JOURNAL OF COMPLEMENTARY MEDICINE RESEARCH
Journal of Complementary Medicine Research, ISSN: 2146-8397 Vol. 13, No. 2, 2022 (pp. 68-72)
RESEARCH ARTICLE
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The Effect of Blood Pressure on the Risk of Developing Systemic Diseases

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ABSTRACT

The article discusses the features of the influence of blood pressure on the risk of developing systemic diseases. The author notes that blood pressure is a factor that, at a certain level of increase, negatively affects the development of systemic diseases. Monitoring of blood pressure indicators and standardization of the level of this parameter will allow to provide the necessary assistance to patients, as well as to select the necessary drugs that will improve the quality of life and will not have significant side effects on the body.

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How to cite this article: Lipina TA, Telegina MA,Grigoriev AV, Kuramshina AV, Ulitin EV, Kiseleva EM. The Effect of Blood Pressure on the Risk of Developing Systemic Diseases Journal of Complementary Medicine Research, Vol. 13, No. 2, 2022 (pp. 68-72).

KEYWORDS:
Blood pressure,
Cardiovascular diseases,
Complex therapy
Hypertension,
Monotherapy,
Systemic diseases .

ARTICLE HISTORY:
Received Feb 23,2022
Accepted Mar 20,2022
Published Apr 22 ,2022

DOI:
10.5455/jcmr.2022.13.02.13

INTRODUCTION

High blood pressure (BP) is one of the most important, as well as the strongest modifiable risk factors for cardiovascular diseases and kidney diseases. Antihypertensive drugs can effectively reduce blood pressure and the risk of concomitant diseases.[1]

The researchers note that a decrease in systolic blood pressure for every 5 mmHg reduces the risk of serious adverse cardiovascular events by 10%, stroke by 13% and death from cardiovascular diseases by 5%. It is noteworthy that there was no evidence that the effect of improving cardiovascular outcomes, expressed in the form of a decrease in relative risk, varies depending on the initial values of blood pressure up to <120 mmHg (the lowest category). However, when expressing an absolute reduction in risk, patients with the highest blood pressure (and, of course, the highest cardiovascular risk) had a greater decrease in cardiovascular events.[2] In general, antihypertensive drugs should be considered as a risk-modifying therapy for primary and secondary prevention of cardiovascular events, regardless of blood pressure values and even in lower blood pressure ranges.

Although the level of awareness about hypertension, its treatment and control has improved significantly in high-income countries since the 1980s and 1990s, control indicators have not changed in the last decade.

In this regard, the aim of the study is to consider the features of the influence of blood pressure on the risk of developing systemic diseases.

MATERIALS AND METHODS

When writing the paper, a certain array of scientific materials was analyzed within the framework of the research topic, a comparative and analytical research method was used in data processing.

RESULTS

Hypertension, a condition so common that it can almost be considered commonplace, is often attributed to the background noise of the patient's medical history. But arterial hypertension is a real systemic disease that affects many organ systems and adds to the incidence of more and more interesting problems that a patient may have.[3] In the last few years, hypertension has been revised in the light of

ohmic technologies that help us redefine most diseases, and this has shown us that hypertension is not at all commonplace.

Over the past few years, all published (updated) guidelines on arterial hypertension have emphasized the exceptional importance of the correct measurement of blood pressure and described in detail the various available measurement methods.

However, the threshold values of blood pressure for the diagnosis of hypertension vary depending on the medical standards of a number of countries.[4]

Accurate and reliable measurement of blood pressure has been and remains the basis of screening, diagnosis and treatment of hypertension. Errors in blood pressure measurement may occur due to factors related to the patient, device and procedure.

