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Systemic arterial hypertension: treatment with Integrative and Complementary Health Practices

Hipertensão arterial sistêmica: tratamento com práticas integrativas e complementares de saúde

Hipertensión arterial sistémica: tratamiento con prácticas de salud integradoras y complementarias

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Abstract

Systemic Arterial Hypertension (SAH) can generate complications such as stroke, myocardial infarction, kidney disease, arteriosclerosis, loss of vision, erectile dysfunction and cognitive dysfunction. Among people who know they suffer from hypertension, 50% use medication and of those only 45% have their blood pressure kept under control. SAH is a multifactorial clinical condition characterized by elevated and sustained blood pressure levels (BP, where systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mmHg). Faced with sparse investigative studies on the causes of SAH in individuals, the dictates of the pharmaceutical industry and the use of in vitro or inconclusive clinical studies, this paper presents the state of the art about the treatment of SAH based on a multifaceted view, including aspects about the physiology of SAH, food and PANC as alternatives for the prevention and control of SAH, as well as an approach on the importance of scientific rigor in the manufacture of medicines.

Keywords: Systemic arterial hypertension; Integrative and complementary health practices; Cardiovascular health; Dictates of the pharmaceutical industry.

Resumo

A Hipertensão Arterial Sistêmica (HAS) pode gerar complicações tais como acidente vascular cerebral, infarto do miocárdio, doença renal, arteriosclerose, perda de visão, disfunção erétil e disfunção cognitiva. Das pessoas que têm conhecimento, 50% fazem uso de medicação e, dessas, apenas 45% têm a pressão controlada. A HAS é uma condição clínica de caráter multifatorial, caracterizada por níveis elevados e sustentados de pressão arterial (PA, onde PA sistólica ≥ 140 mmHg e PA diastólica ≥ 90 mmHg). Diante de parcos estudos investigativos sobre as causas da HAS nos indivíduos, dos ditames da indústria farmacêutica e do uso de estudo clínicos in vitro ou inconclusivos, este artigo se propõe a apresentar o estado da arte sobre o tratamento da HAS a partir de uma visão multifacetada, incluindo aspectos acerca da fisiologia da HAS, da alimentação e das PANC como alternativas para a prevenção e controle da HAS, como também uma abordagem sobre a importância do rigor científico na fabricação de medicamentos.

Palavras-chave: Hipertensão arterial sistêmica; Práticas integrativas e complementares em saúde; Saúde cardiovascular; Ditames da indústria farmacêutica.

Resumen

La Hipertensión Arterial Sistémica (HSA) puede generar complicaciones como ictus, infarto de miocardio, enfermedad renal, arteriosclerosis, pérdida de visión, disfunción eréctil y disfunción cognitiva. De los que saben, el 50% usa medicación y, de estos, solo el 45% tiene la presión bajo control. La HSA es una condición clínica multifactorial, caracterizada por niveles elevados y sostenidos de presión arterial (PA, donde la PA sistólica ≥ 140 mmHg y la PA diastólica ≥ 90 mmHg). Ante los escasos estudios de investigación sobre las causas de la HAS en los individuos, los dictados de la industria farmacéutica y el uso de estudios clínicos in vitro o no concluyentes, este artículo propone presentar el estado del arte sobre el tratamiento de la HAS desde una mirada multifacética. , incluyendo aspectos sobre fisiología de la HAS, alimentos y PANC como alternativas para la prevención y control de la HAS, así como un abordaje sobre la importancia del rigor científico en la fabricación de medicamentos.

Palabras clave: Hipertensión arterial sistémica; Prácticas de salud integradoras y complementarias; Salud cardiovascular; Dictados de la industria farmacéutica.

1. Introduction

Approximately 33% of Brazilians suffer from hypertension. Many of them are unaware that they suffer from this disease and they end up spending most of their lives exposed to complications resulting from high blood pressure (BP), such as stroke, myocardial infarction, kidney disease, arteriosclerosis, vision loss, erectile dysfunction and cognitive dysfunction such as memory disorders. Among people who know they suffer from hypertension, 50% use medication and of those only 45% have their blood pressure kept under control (Savioli & Savioli, 2019).

Malachias et al. (2017), Queiroz, Calzerra & Gomes (2018) and Toledo et al. (2020) define systemic arterial hypertension (SAH) as a multifactorial clinical condition characterized by elevated and sustained blood pressure levels (systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mmHg), according to the VII Brazilian Guideline for Hypertension. These values provide a condition indicated as an important risk factor for early morbidity and mortality caused by cardiovascular diseases. Considering the American College of Cardiology (ACC) and the American Heart Association (AHA), Brook (2018) emphasizes the existence of a new guideline for stage 1 arterial hypertension, when the systolic BP is between 130 to 139 mmHg or when the diastolic BP is between 80 to 89 mmHg.

