Original Article

Suppression of Cardiac Sympathetic Nervous System during Dental Surgery in Hypertensive Patients

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We determined the changes in blood pressure, pulse rate, and heart rate variability during dental surgery in hypertensive patients. The study included 18 essential hypertensives and 18 age and sex matched normotensive controls who underwent tooth extraction at our hospital. Holter electrocardiographic monitoring was used to determine the power spectrum of R-R variability before and during dental surgery. The low frequency (LF: 0.041 to 0.140 Hz), high frequency (HF: 0.140 to 0.500 Hz), and total spectral powers (TF: 0.000 to 4.000 Hz) were calculated, and the ratio of LF to HF and the percentage of HF relative to TF (%HF: $\text{HF/TF} \times 100$) were used as indexes of sympathetic and parasympathetic activities, respectively. The baseline blood pressure for hypertensive patients ($149 \pm 4/85 \pm 2$ mmHg) was significantly higher than that for normotensive patients ($119 \pm 3/71 \pm 2$ mmHg). The baseline pulse rates were similar between the two groups. Blood pressure increased during tooth extraction in both groups; however, changes in blood pressure did not differ between them. Administration of local anesthetic significantly decreased the %HF in normotensive patients (before vs. after anesthesia; 22.3 ± 2.4 vs. $13.8 \pm 2.7\%$, $p < 0.05$). In contrast, the LF/HF significantly decreased during the local anesthesia and tooth extraction in hypertensive patients. These results suggest that pressor response induced by tooth extraction did not differ between normotensive and hypertensive patients, and that suppression of the cardiac sympathetic nervous system during dental surgery might attenuate the pressor response in patients with hypertension.

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Key Words: autonomic nervous system, dental surgery, heart rate variability, hypertension

Introduction

Many patients who visit dental clinics have systemic diseases, such as hypertension, ischemic heart disease, and other atherosclerotic diseases (1). In one study, 64% of the elderly patients who visited the dental clinic were found to have one or more systemic diseases; among these, hypertension was the most common, occurring in up to 30% of the patients (2). Most dental treatments are conducted under local anesthesia, and increases in blood

pressure have been reported during tooth extraction even in normotensive patients (3, 4). Previous studies in our laboratory demonstrated that an increase in blood pressure during tooth extraction is related to the difficulty of the tooth extraction and the volume of local anesthetic used for the treatment (4). In addition, changes in blood pressure during an extraction procedure depend on age; middle-aged and older patients have a greater increase in blood pressure during dental surgery than younger patients (5). However, the response of blood pressure during tooth extraction has not been determined in patients

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with hypertension. It is important to determine the effects of dental surgery on blood pressure response in hypertensive patients, because a fatal subarachnoid hemorrhage and massive bleeding related to dental surgery and hypertension have been reported (6, 7).

Power spectral analysis of R-R variability has been widely used to evaluate the sympathetic and parasympathetic contributions to the activity of the heart (8). Although augmented sympathetic nervous activity in essential hypertension has been reported (9), serial changes of sympathetic and parasympathetic nervous activities during dental surgery have not yet been determined. We hypothesized that tooth extraction augments the activity of the sympathetic nervous system in hypertensive patients, resulting in exaggerated pressor response. It is known that responses of heart rate variability and blood pressure are strongly influenced by patient age (5). Therefore, in the present study, we compared the changes in blood pressure and heart rate variability in hypertensive patients with those in age and sex matched normotensive patients during dental surgery.

Methods

Subjects

The study included 18 patients (7 men and 11 women, ages ranging from 25 to 74 years old; mean age: 57.5 ± 2.6 years) with essential hypertension and 18 age and sex matched normotensive patients, all of whom underwent tooth extraction at our hospital. The details of the protocol were explained to the patients, and written informed consent was obtained. Patients whose systolic and/or diastolic blood pressures were more than 140/90 mmHg or who had been treated with antihypertensive agents were defined as hypertensives in the present study. Patients with diabetes or cardiovascular diseases except for hypertension were excluded from the present study.

