Application of gene polymorphism-oriented individualized medication in patients with hypertension

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Introduction. To compare the clinical efficacy, safety and economic evaluation of antihypertensive drugs and traditional clinical drugs in patients with hypertension under the guidance of gene detection, and to provide accurate drug treatment for patients with hypertension.

Methods. Through the prescription review system, 200 patients with hypertension diagnosed in the hospital from March 2023 to December 2023 were selected. Real-time fluorescence quantitative PCR was used to detect angiotensin II receptor antagonist (ARB) CYP2 C9 * 3, β1 adrenergic receptor blockers (β1) CYP2 D6 * 10. ADRB1, angiotensin converting enzyme inhibitor (ACEI) ACE, calcium channel blockers (CCB) CACNA1C, diuretic ADD 15 antihypertensive drug-related genes. The age, gender, biochemical indicators, blood pressure levels, drug types and economic differences between the two groups were analyzed and compared.

Results. Compared with traditional clinical medication, patients who choose antihypertensive drugs under the guidance of genetic testing can control blood pressure more effectively and earlier, with better safety and higher economy. Among the 100 genomic patients, the sensitivity of patients using calcium channel blockers was better, reaching 47 %. The normal sensitivity rate to angiotensin II receptor antagonists was 38 %. The population with normal sensitivity to β1 receptor blockers accounted for 10 %. The population with high sensitivity to angiotensin converting enzyme inhibitors reached 9 %, and the normal sensitivity rate was only 3 %, while the sensitivity to diuretics was poor. Therefore, among the patients in this study, the population sensitivity rate of calcium channel blockers and angiotensin II receptor antagonists is higher, and the antihypertensive effect is more obvious, which has certain guiding significance in clinical treatment. Compared with the control group, the blood pressure level and the average daily cost

of oral antihypertensive drugs were significantly improved, and the treatment compliance was better, the difference was statistically significant (P<0.01).

Conclusion. The related gene loci of antihypertensive drugs are an important basis for guiding the diversification and individualization of clinical medication. Clinicians need to consider the influence of related genes on drug efficacy and adverse reactions when prescribing.

Keywords. hypertension ; gene detection ; individualized medication

INTRODUCTION

According to a survey,about 17 million people die of cardiovascular diseases every year,which has become the major cause of death worldwide.Hypertension is one of the more common types of cardiovascular diseases,and its prevalence is still increasing day by day in the world[1]. Although there are many types of anti-hypertensive drugs available, hypertension remains a major public health problem, with about one-third of the adult population affected by hypertension, only 13.80% of hypertensive patients have their blood pressure under effective control, and the number of deaths has risen by 56.1% over the past decade [2,3]. It has become one of the common risks that seriously endanger human health [4].

Although the understanding of hypertension and its complications has improved, there are many reasons why blood pressure is not well controlled in different patients, and one possible reason is that it is not possible to predict which antihypertensive drug will be most effective in a given patient. In the last decade, personalised precision medicine has received a great deal of attention from clinicians, researchers, drug developers and others. By studying and evaluating the mechanisms of different patient outcomes through proteomics, molecular biology or genetics, it has been found that low efficacy in certain populations may be related to inter-individual polymorphisms in antihypertensive drug-related genes. Studies have shown that understanding drug sensitivity and metabolic uptake capacity based on the specific location of genes in hypertensive patients can adjust patient treatment regimens, reduce medication uncertainty, decrease adverse effects, and achieve optimal efficacy [5-7]. In this study, the distribution characteristics of gene

polymorphisms were analysed through the detection of antihypertensive drug-related genes at five loci to provide clinical basis for gene-oriented individualized treatment of hypertensive patients.

1 MATERIALS AND METHODS

1.1 General information A total of 200 patients with hypertension diagnosed in our hospital from March 2023 to December 2023 were collected.Inclusion criteria: age ≥18 years; meeting the diagnostic criteria of the 2018 edition of the Chinese Guidelines for the Prevention and Control of Hypertension,Primary hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg measured in the seated position on three consecutive non-same days.Exclusion criteria: renal hypertension and other secondary hypertension; severe liver and renal function abnormalities; severe heart failure; those who refused genetic testing; and those with poor compliance. The study group was divided into 100 cases and the control group into 100 cases by random number method. The study was approved by the Medical Ethics Committee of the hospital. The patients all signed an informed consent form.