Resistant arterial hypertension is defined when blood pressure remains above the recommended limits even with the use of three antihypertensives of different classes, including a blocker of the renin-angiotensin system (Angiotensin-Converting–Enzyme Inhibitor [ACEI] or angiotensin receptor blockers [ARBs]), a long-acting calcium channel blocker (CCB) and a long-acting thiazide-type diuretic (TD) at maximum recommended and tolerated doses, frequently administered; appropriate dosage and proven adherence (Toledo et al., 2020). The autors record that the prevalence of resistant arterial hypertension (RAH) is estimated between 10 and 20% of hypertensive patients in the world. This means that there are approximately 200 million resistant hypertensive patients.

The health system depends on technological developments, sophisticated diagnostic tests, innovative therapeutic techniques, segmentation of healthcare and industry dictates. Thus, the question arises about the efficacy and safety of the patient in the treatment of arterial hypertension, as the holistic care of the human being is often disregarded: body, mind and spirit.

In this sense, this paper prioritizes the treatment of what causes high blood pressure, such as changes in eating habits, smoking outcome, weight control, quality of sleep, reduction in alcohol consumption and exercise; among other integrative measures within the understanding of the current multiplicity that requires views interactions from different areas of knowledge and different social references (multifaceted view). In addition, it is proposed to analyze the dictates of the health industry in the treatment of arterial hypertension, presenting some unconventional food plants and unveiling the importance of scientific rigor in the manufacture and use of medicines.

2. Materials and Methods

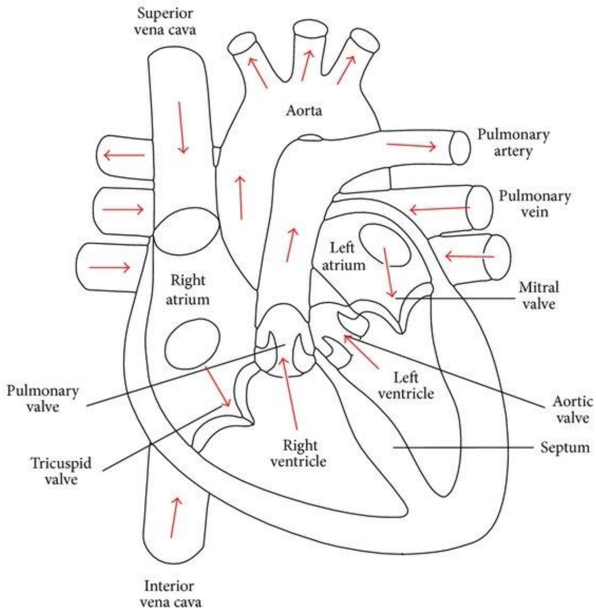
The present qualitative study was based on a systematic review of the literature according to Pereira et al. (2018), which took place through the theoretical deepening and survey of data already published on the topic (secondary source), providing an integrated, synthesized overview of the current state of knowledge.

3. Results and Discussion

3.1 Cardiac work in Systemic Arterial Hypertension (SAH)

Anatomically understood that the heart is formed by four chambers: right atrium (RA), right ventricle (RV), left atrium (LA) and left ventricle (LV). Deoxygenated (low oxygen) or venous blood from the entire organism reaches the RA through the superior and inferior vena cava (systemic circulation), as well as through the cardiac veins and the carotid sinus (coronary circulation); indicating that the RA is in atrial diastole (cardiac relaxation). After that, the blood volume crosses the tricuspid valve, located between the RA and the RV, the moment of atrial systole (cardiac contraction) and ventricular diastole. Then it goes to the four right and left pulmonary arteries (pulmonary circulation or small circulation) when the RV performs the systole. The presence of the valves allows the blood flow to follow a single direction, with no return (reflux) to the anterior chamber, as shown in Figure 1.

Figure 1. Cardiac Anatomy and Physiology.



Source: https://www.researchgate.net/figure/Transverse-section-of-human-heart-5_fig4_276664935.

After the hematosis process (gas exchange that occurs in the lungs through venous and arterial blood) the arterial blood returns from the lungs to the heart (LA) through the two pulmonary veins. This characterizes the moment of atrial diastole. Crossing the bicuspid (mitral) valve, the blood volume reaches the LV and travels through the aorta (systemic circulation or large circulation) and coronary arteries (coronary circulation) to the whole organism, giving rise to maximum pressure or systolic blood pressure [SBP]) during the blood passage, and a minimum pressure or diastolic blood pressure (DBP) coming from the return of the vessel to its initial diameter. This allows the blood to continue its course towards the blood capillaries (Savioli & Savioli, 2019).

Blood pressure changes with everyday situations such as moments of anxiety, physical activity, feelings of pain, medical care and so on. Most of the time, hypertension is asymptomatic or the symptoms are common to some other disease (headache, dizziness, malaise). For this reason, it is called a "silent killer disease". Monitoring BP levels is a lifelong task for hypertensive patients.

