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Clinical effect and safety of nifedipine controlled-release tablets combined with valsartan in the treatment of primary hypertension

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Abstract: To observe and analyze the clinical effect of nifedipine controlled-release tablets combined with valsartan in the treatment of essential hypertension, and to analyze the adverse reactions of patients. A total of 180 patients with primary hypertension treated in our hospital were enrolled as research objects in the study. According to different treatment regimens, they were divided into the control group treated with valsartan dispersible tablets and the research group treated with nifedipine controlled-release tablets combined with valsartan. The therapeutic effects of the two groups of patients were compared and analyzed. Compared with the control group (82.22%), the total treatment effective rate of the research group (95.56%) was higher, $p<0.05$. Comparing the blood pressure level before and after treatment of the two groups, the improvement effect of the research group after treatment was more obvious, $p<0.05$. The incidence of adverse reactions was 6.67% in the research group, which was significantly lower than that (20.00%) in the control group, $p<0.05$. The application of nifedipine controlled-release tablets combined with valsartan in the treatment of patients with primary hypertension can significantly improve the therapeutic effect of patients, and has good safety and reliability, which is a treatment mode worthy of promotion and practice.

Keywords: Primary hypertension, nifedipine, valsartan, combination therapy, security.

INTRODUCTION

Based on the current level of medical development and examination methods, the exact cause of blood pressure rise can be found, known as secondary hypertension; conversely, if the exact cause of blood pressure rise cannot be found, it is called primary hypertension. Most hypertension cases are primary hypertension. but a clear diagnosis of primary hypertension, the first exception to secondary hypertension. To make a definite diagnosis of primary hypertension, secondary hypertension must be excluded first. It is believed that primary hypertension is caused by genetic and environmental factors. In 2005, the American society of hypertension (ASH) proposed that hypertension is a progressive cardiovascular syndrome caused by many causes, which can lead to changes in heart and vascular function and structure (Chen 2019; Wang *et al*., 2018; Liu 2018). Therefore, the primary goal of essential hypertension treatment is to minimize the overall risk of cardiovascular death and disability.

Hypertension is characterized by a continuous increase in arterial blood pressure, which is the main risk factor of cardiovascular and cerebrovascular diseases. Primary hypertension (fig. 1) is one of the most important types of hypertension, and its specific cause is unknown. It is generally believed that primary hypertension may be related to factors such as high-salt diet, obesity, alcoholism, mental stress, genetics and age growth (Graudal *et al*., 2015 and McCallum *et al*., 2015). Valsartan is angiotensin II receptor blocker and nifedipine is dihydropyridine calcium channel blocker, both of which are commonly used in the clinical treatment of hypertension. This study investigated the clinical effect and safety of nifedipine controlled-release tablets combined with valsartan in the treatment of essential hypertension.

MATERIALS AND METHODS

General data

The included patients were 180 patients who had been diagnosed and treated for primary hypertension in our hospital from January 2016 to May 2018. All the included patients met the standards of the Chinese guidelines for the prevention and treatment of hypertension (revised edition in 2004) (Fu 2016) (fig. 2), 140mm Hg≤ systolic blood pressure <160mm Hg (1mm Hg= 0.133kpa), 95mm Hg≤ diastolic blood pressure <110mm Hg and complete examination and treatment data could be collected. The patients have no allergy or discomfort to the drugs studied in this study. The study was approved by hospital ethics association, and all patients signed informed consent. The exclusion criteria were patients with secondary hypertension with poor compliance, who refused to participate in the study and who had diseases that had a serious impact on the study.

The patients were randomly divided into research group and control group. Among the 90 patients in the research group, 53 were male and 37 were female, with an average age of (68.3±3.2) years old. Among the 90 patients in the

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control group, there were 50 males and 40 females with an average age of (66.2±3.8) years old. There was no significant difference in the general data before treatment, p>0.05.

Patients in the control group were subjected to oral administration of valsartan (Xinxiang hengyuan pharmaceutical Co., Ltd., SFDA approval number: H20133189) at dose of 80mg each time, once a day. For the patients in the research group, oral administration of nifedipine controlled-release tablets combined with valsartan was applied, where valsartan method was the same as the control group and nifedipine controlled-release tablets (Shanghai Modern Pharmaceutical Co., LTD., SFDA approval number: H20000079) were taken orally at dose of 30mg each time, three times a day. After one month of treatment, if the patient's diastolic blood pressure is above 90mmHg, the dosage of valsartan can be increased to 160mg and the dosage of nifedipine controlled-release tablets can be adjusted to 60mg once a day.

