

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
DOCTORAL SCHOOL

DOCTORATE THESIS
-SUMMARY -
DRUG ASSOCIATIONS IN ARTERIAL HYPERTENSION

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KEYWORDS:

Arterial hypertension, mortality, cardiovascular diseases, drug associations.

CHAPTER I: Essential hypertension

Arterial hypertension is the leading cause of death worldwide and is one of the most important public health problems. Arterial hypertension is a major cardiovascular risk factor with an increasing incidence¹.

The 2018 ESH-ESC guidelines recommend that the first therapeutic goal be to reduce AT<140 / 90mmHg for all patients and if treatment is well tolerated, BP values should be lowered to 130 / 80mmHg or even below for most patients. In most patients <65 years of age, it is recommended to decrease the SBP in the range 120 -129mmHg.²

The continuous relationship between BP and cardiovascular (CV) and renal events makes the distinction between normal blood pressure and hypertension arbitrary.^{3,4,5} In order to simplify the diagnosis and therapeutic decisions, cut-off values are used.

It is estimated that about one billion people in the world's population suffer from AHT, making AHT the leading cause of death worldwide, but also the main reason why patients see a doctor. Another estimate shows that by 2025 AHT will affect about 1.5 billion individuals worldwide.

The mechanisms involved in the occurrence of over 95% of cases of AHT are multiple, with no single cause. Blood pressure is determined by the product between cardiac output and peripheral resistance. AHT can result from the growth of either factor.

AHT has been called a "silent killer" because it is mostly undiagnosed and untreated, which leads to a silent impairment of blood vessels, heart, brain and kidneys.

AHT assessment involves three steps: BP measurement, global cardiovascular risk assessment, and detection of identifiable or potentially treatable causes of AHT. The diagnosis of hypertension is based on two or more measurements on two or more visits to the doctor according to JNC7⁸. In the medical office, the BP is measured at least twice after five minutes of rest, with the patient sitting in a reclined chair and with the arm at the level of the heart. The patient should not consume alcohol and coffee 30 minutes before the measurement. BP should be measured on both arms and after five minutes of orthostatism.

Chapter II: The treatment of essential hypertension

In order to lower the BP we have several methods at hand: changing the lifestyle, antihypertensive medication and even cardiovascular interventions such as renal denervation. According to the new ESC / ESH guideline of 2018, it is recommended that antihypertensive treatment can be considered even at high normal BP values (130-139/85-89mmHG) if the cardiovascular risk is very high under the conditions of the association with the ischemic heart disease. Except for a few cases of secondary AHT most cases of AHT cannot be cured¹⁰.

The main classes of drugs used in the treatment of AHT are: angiotensin II conversion enzyme inhibitors, angiotensin II receptor blockers, beta blockers, calcium channel blockers and diuretics (thiazide and thiazide-like).

Antihypertensive treatment can be started with a single drug or using two or three drugs given individually or in fixed dose tablets.

OWN CONTRIBUTIONS

Chapter III: The demographic profile of the hypertensive patient in Olt County

The demographic profile of the hypertensive patient in Olt County The study includes a number of 3050 patients with AHT admitted between 2013-2017 in the Municipal Hospital of Caracal, Olt County, for investigations and specific treatment. All patients included in our group were clinically and paraclinically diagnosed with essential AHT. In order to carry out the study, the informed consent of all patients was granted.

Chapter IV: Data processing, results and discussions

IV.1 Data processing

For data analysis, we used the software Microsoft Excel (Microsoft Corp., Redmond, WA, USA), along with the add-on XLSTAT 2014 for MS Excel (Addinsoft SARL, Paris, France) and the software IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA).

The data obtained were entered into Microsoft Excel files then statistically processed, in order to analyze the relationships between the clinical and paraclinical data of the patients.

IV.2 Results

The number of patients with AHT who required hospitalization in the Cardiology Department of the Caracal Municipal Hospital was on average about 610 patients per year, with the lowest number being recorded in 2014 (502 patients) and in 2016 (698 patients). It can be said that the number of hospitalized patients varied from one year to another by a maximum of 16-18% compared to the annual average.

The analysis of the distribution of the group of patients according to gender allowed us to find that most of the patients affected by AHT were female. Thus, out of the 3050 patients, 1756

(57.57%) were female and 1294 (42.43%) were male. The prevalence of AHT in women has been a constant throughout the five calendar years considered in our study.

Regarding the systolic blood pressure (BP) values, we divided our group into three categories of patients:

- with BP values below 160 mmHg (AHT grade I).
- with values between 160 and 180 mmHg (AHT grade II);
- with values over 180 mmHg (AHT grade III).

In our group, most patients had grade II AHT (1401 cases, accounting for 45.94%), whereas the number of patients with grade I and grade III AHT was almost equal: AHT grade I = 810 patients, accounting for 26.55%; AHT grade III = 839 patients, accounting for 28.51%. Female gender was much more numerous than the male gender at all AHT levels.