Several non-governmental organizations, for example, STRIDE BP, an international scientific non-profit organization founded by hypertension specialists in 2019 and officially supported by the European Society of Hypertension (ESH), the International Society of Hypertension and the World League of Hypertension, have identified the need to improve the accuracy of blood pressure measurement (and, consequently, the diagnosis and treatment of hypertension) and provide a detailed list of devices to measure blood pressure, which are recommended in accordance with pre-established quality criteria.[5]

In clinical trials, the protocol used to measure blood pressure is often standardized for different centers to minimize systematic errors and variability. Almost all major epidemiological and clinical studies in the field of hypertension have used the generally accepted standardized measurement of blood pressure. In the systolic blood pressure Intervention trial (SPRINT), a similar approach was used (5 minutes of rest, comfortable sitting and standard measurement), but the staff had to leave the room during the rest period and blood pressure measurement (automatic measurement). The SPRINT results have caused several controversies regarding their applicability to patients with hypertension in everyday practice, including due to the methodological issue of how blood pressure was measured.[6]

In recent years, there has been a paradigm shift in how to start antihypertensive therapy, from monotherapy to, preferably, a combination of one tablet (SPC) from the very beginning. The treatment algorithm was simplified, and the target blood pressure was reduced by about 10 mmHg. Recommendations of the American College of Cardiology/The American Heart Association recommends a single treatment goal of <130 mmHg. for all patients with hypertension, while the recommendations of the European Society of Cardiology (ESC)/ESH advise to individualize the target blood pressure depending on the patient's age, concomitant diseases, cardiovascular risk factors and, very importantly, tolerability within the recommended range of 120 to 140 mmHg systolic blood pressure and from 70 to 80 mmHg of diastolic blood pressure.[7]

In 2018, the ESC/ESH guidelines approve the initiation of antihypertensive medications using SPC, also known as a fixed-dose combination. There are two reasons for this: SPC improves adherence and accelerates the process of achieving the target BP. The target population of this first-line combination therapy includes the majority of patients with arterial hypertension, although it still allows individualization of antihypertensive drugs. In July 2019, the World Health Organization added fixed-dose combination antihypertensive drugs to the List of Essential Medicines of the World Health Organization.

In addition, it should be borne in mind that most patients with hypertension also need other drug therapy for additional diseases, which increases the burden of taking medications. Finally, it was found that non-compliance with the treatment regimen adversely affects the outcome of cardiovascular diseases and, according to the latest study of outcomes, increases overall mortality by 25-49%.

Data from the population cohort showed that a large number of patients who received initial antihypertensive monotherapy could not switch to combination treatment for many years, and this delay affects mortality and cardiovascular events; and recently it was again documented that compared to patients who started monotherapy, patients who started combination therapy, they are more likely to have reached the BP targets .[8]

Table 1: Comparison of the BP category and target BP in medical standards

AD category	*The USA*	*Europe*	*China*	*Korea*	*Japan*	*Canada*
Optimal	—	<120/<80	—	—	—	—
Common	<120/80	120-129/80-84	<120/<80	<120/<80	<120/<80	—
Increased	120-129/<80	—	—	120-129/<80	130-139/80-89	—
Prehypertension	—	—	—	130-139/80-89	—	—
Hypertension						≥135/≥85
Stage 1	130-139/80-89	140-159/90-99	140-159/90-99	140-159/90-99	140-159/90-99	—
Stage 2	≥140/≥90	160-179/100-109	160-179/100-109	≥160/≥100	160-179/100-109	—
Stage 3	—	≥180/≥110	≥180/≥110	—	≥180/≥110	—
Age-related AD						
<65 years	<130/<80	120-130/70-79	<140/<90	<140/<90	<130/<80	<140/<90
65-74 years	<130/<80	130-139/70-79	<140/<90	<140/<90	<130/<80	<140/<90
75-79 years	<130/<80	130-139/70-79	<140/<90	<140/<90	<140/<90	<120
≥80 years	<130/<80	130-139/70-79	<150/<90	<140/<90	<140/<90	<120

DISCUSSION

According to the recommendations, it is necessary to start drug therapy with SPC therapy from the very beginning, so as not to waste time in our efforts to achieve the target BP. According to these recommendations, delaying the start of antihypertensive therapy and waiting for the results of lifestyle changes (in particular, weight loss) is a dangerous strategy. In this regard, an alternative strategy has been proposed in the literature, namely the use of antihypertensive drug therapy in parallel with lifestyle modification (for example, weight loss) and, as soon as this is achieved, reduction of antihypertensive therapy.

