Research Paper

Effect of Valsartan in Essential Hypertension and its Impact on Renal Function and Blood Lipid Levels

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The objective of this study is to explore the drug effect of valsartan in essential hypertension. Through the analysis of the treatment of 122 patients with essential hypertension who were treated in Zhuji Second People's Hospital from June 2022 to June 2023, the patients were divided into group A and group B, with 61 individuals in each group. The patients in group A were treated with valsartan and the patients in group B were treated with amlodipine. The medication cycle of both groups was 8 w. The blood pressure levels, renal function indicators, blood lipid changes, adverse drug reactions and drug effects of the two groups of patients before and after medication were compared. The total effective rate of medication in group A was 91.8 %, and that in group B was 80.33 % ($p<0.05$). After treatment, the systolic blood pressure of group A was lower than that of group B and the diastolic blood pressure was higher than that of group B ($p<0.05$). In terms of renal function indicators, after treatment, the serum blood urea nitrogen, creatinine and other indicators of patients in group A were lower than those in group B ($p<0.05$). In terms of blood lipid levels, group A's serum triacylglycerol, total cholesterol, low-density lipoprotein cholesterol was lower than that of group B ($p<0.05$). There was no significant difference in adverse drug reactions between the two groups ($p>0.05$). Valsartan treatment, as a drug for the treatment of essential hypertension has obvious efficacy, good blood lipid lowering effect, with less adverse effects causing less damage to patients' renal function and high drug safety, which is worthy of clinical drug promotion.

Key words: Valsartan, hypertension, amlodipine, angiotensin-converting enzyme, low-density lipoprotein-cholesterol

As a common cardiovascular disease, essential hypertension has a high incidence worldwide and its clinical characteristics mainly include clinical symptoms of hypertension, target organ damage and other hypertension-related complications[1]. The cause of essential hypertension is caused by many factors and is a complex disease which is affected by multiple factors. Although the academic community is not completely clear about this, it is basically recognized that these aspects are closely related to the cause of essential hypertension[2]. Genetic factors are also responsible for essential hypertension. For instance, people with a family history of high blood pressure are more likely to develop essential hypertension. Similarly, environmental factors and bad life style such as high-salt diet, inactivity, excessive obesity, excessive alcohol consumption and other behaviors will also lead to increased risk of disease. Further, biological factors such as disruption of the balance of vasoconstrictor hormones, renin-angiotensin-aldosterone system and possibly endothelial dysfunction may lead to the occurrence of essential hypertension. Essential hypertension is very harmful and can easily cause cardiovascular, cerebrovascular and kidney diseases. It may also increase the risk of a series of health problems such as diabetes, retinopathy, metabolic syndrome and osteoporosis. Therefore, attention should be paid to the treatment of essential hypertension.

Currently, drug therapy is currently considered to be the major choice of treatment for essential hypertension. The drug treatment of essential hypertension mainly includes 5 categories of drugs. They are diuretics, calcium channel blockers, angiotensin-converting

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enzyme inhibitors, angiotensin receptor blockers and beta-blockers.

Among all of them, diuretics play an important role to reduce blood pressure by increasing the excretion of urine, thereby reducing the amount of fluid in the body. Most commonly used diuretics include thiazides (e.g., hydrochlorothiazide) and loop diuretics (e.g., furosemide), etc. Similarly, calcium channel blockers rely on blocking calcium ion channels in vascular smooth muscle to reduce blood vessel contraction, thereby lowering the blood pressure. The representative drugs of this class include dihydropyridines (e.g., nifedipine and amlodipine), non-dihydropyridines (e.g., verapamil and diltiazem), etc. Angiotensin-converting enzyme inhibitors act by inhibiting angiotensin-converting enzyme, where the growth rate of angiotensin II is slowed down, thereby dilating blood vessels, reducing water and sodium retention in order to achieve the purpose of lowering blood pressure. Some of the examples of representative drugs include captopril, perindopril and enalapril. Further, the mechanism of action of angiotensin receptor blockers is similar to angiotensin-converting enzyme inhibitors. However, they directly block the binding of angiotensin II to its receptors to lower blood pressure. The representative drugs include losartan, valsartan and irbesartan, etc. Eventually, beta-blockers rely on blocking beta-receptors, slowing the heart rate, reducing cardiac contractility and ultimately lowering the blood pressure. These drugs include propranolol, metoprolol and atenolol, etc. Valsartan belongs to the angiotensin receptor blocker class of drugs, and amlodipine belongs to the calcium channel blocker class of drugs. These two drugs are common drugs for the treatment of essential hypertension and are highly representative. Thus, this study selected valsartan and amlodipine for a comparative study. Comparative research between the two has very good guiding significance for the medication of essential hypertension.