Analyzing the distribution of patients by age, the number of patients with AHT increased with age. Most patients with AHT were over 60 years old. Between the 60-89 years age range, a number of 2638 patients were recorded, accounting for 86.49% of the whole group, whereas patients under the age of 60 were 363, accounting for only 11.90%. We believe that the high prevalence of the disease over 60 years is due to the in of the elasticity of the arteries and arterioles, the reduction of the physical effort and the adoption of the sedentary lifestyle, changes in the diet that lead to weight gain, diabetes and obesity.

From our chart, it is easy to see that patients over the age of 60 years showed the most frequent forms of grade II AHT, in all decades of age, a clinical aspect that requires a more frequent monitoring of these people in order to prevent major AHT-generated complications.

If, after 80 years of age, the chart shows a decrease in the number of patients with AHT, this is not due to the "cure" of AHT, but to the death of older people due to cardiovascular disease or other conditions.

From our chart, it can be seen that AHT can occur in individuals under 50 and even in young people. In our group, a person under 10 years of age who had a mild form of AHT (grade I) who required hospitalization in order to establish the diagnosis and appropriate treatment. Also, in the age group 30-39 years (the group of young adults), 6 patients with AHT were recorded, of which 3 patients had AHT stage II and the other 3 patients AHT grade III. In the decade 40-49 years, 57 patients were recorded, of which 21 with AHT stage I, 25 with AHT stage II and 11 with AHT stage III. Our data indicate that AHT may have an early onset, even in adolescents, but given that intense clinical manifestations are absent, it is detected much later.

Convinced that the social environment can be a risk factor that influences AHT, we analyzed the distribution of cases according to the environment of origin. We have found that in the rural area, a number of 2085 patients were recorded, accounting for 68.36%, whereas a number of 965 patients were recorded in the urban area, accounting for 31.64%. It can be easily seen that more than 2/3 of the patients in our group came from the rural area, which proves that the AHT is influenced by the social environment.

Knowing that systolic BP values are a predictive factor for some major complications caused by AHT (strokes, myocardial infarction), in our study we also investigated patients with systolic BP higher than 200 mmHg. Out of a total of 3050 patients, a number of 364 (11.95%) patients had systolic BP values of more than 200 mmHg.

IV.3 DISCUSSIONS

Arterial hypertension (AHT) is a chronic condition in which blood pressure is constantly rising above normal values (120-139 / 80-89 mmHG). Recent studies show that AHT is a major public health problem affecting over one billion people worldwide [6,7].

The high incidence of AHT is a huge worldwide public health problem, as it is the main risk factor for other cardiovascular diseases, including coronary heart disease, stroke and heart failure, kidney failure, etc. Every year, about 17 million people die prematurely from cardiovascular disease, of which 9 million die from AHT complications [2, 9].

A particularity of our group is that the prevalence of AHT was higher in women than in men. Most studies have shown that AHT prevalence is higher in men [11, 12]. It is possible that in Romania, AHT may have a higher prevalence in men, but many of them may not be aware of the presence of the disease, because in its early stages of evolution, AHT may not have any symptoms.

Chapter V: Conclusions

Essential hypertension continues to be a real public health problem, as it is the number-one risk factor in terms of mortality. It is an identifiable, reversible and most common risk factor for diseases such as myocardial infarction, stroke, atrial fibrillation, aortic dissection, and peripheral arterial disease. By determining the vascular remodelling in the brain and heart, it is most commonly associated with stroke and heart failure.

AHT is one of the most common cardiovascular diseases. Of the 3050 patients admitted to the Cardiology Ward of the Caracas Municipal Hospital during 2013-2017, 1756 patients (57.57%) were female and 1294 (42.43%) were male.

In analyzing the distribution of patients by age, it was found that most patients with AHT were over 60 years old. Between the 60-89 years age range, a number of 2638 patients were recorded, accounting for 86.49% of the whole group, whereas patients under the age of 60 were 363, accounting for only 11.90%.

Most patients had grade II AHT (1401 cases, accounting for 45.94%), whereas the number of patients with grade I and grade III AHT was almost equal: AHT grade I = 810 patients, accounting for 26.55%; AHT grade III = 839 patients, accounting for 28.51%. A total of 364 (11.95%) patients had systolic BP values of more than 200 mmHg.

Analyzing the group of 3050 patients in terms of the antihypertensive medication administered, we found that, of all the classes of drugs, the most used was the class of inhibitors of the renin-angiotensin-aldosterone system, and of these, the angiotensin converting enzyme inhibitors.

Regarding the drug combinations, the most used was the association between the conversion enzyme inhibitor and the calcium blocker.

Characterizing the group from the viewpoint of the environment of origin, we found that the highest proportion of patients included patients from the rural area, which can be explained by a poorer medical education, lower addressability, lower compliance with the treatment or non-compliance with the low-salt diet.

Chapter VI: SELECTIVE BIBLIOGRAPHY

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