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Original Article

Interrelations among Smoking Habits, Casual Blood Pressure and Intraocular Pressure in Middle and Old-Aged Japanese Residents

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Abstract

Objectives: To investigate the association of smoking habits with blood pressure (BP) and intraocular pressure (IOP), and to examine whether the smoking-BP association is related to the IOP level.

Methods: This study was conducted on the basis of a cross-sectional design using annual health check-up data during one-year between August, 1999 and August, 2000 for 611 middle and old-aged Japanese residents living in Ibaraki prefecture, Japan.

Results: After adjustment for age, gender, body mass index and alcohol intake score, the proportion of hypertensives, and the mean systolic and diastolic blood pressure (SBP and DBP) of the subjects without antihypertensive medications were the highest (50.4%, 129.6 mmHg and 75.9 mmHg, respectively) in the "smokers of 25 or more cigarettes per day with intraocular pressure (IOP) ≥15 mmHg" of six subgroups crossed by three smoking categories (non-smokers, 1 to 24 cigarettes per day, and 25 or more cigarettes per day) and two IOP categories (less than 15 mmHg, and 15 mmHg or greater). On the other hand, the adjusted proportion of hypertensives, and the adjusted mean SBP and DBP decreased with increasing smoking category in the individuals with less than 15 mmHg of the IOP (p for trend=0.028 for proportion of hypertensives, 0.008 for the SBP, and 0.001 for the DBP, respectively).

Conclusions: Heavy smoking may be specifically related to 'high BP accompanied by high IOP', although the BP may be inversely associated with smoking under the condition without high IOP.

Key words: smoking, intraocular pressure, casual blood pressure, effect modification, health check-up

Introduction

Many previous studies (1–9) have reported that blood pressure (BP) was clearly positively associated with intraocular pressure (IOP). However, the mechanism for progression of high BP with high IOP remains obscure. In respect of the effects of exogenous factors, each of weight gain and alcohol intakes has been recognized to relate to increased BP (10, 11) and IOP (4, 7). On the other hand, although the positive associations of the IOP with smoking were consistently reported in previous studies (5, 7), the effects of smoking on the BP appear to be inconclusive. In contrast, many epidemiological studies (12–15) have suggested that the association of smoking with the BP was negative rather than positive. There have not been any studies analyzing the interrelations among the BP, the IOP and smoking to clarify the background or the reason for the difference in the relation with smoking between the BP and the IOP. Thus, in the present study, after the relations of smoking to the BP and the IOP were separately analyzed, further epidemiological analyses were conducted to examine whether there is an IOP-related effect modification in the relation between smoking and the BP by investigating the smoking-BP association with respect to the IOP level.

Methods

Health check-up

A total of 649 Japanese residents living in Ibaraki prefecture, Japan, were examined between August, 1999 and August, 2000 by a two-days health check-up with lodging being controlled by a general hospital located in Mito-City, the capital city of the prefecture. These examinees were schoolteachers of junior-high schools or high schools, or clerical workers of several companies located in Mito-City or its surrounding area who volunteered to be examined by the check-up system of the hospital. The contents of the health check-up consisted of a questionnaire survey on several demographic and life style-related factors, measurement of height, weight, blood pressure, and intraocular pressure, hematological

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and serum biochemical tests, chest X-ray, electrocardiography and fundus photography. All these examinations were completed in two consecutive days. All subjects were requested not to take any food or alcohol after 9 p.m. of the day before the first examination day. Abstinence from smoking was required for all the examinees throughout these two days. The items of the questionnaire included age, marital status, occupation, residence, current status and past histories of medication, family history, drinking history, smoking history, cigarettes consumption per day, exercise habits, and number of cups of coffee per day. In the questionnaire, the drinking history was classified into the following four categories: never or seldom, several times per month, several times per week, and everyday. The measurement of BP was conducted between 8:10a.m. and 8:50a.m. on the second examination day. It means that the BP measurements were conducted after sufficient physical rest and abstinence from smoking lasting for more than 24 hours. For each examinee, the BP was measured two times after rest at sitting position for at least five minutes using a sphygmomanometer on the right arm. For the IOP, after the objective of the IOP measurement was sufficiently explained for each subject, the consent for measurement from all examinees was confirmed. The IOP was measured three times for each eye with a non-contact tonometer.

