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Clinical study on influences of enteric coated aspirin on blood pressure and blood pressure variability

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Abstract. – OBJECTIVE: We investigated the effects of oral administration of enteric coated aspirin (ASA) on blood pressure and blood pressure variability of hypertension patients before sleep.

PATIENTS AND METHODS: We observed 150 hypertension cases, classified as Grade 1-2, from September 2006 to March 2008. They are divided into a control group with 30 cases, ASA I group with 60 cases and ASA II group with 60 cases randomly. Subjects in the control group had proper diets, were losing weight, exercising and maintaining a healthy mentality and were taking 30 mg Adalat orally once a day. Based on the treatment of control group, patients in ASA I group were administered 0.1 g Bayaspirin (produced by Bayer Company) at drought in the morning. Also, based on the treatment of control group, patients in ASA II group were administered 0.1 g Bayaspirin at draught before sleep.

RESULTS: The course of treatment is 3 months and then after the treatment, decreasing blood pressure and blood pressure variability conditions in three groups will be compared. Through the comparison of ASA II group with the control group, they have differences in terms of systolic blood pressure (SBP), diastolic blood pressure (DBP), decreasing range of blood pressure and blood pressure variability ($p < 0.05$).

CONCLUSIONS: The oral administration of ASA before sleep has synergistic effects on decreasing blood pressure of hypertension patients and improving blood pressure variability.

Key Words:
Oral administration before sleep, Enteric coated aspirin (ASA), Hypertension, Decreasing blood pressure, Blood pressure variability.

Introduction

Hypertension is a clinical syndrome with increasing arterial pressure of systemic circulation as the main clinical manifestation. It is also the most important risk factor of cardiovascular and cerebrovascular diseases which influence important organs such as heart, brain and kidney function and eventually caused organ failure[1]. In recent years, studies or knowledge regarding hypertension are increasing, and related diagnosis and treatment methods are improved[2]. However, it remains one of the main causes of death due to cardiovascular and cerebrovascular diseases. According to epidemiological materials published late in October 2004, there are 160 million hypertension patients in China. The number of patients is increasing year by year with aging population of China. Documents show that reasonable administration of enteric coated aspirin (ASA) is able to lower the prevalence rate of cardiovascular and cerebrovascular events by 30%. ASA plays an important role in primary and secondary prevention for hypertensive patients. There are, however, disputes regarding its effects in decreasing blood pressure for hypertension. Research has shown[3] that administration of ASA at different time and doses will influence the changes of blood pressure. From September 2006 to March 2008, the effects of decreasing blood pressure by oral administration of ASA before sleep are significant for hypertension patients.

Patients and Methods

Patients

All study subjects are 1-2 grade 150 hypertension cases from September 2006 to March 2008, (140 mmHg ≤ SBP ≤ 179 mmHg, 90 mmHg ≤ DBP ≤ 109 mmHg), and they are divided randomly into control group with 30 cas-

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es among which there are 16 males and 14 females; their ages are 42-70 years old, their average age is 60.4 ± 7.7 years old. For the ASA I group, there are 60 cases and 31 are males and 29 are females, their ages are 44-78 years old with average 62.4 ± 8.7 years old. For the ASA II group, there are 60 cases with 29 males and 31 females; their ages are 43-77 years old and average is 61.1 ± 8.1 years old. There are no differences among the 3 groups in terms of age, gender, hypertension degree and risk level ($p > 0.05$). Subjects in the control group had proper diets, were losing weight, exercising and maintaining a healthy mentality and were taking 30 mg Adalat orally once a day. Based on the treatment of control group, patients in ASA I group were administered 0.1 g Bayaspirin (produced by Bayer Co., Leverkusen, Germany) at drought in the morning. In addition, based on the treatment of control group, patients in ASA II group were administered 0.1 g Bayaspirin at draught before sleep. Blood pressure conditions were recorded 24h till when the course of treatment was completed (3 months) and decreasing conditions of blood pressure in two groups are compared.

Methods

Blood Pressure Testing

For three groups, their 48h blood pressure changing conditions before and after treatment were tested. The testing was performed every 20 minutes in the daytime and every 30 minutes at the nighttime. Testing parameters include the mean values of systolic blood pressure and diastolic blood pressure at 24h. For blood pressure variability (BPV), the standard deviation (s) of blood pressure in a certain period of time shall be taken as the quantitative index, including the variability of SBP and DBP at 24h.

Administration and Observation Method

150 hypertension cases are divided into (1) control group with 30 cases and (2) two observation groups with 60 cases each. Conventional blood pressure decreasing treatment was performed in three groups. For ASA II group, 0.1 g Bayaspirin oral administration before sleep was performed based on conventional blood pressure decreasing treatment. For ASA I group, the same dose of Bayaspirin was taken in the morning, and the course of treatment was 3 months. After the course of treatment was finished, their decreasing conditions of SBP and DBP and BPV in two groups was compared.

Statistical Analysis

All measurement data are presented as (x±s) and through *t*-testing. SPSS12.0 statistical software (SPSS Inc., Chicago, IL, USA) is used for processing. $p < 0.05$ was considered statistically significant.

Results

For patients in all groups, their SBP, DBP blood pressure levels and BPV are decreasing obviously or significantly before and after treatment ($p < 0.05$ or $p < 0.01$), there were no differences in ASA I group in terms of decreasing range of blood pressure and BPV compared with the control group before and after treatment ($p > 0.05$). There are no differences in ASA II group in terms of decreasing range of blood pressure and BPV compared with ASA I group before and after treatment ($p > 0.05$). For ASA II group, there are significant differences in terms of decreasing range of blood pressure and BPV compared with control group before and after treatment (Table I) ($p < 0.05$ or $p < 0.01$).

