (RAS), of the sympathetic system and of the endothelium in the maintenance of blood pressure is well known. Moreover, in the last years, evidences of correlations between the fluid and ionic homeostasis and the regulation of blood pressure have been found. In fact, changes of the volume of body fluids, in particular of the interstitial fluid, seem to effectively reflect the hypertensive state[2-7]. Since there are many difficulties in obtaining data about body fluid shifts, it is not known if these body fluid changes represent the cause or rather the effect of the blood pressure rise. Clarifying the exact mechanism underlying this correlation could offer new therapeutic approaches with remarkable impact on this affection. Distinc-

Corresponding author: Antonino De Lorenzo, MD; e-mail: lab.immunol.2@rm.unicatt.it

tion of water rich and water poor body compartments is currently performed by bioimpedenzometry, measuring the bioelectrical impedance (z), the opposition that the body (a biological conductor) offers to the passage of an electrical alternated current. Body impedance is then inserted in appropriate formulas for the determination of the total body water (TBW) and the free fat mass (FFM). FFM contains approximately 73% of the TBW in healthy subjects and in patients affected by different diseases. New equipments, carrying out impedance measurements at various resolutions modifiable by the operator (Bioimpedance Spectroscopy, BIS), obtain broader bioelectrical informations, enabling the operator to estimate some fluid under-districts, like extracellular water (ECW) and intracellular water (ICW). The BIS uses more physiology-related mathematical-statistical models in order to extrapolate parameters like extracellular resistance (RECW) and intracellular resistance (RICW), carrying out a scansion of currents to variable frequencies (from 1 kHz to 1 MHz) and measuring values of resistance®, reactance (Xc) and phase angle (φ). This technique enables the operators to monitorize the hydratation of single body tissues or single fluid compartments[7-9]. The continuous and progressive improvements of this methodological approach and its international standardization explain the interest for its possible applications in research and in clinical context.

Aim of this study was the assessment of body fluids and the estimation of the compartmental distribution in ICW and ECW by means of the BIS in a hypertensive population compared to control subjects.

Methods

The study was first approved by the Ethical Committee of the “Tor Vergata” University, Rome. Each subject gave written informed consent to participate to the study. Body fluid compartments of 28 essential hypertensive patients (14 females, 14 males, mean age 47 ± 5) was assessed by BIS.

Hypertension degree of these subjects was classified according to WHO-ISH guidelines[10]. These subjects were not on antihypertensive treatment and did never take antihypertensive drugs in the last 6 months. Moreover, they were not affected by any disease that could interfere with the study.

A group of 37 healthy subjects sex- and age-matched (17 females and 20 males, mean age 45 ± 8) was used as control group.

All subjects have been submitted haematologic screening in order to exclude metabolic diseases. They underwent also to echocardiography, fundus oculi assessment, urine test and 24-h ambulatory blood pressure monitoring (ABPM). Thyroid tests, urinary catecholamines, and an echo-Doppler scan of renal arteries were performed in order to exclude secondary causes of hypertension.

Body weight was measured to the nearest 0.1 kg on an electronic beam scale (Invernizzi, Bologna Italy), without clothes and shoes and after subjects voided. Height was measured to the nearest 0.5 cm with a stadiometer (Invernizzi, Bologna Italy). Body mass index (BMI) was calculated as weight (kg)/height (m^2).

Bioimpedance Spectroscopy (BIS) Analysis

After measurement of body weight and height, and with subjects in a fasted state after voiding, single wrist-to-ankle (i.e., whole body) complex impedance (Z) measurements were taken using BIS (Xitron 4000B, Xitron Technologies Inc., San Diego, CA, USA). Resistance (R) and Reactance (X_C) were measured at 21 frequencies, ranging from 1 kHz to 1.248 Mhz, using Littmann 2325VP adhesive electrodes (3M, St. Paul, MN, USA). The measurements were taken within the first several minutes after subjects assumed the supine position, as previously described by De Lorenzo et al[8]. FFM was calculated by using the formula developed by Segal et al[11].

Statistical Analyses

Differences among groups for all variables were calculated using a one-way analysis of variance (ANOVA). If significant main effects or interactions occurred, Bonferroni’s post-hoc test was utilized to detect the differences. The data were analyzed using the Statistical Program for the Social Sciences (SPSS) version 9.0 for Windows statistical software. Statistical significance was set at p = 0.05 level of probability. All values are expressed as means ± standard deviation (SD).

Table I. Weight, Body Mass Index (BMI), diastolic (PAD) and systolic (PAS) blood pressure mean values ± standard deviation (SD) in the study control group and hypertensive patients.