Subjects

Of the examinees for the health check-up, 611 individuals (474 males and 137 females) who had completed the answers for the questionnaire and the physical examinations by the health check-up were selected as the subjects of this study. The age of the subjects were distributed from 29 yrs old to 79 yrs old. On the basis of the criteria for hypertension from the sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (16), these subjects were classified into normotensives (systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg) without antihypertensive medications, hypertensives (SBP≥140 mmHg and/or DBP≥90 mmHg) without antihypertensive medications, and subjects with antihypertensive medications. Then, the latter two groups (hypertensives with or without antihypertensive medications) were defined as "hypertensives". The numbers of "hypertensives" were 133 males and 25 females. The numbers of subjects in the former two groups (subjects without antihypertensive medications) were 396 males and 126 females. For the analyses of the interrelations of smoking habits, the BP and the IOP, the subjects were classified into subgroups according to smoking habits, and high or not high IOP. As the criteria for high IOP, we arbitrarily adopted the 75 percentiles or greater of the IOP level for all the subjects. That is, the subjects were classified into the following six groups: Group A: Non-smokers with less than 75 percentiles of the IOP, Group B: Non-smokers with 75 percentiles or greater of the IOP, Group C: Smokers of 1–24 cigarettes per day with less than 75 percentiles of the IOP, Group D: Smokers of 1–24 cigarettes per day with 75 percentiles or greater of the IOP, Group E: Smokers of 25 or more per day with less than 75 percentiles of the IOP, Group F: Smokers of 25 or greater per day with 75 percentiles or greater of the IOP. Here, from the analysis on the distribution of the IOP level among all the subjects, 75 percentiles of the IOP turned out to be 15 mmHg.

Statistical analysis

The mean value of the two measurements was used as the blood pressure measurement for each of the SBP and the DBP. With regard to the IOP, at first, the mean value of the three measurements was calculated for each eye. However, since there was a strong correlation (r=0.84) of the mean IOP between right and left eyes among 611 subjects, the mean level of each mean IOP of the right and left eyes was defined as the IOP for each subject. In the basic analyses of the study, the associations of age with the proportion of hypertensives and the IOP were evaluated by the comparisons of the mean values across six age classes (44 or less, 45 to 49, 50 to 54, 55 to 59, 60 to 64, 65 or greater) for all the subjects according to Bonferroni's multiple comparison (17) by gender, while gender differences in the mean SBP, DBP and IOP levels were tested using Student's *t*-test by age class. Similarly, the associations of age with the SBP and the DBP were evaluated by the comparisons of the mean values across six age classes for the subjects not receiving antihypertensive medications. For the analyses on the relation of the IOP to the BP or smoking habit, the adjusted mean levels of the IOP calculated from the analyses of covariance were compared between the aforementioned three categories of the BP or between the three categories of cigarettes consumption (non-smoker, smoker with 1 to 24 of cigarettes consumption per day, and smoker with 25 or more of cigarettes consumption per day). In the former analysis, gender, age, body mass index (BMI) corresponding to weight (kg) divided by the square of height (m^2), alcohol intake score (daily drinkers: "3", "several times per week" drinkers: "2", "several times per month" drinkers: "1", non- or ex-drinkers: "0") and smoking history (Non- or Ex-smokers: "1", Current smokers: "2") were included as adjusted for variables. Similarly, in the latter analysis, gender, age, BMI, and alcohol intake score were included as adjusted for variables. For the analyses on the association of smoking with the BP, the proportion of hypertensives, and the mean SBP and DBP among the subjects without antihypertensive medications were compared between the three categories of cigarettes consumption, adjusting for gender, age, BMI, and alcohol intake score. Similarly, after adjustment for gender, age, BMI and alcohol intake score, the proportion of hypertensives, and the mean SBP and DBP among the subjects without antihypertensive medications were compared among six subgroups (Group A to Group F). Furthermore, to test whether the IOP or the BP increased with increasing level of smoking in all the subjects and whether the BP increased with increasing level of smoking in the subgroups with or without high IOP, the p-values for trend were calculated. The p-values for trend were estimated as the p-values of the partial regression coefficients of the smoking level as an independent variable shown by a continuous value ('0' for non-smokers, '1' for smokers of 1 to 24 cigarettes per day, and '2' for smokers of 25 or more cigarettes per day) in the multiple regression models. All these statistical analyses were conducted using the SAS statistical package (18).

