

学位論文の要旨

氏名 伊藤 智子

学位論文名 Effect of Salt Intake on Blood Pressure in Patients Receiving Antihypertensive Therapy: Shimane CoHRE Study

発表雑誌名 European Journal of Internal Medicine (in press)
(巻, 初頁～終頁, 年)

著者名: Tomoko Ito, Miwako Takeda, Tsuyoshi Hamano, Tsunetaka Kijima, Masayuki Yamasaki, Minoru Isomura, Shozo Yano, Kuninori Shiwaku, Toru Nabika

論文内容の要旨

INTRODUCTION

Hypertension is the most prevalent lifestyle-related disease in the world, with the number of hypertensive patients being one billion worldwide, including 40 million in Japan. Hypertension is a well-known risk factor for stroke, cardiac disease, and kidney disease, all of which may reduce life expectancy. However, it has been reported that 50% of Japanese patients on antihypertensive drugs do not reach their target BP. Although lifestyle modification is also important for patients on antihypertensive therapy, patients may rely too much on their medication and disregard instructions about lifestyle modification, resulting in a low proportion of patients achieving an appropriate BP despite drug treatment. The most important lifestyle factor with an influence on BP is salt intake. Therefore, we hypothesized that salt intake could have a significant influence on BP, even among patients taking antihypertensive medications. In this cross-sectional study, we showed that salt intake (estimated from spot urine) was correlated with BP in patients on antihypertensive therapy.

MATERIALS AND METHODS

A total of 1501 consecutive participants (571 men and 930 women) were recruited from among persons undergoing health screening examinations in rural areas of Shimane Prefecture during 2012. Participants were limited to the age range between 40 and 74 years. Information about physical activity, smoking, drinking, and use of antihypertensive medications was obtained by interview, and the actual medications were confirmed by checking prescriptions. After

excluding 5 subjects with a history of treatment for renal disease, the remaining 1496 participants were divided into groups with or without antihypertensive medication. This yielded a group of hypertensive subjects on medication (treated subjects: N=491) and a group of normotensive or hypertensive subjects without medication (untreated subjects: N=1005). The International Standardized Physical Activity Questionnaire was employed to assess 24-hour physical activity and the exercise count (ex) was calculated according to the method reported previously.

Participants were categorized into two groups (low and high physical activity groups) based on the median exercise count (56 ex/week). Habitual smokers and habitual drinkers were defined as persons who smoked at least 1 cigarette/day and persons who drank at least 20g of ethanol/day, respectively. Systolic BP and diastolic BP (SBP and DBP) were measured by standard methods. A venous blood sample was collected from each subject after an overnight fast. Triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured by standard enzymatic methods. Sodium and creatinine were measured in spot urine collected at the health screening examination, and 24-hour urinary sodium excretion was estimated with the formula proposed by Tanaka et al .

Correlations between BP and other continuous variables were analyzed by calculating Spearman's rank correlation coefficients. The influence of categorical parameters on BP was determined by Student's t-test. Multiple regression analysis was performed to assess the influence of each variable on BP. Written informed consent was obtained from each participant.

The study protocol was approved by the ethics committee of Shimane University.

RESULTS AND DISCUSSION

There was no significant difference of estimated salt intake between the untreated and treated subjects. Individuals with low physical activity were slightly, but significantly, more prevalent among the treated subjects, and there were no significant differences of smoking and drinking habits between the two groups. Twenty-three of the treated subjects were using diuretics. Since these drugs could cause overestimation of the salt intake if they were prescribed temporally, we compared the estimated salt intake between subjects with and without diuretics. The estimated salt intake of the subjects using diuretics was 10.5 ± 3.1 g/day (N=23), which was not significantly different from that of subjects without diuretics (9.6 ± 2.5 g/day; N=305, $p=0.1$).

Therefore, we included all of the treated subjects in the following analyses. Univariate analysis showed a significant positive correlation between salt intake and SBP/DBP in both the treated and the untreated subjects. Multiple linear regression analysis was performed using the parameters that showed a significant correlation with BP in univariate analysis to find variables with an independent influence on SBP or DBP. The results showed that salt intake was

independently associated with SBP and DBP in the untreated subjects (SBP: $\beta=1.45\pm0.26$, $p<0.001$, DBP: $\beta=0.52\pm0.16$, $p=0.001$). Even in the treated subjects, salt intake had an independent association with SBP together with age and BMI (SBP: $\beta=0.75\pm0.27$, $p=0.01$).

This result seemed to be robust because analysis after excluding the 23 subjects using diuretics also revealed a positive correlation between salt intake and SBP ($\beta=0.72\pm0.28$, $p=0.01$).

Female sex had a significant negative influence on DBP despite no significant effect on SBP, so we assessed the effect of sex on pulse pressure by multiple linear regression analysis. As expected, female sex had a significant positive influence on pulse pressure in both the treated and the untreated subjects (the treated: $\beta=-4.36\pm1.42$, $p=0.002$, the untreated: $\beta=-4.17\pm0.90$, $p<0.001$) The effect of salt intake on pulse pressure was also significant.

In the present study, we showed that salt intake estimated from the sodium concentration in spot urine was positively correlated with SBP in subjects on antihypertensive therapy. Accordingly, it may be important to control salt intake in hypertensive patients receiving the pharmacotherapy to ensure that their treatment is effective. Multiple linear regression analysis confirmed that female sex had a strong positive influence on pulse pressure. This observation is interesting when we consider the relationship of pulse pressure to arterial stiffness in the elderly. However, as multiple factors are known to influence pulse pressure, further evaluation will be necessary to clarify the pathophysiological significance of the larger pulse pressure observed in women of our study population. While the present study provided epidemiological evidence of a positive correlation between salt intake and BP in subjects on antihypertensive therapy, it has limited clinical applicability because the method of estimating salt intake used in this study is not reliable enough to assess salt intake of individual patients. Probably because of this limitation, the correlation between SBP and estimated salt intake was only modest. Therefore, it would be necessary to confirm the present results by using 24-hour urine data before the clinical application is considered.

CONCLUSION

We showed that salt intake estimated from a spot urine sample had an independent influence on SBP and pulse pressure in patients on antihypertensive therapy. Careful control of salt intake may be important to achieve better therapeutic outcomes in treatment of hypertension.