MATERIALS AND METHODS

General information:

A retrospective analysis was conducted with 122 individuals with essential hypertension who were treated in Zhuji Second People's Hospital from June 2022 to June 2023. Based on the actual data, 61 individuals who were treated with valsartan were considered to be into group A while 61 individuals taking amlodipine drug treatment were considered to be into group B. There were no significant differences in gender, age and course of disease between the two groups of patients.

Inclusion criteria:

The patients who met the diagnostic criteria according to the essential hypertension in the "2018 revised edition of the Chinese guidelines for the prevention and treatment of hypertension"; patients who were not treated with other antihypertensive drugs 1 w before treatment; those patients who had good compliance and patients who have signed the informed consent were included in this study.

Exclusion criteria:

Patients having hypertension caused by other causes; patients with malignant tumors; patients with mental illness and patients having liver, kidney and other organ dysfunction, etc., were excluded from the study.

Methods:

Before conducting the basic treatment, it was ensured that patients of both the groups need to pay attention to diet and exercise, involving low-salt and sodium diet and abstinence from alcohol with daily quantitative exercise.

Patients in group A were given 2 valsartan tablets once every day for 8 w. The manufacturer of valsartan tablets is Zhejiang Huahai Pharmaceutical Co., Ltd., approved by the standard H20183128, whose specification is 40 mg×28 tablets/box.

Similarly patients of group B were given amlodipine besylate tablets. The starting dose given was 5 mg for 1 w. Then the dose was adjusted according to the actual effect of the patient's medication, with the maximum dose not exceeding 10 mg/day. The manufacturer of amlodipine besylate tablets is Zhejiang Weikang Pharmaceutical Co., Ltd., approved by the standard H20066835, whose specification is 5 mg×14 tablets. The total course of treatment was 8 w.

Outcome measures:

Evaluation of drug effects: The reference standards of drug efficacy included 3 grades namely, markedly effective, effective and invalid. If the diastolic blood pressure after medication is ≤90 mmHg and is reduced by >10 mmHg compared with before medication or if the diastolic blood pressure is >90 mmHg after taking the medicine, but it is reduced by >20 mmHg than before the medicine or even if the systolic blood pressure is reduced by >10 mmHg

than before the medicine, then it is considered to be markedly effective. Similarly, if the diastolic blood pressure is <20 mmHg after medication and the diastolic blood pressure is >90 mmHg or if the systolic blood pressure decreases by >30mmHg, then it is considered to be effective. Finally, if none of the above mentioned conditions were observed, such condition is considered as invalid.

Total effective rate=significant rate+effective rate

Renal function: It includes renal indicators and evaluation criteria. The renal function indicators in this study were Blood Urea Nitrogen (BUN) test and Creatinine (Cr). According to the evaluation standard, if the BUN and Cr levels are reduced compared with before treatment then the renal function is considered to be better.

Blood lipid levels: They include indicators such as Total Cholesterol (TC), Triglycerides (TG) and Low Density Lipoprotein-Cholesterol (LDL-C). As per the evaluation criteria, lower the values of TC, TG and LDL-C, healthier is the blood lipid level.

Serum inflammatory indicators: Serum inflammatory indicators such as Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and White Blood Cell (WBC) count were detected using Enzyme-Linked Immunosorbent Assays (ELISAs).

Statistical analysis:

This study used Statistical Package for Social Sciences (SPSS) version 22.0 software to process the data of the study. We have used t-test to determine if there is any significant difference and $p<0.05$ was regarded to be statistically significant.

RESULTS AND DISCUSSION

Drug effects of the two groups were compared and tested between both the groups. The total effective rate of medication in group A was 91.8 %, and that in group B was 80.33 % (Table 1).

Subsequently the blood pressure levels in both the groups were evaluated. The blood pressure levels of patients are presented in Table 2. The renal function indicators of the two groups of patients were compared and presented in Table 3. Similarly, the blood lipid levels were examined in the two groups to evaluate the blood lipid indicators as shown in Table 4. Finally, the drug safety was estimated as shown in Table 5.