On the day of dental surgery, each patient was asked to complete a questionnaire concerning medical history and medication use. After a 12-lead electrocardiogram had been recorded, continuous two-channel Holter electrocardiographic monitoring was performed and recorded on tape (SM-50, Fukuda Denshi, Tokyo, Japan). The patients were kept in a supine position for at least 10 min in a quiet room, and blood pressure and pulse rate were measured every 2 min by an oscillometric method using an automatic device (BP-203i, Nippon Colin, Komaki, Japan). The averages of the last two measurements were defined as the baseline blood pressure and pulse rate. The patients were then moved to the dental department to undergo tooth extraction. The patients were kept in supine position throughout the entire treatment period. Local anesthetic was administered after a control period of at least 10 min. Lidocaine, 2% with epinephrine (1:

80,000), was used as anesthetic for all patients. Surgery was begun 10 min after injection of the local anesthetic. After surgery, the patients were kept in a supine position during a recovery period of at least 10 min. Blood pressure and pulse rate were measured every 2 min throughout the study. Blood pressure and pulse rate in each patient were averaged for each treatment period (before surgery, during local anesthesia, during surgery, and after surgery) for further analysis. In order to eliminate the effects of the duration of the surgery or the volume of local anesthetic administered, we used the data from the initial 10 min of the surgery.

Power Spectral Analysis of R-R Intervals

Two-channel electrocardiographic monitoring was performed to record R-R intervals on magnetic tape. These intervals were converted to digital signals (SCM-3000 System, Fukuda Denshi), and periods of 256 s were sampled for further analysis. The autoregressive parameters were then calculated, and power spectral densities were computed by the maximum entropy method using a commercially available program (HPS-RR version 2.01, Fukuda Denshi). The power spectrum was divided into the low frequency (LF) band (0.041 to 0.140 Hz), which is an index of both sympathetic and parasympathetic activity, and the high frequency (HF) band (0.140 to 0.500 Hz), which reflects parasympathetic activity. The total frequency (TF) band was defined as the frequency range from 0.000 to 4.000 Hz. The ratio of LF to HF, which is an index of sympathovagal balance, was calculated (8, 10). The percentage of HF relative to TF (%HF) was calculated as $\text{HF/TF} \times 100$. These frequency components were calculated for each patient in each treatment period between 5 and 10 min before surgery, during local anesthesia, during surgery, and after surgery.

Statistics

All values are expressed as the mean $\pm$ SE. Student's *t*-test was performed to compare the blood pressure, pulse rate, and volume of local anesthetic used for tooth extraction in normotensive and hypertensive patients. In order to analyze the effects of local anesthesia and dental surgery on blood pressure and heart rate variability, a paired *t*-test was used to determine which means were significantly different from the baseline values. *P* values < 0.05 were considered statistically significant.

Results

Table 1 summarizes the clinical characteristics of the patients. The reasons for tooth extraction were similar in both groups. Ten of the hypertensive patients were taking antihypertensive drugs (diuretics, calcium channel antag-

Table 1. Clinical Characteristics of the Subjects

Variables	Normotensives	Hypertensives
N	18	18
Age (years)	59.7±3.4	57.5±2.6
Male/Female	11/7	11/7
Antihypertensive treatment	0	10
Diuretics	0	2
Ca channel antagonists	0	6
ACE inhibitors	0	3
Baseline SBP (mmHg)	119±3	149±4 **
Baseline DBP (mmHg)	71±2	85±2 **
Baseline PR (beats/min)	68±2	68±2
Reasons for tooth extraction		
Pericoronitis	4	2
Periodontitis	8	10
Stump tooth	6	5
Others	0	1
Total volume of anesthetic (ml)	2.5±0.3	2.0±0.2

Values are mean±SE. N, number of the patients; ACE, angiotensin converting enzyme; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate. ** $p < 0.01$ vs. normotensive patients by Student's *t*-test.

onists, or angiotensin converting enzyme inhibitors). One hypertensive patient was being treated with both a calcium channel antagonist and an angiotensin converting enzyme inhibitor. The baseline levels of systolic and diastolic blood pressures for hypertensive patients were significantly higher than those for normotensive patients. However, the baseline pulse rate was similar between the two groups. No difference in the total volume of local anesthetic used for tooth extraction was observed between the two groups.