1.2 Methods Gene sensitivity screening: 2 ml of whole blood specimens from all included genomic hypertensive patients were collected clinically, genomic DNA was extracted, and fluorescence signals of gene loci related to the five major classes of antihypertensive drugs were collected by fluorescence quantitative polymerase reaction method, and the results were tested. All included hypertensive patients were considered to have reached the blood pressure standard when their blood pressure reached systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg, and the time was counted from the time when the blood pressure standard was maintained stably for 3 days after the start of medication. The observation period was 3 months. Relevant indicators before and after drug administration were evaluated: blood pressure control (DBP/SBP), time to blood pressure stabilisation, number of drugs used, and general information.

1.3 Statistical methods Graphad Prism 7.0 software was used for statistical analyses and the production of statistical graphs, all data were expressed as the mean standard deviation (SD), one-way analysis of variance (ANOVA) was used to compare the information between multiple groups, and LSD-t test was used to compare two by two between multiple groups.$P<0.05$ indicated that the difference was statistically significant.

2 RESULTS

2.1 Baseline data Among the 200 subjects included in the study, there were no statistically significant differences in age, gender, and biochemical indicators ($P>0.05$), Table 1.

Table 1 Baseline data

roups		ge	/F	LT	r	A	LU	G	DC-C
ontrol group	00	9.76±12.48	5/45	4.01±27.19	7.76±17.70	4287±96.30	.77±3.18	.10±1.63	.57±0.89
enomics group	00	0.75±16.08	2/38	4.46±37.10	1.46±45.97	53.54±112.46	.21±2.33	.09±1.84	.68±0.86
		.6289	.3893	.9244	.4643	.4849	.1801	.9567	.404

Note: ALT: alanine aminotransferase Cr: creatinine UA: uric acid GLU: blood glucose TG: triacylglycerol LDC-C: low-density lipoproteins

2.2 Comparison of the efficacy of the two groups after the intervention Before treatment, the differences in systolic and diastolic blood pressure levels between the two groups were not statistically significant ($P>0.05$); after treatment, the levels of SBP and DBP decreased in both groups compared with those before treatment, whereas the decrease in the levels of systolic and diastolic blood pressure was more pronounced in the

genomics group after treatment, and the differences were statistically significant (*P<0.05 vs. control group post-treatment diastolic blood pressure , **P<0.01 vs. control group post-treatment systolic blood pressure, Figure 1).

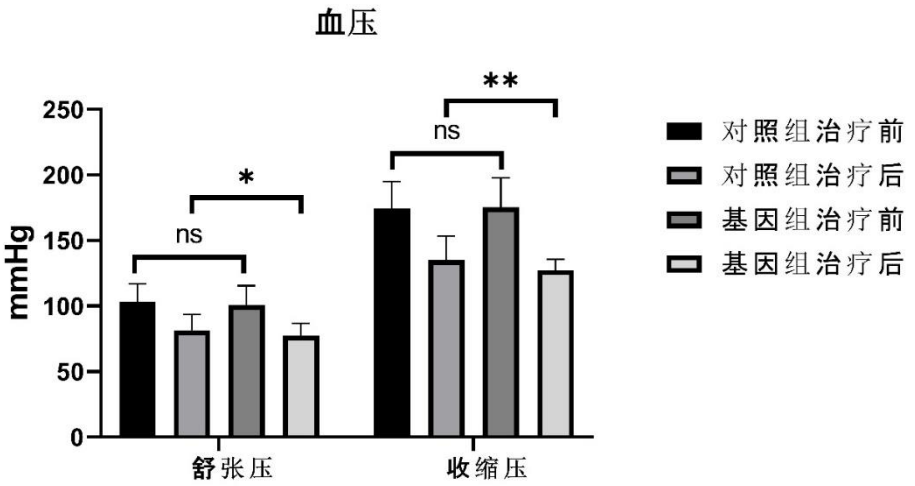

Figure 1 Comparison of blood pressure and heart rate control before and after treatment in control group vs. before and after treatment in genomics group (*P<0.05 vs. diastolic blood pressure after control group treatment, **P<0.01 vs. systolic blood pressure after control group treatment)