Blood pressure is measured using an aneroid sphygmomanometer (without mercury and with a diaphragm), which must be periodically tested and calibrated. This calibration can be done using digital devices that must be used with great care, as they are susceptible to many errors. Monitoring can also take place with instruments such as ABPM (Ambulatory Blood Pressure Monitoring) or HBPM (Residential Blood Pressure Measurement), blood pressure measurement tests outside the clinic to confirm inadequate pressure control, which is usually higher in relation to household measurement (white coat effect) (Toledo et al. 2020).

By keeping BP under control, health benefits include a significant reduction in coronary events such as myocardial infarction, stroke and death. A decrease in SBP of 5 mmHg is associated with a 4% decrease in mortality from stroke, 9% from coronary artery disease and 7% in mortality from all causes (Santos, Costa & Kruel, 2014).

According to Savioli & Savioli (2019), tt is assumed that genetic and environmental factors are involved in the origin of arterial hypertension and, because of its unknown etiology, it is called primary hypertension. Several risk factors are strongly and independently associated with this disease: age (advanced); obesity (increase in weight and fatty body mass); family history (hypertensive mother and / or father twice increases the chance of developing high blood pressure); race (more common in blacks); high sodium diet; excessive alcohol consumption; physical inactivity; diabetes and dyslipidemia; personality traits and depression (disease can be more common in individuals with hostile attitudes, impatience, depression and anxiety).

Some conditions can increase BP and lead to secondary hypertension, which, due to its defined etiology, may be possible to cure. The main causes of this hypertension include: oral contraceptives (particularly those containing high doses of estrogen), non-steroidal anti-inflammatory drugs (particularly those with chronic use), antidepressants, corticosteroids, nasal decongestants, weight loss medications, stimulants, illicit drugs , smoking, primary kidney disease, renovascular hypertension (alteration of the arteries that carry blood to the kidneys) and obstructive sleep apnea (Savioli & Savioli, 2019).

Patients' adherence to pharmacological and non-pharmacological treatment is always a major challenge, especially in public services. It may be related to rejection of the excessive number of drugs in complex dosages (many administrations and many pills), side effects of medications, sociocultural problems and ignorance of the natural history of the disease, difficulty in accessing doctors, medications and complementary tests. In addition, there are reasons related to the doctor, such as: bad doctor-patient relationship, non-synergistic dosages or wrong doses, and omission or lack of knowledge in the investigation of treatable secondary causes (Toledo et al., 2020).

The change in the doctor-patient relationship, the excessive use of technology and the inability of the medical system to adequately treat chronic disease contributed to the expansion of complementary medicine, currently called integrative medicine. It uses the accumulated scientific knowledge for the timely treatment of the patient, allowing the professional to use other techniques, in addition to the classic ones. From the point of view of integrative medicine, the relationship between mind, body, spirit and environment is understood, through medicines, surgery, phytotherapy, psychology, nutrition, spirituality, meditation, among others (Brasil, 2013).

The philosophy of integrative medicine is not new. Long before the existence of magnetic resonance images and computed tomography, Aristotle (384-322 BC) experimented, observed and reflected on the human condition, representing one of the first holistic doctors who considered that each person was a combination of physical and spiritual properties, no separation between body and mind. Thus, Hippocrates (370 BC), considered the Father of Medicine, brilliantly elucidated that the remedy is food, and that this food is the remedy for the human, physical, psychic and spiritual. This concept persisted until the 16th century, when René Descartes (1596-1650) separated mind and spirit in order to protect science, leading to the “Cartesian division” of mind-body duality. He believed that the mind and spirit should be the focus of the Church, leaving science to the study of the physical body (Savioli & Savioli, 2019).

Later, John Locke (1632-1704) and David Hume (1711-1776) started the reductionist movement that shaped our current science and medical system. This caused natural phenomena to be reduced to greater simplicity in order to understand the greater whole. At the beginning of the 20th century, applied science began to transform medicine through the development of medical technologies, emphasizing the triad that still prevails in academies today: research, education and clinical practice. Reductionism and the scientific method produced a greater compression of diseases and the development of tools to help fight them. Currently, the overspecialization of medicine presents professionals with skills in segments of the human being, fragmenting it more and more (Savioli & Savioli, 2019).

The non-pharmacological treatments indicated for arterial hypertension and included in this paper are control of body weight, attention to the intestinal microbiota, control over salt and alcohol intake, physical exercise, sleep quality and meditation, as well as the use of Unconventional Food Plants (PANC).

Toledo et al. (2020) mention that several mechanisms favor the maintenance of a high BP in obese hypertensive patients, such as obstructive sleep apnea, sympathetic hyperactivity, endothelial dysfunction and modification of the intestinal microbiota. All of these factors are capable of promoting an inflammatory phenotype and perpetuating the vicious cycle. According to the authors, patients with body mass index (BMI) ≥ 30kg/m2 are 50% more likely to have uncontrolled BP than those with normal BMI (< 25kg/m2). On the other hand, a

BMI > 40kg/m2 triples the chances of requiring multiple drugs to control BP. A weight loss of 10kg is associated with an average reduction of 6.0 mmHg in systolic BP and 4.0 mmHg in diastolic BP.

