Effects of Phenylephrine and Prazosin on Axial Movement of the Rat Incisor and Arterial Blood Pressure

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ABSTRACT—We investigated the dose-response effects of phenylephrine and antagonistic effects of prazosin on axial movement of the rat incisor and arterial blood pressure. Phenylephrine caused a temporal extrusive tooth movement and an increase in blood pressure at all doses. With increasing phenylephrine doses, the maximum extrusive tooth movement and maximum increase in blood pressure were enhanced. The maximum extrusive tooth movement and increase in blood pressure induced by phenylephrine were markedly suppressed after pretreatment with prazosin. These results suggested that extrusive tooth movement is closely related to the rise in blood pressure due to stimulation of vascular α1-receptors.

Keywords: Phenylephrine, Prazosin, Tooth movement

A pulsatile movement of the erupting human premolars is observed in concert with the arterial pulse (1). The extrusive movements evoked by increases in aortic pressure are also observed (2). It seems that vascular pressures can produce forces sufficient to move a tooth under physiological conditions. Adrenaline and noradrenaline induce a rapid extrusive movement of the rat incisor almost simultaneously with an increase in systemic arterial blood pressure (3); it has been suggested that extrusive tooth movement is related to a rise in arterial blood pressure due to stimulation of vascular α-adrenergic receptors. However, noradrenaline induces intrusive tooth movements in the rabbit incisor (2, 4) and in the cat canine (5). Recently, we reported that the extrusive tooth movement induced by adrenaline was not suppressed by pretreatment with tolazoline (an α-blocker), although an increase in blood pressure induced by adrenaline was significantly suppressed (6). Thus, the precise relationship between extrusive tooth movement and the stimulation of vascular α-receptors in continuously erupting incisors remains unclear. To provide a clue to the relationship between extrusive tooth movement and the stimulation of vascular α1-adrenergic receptors, we investigated the dose-response effects of phenylephrine and the antagonistic effects of prazosin on axial movement of the rat mandibular incisor and arterial blood pressure.

Male Wistar rats (n=10, 347–366 g) were used. The experimental setup has been described previously (7, 8). To examine the dose-response effects of the α1-agonist, each animal was given intravenous injections of 5, 10 and 20 μg/kg of phenylephrine (Kowa Co., Nagoya) at 1-hr intervals. To examine the antagonistic effects of an α1-blocker, each animal was given an intravenous injection of prazosin (1 mg/kg, Sigma, St. Louis, MO, USA), and 1 and 2 hr later, was given intravenous injections of phenylephrine (20 μg/kg). Axial movement of the left mandibular incisor was measured by a non-contacting displacement detector (503-FD; Emic, Tokyo). The arterial blood pressure was measured from the mid-tail artery using a pressure transducer (MP-15; Micron Instruments, CA, USA). The data were stored on a computer (PC-9801DA; NEC, Tokyo) at 1-msec intervals during the experimental period. Positions of the teeth at the maximum extrusive movement and arterial blood pressure at the maximum increase were measured following the injection of phenylephrine before and after pretreatment with prazosin. Difference of the mean values was compared by Scheffe’s method for multiple comparisons after analysis of variance (ANOVA). Regression analyses were made to examine the correlations between doses and maximum tooth movements and between doses and changes in arterial blood pressure. Student’s t-test was used to determine the degree of significance of the correlation coefficients.

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Phenylephrine induced a temporal extrusive movement of the incisor and increase in blood pressure at all doses. With increasing phenylephrine doses, the maximum extrusive tooth movement and maximum increase in blood pressure were enhanced (Fig. 1). The maximum increase in blood pressure was significantly dose-dependent (ANOVA, \( P < 0.001 \)); the formula of the regression line was estimated as \( y = 1.07x + 34.30 \), where \( y \) is the change in blood pressure (mmHg) and \( x \) is the dose. The correlation coefficient (\( r \)) was 0.613 and significantly different from zero (\( t \)-test, \( P < 0.001 \)). However, the maximum extrusive tooth movement was not significantly dose-dependent. The mean value of the maximum extrusive tooth movement increased in parallel with the mean value of the maximum increase in blood pressure (Fig. 1).