Results

The associations of age with the proportion of hypertensives and the IOP are shown in Table 1. In Table 2, the relation of age to the SBP and the DBP among the subjects without antihypertensive medications are shown. In both genders, the mean IOP, SBP, and DBP levels were the highest in the age group "60–64" of the six

Table 1 Distribution of age, and age-specific proportion of hypertensives and intraocular pressure by gender in all subjects

Age class	Nr. of subjects		Proportion of hypertensives†		P-value for the difference between males and females	Mean intraocular pressure (±SD) (mmHg)		P-value for the difference between males and females
	M	F	M	F		M	F	
–44	51	16	0.16 [e,f]	0	0.004	12.5±2.2	12.0±1.5	0.25
45–49	79	16	0.15 [e,f]	0	<0.001	12.2±2.7 [e]	11.4±3.0	0.309
50–54	91	30	0.22 [e]	0.2	0.819	12.9±2.7	12.0±2.1	0.057
55–59	133	33	0.31	0.15	0.041	13.3±3.4	13.0±3.6	0.641
60–64	88	22	0.43 [a,b,c]	0.32	0.329	13.6±3.1 [b]	14.3±4.1 [f]	0.484
65–	32	20	0.47 [a,b]	0.3	0.229	12.2±2.8	11.0±2.8 [e]	0.146
Total	474	137	0.28	0.18	0.006	12.9±3.0	12.4±3.2	0.06

†: Subjects receiving antihypertensive medications, or those with 140 mmHg or greater systolic blood pressure and/or 90 mmHg or greater diastolic blood pressure, M, Males, F, Females, Significant differences noted at the 0.05 level on the basis of Bonferroni's multiple comparison : [a] : vs Age "–44", [b] : vs Age "45–49", [c] : vs Age "50–54", [d] : vs Age "55–59", [e] : vs Age "60–64", [f] : vs Age "65–"

Table 2 Distribution of age, and age-specific blood pressure by gender in the subjects not receiving antihypertensive medication

Age class	Nr. of subjects		Mean systolic blood pressure (±SD) (mmHg)		P-value for the difference between males and females	Mean diastolic blood pressure (±SD) (mmHg)		P-value for the difference between males and females
	M	F	M	F		M	F	
–44	48	16	119.2±13.8 [e]	111.1±9.2 [e]	0.011	70.7±10.3 [e]	63.9±6.5 [e]	0.004
45–49	74	16	121.4±13.5 [e]	115.2±10.3	0.047	71.5±9.5 [e]	67.4±7.3	0.068
50–54	78	28	122.2±14.0	121.3±15.4	0.793	70.8±8.0 [e]	69.9±7.6	0.572
55–59	107	31	123.7±13.4	118.6±13.5	0.068	73.5±8.8	69.6±8.2	0.025
60–64	67	19	128.8±13.5 [a, b]	127.7±12.3 [a]	0.752	76.2±10.3 [a, b, c]	73.2±9.8 [a]	0.253
65–	22	16	128.6±14.7	122.9±16.1	0.267	71.4±10.1	66.8±8.2	0.13
Total	396	126	123.6±13.9	119.7±14.0	0.008	72.6±9.4	68.8±8.3	<0.001