Figure 1 illustrates the changes in blood pressure and pulse rate in the two groups. Blood pressure gradually increased, and the peak values were obtained during tooth extraction in both groups. Systolic blood pressure showed similar significant increases in both groups; however, diastolic blood pressure significantly increased during tooth extraction only in normotensive patients. Absolute values of systolic and diastolic blood pressure during tooth extraction in hypertensive patients were significantly higher than those in normotensive patients (normotensives vs. hypertensives; $136 \pm 5/77 \pm 3$ vs. $162 \pm 5/89 \pm 3$ mmHg, $p < 0.01$). However, changes in systolic and diastolic blood pressure from baseline blood pressure during tooth extraction did not differ between the groups; the changes were $17 \pm 4/6 \pm 2$ and $15 \pm 5/5 \pm 3$ mmHg, respectively. Pulse rate showed a significant increase and similar time course between the two groups.

Figure 2 shows the time course for LF/HF and %HF elicited by administration of local anesthetic and extraction of the tooth. The LF/HF decreased significantly during the local anesthesia and tooth extraction in hypertensive patients. However, LF/HF did not change during

Fig. 1. Line graph showing the time course of changes in blood pressure and pulse rate elicited by administration of local anesthetics and tooth extraction. Open and solid circles show normotensive ($n=18$) and hypertensive patients ($n=18$), respectively. * $p < 0.05$, ** $p < 0.01$ vs. baseline by paired *t*-test.

Fig. 2. Line graph showing the time course of %HF ((power of high frequency/power of total frequency) $\times 100$) and LF/HF (power of low frequency/power of high frequency) elicited by administration of local anesthetics and tooth extraction. Open and solid circles show normotensive ($n=18$) and hypertensive patients ($n=18$), respectively. * $p < 0.05$, ** $p < 0.01$ vs. control period by paired t-test.

tooth extraction in normotensive patients. In contrast, the %HF significantly decreased in normotensive patients during local anesthesia and the recovery period. The %HF in hypertensive patients failed to change throughout the treatment period.

Discussion

The two principal findings of the present study are that blood pressure response during dental surgery did not differ between normotensive and hypertensive patients, and that the responses of cardiac sympathetic and parasympathetic nervous systems were different in the two groups. To the best of our knowledge, this is the first study to investigate the power spectral analysis of R-R variability during dental surgery in hypertensive patients.

Few studies have been conducted to determine the changes in blood pressure in hypertensive patients during dental surgery. Abraham-Inpijn *et al.* (11) showed that the increase in blood pressure during dental procedures is greater in hypertensive patients than in normotensive patients. In their study, however, they did not control for patient age; given that older patients have a higher baseline blood pressure and greater changes in blood pressure during dental surgery (5), their results might have been

influenced by the age of the patients. In contrast, Meyer (12) demonstrated that changes in blood pressure and heart rate induced by tooth extraction are similar in normotensive and hypertensive patients. In the present study, patient characteristics including those of age and sex were adjusted for normotensive and hypertensive patients, and one dentist (Ko. M.) carried out the tooth extraction for all patients. After adjustment for patient profiles and surgery bias, blood pressure response during dental surgery was not found to differ in normotensive and hypertensive patients. Our previous studies (4, 5), in agreement with our findings here, suggest that one of the important factors influencing changes in blood pressure during tooth extraction is not the baseline level of blood pressure but patient age, although achieved blood pressure during tooth extraction is higher in hypertensive patients than in normotensive patients.

The %HF significantly decreased during the administration of local anesthetic in normotensive patients, suggesting the suppression of the parasympathetic nervous system. In contrast, the LF/HF significantly decreased during the administration of local anesthetic and tooth extraction in hypertensive subjects, suggesting the suppression of the cardiac sympathetic nervous system. Heart rate is regulated by many factors, such as cardiac or systemic autonomic function and closed loop baroreceptor reflex. In addition, the administration of epinephrine, present in local anesthetic, elicits an increase in heart rate. The present study suggests that responses of sympathetic and parasympathetic outflow to the heart differed between normotensive and hypertensive patients, although responses of blood pressure and heart rate between the groups were similar. These converse responses between the groups were not attributable to the age of the patients, because the age and the gender of the patients in normotensive and hypertensive groups were adjusted in the present study.