Savioli & Savioli (2019) consider that any excess body fat is harmful to health in general and weight gain is directly related to the increase in blood pressure levels in both adults and children. Visceral fat, located more deeply around important organs such as the liver, pancreas and kidneys, is an even greater risk factor than subcutaneous fat. Adipose tissue is considered an endocrine organ, releasing a series of hormones into the bloodstream. In addition, the authors cite that excess fat is pro-inflammatory because it eliminates small proteins (cytokines), such as Interleukin-6 (IL-6), which stimulate the production of other proteins of the acute phase of inflammation and increase the secretion of triglycerides by the liver, contributing to hypertriglyceridemia associated with visceral obesity.

Excessive alcohol consumption also contributes significantly to the uncontrolled BP. The daily consumption of more than two drinks (about 24 g / day) is associated with an increase in blood pressure levels (Toledo et al., 2020). The association between serum uric acid and cardiovascular disease such as hypertension, metabolic syndrome and coronary and cerebral vascular diseases has been reported in several epidemiological studies. According to Kan et al. (2019), excessive beer intake can increase serum uric acid levels (hyperuricemia), leading to a high risk of gout, previously attributed to the high purine content in beer. Johnson et al. (2003) report that hyperuricemia is associated with hypertension, vascular disease, kidney disease and cardiovascular events. They affirm that controlling hyperuricemia would be more effective in preventing than treating hypertension.

Sleep disorders contribute to the establishment of arterial hypertension, with obstructive sleep apnea (OSA) being a problem present in 35% of hypertensive patients, reaching 70% of resistant hypertension cases. Defined as total or partial cessation of respiratory flow during sleep, this syndrome promotes oxyhemoglobin desaturation and micro-arousals during sleep (Toledo et al., 2020). OSA is one of the causes of secondary hypertension, having as risk factors an increase in the circumference of the neck and abdomen (obesity), changes in the mandible and maxilla, hypertrophy of the tonsils, adenoids and reduction of the nasal cavities as well as the use of tobacco. Snoring and daytime sleepiness are frequent symptoms, in addition to periods of respiratory arrest after sound snoring, indicating sleep treatment to reduce cardiovascular risk (Savioli & Savioli, 2019). Toledo et al. (2020) add that the activation of the sympathetic nervous system and humoral changes are responsible for changes in the integrity of the vascular endothelium, and its consequences in patients with OSA include increased BP, development of atherosclerotic disease, cardiac arrhythmias, among others.

The association between dietary sodium intake and blood pressure variability in hypertensive patients remains uncertain. Wang et al. (2020), in a study with Chinese patients with hypertension, reported that the intake of sodium in the diet is associated with the variation in systolic blood pressure at night. According to the authors, blood pressure variability, as a measure of BP fluctuation, is also associated with increased cardiovascular risk, regardless of BP level. For Toledo et al. (2020), the salt intake must always be checked, if possible with the sodium check in 24-hour urine. This is because the sodium intake is usually excessive due to the consumption of processed foods and the lack of knowledge of patients in relation to excessive salt consumption. Sensitivity to sodium and volume overload account for the main pathophysiological mechanism in most cases, restricting the ability of excretion of water and sodium by the kidneys, which makes BP more dependent on volume variations.

Aerobic physical exercises are recommended for primary prevention, treatment and control of hypertension, based on a planned, structured and repetitive physical activity. Such exercises are related to neuromuscular, metabolic and psychological improvements. Regular exercise promotes physical health, avoids diseases and disorders arising from routine, tiredness, thoughts and feelings and decreases the BP registered in the office and the outpatient clinic in resistant hypertensive patients, in addition to attenuating the characteristic of neurohumoral activation (Toledo et al., 2020). Exercise programs that mainly involve resistance activities, such as weight training, prevent the development of hypertension and lower BP in adults through neurohumoral, vascular and structural adaptations, decreasing catecholamines and total peripheral vascular resistance, improving sensitivity insulin, and altering vasodilators and vasoconstrictors (Pescatello et al, 2004). According to Santos, Pedroso & Silva (2018), the effect on blood pressure of hypertensive elderly people immediately after resistance exercise is high when compared to resting levels, which is a physiological effect considered normal, but after a period of approximately 15 minutes of recovery it is possible to see reductions in SBP and DPB. Another important modality in BP reduction is isometric exercise, showing an expressive hypotensive effect after exercise, which strengthens its auxiliary therapeutic role in controlling the disease (Abreu, 2019).