2.3 Comparison of drug sensitivity and probability of adverse reactions in populations

Among the 100 patients included in the genomics group, there were 62 males and 38 females, with a mean age of 60.75±16.08 years. genomics group antihypertensive drug gene sensitivity is shown in Figure 3, the total population was better for CCBs, with a normal sensitivity rate of 47%, and normal sensitivity for β1 drugs and ARBs reached reached 38% and 10%, ACEIs were moderately effective, with a high sensitivity rate of 9% but a normal sensitivity rate of only 3%, and diuretics had the worst sensitivity, with a low sensitivity rate of 6%. Through the follow-up follow-up found that the genomics group with drugs to lower blood pressure effect is more obvious study group adverse reactions mainly manifested: headache, ankle oedema, the study

process, no subject withdrew; control group adverse reactions mainly dry cough, lower limb oedema, adjust the medication to continue to carry out observation, see Figure 2.

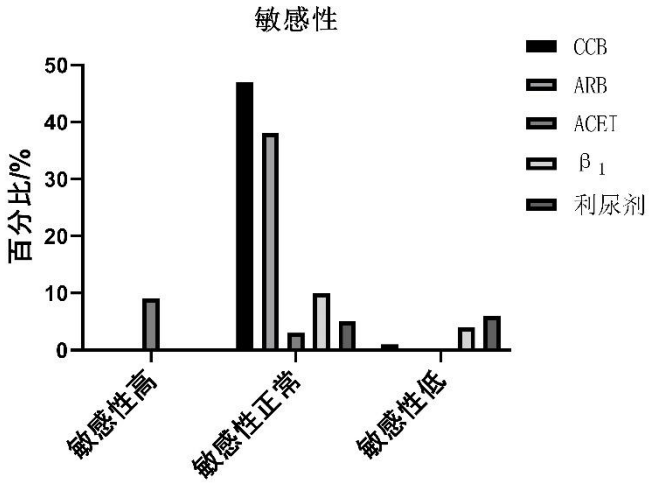

Figure 2 Hypertensive drug gene sensitivity testing

2.4 Comparison of the economics of the two groups after the intervention Genetic testing to guide individualised medication can, to a certain extent, reduce the types of medication patients take, increase patient compliance and reduce the economic burden (Figure 3). Individualised medication can reduce the risk of adverse reactions, improve patients' acceptance of and adherence to medication, and reduce their financial burden to a certain extent by selecting the medication and dosage that is most suitable for their individual situation based on their genetic information and drug metabolism characteristics, and by reducing unnecessary medication adjustments and trial-and-error processes.

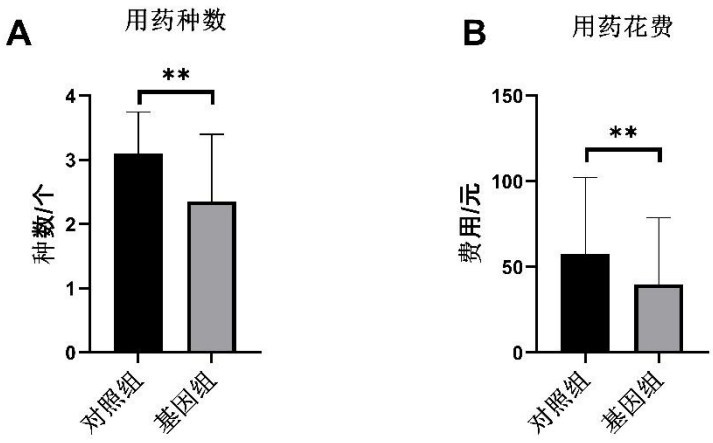

Figure 3 Genetic testing to guide individualised medication can reduce the number of types of medication used and alleviate the economic burden on patients A: number of types of medication used B: medication cost (**P < 0.01 vs. control group)

3 DISCUSSION

With rapid socio-economic development, people's lifestyles have changed significantly. Factors such as changes in dietary structure, reduced physical activity, and increased stress may lead to a gradual increase in the risk of chronic diseases, especially hypertension as a high prevalence of chronic diseases. High-salt and high-fat diets, physical inactivity, and poor ways of coping with stress may increase the risk of hypertension [8]. Uncontrolled hypertension may cause damage to blood vessels, heart and brain, and it has been reported that the number of deaths from hypertension complication-related diseases ranks first among chronic diseases in China, and the prevalence of hypertension among residents aged 18 years and older is increasing year by year [9]. There are a wide variety of antihypertensive drugs, and there are obvious individual differences in patients' response to medication. The anti-drug trial process in conventional antihypertensive treatment not only causes waste of resources and time, but also may cause adverse drug reactions, which reduces the adherence of hypertensive patients and leads to a low compliance rate.