The handbook The Kidney Disease: Improving Global Outcomes (KDIGO) for the management of hypertension in chronic kidney disease (CKD) now recommends target values of systolic blood pressure <120 mmHg, if tolerated, using a standard office blood pressure measurement. This is in stark contrast to other guidelines that recommend values of <140 and 130 mmHg, respectively, with a note to avoid BP < 120 mmHg. In the summary of the KDIGO manual, the authors state that the recommendations are "largely based" and then "based on one" test, namely SPRINT. This discrepancy between the KDIGO recommendations and other recommendations can be explained by the fact that SPRINT used a special method for measuring blood pressure. The average difference between systolic blood pressure measured in SPRINT and normal office blood pressure differs significantly in individual patients (by 5 and 15 mmHg).[9]

Moreover, in SPRINT, patients with type 2 diabetes (the most common cause of CKD), patients with proteinuria (>1 g/day or >1 g/g of creatine) and stroke patients (one of the most common causes of hypertension). complications) were excluded. In the face of these two limitations, the study-specific blood pressure measurement method, and exclusion criteria that strongly select the studied population (and, according to the authors, do not allow generalizing the results to other populations), it is unclear why KDIGO relied heavily on SPRINT data and recommended a blood pressure value <120 mmHg. Later, the authors of KDIGO recognized the "recommendation as weak", which is reflected by the recommendation of level 2B, while the target values of blood pressure in the recommendations of the American Heart Association and ESC/ESH are estimated as 1A.

It is obvious that the recommendations of KDIGO can be misunderstood by general practitioners and nephrologists, which can harm patients if they follow the recommendations of KDIGO and reduce office blood pressure to <120 mmHg, measured using a generally accepted standardized methodology that is used worldwide. The lesson from this is that we need to carefully link any recommendations with relevant information about how BP was measured, and thus any recommended BP value should accurately indicate the measurement conditions.

The prevalence of hypertension increases with age (for example, about 75% of people aged 75), and the lifetime risk of developing hypertension is >90% if a person lives long enough. When comparing different recommendations, it was found that the target values of blood pressure differ between different national and international recommendations for hypertension. In the Hypertension in the Very Elderly Trial (HYVET) study conducted among elderly patients, a significant reduction in mortality, fatal strokes and cases of heart failure was observed in the more intensive treatment group (target value <150 mmHg). Analysis of the Berlin Initiative study, which included patients aged 70 years and older who received antihypertensive drugs at baseline, showed that blood pressure values <140/90 mmHg. They may be associated with an increased risk of mortality in elderly patients and patients with a history of cardiovascular events.[10]

In general, when working with elderly patients, the authors emphasize the importance of an individual approach to blood pressure, since this will make it possible to evaluate such therapy to determine the benefits and harms of lowering blood pressure.

In most guidelines, treatment-resistant hypertension (TRH) is defined as BP ≥ 140/90 mmHg. The importance of TRH is due to the increased risk of adverse cardiovascular and renal outcomes compared to non-TRH, and at this stage it is necessary to conduct a thorough examination.[11]

First, it is necessary to eliminate pseudoresistance in order to eliminate the false variant of the TRH classification, which includes ensuring accurate measurement of blood pressure. It is necessary to ensure confidence in adherence to prescribed antihypertensive drugs, since non-compliance with the treatment regimen is widespread in patients with TRH.

Then, potential changes in lifestyle factors such as obesity, nutrition (high salt and alcohol intake) and physical inactivity should be identified. Lifestyle changes undoubtedly reduce blood pressure, thereby reducing the associated cardiovascular risk. In addition, it is necessary to control the increase in blood pressure due to concomitant treatment, since some drugs and substances (for example, steroids, nonsteroidal anti-inflammatory drugs, immunosuppressants and erythropoietin) can increase blood pressure or counteract the hypotensive effect of antihypertensive drugs. It was found that the individual effects of these agents vary greatly from a slight effect or lack thereof to a sharp increase in blood pressure values.

In general, the prevalence of secondary causes of hypertension ranges from 5 to 15% in patients with hypertension. The most common types of secondary hypertension include kidney parenchyma disease, primary hyperaldosteronism, and renovascular hypertension.

Antihypertensive treatment should be optimized. After a triple combination of one tablet (algorithm: A + C + D) the next step may be the appointment of a mineralocorticoid receptor antagonist or the replacement of a diuretic with a loop diuretic if the estimated glomerular filtration rate decreases from <30 to 40 ml/min by 1.73 m^2, as well as the selection of hardware antihypertensive therapy.