In order to control emotional, mental, social, spiritual and behavioral factors that can directly affect health, Integrative and Complementary Health Practices are described as tools to strengthen the interactions between brain, mind, body and behavior. Breathing during meditation, for example, stimulates receptors in the lungs that, through specific nerve pathways, send stimuli to the area of the brain responsible for controlling blood pressure. Chandler et al. (2020) indicate changes in lifestyle as treatment of first-line hypertension (patients in stage 1 of non-medicated systolic arterial hypertension). Using a respiratory awareness meditation program delivered through a health application, practiced twice a day, the primary result was to change the SBP at rest and the secondary outcome to change the BPD at rest. The preliminary effects of respiratory awareness meditation on controlling SBP look promising with appropriate practical techniques and high levels of compliance.

The regulation of blood pressure and homeostasis of the body also involves the activation of the renin-angiotensin system (RAS). The increase in sympathetic activity and changes in the concentration of vascular sodium chloride (NaCl) activate RAS, initially triggering the release of renin, an enzyme produced and stored by renal cells (Silva et al., 2019). The authors add that, when renin is converted into the bloodstream, it converts angiotensinogen, an alpha-2-globulin synthesized mainly in the liver, into angiotensin I (Ang I) which, due to the influence of the angiotensin-converting enzyme (ACE), protease found especially in the vascular endothelial cells of the lung, forms angiotensin II (Ang II). Ang II, according to Silva et al. (2019), promotes actions locally, at tissue level or by transporting its components in the bloodstream, with vasoconstrictor, pro-oxidant and pro-inflammatory responses.

Under conditions of hyperactivity, RAS contributes significantly to a series of harmful events to the kidneys, vessels and heart, mainly associated with myocardial infarction, cardiac hypertrophy, atherosclerosis and heart failure (Silva et al., 2019; Queiroz, Calzerra & Gomes, 2018; Paul, Mehr & Kreutz, 2006). RAS hyperactivity can also cause vascular injury induced by vasoconstriction, proliferation and hypertrophy of smooth muscle cells and vascular inflammation with degradation of the cellular matrix (Queiroz, Calzerra & Gomes, 2018; Paul, Mehr & Kreutz, 2006).

Oxidative stress has been shown to play a critical role in the development of endothelial dysfunction and hypertension and atherosclerosis (Paul, Mehr & Kreutz, 2006), in addition to premature aging and cancer, since oxygen free radicals are the main causes tissue injury. The inflammation produced by the increase in free radicals to the detriment of a lower amount of the antioxidant system can be reduced by adequate intake of foods that contain antioxidant compounds (Silva at al, 2020).

Finally, Hermida et al. (2020) highlight that the time of administration of antihypertensive medication helps to maintain low BP values. According to the authors, the intake of the entire daily dose of the medication prescribed to lower blood pressure at bedtime controls BP and improves sleep, reducing morbidity and mortality from cardiovascular disease, when compared to the usual administration of all these drugs upon waking up.

3.2 Food and SAH

A supplementation rich in nutritious, functional and antioxidant foods, such as the B vitamins (mainly B6), D, C and E can more effectively reduce SAH (Ahhmed & Muguruma, 2010), as well as mineral salts (magnesium and zinc). Functional foods are an interesting option for hypertensive patients, as they contain bioactive and nutraceutical compounds that promote physiological benefits in reducing the risk of acquiring chronic diseases and their complications, in addition to being vehicles of basic nutritional functions.

In the literature review by Kostov & Halacheva (2018), evidence is found that magnesium deficiency increases the risk factors for SAH. As magnesium is a natural calcium antagonist, it both prevents calcification of arteries and stimulates the production of local vasodilator mediators (prostacyclin and nitric oxide). In this way, magnesium alters vascular responses to a variety of vasoactive substances (endothelin-1, angiotensin II and catecholamines). Magnesium deficiency stimulates the production of aldosterone and potentiates the vascular inflammatory response, as well as reducing the activity of several antioxidant enzymes (glutathione peroxidase, superoxide dismutase and catalase) and levels of vitamin C, vitamin E and selenium. This deficiency is also related to insulin resistance, hyperglycemia and changes in lipid metabolism. Magnesium balances the effects of catecholamines on acute and chronic stress, mitigates atherosclerosis, regulates the renewal of collagen and elastin in the vascular wall. It also acts in the regulation of the matrix metalloproteinase activity, helps to protect the elastic fibers from calcium deposition and maintains the elasticity of the vessels. Given the relevance of the benefits of magnesium, it is essential that the daily food diet has foods that have bioavailable amounts of magnesium, while this one helps substantially in the control of SAH.

We list foods that have more than 100mg of magnesium in 100g of their composition, according to Taco (2011): almond, peanut, brown rice, oats, cashews, Brazil nuts, rye, amaranth slender, coriander, dark chocolate , roasted coffee powder, spinach, beans (all), sesame, pigeon pea, chickpeas, skimmed milk powder, flaxseed, molasses, pine nuts (Araucaria angustifolia seeds) and soy. It should be noted here that pigeon pea and slender amaranth are considered PANC. Benevides et al. (2019) point out that the pigeon pea has a significant amount of mineral salts, including magnesium (166mg in 100g of pigeon pea), and should be part of the daily life of healthy and hypertensive people.