Advances in hypertensive drug genomics group science provide new hope for individualised medication, compared with the traditional empirical selection of antihypertensive drugs, genetic testing to guide personalised medication can accurately select the most suitable drug for a patient's genotype based on his or her genetic information, thus improving the relevance and effectiveness of the treatment as well as shortening the time to reach the blood pressure target [10]. Meanwhile, through more precise drug selection and dose adjustment, individualised medication can control hypertension more effectively and reduce the risk of cardiovascular complications, thus helping to improve the long-term prognosis of patients [11]. Individualised medication can also predict patients to be more sensitive to adverse reactions to certain drugs based on their genetic information, reducing the risk of adverse reactions in patients and reducing damage to other target organs by avoiding drugs that may trigger adverse reactions [12]. In addition, gene-directed individualised medication as an example of precision medicine, by analysing real-world clinical cases and combining individual patient characteristics with treatment options, it has been found that the selection of antihypertensive medications based on drug GENOMICS GROUPSTUDY guidance may be more effective in controlling blood pressure compared to clinical experience with medication, and can lead to a more effective and customised medical care.

In this study, we followed up and observed the differences in antihypertensive efficacy and adverse drug reactions between traditional clinical experience of medication and gene testing-guided selection of antihypertensive drugs. A study of 200 hypertensive patients found that there was a significant difference in the rate of blood pressure attainment between the gene-guided group and the non-gene-guided group ($P<0.05$), and that patients were able to achieve blood pressure attainment more easily and earlier by using medication under the guidance of genetic testing. Although there was no statistically significant difference between the two groups in terms of blood pressure level and the number of medications used, the gene-guided group showed a lower trend than the non-gene-guided group. Therefore, the selection of antihypertensive medications by patients with hypertension guided by the genetic test may lead to a greater decrease in

blood pressure and a reduction in the number of medications used, and the patient's compliance is better, so that the purpose of lowering blood pressure can be achieved efficiently and accurately. In the collection of patients' adverse drug reactions, both groups showed different kinds of adverse reactions, the difference was not statistically significant, and we can continue to observe and track the relevant results of the patients; at the same time, it may be related to the small number of cases, the sample size is insufficient, and we should expand the collection of the sample size in the future. In the comparison of the economy of the two groups, we found that genomics group can reduce the economic burden of patients to a certain extent by guiding patients to individualise their medication and reduce unnecessary medication adjustments and trial-and-error processes.

Poor adherence is reported to be one of the important reasons for the low rate of hypertension control [13], and the more types of medication and the higher the cost, the worse the adherence [14]. In this study, adherence was higher in the genomics group than in the control group, probably because the use of medication under the guidance of genetic testing reduced the cost of lowering blood pressure, improved the accuracy of medication, and led to a significant reduction in systolic blood pressure, which enhanced the patients' confidence in treatment. It may also be because gene-directed individualised medication can reduce the types of medication used, can accurately adjust the regimen, and improve the efficiency of blood pressure reduction [15].

In summary, the relevant gene loci of antihypertensive drugs are an important basis for guiding the diversification and individualisation of clinical medication, and gene-directed individualised therapy can control blood pressure more effectively. However, it is still important to note that despite the theoretical potential of individualised drug therapy, it still faces some challenges in practical application. Collecting, interpreting and applying genetic information requires expertise and appropriate equipment, and the relationship between genes and drug response can be complex and influenced by other environmental factors. In addition, individualised therapy may also increase the cost and time of treatment. Therefore, the implementation

of individualised drug therapy needs to take into account the patient's specific situation, medical resources and the latest advances in scientific research.

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