M, Males, F, Females, Significant differences noted at the 0.05 level on the basis of Bonferroni's multiple comparison : [a] : vs Age "–44", [b] : vs Age "45–49", [c] : vs Age "50–54", [d] : vs Age "55–59", [e] : vs Age "60–64", [f] : vs Age "65–"

Table 3 Adjusted† mean levels of intraocular pressure according to blood pressure categories

	N	Adjusted mean IOP (±SE) (mmHg)	P-value for the difference
Males			
Normotensives¶ without antihypertensive medications	340	12.8±0.2	
			0.054
Hypertensives‡ without antihypertensive medications	56	13.6±0.4	0.486
			0.273
Subjects with antihypertensive medications	78	13.1±0.3	
Females			
Normotensives¶ without antihypertensive medications	113	12.4±0.3	
			0.742
Hypertensives‡ without antihypertensive medications	13	12.7±0.9	0.344
			0.314
Subjects with antihypertensive medications	11	11.4±1.0	
Total			
Normotensives¶ without antihypertensive medications	453	12.7±0.1	
			0.061
Hypertensives‡ without antihypertensive medications	69	13.5±0.4	0.755
			0.189
Subjects with antihypertensive medications	89	12.8±0.3	

†: The variables adjusted for were age, body mass index, alcohol intake score (daily drinker : 3, "several times per week" drinker: 2, "several times per month" drinker: 1, non-drinker or ex-drinker: 0) and smoking history (non- or ex-smoker: 1, smoker: 2) for gender-specific analyses, and age, body mass index, alcohol intake score, smoking history and gender (male: 1 and female: 2) for overall analysis, respectively.
¶: Subjects with 139 mmHg or less systolic blood pressure and 89 mmHg or less diastolic blood pressure.
‡: Subjects with 140 mmHg or greater systolic blood pressure and/or 90 mmHg or greater diastolic blood pressure IOP, Intraocular pressure.

Table 4 Adjusted† proportion (±SE) of hypertensives‡ and adjusted† mean (±SE) levels of intraocular pressure by three categories of smoking habits in all the subjects

	Non-smokers (N=393)	Smokers of 1–24 cigarettes per day (N=145)	Smokers of 25 or more cigarettes per day (N=73)	P-value based on F value	P-value for trend
Proportion of Hypertensives	0.28±0.02	0.22±0.04	0.22±0.05	0.252	0.128
IOP (mmHg)	12.6±0.2	13.0±0.3	13.3±0.4	0.193	0.071

†: Age, gender (male: 1 and female: 2), body mass index and alcohol intake score (daily drinker: 3, "several times per week" drinker: 2, "several times per month" drinker: 1, non-drinker or ex-drinker: 0) were selected as adjusted for variables.
‡: Subjects receiving antihypertensive medication, or those with 140 mmHg or greater systolic blood pressure and/or 90 mmHg or greater diastolic blood pressure, IOP, Intraocular pressure

Table 5 Adjusted† mean (±SE) levels of systolic and diastolic blood pressure by three categories of smoking habits in the subjects not receiving antihypertensive medications

	Non-smokers (N=331)	Smokers of 1–24 cigarettes per day (N=125)	Smokers of 25 or more cigarettes per day (N=66)	P-value based on F value	P-value for trend
SBP (mmHg)	123.4±0.7	121.0±1.2	122.0±1.6	0.245	0.219
DBP (mmHg)	72.5±0.5	70.9±0.8	70.3±1.1	0.035	0.019

†: Age, gender (male: 1 and female: 2), body mass index and alcohol intake score (daily drinker: 3, "several times per week" drinker: 2, "several times per month" drinker: 1, non- or ex-drinker: 0) were selected as adjusted for variables. SBP, Systolic blood pressure, DBP, Diastolic blood pressure.

age categories. The proportions of hypertensives were relatively high in the age group "60–64" and "65 or greater". In contrast, these values were relatively low in younger groups aged 49 or less. However, the lowest levels of mean IOP were noted for the age group "65 or greater", the oldest age class. In all the age classes, these parameters were higher in males than in females with one exception for the IOP in the age group "60–64".

