MULTIFACTORIAL HEMODYNAMIC ENTITIES OF HYPERTENSION AT THE ELDERLY

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ABSTRACT

***Introduction**: Hypertension is currently considered one of the most frequent diseases and an important risk factor for cardiovascular diseases. Approximately 20% of the world's adults are estimated to have hypertension, and the prevalence dramatically increases in patients over 60 years. Essential hypertension is a result of the alteration in any of the following hemodynamic modulators: intravascular volume, inotropy, vasoactivity, or any combination thereof.*

***Methods**: The observational five months study (February-June 2013) on 44 inpatients, 72.7% female; with the average age of 72.68±7.49 years. We evaluated the hemodynamic modulators (volemia, inotropy and vasoconstriction), cardiac index and mean arterial pressure as the hemodynamic status. We used the Hemodynamic Management System of patients' hemodynamics and oxygen transport dynamics Thoracic Electrical Bioimpedance (TEB) method (HOTMAN® System).*

***Results**: The rates frequency of associated diseases are: coronary ischemia (75%), obesity (34%), diabetes mellitus (23%), heart failure (7%). 20.5% of the patients were uncontrolled despite antihypertensive treatment. Antihypertensive drugs used: diuretics 52.3%, vasodilators and beta-blockers 61.4% equal. Hemodynamic measurement showed that 95.5% ($p<0.0001$) of all subjects presented at least one altered modulator (hypervolemia, hypo/hyper inotropy or vasoconstriction/vasodilation). 20.3% of patients was hypodynamic, while mean arterial pressure was in normal ranges in the majority of the patients. More than half of the patients (52.3%) have a low cardiac index that was correlated with hypoinotropy ($p=0,004$). Out of patients with controlled hypertensive treatment, 93.1% presented at least one altered modulator ($\chi 2=21.55$, $p<0.0001$).*

***Conclusion**: The patients under controlled hypertensive treatment showed at least one altered modulator. The most affected modulators were hypoinotropy and hypervolemia responsible for side effects related to hypo perfusion. Being aware of the mode of action of classes of antihypertensive and measuring the patient's hemodynamic profile can prepare an effective therapeutic algorithm, both in lowering blood pressure (BP) and in normalization of hemodynamic status.*

***Key words**: hemodynamic entities, old people, hypertension.*

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Introduction

Hypertension is currently considered one of the most frequent diseases and an important risk factor for cardiovascular diseases. Despite extensive awareness and an impressive number of available antihypertensive medications, blood pressure (BP)control rate is still reported as suboptimal, with figures that vary from approximately 30% control rate[(1)] to 12% uncontrolled hypertensive resistant patients[(2)].

Approximately 20% of the world's adults are estimated to have hypertension, and the prevalence dramatically increases in patients over 60 years. The prevalence further increased to 22% in the group aged 40-49 years, to 37.5% in the group aged 50-59 years, and to 51% in the group aged 60-74 years[(3)]. In a different study, the incidence of hypertension appeared to increase approximately 5% for each 10-year age range. Different factors are incriminated in poor control rates, such as lifestyle habits, patient poor compliance due to side-

effects, or the so-called "resistant" hypertension[4]. But the lack of treatment success could be also explained by an inadequate/suboptimal treatment scheme, especially if only BP target is considered, while other hemodynamic parameters are neglected. Essential hypertension is a result of alteration of any of the following hemodynamic modulators: intravascular volume, inotropy, vasoactivity, or any combination thereof. In each patient all these hemodynamic parameters are in a mutual relation and determine a specific hemodynamic profile[5, 6].

Treating only high BP and setting aside the other hemodynamic parameters like cardiac output, left ventricle contractility or vascular resistance, despite the fact that used antihypertensive drugs modify the entire hemodynamic status, could be an explanation for the suboptimal efficacy, as well as for important associated side effects in about half of the patients treated for hypertension.

At present, few data regarding the hemodynamic status of older patients are available, considering that most clinical studies were directed towards adult patients' population. This is the rationale for our observational study.

Methods

(February-June 2013) on 847 patients aged over 60 years, hospitalized in our in Department of Geriatrics, in the treatment for hypertension and other comorbidities. The patients were included in the study after signing the Informed Consent Form. The exclusion criteria were: history of the following pathologies within the last 6 months: myocardial infarction, unstable angina pectoris, percutaneous coronary intervention, bypass surgery, congestive heart failure stage III-IV, hypertensive encephalopathy, stroke, as well as patients with conditions that could limit the bioimpedance method (obesity BMI>40, rhythm and conduction disturbances such as atrial fibrillation, left bundle block etc.).