	Control group			***Hypertensive patients***		
	Females (No 17)	***Males (No 20)***	***Total (No 37)***	***Females (No 14)***	***Males (No 14)***	***Total (No 28)***
Age (year ± SD)	43.6 ± 8	46 ± 7	45 ± 8	46 ± 5	45 ± 6	47 ± 5
Weight (kg ± SD)	61.6 ± 9.1	78.5 ± 9.3	70.9 ± 9.3	74.5 ± 9.2	91.5 ± 10.3	84.5 ± 10.1*
Height (cm ± SD)	160 ± 5	173 ± 6	167 ± 6	167 ± 7	173 ± 6	168 ± 7
BMI (kg/m^2 ± SD)	23.9 ± 2.5	26.2 ± 2.6	25.2 ± 2.6	28.5 ± 3.2	30.4 ± 4	29.6 ± 4.6*
PAD (mmHg ± SD)	80.4 ± 1.3	80.0 ± 1.2	80.2 ± 1.2	96.1 ± 5.4	101.0 ± 12.0	99.0 ± 9.9†
PAS (mmHg ± SD)	126.6 ± 3.6	126.2 ± 3.3	126.4 ± 3.4	151.1 ± 11.2	154.5 ± 16.2	153.1 ± 14.1†

*$p < 0.05$; †$p < 0.0001$.

Results

Table I reports the anthropometric data of hypertensive patients and controls. Both mean weight and BMI of hypertensive patients resulted significantly higher than the control group ($p < 0.05$). Diastolic and systolic blood pressure values in the control group resulted within normal ranges (80.2 ± 1.2 mmHg as regards diastolic blood pressure, 126.4 ± 3.4 as regards systolic blood pressure), while hypertensive subjects showed significant higher blood pressure values (99 ± 9.9 mmHg as regards diastolic blood pressure, 153.1 ± 14.1 mmHg as regards systolic blood pressure) ($p < 0.0001$). Hypertensive subjects showed increased TBW, ICW and ECW compared to normotensive control subjects (Table II). In particular, the control group showed mean TBW values within normal ranges (36.5 ± 7.3 liters), while hypertensive subjects showed increased TWB values (40.0 ± 9.8 liters). We found higher ICW values in hypertensive patients compared to normotensive subjects (22.1 ± 6.1 vs 18.1 ± 4.4) and this difference was proportional to the difference of mean blood pressure values, reaching statistical significance only as regards the stage II hypertensive subgroup when compared to normal subjects ($p < 0.03$). Differences of ECW (17,7 ± 3.5 liters in normal subjects vs 17.9 ± 3.9 liters in the hypertensive patients) did not reach statistical significance. Moreover, FFM values appeared to be higher in hypertensive individuals compared to normotensive subjects (29.2 ± 7.1 kg vs 26.6 ± 5.3 kg) even if such differences did nor reach statistical significance.

Discussion

Our data showed that hypertensive subjects had an increased TBW, reflecting an increase of both ICW and ECW. In particular, hypertensive

Table II. TBW, ICW and ECW mean values ± SD in the study control group and hypertensive patients.

	Control group	***Hypertensive patients***		
	Total (No 37)	***Total (No 28)***	***Females (No 14)***	***Males (No 14)***
TBW (l ± SD)	36.5 ± 7.3	40.0 ± 9.8	39.4 ± 6.1	42.4 ± 12.5
ICW (l ± SD)	18.1 ± 4.4	22.1 ± 6.1	21.2 ± 3.3	23.9 ± 7.9*
ECW (l ± SD)	17.7 ± 3.5	17.9 ± 3.9	18.2 ± 2.9	18.5 ± 4.7
FFM (kg ± SD)	26.6 ± 5.3	29.2 ± 7.1	28.8 ± 4.4	31.0 ± 9.1
ECW/ICW	1.0 ± 0.2	0.9 ± 0.2	0.9 ± 0.1	0.8 ± 0.1†

* $p < 0.05$; †$p < 0.01$.

patients showed a progressive increase of the ICW that becames significant when compared to healthy subjects in stage II hypertension ($p < 0.03$). The significant decrease of the ratio ECW/ICW compared to controls ($p < 0.02$) appeared to be even more interesting, indicating that water content increases in hypertensive patients were attributable mostly to ICW increases. These ICW increases were well correlated to blood pressure values. These results are consistent with previous observations[11-16], confirming that the blood pressure increases are associated to TBW, and caused mainly by ICW increases. Moreover, the ICW increases seemed to be somewhat proportional to the blood pressure rise. Possible explanations of such volumetric dysregulations in arterial hypertension could be due to a dysfunction of the Na/K^+ pump, an alteration of the RAS or to possible dysfunctions of the sympathetic nervous system.

Even if a definite explanation of such changes of body water content in hypertension is still lacking, the BIS, a simple, reliable, non invasive and cost effective methodical approach that supplies an estimation of the distribution of body fluids offers new possibility of management of the hypertensive disease. The BIS is currently used in the management of the obese patients, hypertensive pregnant women and other diseases[17]. Bioelectrical impedance analysis is a practical tool in the follow-up of anti-hypertensive therapy at term gestation[18,19]. The BIS, supplying fluids volume data, may be useful to establish a more appropriate antihypertensive treatment. Moreover, the BIS, estimating volume restoration of the different body compartments may be helpful in evaluating the effectiveness of pharmacological antihypertensive treatment.

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