TABLE 1: COMPARISON OF DRUG EFFECTS BETWEEN THE TWO GROUPS, n (%)

Group	n	Effective	Efficient	Invalid	Total effective rate
A	61	27 (44.26)	29 (47.54)	5 (8.2)	56 (91.8)
B	61	22 (36.07)	27 (44.26)	12 (19.67)	49 (80.33)
x^2					5.127
p					0.001

TABLE 2: COMPARISON OF BLOOD PRESSURE LEVELS BETWEEN THE TWO GROUPS OF PATIENTS (x̄±s)

Group	n	Systolic blood pressure		Diastolic blood pressure	
		Before medication	After medication	Before medication	After medication
A	61	144.62±2.36	108.24±2.12	105.58±8.36	85.46±4.66
B	61	144.54±2.35	123.34±2.28	104.82±8.42	77.51±4.22
t		1.326	4.629	1.082	3.625
p		0.627	0.001	0.816	0.001

TABLE 3: COMPARISON OF RENAL FUNCTION BEFORE AND AFTER MEDICATION (x̄±s)

Group	n	Cr (μmol/l)		BUN (mmol/l)	
		Before medication	After medication	Before medication	After medication
A	61	94.26±7.18	73.46±6.12	5.61±0.82	4.36±0.11
B	61	95.22±7.28	82.39±7.26	5.62±0.83	4.92±0.12
t		1.627	4.962	1.429	4.812
p		0.418	0.001	0.545	0.001

TABLE 4: COMPARISON OF BLOOD LIPID LEVELS (x̄±s, mmol/l)

Group	n	TC		TG		LDL-C	
		Before medication	After medication	Before medication	After medication	Before medication	After medication
A	61	6.13±0.79	3.71±0.59	2.90±0.69	1.55±0.32	3.46±0.55	1.56±0.42
B	61	6.12±0.80	4.36±0.62	2.89±0.69	2.12±0.36	3.47±0.54	2.49±0.48
t		1.468	5.837	1.459	5.354	1.471	5.624
p		0.527	0.001	0.508	0.001	0.512	0.001

TABLE 5: COMPARISON OF ADVERSE DRUG REACTIONS BETWEEN THE TWO GROUPS, n (%)

Group	n	Gastrointestinal issues	Dizziness	Headache	Hypotension	Overall incidence
A	61	1 (1.64)	1 (1.64)	1 (1.64)	0 (0)	3 (4.92)
B	61	2 (3.28)	1 (1.64)	0 (0)	1 (1.64)	4 (6.56)
x^2						0.286
p						0.628

Studies have shown that essential hypertension is largely related to genetics[3]. Specific genetic mutations may increase an individual's risk of essential hypertension. Some studies have also shown that the kidneys play an important role in balancing blood pressure. Once kidney function is abnormal, this balance will be destroyed and hypertension will occur[4]. Jing *et al*.[5] also affirm this view, pointing out that kidney damage may lead to the emergence of essential hypertension. Looking deeper into the reason, it may be that there is a problem with the function of the glomeruli and renal tubules in the kidneys, which leads to an increase in blood pressure. Some studies have also pointed out that the Renin Angiotensin Aldosterone System (RAAS) in the kidney plays a key role in regulating blood pressure[6], ultimately explaining the relationship between renal function and hypertension. In fact, it is to explain the rationality of renal function including indicators of this study.

Some studies have pointed out that high LDL-C may promote the progression of essential hypertension, and the same is true for reduced levels of High (H) DL-C. High levels of LDL-C can easily lead to atherosclerosis whose direct consequence is increased blood pressure[7]. Low HDL-C is often associated with vascular damage or inflammation, both of which can increase blood pressure. In addition, elevated TG values are often closely related to insulin resistance, obesity and metabolic syndrome, all of which can increase blood pressure[8]. Bellien *et al*.[9] have pointed out that high levels of high sensitivity-C-Reactive Protein (hs-CRP) may be related to abnormal vascular endothelial function, atherosclerosis and inflammatory reactions, which can easily cause hypertension. We have to admit that although there are many research conclusions pointing out the relationship between blood lipids and essential hypertension, the entire system is relatively complex and is interfered by multiple factors. From a practical point of view, this study recognizes the relationship between blood lipids and hypertension, thus using it as a research indicator.