Recently, we investigated the serial changes of plasma catecholamine concentrations during dental surgery with use of local anesthesia in normotensive patients. Peak value of plasma epinephrine concentration was obtained just after the administration of local anesthetic with epinephrine, while the peak value of plasma norepinephrine concentration was obtained during dental surgery (unpublished observations). The time courses of plasma catecholamine concentrations were consistent with previous findings (13, 14). These results suggest that epinephrine (1:80,000) administered in local anesthetic leaks into the systemic circulation. In contrast, an increase in plasma norepinephrine concentration seemed to be attributable to the activation of the systemic sympathetic nervous system induced by dental treatment. Augmented activity of the systemic sympathetic nervous system during dental surgery probably elicited the increases in blood pressure and pulse rate in both groups. On the other

hand, the contribution of epinephrine in local anesthetic solution to the response of blood pressure remains to be investigated. Köhler-Knoll *et al.* (15) showed that injected epinephrine failed to cause any significant changes in blood pressure and heart rate. However, different cardiovascular regulations in hypertensive patients have been suggested (16, 17), thus injected epinephrine might elicit different cardiovascular responses in normotensive and hypertensive patients. Further studies are necessary to determine whether epinephrine in local anesthetics elicits an increase in blood pressure in hypertensive patient.

Based on the results of the power spectral analysis of R-R intervals and the responses of plasma catecholamine concentrations, it may be concluded that differential regulations of the cardiac and systemic sympathetic nervous system were functioning during dental surgery in hypertensive patients. In hypertensive patients, LF/HF was suppressed after local anesthesia. Administration of epinephrine *via* local anesthetic solution might elicit this response; however, the response differed between normotensive and hypertensive patients. Moreover, the LF/HF was further suppressed during tooth extraction in hypertensive patients. Thus, this reduction of LF/HF value was induced, at least in part, by an increase in blood pressure or the activation of the systemic sympathetic nervous system. One possible explanation for this response is the baroreceptor reflex-mediated suppression of the cardiac sympathetic nervous system. An increase in blood pressure elicited by administration of local anesthetic or tooth extraction might suppress cardiac sympathetic nervous activity *via* the baroreceptor reflex; these mechanisms might inhibit further increase in blood pressure in hypertensive patients.

The present study is limited by the fact that 56% of the hypertensive patients were being treated with antihypertensive agents, which might have influenced the results of the present study. The association between blood pressure and bleeding during dental surgery has been debated (18); however, massive bleeding associated with higher blood pressure has been reported (7). Therefore, in the present study, some patients with higher blood pressure were treated with antihypertensive drugs before conducting the tooth extraction. Meiller *et al.* (19) showed that hypertensive patients without medication had a slightly greater increase in systolic blood pressure compared with that of patients taking antihypertensive drugs. In our preliminary analysis, however, an increase in systolic blood pressure during dental surgery was greater in medicated patients than in unmedicated patients (20.6 ± 5.4 and 7.9 ± 8.9 mmHg, respectively), although baseline systolic blood pressure was similar between groups (147.9 ± 6.3 vs. 150.3 ± 3.8 mmHg). These different responses might be attributed to the age of the patients of respective subgroups (5); the patients treated with antihypertensive drugs were older than those without medications

(63.1 and 55.5 years, respectively). In addition, LF/HF decreased during dental surgery in both medicated and unmedicated hypertensive patients. These results suggest that the effects of antihypertensive treatment on the responses of blood pressure and heart rate variability during dental surgery might have been minimized in the present study.

In conclusion, the responses of blood pressure were similar in normotensive and mildly hypertensive patients; however, the responses of cardiac sympathetic and parasympathetic nervous systems assessed by heart rate variability differed between groups. Differential regulations of the cardiac and systemic sympathetic nervous system in hypertensive patients might suppress further increase in blood pressure during dental surgery. Further studies are necessary to determine the effects of antihypertensive treatment on the responses of blood pressure and sympathetic nervous system during dental surgery.

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