There are only a few comparative studies analyzing the strategies of pharmacological treatment of TRH. In one of the studies, spironolactone turned out to be the most effective additional drug, superior to beta-blockers and alpha-blockers. However, side effects due to its antiandrogenic properties (for example, gynecomastia), as well as electrolyte imbalance may limit use

(the frequency of discontinuation after 1 year is up to 50%), in particular, if renal function is reduced.[12]

It is also necessary to consider the status of diuretics as first-line therapy. There have been changes in the recommended classes of first-line drugs; for example, beta-blockers should be preferred only in the presence of concomitant heart diseases with the need to prescribe beta-blockers or arterial hypertension in pregnant women. Nevertheless, diuretics were still considered the cornerstone and equivalent first-line treatment options in the recommendations of the American College of Cardiology/American Heart Association and ESC/ESH. On the contrary, in the recommendations of the International Society of Hypertension 2020, in general, diuretics are not recommended as the first two steps of the treatment algorithm, which consists in starting taking antihypertensive drugs.

However, there are several potential salt-sensitive conditions in which treatment with diuretics is beneficial, for example, in patients with diabetes, renal insufficiency, heart failure or TRH.

As for diuretics as such, there is a long and controversial debate about whether thiazide-like diuretics (for example, chlorthalidone and indapamide) should be preferred to classical thiazides, in particular hydrochlorothiazide. It was found that thiazide and thiazide-like diuretics may not have the same effect on blood pressure, but a direct comparison does not allow us to draw a definite conclusion. In addition, diuretics are often used in combination with other antihypertensive drugs, and potential differences in lowering blood pressure may disappear. However, in the "class of diuretics" significant pharmacokinetic and metabolic differences exist and suggest a difference between thiazide and thiazide-like diuretics and even within thiazide-like diuretics (for example, indapamide has a more favorable metabolic and renal profile).

In recent decades, the potential side effects of antihypertensive drugs against cancer have been repeatedly suggested. More recently, several observational studies have revealed an increased risk of developing several types of skin cancer when using thiazide diuretics. Although there is no evidence that thiazide diuretics, and in particular HCT, cause skin cancer by themselves, their photosensitizing properties can enhance the harmful effects of sun exposure and potentially increase the risk of developing several types of skin cancer.

However, not only diuretics have photosensitizing properties, but also the most commonly used antihypertensive drugs. Indeed, another meta-analysis found no association between thiazide diuretics and the risk of skin cancer, while calcium channel blockers seem to increase the risk of skin cancer, and beta blockers increase the risk of skin melanoma.

At the session "News of Hypertension Science" at the ESC 2020 virtual Congress, data from the third cycle of cooperation between specialists in the treatment of blood pressure reduction were presented. Based on 31 randomized controlled trials with individual data of participants from 261,000 participants, 5 main classes of antihypertensive drugs were studied in comparison with placebo or other drugs that reduce blood pressure. The use of antihypertensive drugs of any class did not significantly affect the risk of developing any cancer or cancer mortality. In particular, there was no convincing evidence that the use of any class of antihypertensive drugs affects the risk of developing breast, colon, lung, prostate or skin cancer. In addition, no trend was found over time for any outcome.

Consequently, there are no clear indications for the exclusion of diuretics, which are one of the cornerstones of antihypertensive (but also other conditions, for example, heart failure) drug therapy, but the restriction of sun exposure, the use of adequate sun protection, as well as regular checks of suspicious skin lesions should be carried out by all patients, including hypertensive patients.

In the future, additional options for interventional therapy aimed at high blood pressure will definitely become available, while renal denervation (RDN) will become the most advanced technology. The rationale for catheter-based RDN is based on knowledge of the pathophysiological role of sympathetic nervous system activity in the initiation, maintenance and progression of hypertension and hypertension-mediated diseases. Clinical data from the pre-drug era showed an improvement in blood pressure and life expectancy after surgical paralumbal sympathectomy, but the side effects were significant.

CONCLUSION

Thus, blood pressure is a factor that, at a certain level of increase, negatively affects the development of systemic diseases. Monitoring of blood pressure indicators and standardization of the level of this parameter will allow to provide the necessary assistance to patients, as well as to select the necessary drugs that will improve the quality of life and will not have significant side effects on the body.

Author Contributions

All authors contributed in reviewing the final version of this paper.

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