Zinc influences arterial hypertension in such a way that its deficiency results in an increase in blood pressure. Additionally, the low concentration of zinc in the extracellular spaces makes the blocking of calcium channels less efficient, favoring the influx of calcium ions into the cell and its accumulation, leading to increased tension and hypertrophy of the smooth tissue of the muscle layer and vessels cardiac (Tubek, 2007).

Ahhmed & Muguruma (2010) exemplify that yogurts and soy derivatives, fresh vegetables such as olives and fruits that contain antioxidants, vitamins and minerals can have blood pressure reducing effects. In a positive way, meat is a fundamental food because it has a great wealth of peptides and proteins that significantly reduce the risk of chronic diseases such as diabetes, osteoporosis and SAH.

This analysis reflects the importance of training hypertensive people in issues of life quality versus longevity and in offering integrated nutrition with their treatment and lifestyle, instead of only the alternative medications. For hypertensive and normotensive individuals, chemically based drugs can have harmful side effects. Functional food rich in antioxidant vitamins, and biologically active proteins or peptides, can lower blood pressure in people with SAH, possibly preventing an underlying cause of the disease. Deficiencies in the consumption of crucial nutrients (such as meat proteins), in addition to abnormalities in the metabolism of carbohydrates and fats, may be underlying the etiology of the clinical course of hypertension. Foods derived from nutrient-rich meat can provide physiologically functional peptides, in addition to improving the digestion and metabolism of carbohydrates and fats, thereby lowering blood pressure and normalizing biochemistry and histopathological changes. The authors found in the studies, that meat had value, because the proteolysis of meat muscle generated a substantial number of amino acid peptides that have non-functional functions, and some of which have a strong participation in the conversion of angiotensin as an enzyme inhibiting activity. It also demonstrates that meat proteins can minimize health problems and help find more effective approaches to meet the needs of all hypertensive patients, both nutritionally and therapeutically. However, meat consumption should not be too high. A fundamental aspect is the choice of meat, that is, industrialized meat is not interesting due to the insertion of chemical additives that often corroborate for the elevation of diseases and the development of allergies. So, the choice of what to eat should always come from the origin and quality of its processing. The more natural this food, the better for health.

3.3 PANC: a possible natural alternative for prevention and control of SAH

The plant kingdom has an unlimited biodiversity of individuals and specimens scattered throughout the earth's crust. The use of plants by humanity for food, medicine, ornamentation, housing, among others, dates back to millennia. Many disease cures were made from elements taken from nature. Every day the volume of studies and scientific articles about the use of natural elements, such as vegetables for the reduction of symptoms and control of certain diseases, grows. Many plants have been used for millennia to control diseases, hence they are called medicinal plants. In this sense, research on these plants has greatly increased. In particular, we will emphasize the PANC that interfere with arterial hypertension in the scientific literature.

PANC's are so named because they are not consumed by the population as a whole, nor are they widely traded in fairs and markets. According to Kinupp & Lorenzi (2014), these plants are born spontaneously. They are cosmopolitan, exotic, food and even medicinal with interesting therapeutic effects for human health. PANCs can be fruits, herbs, vegetables, trees or roots. In addition to food, many can be used to prevent diseases or to treat symptoms of various diseases such as high blood pressure.

One of the plants widely studied worldwide is Moringa oleifera, considered by many to be the “tree of life”. In the study, in a laboratory by Randriamboavonjy et al. (2016), the moringa specifically decreased heart rate during the night without, however, affecting the rate during the day, as well as blood pressure. This is particularly important, because the decrease in heart rate is associated with vascular changes in heart protection, having a direct relationship between the prevention of coronary atherosclerosis and cardiovascular morbidity. Moringa treatment did not change blood pressure in hypertensive rats, but it did moderate moderate heart rate and improve cardiac diastolic function. The thickness of the left ventricular anterior wall, interseptal thickness in the diastole and the relative thickness of the wall were reduced after treatment with moringa seed flour, where the relative thickness of the wall is equal to the sum of the thickness of the posterior wall of the LV plus interventricular septum thickness divided by LV diameter, all in diastole. In addition, a significant reduction in fibrosis in the left ventricle. This anti-hypertrophic and antifungal effect of moringa was associated with increased expression of peroxisome proliferator-activated receptors, reduced level of triglycerides and improved plasma prostacyclins. Finally, the researchers identified the benefit of moringa seeds against the functional and structural function induced by arterial hypertension and cardiac muscle restructuring.

Another PANC investigated in relation to SAH is Echinodorus grandiflorus, popularly called "chapéu-de-couro". In the study by Tibiriçá et al. (2007) the vascular effects of the crude aqueous extract of the leaves of the "chapéu-de-couro" were investigated, using in vitro experimental models of the isolated aorta from rabbit and perfused kidney. Leaf extract was injected into the renal circulation of rabbit pre-contracted with noradrenaline and induced marked and dose-dependent vasodilatory responses. In addition, the extract caused significant, concentration-dependent relaxation in the intact aortic rings. The authors suggest that the blood pressure lowering effects of the "chapéu-de-couro" leaf extract may be due to its potent systemic vasodilator effect.