Finally 44 inpatients were included, 72.7% female, average age of 72.68±7.49 years. We evaluated the hemodynamic profile regarding the hemodynamic modulators (volemia, inotropy and vasoconstriction) and the hemodynamic status (cardiac index and mean arterial pressure) using HOTMAN® Integrated Thoracic Electrical Bioimpedance (TEB) method[7, 8].

The blood pressure is measured and treatment management according to 2013 European Society of Hyperthension(ESH) Guidelines[9,10].

The study was approved by the Ethical Committee at "Sf. Luca" Hospital.

All statistical analyses were done with the Statistical Package for the Social Sciences. All variables were tested by chi-square, binomial, Mann-Whitney U, Kruskal-Wallis, Friedeman and Wilcoxon tests for statistical significance of differences between proportions and, respectively, means.

Results

The average age of patients included is 72.68±7.49 years. Women's average age was similar to men's (p=00854). As far as gender it was registered a female preponderance (F:M=2.67, p=0,003). Body mass index (BMI) registered a mean value of 28±4,47 kg/m2 (overweight). BMI values were statistic similar both in men and women (p=0.842). Antihypertensive classes used were vasodilators 61.4%, beta-blockers 61.4% and diuretics 52.3%. From vasodilators drugs, calcium-antagonists represents only 22,7%, while angiotensin-converting enzyme inhibitors class represents more than 60%. (Fig.1)

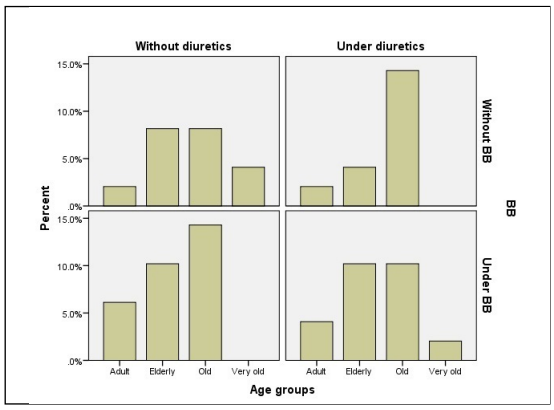

Figure 1: Prevalence of diuretics and beta-blockers by age.

About the hemodynamic profile, 20.5% of all patients were uncontrolled hemodynamically despite antihypertensive treatment. The majority of the patients showed normal BP values according to current ESH Guidelines[8, 9]. Except for diastolic blood pressure, which values were statistically significant higher in men, mean difference 6,04 mmHg, both systolic blood pressure(SBP) and mean arterial pressure(MAP) were similar in both gender groups. Hemodynamic measurement showed that 95.5% of all subjects presented at least one altered modulator ($\chi 2=36.36$, $p<0.0001$).

The distribution of altered modulators was: 72,7% hypervolemia, 52.3% hypoinotropy vs. 6.8% hyperinotropy and 43,2% vasoconstriction vs. 6.8% vasodilation (Table 1).

Modulators	Modulators profile	All subjects (%)	Subjects with BP controlled (%)
Chronotropism	Hypo	54.5	65.5
	Normo	34.1	24.1
	Hyper	11.4	10.3
Volemia	Hypo	2.3	-
	Normo	25	34.5
	Hyper	72.7	65.5
Inotropism	Hypo	52.3	58.6
	Normo	40.9	34.5
	Hyper	6.8	6.9

table 1: Differences of hemodynamic modulators between patients with controlled BP and all patients.

Out of the patients (79.5%) with controlled hypertensive treatment, 93.1% (p<0.0001) presented at least one altered modulator. The most affected modulators were inotropy (58,6% hypoinotropy) and volemia (65% hypervolemia). Data suggest that even blood pressure controlled patients have not a normalized hemodynamic status, which can be responsible for side effects related to hypoperfusion (low cardiac index).

Cardiac output (CO)- 75% of all patients were recorded normal values of CO (4-8ml/min) and 20.5% of all subject having low CO (<4ml/min) [p<0.0001].