In Table 3, the adjusted mean IOP were compared by the three categories of blood pressure according to gender. In both genders, there were no significant differences in the mean IOP at the 0.05 level among the normotensives, the hypertensives not receiving antihypertensive medications and the hypertensives currently under blood pressure-lowering medications, although the highest levels were noted for the hypertensives not receiving antihypertensive medications. The associations of smoking habits with the adjusted proportion of hypertensives and the adjusted IOP for all the subjects are shown in Table 4, while the relations of the adjusted mean SBP and DBP to smoking habits among the subjects without hypertensive medications are shown in Table 5. The adjusted mean IOP increased with increasing level of the three smoking categories, although this linear trend did not reach a significant level (p-value for trend=0.071). The adjusted levels of the proportion of hypertensives and mean DBP were higher in non-smokers than in smokers of 25 or more cigarettes per day by 0.06 (6%) for the proportion of hypertensives and by 2.2 mmHg for the DBP, respectively. The decrease in the adjusted mean DBP with increasing smoking category was found to be significant (p-value for trend=0.019).

In Figs 1 and 2, the interrelations between the BP, the IOP and smoking are shown. The proportion of hypertensives, and the mean SBP and DBP among the subjects without antihypertensive medications was the highest in the "smokers of 25 or more cigarettes per day with high IOP (IOP≥15 mmHg)" (Group F) of six subgroups classified by smoking habits and the IOP level. For Group F, the adjusted proportion of hypertensives corresponded to 0.504 (50.4%), and the adjusted mean SBP and DBP among the subjects without hypertensive medications were 129.6 mmHg and 75.9 mmHg, respectively. In contrast, these three parameters regarding blood pressure were the lowest in the "smokers of 25 or more cigarettes per day without high IOP" (Group E), showing that the adjusted proportion of hypertensives was 0.100 (10.0%), and the adjusted mean SBP and DBP among the subjects without antihypertensive medications were 119.2 mmHg and 68.2 mmHg, respectively. The differences in the adjusted proportion of hypertensives, and the adjusted mean SBP and DBP among the subjects without antihypertensive medications between Group E and Group F were found to be significant (p-value=0.0002 for a proportion of hypertensives, 0.003 for the SBP, and 0.001 for the DBP, respectively). On the other hand, the adjusted proportion of hypertensives, and the adjusted mean SBP and DBP decreased with increasing smoking category in the individuals with less than 15 mmHg IOP (p for trend=0.028 for a proportion of hypertensives, 0.008 for the SBP, and 0.001 for the DBP, respectively).

Discussion

The results of this study showed that heavy smoking was associated with increased BP accompanied by increased IOP, whereas the BP was inversely associated with smoking under the condition without high IOP. The IOP was, as a whole, positively associated with smoking. In addition, the IOP was, though weakly, positively related to the BP, as shown in many previous studies (1–9). These results suggest that the effects of smoking on the BP may be diverse, depending on the particular physical conditions represented by the IOP level. The volume of aqueous humour that is ultra-filtrated from the ciliary artery and reabsorbed into the episcleral vein determines the IOP. The high BP may raise the IOP by increasing the ultrafiltration of the aqueous humour through elevation of ciliary artery pressure (4, 7, 19, 20). In addition, the high BP can at least partly derive from increased vascular resistance due to degenerative changes in the blood vessel wall of small arteries (21, 22), as represented by arteriosclerosis. Therefore, one possible explanation for the association of heavy smoking with high BP accompanied by high IOP is that heavy smoking-induced degenerative changes or remodeling of the small arteries led to increased BP with increased IOP.