The number of PANC studies that interfere with arterial hypertension is vast. Pages referring to the use of plants in medicinal uses would be necessary. Based on this statement, we brought a study by Teixeira (2011) where the author places a series of plants and their effects on hypertension. However, we warn that despite the beneficial effect of these plants, we can not neglect the ways of use and quantity of them. Each vegetable has different substances that act in different ways, in addition, each person can have a greater or lesser effect, including developing allergies and even causing greater problems. Treatment for hypertension with medicinal plants must be accompanied by a specialist in the field, who will indicate the quantities, times, forms of consumption and frequency of therapeutic use.

Thus, the plants researched by Teixeira (2011) as hypotensive PANCs are: Arctium lappa Arctium minus (common name: bardana, pegamassa); Baccharis trimera (common name: Carqueja); Bidens pilosa L.(common name: picão); Boerhavia diffusa L. and Boerhavia coccinea (common name: celidônia, erva-tostão, pega-pinto, tangará); Britoa guazumaefolia (common name: capoteira, sete capotes); Coleus barbatus (common name: boldo-do-reino, falso-boldo, malvasanta); Costus spicatus (common name: cana-de-macaco); Costus spiralis (common name: cana-do-brejo); Cuphea balsamona, Cuphea carthagenensis and Cuphea gutinosa (common name: sete-sangrias, erva-de-sangue, pé-de-pinto); Cymbopogon citratus (common name: capim-santo, capim-cidreira, capim-limão, capim-cidró, erva-cidreira); Erythrina falcata (common name: corticeira, corticeira-da-serra, mulungu, suinã); Eugenia uniflora L. (common name: ginja, ibipitanga, pitanga, pitanga branca, pitangueira); Foeniculum vulgare Mill. (common name: erva-doce, funcho); Hedychium coronarium (common name: gengibre branco, lágrima-de-moça, lírio-do-brejo, napoleão); Hibiscus sabdariffa (common name: hibisco) (McKay et al., 2010); Jatropha gossypiifolia L. (common name: (common name: erva-purgante, jalapa, mamoninha, peão-roxo, pinhão roxo, raiz-de-tiu); Ocimum basilicum and Ocimum selloi (common name:

alfavaca, alfavacão, alfavaca-cravo); Peperomia pellucida L. (common name: erva-jaboti, mariamole, ximbuí); Plantago major L. (common name: plantagem, sete-nervos, tansagem, tanchagem); Polygonum acre and Polygonum punctatum (common name: erva-de-bicho); Portulaca pilosa (common name: amor crescido, alecrim-de-são-josé, beldroega, perrexi); Taraxacum officinalis (common name: dente-de-leão) and Urera baccifera L. and Urtica dioica L. (common name: cansanção, urtiga, urtigão, urtiga-vermelha).

According to Teixeira (2011), plants have active principles that can act in different ways. For example, the presence of flavonoids with diuretic action and amines with vasodilatory action in vasomotor centers, which may be able to exert vasodilation and hence the reduction of hypertension; they also have a vasodilating action by blocking calcium channels; can induce inhibition of the angiotensin-converting enzyme; they have antagonistic properties over the alpha 2-adrenoreceptor; some fruits of these plants have a diuretic effect, among others.

According to the studies referenced here by the scientific literature, the path to the formulation of efficient and natural medicines and reduced side effects for humanity is promising. It is up to society, health agencies and authorities to demand broader, more transparent and credible research and studies on the active principles of medicinal plants and their large-scale production, with commercialization at popular prices and free from vicious development policies and trade of the large pharmaceutical industries.

3.4 The importance of scientific rigor in the manufacture of medicines

The drug manufacturing process, which involves the stages of preparing the drug, purchasing materials, production, quality control, release, storage, shipping of finished products, as well as the controls related to these; must meet minimum quality requirements, according to RDC 310 (Brasil, 2019). In addition to controlling the stages, the manufacturing companies must ensure the purpose of the intended use of the medication, so as not to put patients at risk, as to safety, quality or adequate effectiveness, always complying with Good Manufacturing Practices (GMP).

The process of manufacturing and selling medicines, whether for the control of SAH or other comorbidity, became a point of attention and concern after the evolution of public health policies. When it comes to the manufacture of medicines for public use, all their production must always be guided by fundamental pillars, among which are safety, efficacy and quality, with the principle of GMP being the expression of quality assurance in this process, bringing benefits, mainly , to consumers. GMPs must express the responsibility shared with the health of the population by manufacturers and the State, and the role of the Brazilian Health Regulatory Agency (ANVISA) is to guarantee conditions for the safety and quality of the drugs consumed, and to demand the adoption of the principles of quality assurance in drug manufacturing processes, with the aim of ensuring that the State complies with the Constitution with regard to the health care of the population.