Valsartan is white crystal or white powder. It is easily soluble in ethanol, easily soluble in methanol, slightly soluble in ethyl acetate, and almost insoluble in water. Its molecular formula is $C_{24}H_{29}N_5O_3$, and molecular weight is 435.51900. The preparation method can be described as follow. First 2'-cyano biphenyl-4-methyl aldehyde (I) and L-valine were subjected to reductive amination, resulting in compounds (II), which was then treated by acylation and chromatography to obtain compounds (II). After that it reacted with Bu3SnN3, tetrazoles were introduced followed by hydrolysis to obtain the final product. As a antihypertensive drug, valsartan is the receptor antagonist for angiotensin II (Ang II), which can selectively block Ang II from binding with AT1 receptor (antagonism effect of AT1 receptor is about 20000 times greater than that of AT2), thus inhibiting vascular contraction and the release of aldosterone, and exerting antihypertensive effects. Nifedipine sustained release tablets are mainly composed of nifedipine, chemical name is 2, 6-dimethyl-4 - (2-nitrophenyl) -1, 4-dihydro-3, 5 pyridine dimethyl diformate, molecular formula is C 17H 18N 2O 6, molecular weight is 346.343. Nifedipine is a calcium ion antagonist of 1, 4 dihydropyridine, which can reduce calcium ions entering cells through slow calcium channels. Nifedipine specifically acts on the smooth muscle cells of cardiac muscle cells, coronary arteries and peripheral resistance vessels. It can dilate coronary artery and the incomplete occlusion area sound blood vessel, weaken the coronary artery smooth muscle tension, avoid vasospasm, increase blood flow to narrow vessels and increase oxygen supply.

Observational indexes

The blood pressure levels of the two groups before and after treatment were compared, and the overall treatment effective rate was calculated. According to the guiding principles of drug clinical research, the therapeutic effect was evaluated (Luo *et al*., 2015). The criterion for significant effectiveness is that after treatment, the diastolic blood pressure is decreased by more than 20mmHg or falls to the reference range. The criterion for effectiveness criterion is a 30mmHg reduction in diastolic blood pressure after treatment. The criterion of ineffectiveness refers so no significant improvement in blood pressure after treatment. Meanwhile, the rate of adverse reactions was calculated.

STATISTICAL ANALYSIS

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean ± average ($\bar{x}$ ± s), with t test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with X^2 used for intergroup comparison. The intergroup difference is of statistical value when P<0.05.

RESULTS

The improvement effect of blood pressure level in two groups

As shown in table 1 below, the improvement degree of blood pressure in the research group was significantly better than that in the control group (p<0.05).

Comparison of overall treatment effective rate between the two groups

As shown in table 2, the overall effective rate of the research group was higher than that of the control group, p<0.05. Imaging examination of 1 patient after treatment is shown in fig. 3.

Comparison of adverse reaction rate between the two groups

As shown in table 3, the adverse reaction rate of the research group was significantly lower than that of the control group, p<0.05.

DISCUSSION

In recent years, the number of patients with primary hypertension has been continuously increasing, and the sharp increase of blood pressure is the main clinical manifestation, which can impact patients' health to different extent (Pulgar 2015). Therefore, timely applying effective drugs to control the blood pressure level of patients with primary hypertension is of great importance to improve clinical symptoms and obtain a better quality of life. As a new type of cardiovascular drugs, calcium ion blockers can effectively reduce the peripheral resistance, significantly increase the blood flow of organs and effectively prevent and control the remodeling of target organs.

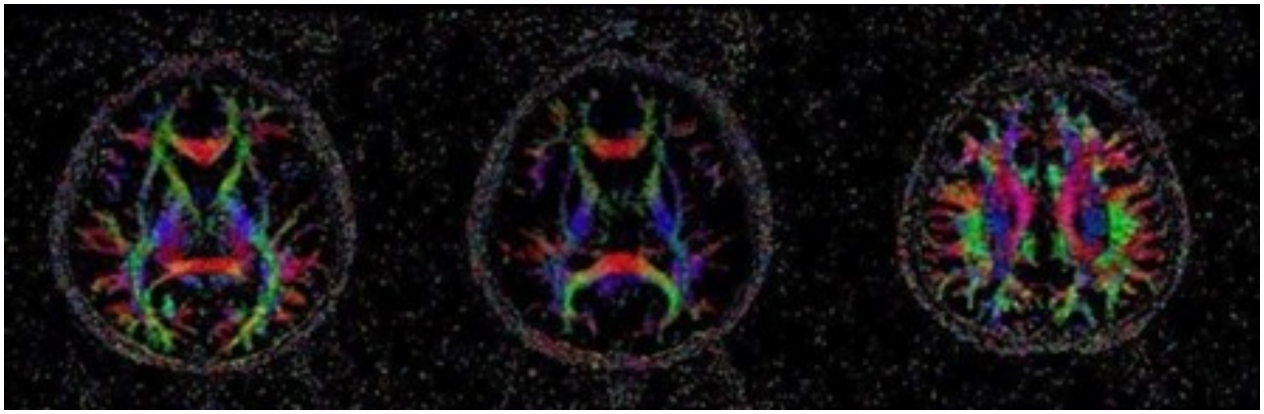

Fig. 1: color tensor imaging of hypertension

Table 1: The improvement effect of blood pressure level in two groups ($\bar{x}\pm s$)

Group	Diastolic blood pressure (mmHg)		Systolic pressure (mmHg)	
	Before treatment	After treatment	Before treatment	After treatment
Research group (n=90)	96.79±6.70	80.13±7.08	149.70±10.24	130.28±9.25
Control group (n=90)	95.78±8.16	90.22±9.04	148.66±11.27	140.27±9.23
t	0.27	8.94	0.18	12.36
p	>0.05	<0.05	>0.05	<0.05