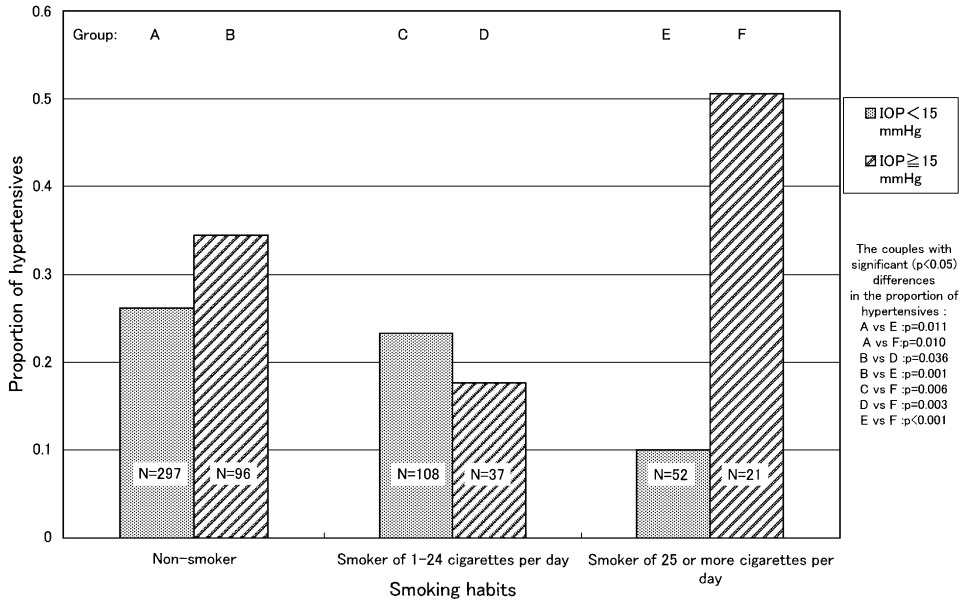

Fig. 1 Proportion of hypertensives† adjusted for age, gender, body mass index and alcohol intake score‡ according to smoking habits and intraocular pressure.
†: Subjects receiving antihypertensive medications, or those with 140 mmHg or greater systolic blood pressure and/or 90 mmHg or greater diastolic blood pressure,
‡: Daily drinkers: 3, "several times per week" drinkers: 2, "several times per month" drinkers: 1, Non- or ex-drinkers: 0,
IOP, Intraocular pressure.

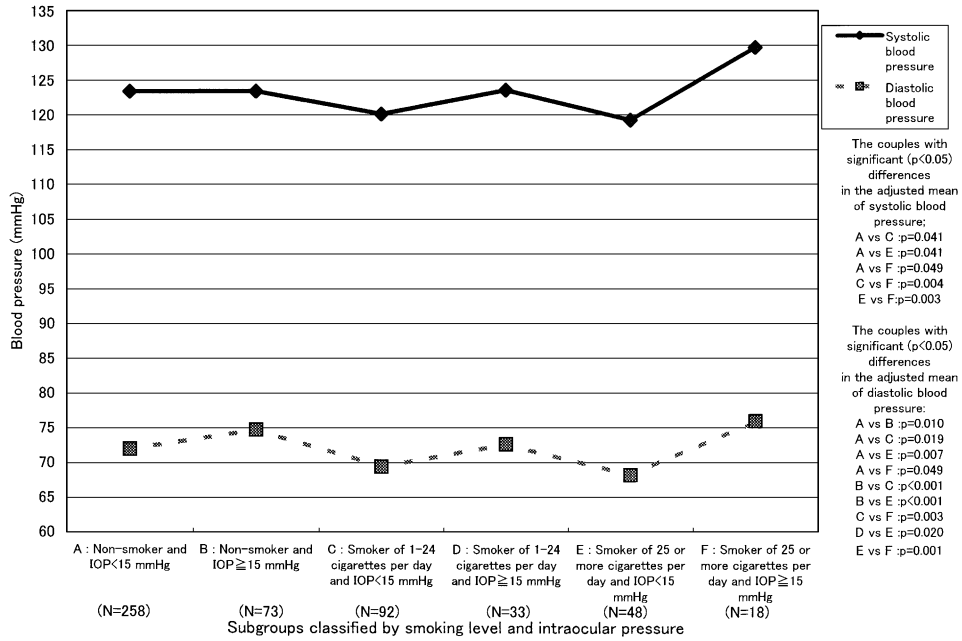

Fig. 2 Mean systolic and diastolic blood pressure adjusted for age, gender, body mass index and alcohol intake score‡ according to smoking habits and intraocular pressure among the subjects without antihypertensive medication.
‡: Daily drinkers: 3, "several times per week" drinkers: 2, "several times per month" drinkers: 1, Non- or ex-drinkers: 0,
IOP, Intraocular pressure