Discussion

Cardiovascular and cerebrovascular diseases are the biggest cause of death in China, with hypertension being the main risk factor[3]. Blood pressure levels are positively correlated to the prevalence rate of cardiovascular and cerebrovascular diseases. Increasing blood pressure is the independent risk factor of the prevalence of stroke and coronary heart disease. Increasing blood pressure also increases the risk of heart failure and kidney diseases[4]. In addition, increasing pulse pressure is significantly positively related to the occurrence of total death, cardiovascular death, stroke and coronary heart diseases. Treatment can only decrease the death rate and disability rate of stroke while prevention is able to decrease three rates occurrence rates as well. Since the 1970's, it has been proved by more than 250 clinical and random control studies that ASA is able to effectively prevent thrombus events[5,6]. 75-100 mg ASA per day is able to decrease the occurrence of stroke by 1/4 and car-

Table I. Comparison of blood pressure and BPV before and after treatment for patients in different groups.

Group	Cases		Blood pressure (KPa)			24h BPV	
			Before treatment	After treatment	Decreasing range	Before treatment	Afte treatment
Control group	30	SBP	164.5 ± 11.6	143.5 ± 9.4*	21.0 ± 5.1	1.92 ± 0.53	1.52 ± 0.29*
		DBP	98.3 ± 7.7	89.0 ± 7.1*	9.3 ± 6.4	1.60 ± 0.42	1.26 ± 0.25*
ASA I group	60	SBP	163.4 ± 11.5	140.2 ± 8.6*	23.2 ± 5.6	1.95 ± 0.38	1.48 ± 0.27*
		DBP	99.5 ± 7.0	88.6 ± 6.8*	10.9 ± 3.8	1.57 ± 0.31	1.25 ± 0.23*
ASA II group	60	SBP	164.1 ± 10.8	136.5 ± 6.9**▲	27.6 ± 6.0*▲	1.96 ± 0.50	1.22 ± 0.21**▲▲
		DBP	99.8 ± 8.4	86.3 ± 7.5*#	13.6 ± 4.2*#	1.62 ± 0.43	1.14 ± 0.19**#

Note: *t*-testing is used, comparison before and after treatment is $*p < 0.05$, $**p < 0.01$; compared with SBP in control group SBP, $^{\blacktriangle}p < 0.05$, $^{\blacktriangle\blacktriangle}p < 0.01$; compared with DBP in control group, $^{\#}p < 0.05$.

diovascular death by 1/6. Therefore, ASA has become the cornerstone of preventing cardiovascular and cerebrovascular diseases, which is due to the effect of applying ASA antiplatelet aggregation[7,8]. Currently, application of ASA in hypertension patients is also based on above-mentioned reasons. However, there are less clinical studies and exploration in terms of the relation between its pharmacologic effect and blood pressure. In recent years, some researchers have noticed that the administration of ASA at different times may influence blood pressure and they have obtained data to support that. Various publications have shown that administration of ASA before sleep is able to significantly decrease blood pressure level of slight and mild hypertension patients while there are no similar results for administration in the morning[9]. It is also shown in this study that administration of ASA before sleep has a more significant effect of decreasing blood pressure when compared to the other two groups.

BPV is also called blood pressure variability and shows the changing condition of blood pressure for one individual during a certain period of time (it is presented as the standard deviation of blood pressure changes in a certain period of time)[10]. The autonomic nerves system is an important mechanism that influences and regulates BPV, which mainly reflects the dynamic balance of cardiovascular regulation by sympathetic nerve and vagus as well as the completeness of autonomic nervous function. For hypertension, baroreflex function is injured and secondary baroreflex sensitivity decreased, which results in increasing BPV[11]. Long-range BPV is mainly influenced by the effects of autonomic nerve on cardiovascular center. Autonomic nerve function is injured and the sympathetic activity is increased. Decreasing vagal activity may be the main mechanism of primary hypertension on increasing BPV. Decreasing BPV and target organ injury can be regarded as one of the good options for controlling blood pressure in cardiovascular disease[12]. Long-range BPV index is used in this study to compare BPV conditions between conventional blood pressure treatment with ASA administration in the morning or before sleep. Results show that ASA administration before sleep will significantly decrease BPV ($p<0.05$ or $p < 0.01$).

ASA administration before sleep is good for decreasing blood pressure and BPV which may be related to its special pharmacokinetic and pharmacodynamic features. For ASA, it needs more time to be absorbed by the digestive tract. At the beginning, small dose shall be taken; t1/2 is about 2-3 hours. For long term and repeated administration, it shall reach 5-18 hours[12]. At 6h after administration of ASA, blood concentration reaches the peak and angiotensin also reaches the high of the end of the range. In addition, at this time, ASA is able to cause increased blood pressure caused by increased Angiotensin. In addition, since patients of this disease have slow blood flow at night time, inflammatory factors easily adhere to the inner blood vessel wall. Meanwhile, it has been proven that the inflammatory response of the blood vessel inner wall is one important factor that causes increasing blood pressure[13]. ASA is cyclooxygenase inhibitor and it is able to inhibit thromboxane (TxA_2) and prostaglandin from synthesis. Decreasing synthesis of prostaglandin at night time will indirectly influence the secretion of active renin the next morning and activate inactive renin. It decreases

the changes of renin-angiotensin-aldosterone system (RAAS) activity. Therefore, valley values generated by nitric oxide at night are eliminated, peak effects of blood pressure in the morning are decreased and BPV is improved[14].

Conclusions

We discovered in this study that oral administration of ASA before sleep is good for decreasing blood pressure and BPV, which is worth of recommendation.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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