There are many drugs for the treatment of essential hypertension, which were explained at the beginning of this study. This study selected valsartan and amlodipine as a single drug comparative study, which has certain value considerations. As an angiotensin II receptor antagonist, valsartan relies on blocking the effects of angiotensin II on vasoconstriction and aldosterone release, thereby dilating blood vessels and lowering the blood pressure. One study compared the therapeutic effects of valsartan and placebo in the treatment of patients with essential hypertension. The results showed that within 12 w of medication, valsartan significantly reduced both systolic and diastolic blood pressure and the drug was highly safe[10]. Yang *et al*.[11] have also conducted comparative studies on valsartan and lotenin, and the results showed that valsartan is better than lotenin in lowering blood pressure and reducing cardiac events. As mentioned earlier, there is a certain relationship between essential hypertension and kidney damage. Jaglinska *et al*.[12] have conducted research on valsartan and essential hypertension. This study compared the renoprotective effects of valsartan and ramipril in patients with hypertension. Results showed that patients taking valsartan had a lower risk of worsening renal function and lower urinary protein excretion. There are also studies

comparing amlodipine with benazepril in the treatment of hypertension. These results depicted that patients in the amlodipine group had lower urinary protein excretion and lower risk of kidney-related cardiovascular events[13].

In this study, the Cr and BUN indicators of patients in the valsartan and amlodipine groups reduced after treatment, indicating that these two drugs have certain effects on patients' renal function. But valsartan is more effective in improving patients' renal function. The conclusion of this study is also supported by the same research literature. For example, one study compared the renal protective effects of valsartan and amlodipine in patients with hypertension. The results showed that patients in the valsartan group had lower urinary protein excretion and slower progression of renal function deterioration, while the amlodipine group showed relatively poor effects[14]. Similarly, Sultan *et al*.[15] have concluded that the valsartan group has lower risk of renal function deterioration and lower protein excretion, but the amlodipine group shows higher protein excretion and higher risk of renal function deterioration.

A retrospective study regarding the adverse drug reactions between both drugs pointed out that the most common adverse reactions in patients taking valsartan to treat hypertension were headache, hypotension and fatigue[16]. These adverse reactions are usually mild and self-limiting, and only a small number of patients may need to adjust the dosage or stop taking the drug. Another systematic review pointed out that about 5 %-10 % of patients will experience adverse reactions when valsartan is used to treat hypertension. These adverse reactions are mainly hypotension, headache, dizziness and vomiting[17]. Moreover, these adverse reactions are often mild and few patients need to stop taking the medication. Judging from the results of other people's studies, the adverse drug reaction rate of valsartan in this study was 4.92 %, which is almost the same as the conclusions of other studies. So, it can be considered that the adverse drug reactions in this study were almost the same as compared with those in other studies. This supports the scientific nature of this study to a certain extent.

Regarding the adverse drug reactions of amlodipine, a retrospective study pointed out that the most common adverse reactions of patients after using amlodipine were headache, edema and facial flushing, and these adverse reactions were mild and self-limiting[18]. There is also a large-scale randomized controlled study that compared the adverse reactions of amlodipine and other hypertension drugs. The results showed that the incidence of adverse reactions in the two groups of patients was almost the same, and the most common adverse reactions were headache, edema, facial flushing, gastrointestinal discomfort, etc.[19]. Overall, the adverse drug reactions of amlodipine are mild and similar to other antihypertensive drugs. This also supports the conclusion that there is no significant difference in the adverse drug reactions of valsartan and amlodipine in this study.

This study did not use combination drugs, but compared only single drugs. The reason is that many studies have shown that valsartan monotherapy can effectively reduce blood pressure in the treatment of essential hypertension and has a good protective effect on the risk of cardiovascular events[20]. Different antihypertensive drugs have certain side effects. When valsartan has a good effect in treating essential hypertension, choosing a single drug can better explore the true situation of the drug.

In summary, both valsartan and amlodipine have good effects in treating essential hypertension. Valsartan is better at improving patients' blood pressure levels, renal function indicators, and blood lipid levels; both drugs are highly safe. Thus, in terms of clinical guidance, valsartan is a better choice. This study also has a limitation; compared with single drugs, combination of drugs are more complex and may involve reactions between drugs. In particular, it is difficult to determine whether a drug safety event is caused by a certain drug or a combination. So, there is no study that compared single drug with a combination of drugs which should be studied in future.

Conflict of interests:

The authors declared no conflict of interests.

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