Table 2: Comparison of overall treatment effective rate between the two groups [n(%)]

Group	Significantly effective	Effective	Ineffective	Overall treatment effective rate
Research group (n=90)	60	26	4	86(95.56)
Control group (n=90)	42	32	16	74(82.22)
X^2				6.72
p				<0.05

Table 3: Comparison of adverse reaction rate between the two groups [n(%)]

Group	Dizziness and headache	nausea and vomiting	constipation	edema of lower limbs	rate of adverse reactions
Research group (n=90)	3	2	1	0	6(6.67)
Control group (n=90)	7	4	3	4	18(20.00)
X^2					8.86
p					<0.05

Nifedipine controlled-release tablet is a calcium antagonist that can dilate the coronary arteries and at the same time can well dilate the healthy blood vessels in the incomplete blocked area. Nifedipine controlled-release tablets can effectively reduce the tension of coronary smooth muscle, prevent the problem of vasospasm, and provide more oxygen to the body by increasing the blood flow of narrow vessels.

Valsartan belongs to angiotensin II (Ang II) receptor antagonist, which improve left ventricular hypertrophy by blocking the combination of angiotensin Ⅱ and its receptors. Valsartan can prevent all kinds of ways to produce Ang II, block blood vessels contraction induced by angiotensin II, increase blood catecholamine and aldosterone. Compared with angiotensin converting enzyme inhibitors (ACEI), valsartan has obvious advantages. In addition, by inhibiting peripheral vascular exercise and promoting the release of nitric oxide and prostacyclin, the blood pressure variability can be well reduced, and the heart rate will not be increased, so that the blood pressure can be maintained at a stable level for 24 hours.

The results of this study showed that, compared with the control group (82.22%), the overall treatment effective rate of the research group (95.56%) receiving valsartan combined with nifedipine controlled-release tablets was higher, $p<0.05$. Compared with the control group, the improvement effect of blood pressure level in the research group after treatment was more significant, $p<0.05$. The rate of adverse reactions was 6.67% in the research group, which was significant lower than 20.00% in the control group, $p<0.05$. The results fully demonstrate the

effectiveness of valsartan combined with nifedipine controlled-release tablets in the treatment of primary hypertension, which is consistent with the relevant research results (Buchhorn and Ross 2018, Fang *et al*., 2017).

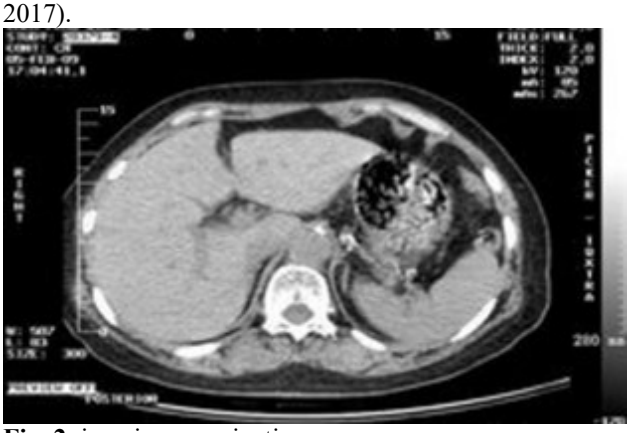

Fig. 2: imaging examination

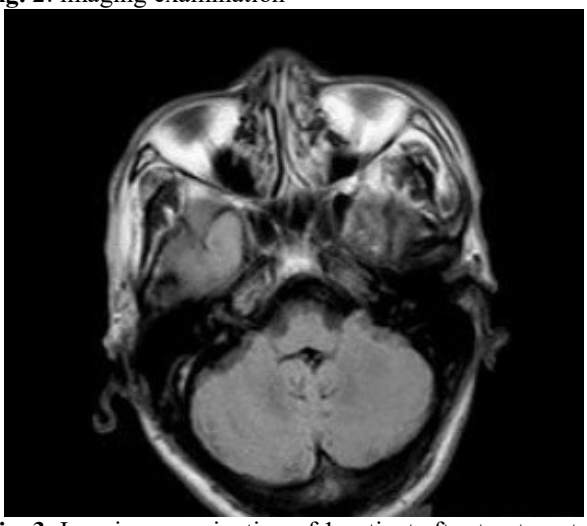

Fig. 3: Imaging examination of 1 patient after treatment

CONCLUSION

Valsartan combined with nifedipine controlled-release tablets in the treatment of essential hypertension has a significant curative effect. Such combination therapy can significantly improve the blood pressure level of patients and has a high safety, which an effective treatment model that can be popularized in practice. Nifedipine is a calcium antagonist, which has a significant effect on the treatment of hypertension. However, different dosage forms of nifedipine also have a significant difference in the antihypertensive effect. In this study, nifedipine sustained-release tablets combined with nifedipine controlled-release tablets were used to treat primary hypertension and the clinical effects were more satisfactory, which provides a reference for clinical rational anti-hypertension. However, due to the small sample size of this study, more large sample data studies are needed in the future to support the results of this study.

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