The literature reports that the evolution of rigor in the manufacture of medicines is associated with disasters of great repercussion in the media, involving the use of poor quality medicines that have brought serious damage to the health of users and, in some cases, they have killed dozens of patients . Among the cases with the greatest repercussion, Vogler et al. (2017) cite the incidents involving the medication sulfatiazol, in 1941, in the United States of America (USA), which left approximately 300 victims (deaths or sequelae) due to ingestion of pills contaminated by phenobarbital; and the case of the failure in the process of viral inactivation of a batch of polio vaccine in the 1950s, which caused 60 people to develop polio and 89 other family members to contract the disease, also in the USA. Here in Brazil, some episodes involving the lack of quality in the manufacture of drugs can also be cited, such as the cases of the oral contraceptive Microvlar® and the drug Celobar®, which led to the death of 20 patients in Goiânia (Tubino & Simoni, 2007). Even today, doubts about quality in manufacturing and the suspension of the sale of medicines continue to exist, as can be seen on the ANVISA website (Brasil, 2020).

The agreements established by the World Trade Organization were the reference framework for the implementation of quality standards for medicines and health products. This event corroborated with the existence of an awareness that assessing the quality of medicines to be offered to society has always been indispensable to ensure the health of people who need to consume them. However, only from 1999, with the creation of ANVISA in Brazil, as an autarchy, the inspection of all health sectors and, consequently, of the pharmaceutical industries and their processes were approached differently (Deus & Sá, 2011).

Since then, there have been several discussions about scientific rigor, denoting a concern with criteria of scientific validity and reliability, which were initially described in quantitative research. After being well established and accepted, these criteria were extended to qualitative research (Moreira, 2018). Then, the scientific rigor provided by safe manufacturing practices was adopted to serve society and individuals, using Quality Management concepts and practices. These concepts have evolved over the years, in order to ensure the main safety criteria both in scientific research and in the manufacture of medicines.

The introduction of concepts and criteria from scientific research to the manufacture of medicines to ensure scientific rigor, started another and new movement, in which, through scientific research, pharmaceutical products started to be legitimized, thus strengthening the pharmaceutical industry. Scientific knowledge and disclosures are used as a marketing argument, directing economic interests in the area of medicines and often leading to bias in their results. Here is a new logic and a promising market, based on the funding of research programs, on the production and publication of scientific articles, often in accordance with the interests of the pharmaceutical industry. The latter, in turn, now understands that it is easier to introduce a medical substance or product on the market, if it is associated with the scientific knowledge generated by a powerful and articulated gear (Miguelote et al., 2010).

Finally, regardless of whether or not there is a possible direction of scientific research sponsored by the market, we cannot ignore the fact that the standardization proposed by GMPs associated with the consolidation of inspection by regulatory agencies, contributes to a fairer competitiveness even considering different manufacturers.

4. Conclusion

The health industry subjects individuals to treatment for the consequences of hypertension, neglecting the causes that led the body to adapt to cardiac output and vascular resistance. Thus, the need to change eating habits, smoking outcome, weight control, quality of sleep, reduced consumption of alcoholic beverages and physical exercise is little appreciated.

To reverse this dynamic, health professionals need to understand the patient as a human being, enabling, among other integrative measures, using PANC to treat causes within the understanding of the current multiplicity that requires the interaction of views from different areas of knowledge and different social references (multifaceted view).

In addition, in the process of manufacturing and developing new drugs, there are specific GMP criteria, strictly following the different pre-clinical and clinical phases. In the preclinical phases, the drugs undergo preliminary tests on animals, the most common being rats and dogs because they are easy to access and have a low cost, in addition to presenting low toxicity, among other characteristics. Once these tests are approved in guinea pigs, the phase called the clinic begins, where the drug has its effectiveness tested from its use in humans, initially in a small group (PHASE I), and then evolve in large groups of people. (PHASES II and III). In all these phases, criteria such as safety, quality and efficacy of the drug are verified and it can take years before a new drug is then made available for consumption on the market, which costs manufacturers some good millions of dollars.

All of this development opens up a new range of discussions and questions about the need to use guinea pigs, whether animal or human, as well as the effectiveness of responses throughout this journey. Although the regulation requires ethical rigor, it is still questioned, whether by animal protection agencies or by civil society, which sees in this process a vulnerability of people, especially the least favored. If, on the one hand, there are advocates that this process is necessary because there are no techniques to replace it, on the other are the arguments that technological advances need to make it possible to investigate the effect of substances on the human body without the use of a guinea pig. This discussion is far from over and needs to be further investigated by scientists in partnership with civil society and regulatory bodies.

Finally, as a proposal for future work in the study of SAH, the importance and the result of understanding the endocrine system in the control of hypertension can also be raised and evaluated. In contrast, discuss the problems in drug interactions with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or direct renin inhibitors. Health technologies must be at the service of society as an alternative for validating treatments and clinical research, including pharmacological and non-pharmacological, safeguarding life.

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