Many previous epidemiologic studies (12, 14, 15, 23, 24) have reported that smoking was inversely associated with blood pressure. On the other hand, cigarette smoking has been reported to produce an acute rise in the BP (25, 26). Furthermore, recent cross-sectional studies (27, 28) have suggested that the daytime level of ambulatory blood pressure was significantly higher in smokers than in non-smokers among hypertensive patients. The most plausible explanation for such a discrepancy in the relation between smoking and the BP is that there is a "withdrawal phenomenon" by which the BP drops below the baseline during abstinence, while the BP rises during the act of smoking. The relatively low BP in smokers shown by previous epidemiologic studies might reflect the low casual blood pressure measured during abstinence. The inverse association between smoking and the BP under the condition without the increased IOP shown in the present study might also reveal that there can be a "withdrawal phenomenon", if the degenerative changes or remodeling of the arteries by smoking are not large. At any rate, in studies of the effects of smoking on the BP, casual blood pressure during abstinence should be distinguished from the mean BP derived from

ambulatory blood pressure.

Although there was a positive relation between the BP and the IOP, the overall positive association between smoking and the IOP cannot be explained only by the smoking effects on the BP because the association between smoking and the BP was, as a whole, negative rather than positive, especially for the DBP. Increase in blood viscosity, or other unknown smoking-induced changes in the ciliary artery, Schlemm's canal, or episcleral vein might relate to the increase in the IOP.

Smoking is a potent risk factor for cardiovascular diseases (29, 30). This finding appears to be compatible not with smoking-induced BP decrease but with simultaneous increase in the BP and the IOP due to smoking that was suggested in the present study. In this sense, the high IOP may be a key marker for the development of "smoking-related hypertensive diseases". Moreover, the high IOP might be considered as a risk indicator not only for glaucoma but also for cardiovascular diseases.

One interesting finding of this study is that the IOP level was slightly lower in treated hypertensives than in untreated hypertensives in both genders. Although no definite conclusions can be drawn from this finding alone, because the difference was small and not significant, there might be a possibility that blood pressure-lowering medications lead to the IOP decrease in some hypertensive patients.

According to the findings of the present study, the associations of age with the IOP were positive in both genders among the population aged 64 years old or less. Age-IOP positive relations have been similarly reported by some cross-sectional studies (31–34) in Western countries. This positive association may be due to the concomitant increase in the BP or the BMI with aging. On the other hand, Mori et al. (4) suggested that the IOP decreased with increasing age when the IOP was adjusted for the BP and the BMI in a Japanese population. In the present study, the lowest levels of mean IOP were noted for the age group "65 or greater" in both genders. Although the reason for these phenomena is unclear, the particular mechanism for an IOP decrease with aging possibly exists.

Since this study was based on a cross-sectional design, there were basic limitations for evaluations of the biological effects of smoking. For example, although non-smokers were a relatively high proportion of hypertensives and showed a high mean DBP among the subjects not receiving antihypertensive medications in this study, it could be in part due to the finding that some individuals diagnosed as hypertensive or treated for hypertension had stopped smoking as a result of self-control. Therefore, it should be considered that the observed association between smoking and the BP might be somewhat biased from the real biological relation toward an inverse direction.

In conclusion, the results of this study suggested that the effects of smoking on casual blood pressure may be complicated, as suggested by the finding that heavy smoking is related to 'high blood pressure accompanied by high intraocular pressure', although the BP was inversely associated with smoking under the condition without high IOP. The measurement of IOP may be useful for understanding the development or the risk of "smoking-related hypertensive diseases".

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