Cardiac index(CI)- 36.4% of all patients have normal values of the cardiac index (2.8-4.2mL/min/m2) and 52.3% of total patients have low values of cardiac index (<2.8 mL/min/m2) [p=0.004]. More than half of the patients (52.3%) have a low cardiac index that was correlated with hypoinotropy (p=0,004). Bivariate correlation analysis revealed a strong correlation directly proportional between inotropism and cardiac output and cardiac index respectively [rs = 0.771; rs2 = 0.594; p < 0,0001] (Fig 2).

Hypoinotropy cases frequently associated with low cardiac output while hyperinotropy cases were most commonly associated with increased cardiac output [rs = 0.568; rs2 = 0.323; p <0,0001]. Most patients (54.5%) had hypochronotropism [p=0.002]. 72.7% of the batch showed hypervolemia [p<0.0001]. 52.3% of the batch showed hypoinotropy [p=0.001]. Most patients showed a normal vasoactivity [p=0.001]. The most frequent combination of affected modulators, both in total study population and in controlled hypertensive group was: hypoionotropy+hypervolemia+normal vasoactivity+hypochronotropy.

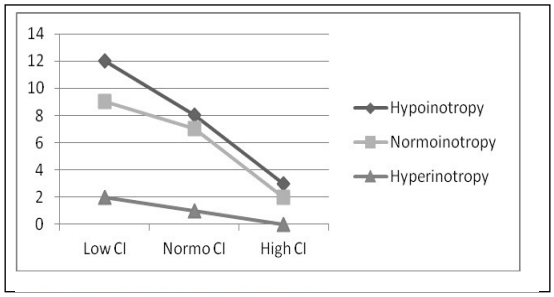

Figure 2: Correlation between inotropy and cardiac index.

Discussion

At this stage of knowledge there are no data on the hemodynamic status of hypertensive patients by age, sex, or drug interactions. Many researches disclose the importance of identification of the hemodynamic profile in hypertensive patients as a valuable tool in hypertension management[11, 12]. A recently published observational study, that involved nine European Hypertension Excellence Centers, emphasizes the need for understanding the hemodynamic profile before treating a hypertensive patient[13]. The presence of hypervolemia in most of the patients (some of them treated with diuretic), in the absence of edema or other clinical signs of volemic overload, indicated the need of a more intense therapy, with more focus on the volemia control. The hemodynamic management system helped identify the causes of the lack of therapeutic control (vasoconstriction, hypervolemia, hyperinotropy). But, we have to mention that in studies whose purpose was to reach the target blood pressure values, the BP control was obtained in a quite high percentage–up to 2/3 of the patients in the ALLHAT study[14]. In addition, cardiac output declines approximately 1% per year from age 30 years, and brain and cardiac vessel blood flow rates decline 0.35% to 0.5% and 0.5% per year, respectively, over 25 years. Additionally, frailty and concurrent disease may result in substantial changes in the serum concentrations of the two major drug-binding plasma proteins (albumin, which binds acidic drugs, decreases, while α1 acid glycoprotein, which binds basic

drugs, remains the same or rises) (15). Careful analysis of all hemodynamic modulators by TEB should precede pharmacological treatment modification in order to achieve a normohemodynamic status as a useful method for a customized treatment of hypertension[16]. The clinical benefits potentially offered by a larger use of this technique in the daily management of patients would require to be tested by future longitudinal outcome studies[1] and hemodynamic status in uncontrolled hypertensive patients. In the elderly, prescribing thiazides is associated with an increased risk of falling and this is strongest in the 3 weeks following the first prescription[17]. Drug-drug and drug-disease interactions are common in older adults and may have a negative impact on health-related quality of life[18].

Conclusions

The patients with controlled hypertensive treatment presented at least one altered modulator. The most affected modulators were hypoinotropy and hypervolemia responsible for side effects related to hypoperfusion. Knowing the mode of action of classes of antihypertensive and measuring the patient's hemodynamic profile can prepare an effective therapeutic algorithm both in lowering BP and a normal hemodynamic status. This method might be helpful in the treatment individualization in hypertensive aged patients, especially considering the challenges in this age group: presence of multiple comorbidities, multiple medication, increased adverse events, like falls etc. A treatment decision guided by hemodynamic profile of the patient can increase both the efficiency and safety of the antihypertensive therapy at the elderly if we consider as treatment goal not only BP reduction but a normalized hemodynamic profile.

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