Figure 2 shows records of tooth displacement and arterial blood pressure following the injection of 20 \( \mu \)g/kg of phenylephrine 1 hr before (control) and 1 and 2 hr after pretreatment with prazosin (1 mg/kg). The eruptive tooth movement was observed before and after the temporal extrusive tooth movement induced by phenylephrine (Fig. 2). At 1 hr after pretreatment with prazosin, the extrusive tooth movement induced by phenylephrine was markedly suppressed, but the successive intrusive

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**Fig. 1.** Graph showing the dose-response effects of phenylephrine on the extrusive tooth movement (●) and on the increase in blood pressure (■). Each point and vertical bar represents the mean ± S.D. of 10 rats. The y-axis shows the extrusive tooth movements or increases in blood pressure, and the x-axis shows the log-doses of phenylephrine. Significant differences were found between the log-doses of phenylephrine and increases in blood pressure, *\( P < 0.001 \) (ANOVA).

**Fig. 2.** Records of tooth displacement (upper column) and arterial blood pressure (lower column) following the injection of phenylephrine (20 \( \mu \)g/kg) 1 hr before (control) and 1 and 2 hr after pretreatment with prazosin (1 mg/kg). The time of phenylephrine injection was designated as 0 min. Each curve was obtained from the combined values for ten animals.
tooth movement was similar to the control. Arterial blood pressure decreased from approximately 80 to 65 mmHg following injection of prazosin and was maintained at this low level during the experimental period. The phenylephrine-induced increase in arterial blood pressure was markedly suppressed. There was a slight but distinct decrease in blood pressure (approximately 10 mmHg). At 2 hr, both the extrusive and intrusive tooth movements were similar to those at 1 hr. The increase in blood pressure was still markedly attenuated and the decrease in blood pressure was less than that at 1 hr. The maximum extrusive tooth movements were significantly (Scheffe's method, P<0.001) suppressed at 1 and 2 hr (27% and 33% of the control value, respectively) after pretreatment with prazosin (Table 1). The maximum increases in arterial blood pressure were also significantly (Scheffe's method, P<0.001) suppressed at 1 and 2 hr (5% and 4% of the control value, respectively).

In the present study, a dose-dependent increase in systemic arterial blood pressure was observed following the injection of phenylephrine (Fig. 1), as reported in previous studies (9, 10). Extrusive tooth movement occurred almost simultaneously with increases in blood pressure following the injection of phenylephrine (Fig. 1), as has been reported for injections of adrenaline or noradrenaline (3). The present and previous results support the view that extrusive tooth movement of the rat incisor is related to a rise in arterial blood pressure due to stimulation of vascular α-receptors (3). In contrast, it has been suggested that intrusive tooth movement is due primarily to activation of α-adrenergic receptors and changes in the vasculature or interstitial fluid in the socket (5, 11). The discrepancy between our results and those by other investigators might be due to the differences of animals, teeth, drugs, methods to measure tooth displacements and other experimental conditions.

In the present study, the phenylephrine-induced increase in arterial blood pressure was markedly suppressed by prazosin (Fig. 2, Table 1), which is consistent with previous reports (9, 12). The extrusive tooth movement induced by phenylephrine was also suppressed by prazosin, correlating with changes in blood pressure (Fig. 2, Table 1). Therefore, this suggests that the extrusive tooth movement is closely related to vasoconstriction and the rise of arterial blood pressure (3) due to stimulation of vascular α1-receptors. In contrast, the extrusive tooth movement induced by adrenaline was not suppressed by pretreatment with tolazoline (6): In the previous study, a slight increase in arterial blood pressure induced by adrenaline after pretreatment with tolazoline would have caused a marked increase in pressure within the socket, particularly when blood flow was increased by potentiation of cardiac β1-receptors and vascular β2-receptors, resulting in the extrusive movement of the incisor.

The maximum extrusive tooth movements induced by phenylephrine, however, were reduced to 27% and 33% of the control, and the maximum arterial blood pressure was reduced to 4% and 5% after pretreatment with prazosin (Table 1). The cause of such a discrepancy cannot be explained at present. In addition, prazosin did not potentiate the intrusive tooth movement induced by phenylephrine (Fig. 2), probably because the β-adrenergic action of phenylephrine was too weak to induce a marked intrusive tooth movement even when extrusive tooth movement was blocked by prazosin. Yet, this suggests that extrusive tooth movement is regulated not only by changes in arterial blood pressure but also by other factors such as resistance of periodontal/pulpal blood vessels, local blood flow (6), resisting force of the periodontal ligament (3, 13) and low compliant environment within the socket (14, 15).

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