Dominant Vasodilator Action of Norepinephrine in Isolated, Non-Preconstricted Simian Facial Veins

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Abstract—Using the cannula inserting method, we investigated the vascular responses to norepinephrine (NE), phenylephrine and isoprenaline (Isp) in isolated, perfused simian facial veins. NE usually induced only a vasodilation in non-preconstricted veins. Phenylephrine consistently induced only a slight vasoconstriction, and Isp produced only a vasodilation. NE-induced vasodilations were reversed to vasoconstrictions after treatment with a relatively larger dose of propranolol. It is concluded that simian facial veins have a spontaneous intrinsic tone and dominant abundant beta-adrenoceptors but sparse alpha₁-adrenoceptors.

In 1976, Pegram et al. (1) reported that norepinephrine (NE) and transmural nerve stimulation (TNS) readily produced vasodilation in a segment of the facial vein of the rabbit. In 1982, Mellander et al. (2) reported that beta-adrenoceptor-mediated relaxation was observed in a ring preparation of the superficial buccal segment of the human facial vein by use of TNS or NE. More recently, Tsuru and Negita (3) also reported that NE and epinephrine readily caused a relaxation in isolated, canine precontracted facial veins without alpha-blockade. In the three animals used, isolated facial veins showed the common characteristic of vascular relaxation readily induced by NE, suggesting physiologically specific characteristics of mammalian facial veins. In the present study, we studied the effects of NE, phenylephrine and isoprenaline on isolated simian facial veins, using the cannula inserting method which was developed and modified by Hongo and Chiba (4) and Tsuji and Chiba (5), because there are yet no reports on the effects of NE on isolated simian facial veins.

Japanese monkeys (Macaca fuscata, n=8) of either sex, weighing 3–10 kg, were anesthetized with ketamine hydrochloride (10 mg/kg, i.m.). After treatment with sodium heparin (200 units/kg, i.v.), the animals were sacrificed by rapid exsanguination from the right common carotid artery. Facial veins were then carefully isolated, and small branches were ligated as much as possible, and segments (1.4–4.0 mm outer diameter and 15–30 mm in length) were cut from each isolated vessel. We usually made two vessel preparations from each monkey.

Each segment was inserted with a stainless steel cannula with one small side hole at a 5-mm distance from the distal blind end (13–21 gauge, with an outer diameter of 0.8–2.4 mm and 4 cm in length). The cannula with vascular segment was placed in a cup-shaped glass container maintained at 37°C and perfused with Krebs’ solution at a constant flow rate (2.0–3.8 ml/min) by means of a peristaltic pump. The perfusate contained 118 mM NaCl, 4.7 mM KCl, 2.5 mM CaCl₂, 1.2 mM KH₂PO₄, 1.2 mM MgCl₂, 25 mM NaHCO₃ and 10.0 mM glucose, and bubbled with 95% O₂ and 5% CO₂.

The speed of perfusion was initially adjusted so that the perfusion pressure was maintained at 20–35 mmHg and kept constant throughout the experiments. Therefore, the vasoconstriction or dilatation was observed as an increase or a decrease in perfusion pressure, respectively. The perfusion pressure was continuously measured with an electric manometer.

Drugs used in this study were dl-norepinephrine hydrochloride (Sankyo), phenylephrine hydrochloride (Kowa), isoprenaline
hydrochloride (Kaken), propranolol hydrochloride (ICI) and bunazosin hydrochloride (Eisai). The drug solution was administered into the rubber tubing close to the cannula in a volume of 0.001–0.01 ml for 2 sec by using a microinjector (Terumo).

When a bolus injection of NE was performed into the cannulated facial vein, a transient decrease in perfusion pressure was immediately induced in a dose-related manner. This vasodilatory response was reproducible when NE was added after completion of the previous response. Isoprenaline was a more potent vasodilator than NE, and its effect was dose-related. On the other hand, phenylephrine induced only vasoconstrictions. The constrictor response was usually not so great, i.e., the maximal increases in perfusion pressure were approximately 5 mmHg at 3 μg. Summarized data are shown in Fig. 1.

NE-induced vasodilations were inhibited by treatment with propranolol. As shown in Fig. 2A, NE-induced vasodilations were clearly suppressed after 0.1 μg of propranolol, and these were reversed to vasoconstrictions after treatment with 1 μg propranolol, and

![Graph of vascular responses to isoprenaline, norepinephrine (NE) and phenylephrine of isolated, perfused simian facial veins. PP, perfusion pressure. Values represent the mean±S.E.M.](image)

![Graph of effects of three doses of propranolol on (A) norepinephrine (NE)- and (B) isoprenaline-induced vasodilatory responses in isolated, perfused simian facial veins. P-0.1: after treatment with 0.1 μg propranolol, P-1: after treatment with 1 μg propranolol and P-10: after treatment with 10 μg propranolol.](image)
NE produced only vasoconstrictions after 10 μg propranolol. After 10 μg bunazosin, NE-induced vasoconstrictions were significantly suppressed from 8.4±1.5 mmHg (by 3 μg NE) to 0.6±0.4 mmHg in 4 propranolol-treated preparations. As reported previously (6), phenylephrine-induced vasoconstrictions were strongly suppressed by bunazosin but xylazine-induced ones were not influenced, indicating that bunazosin is a selective alpha, adrenoceptor antagonist. Isoprenaline-induced vasodilations were also inhibited by propranolol treatment, but did not reverse to constrictions in concentrations up to 1 μg propranolol (Fig. 2B). In 3–4 experiments, a selective alpha2-adrenoceptor agonist, 1 μg clonidine caused no change in perfusion pressure; and 1 and 10 μg xylazine, another selective alpha2-agonist, had produced no significant vasoconstrictions (data not shown).

Pegram et al. (1) reported that a ring segment of the facial vein of the rabbit responds to NE and TNS by brisk biphasic dilation after passive stretch. The dilation in response to both procedures was reversed by prior exposure to propranolol. Thus, they considered that there is a population of beta-adrenoceptors that predominates over alpha-adrenoceptors, and the presence of a dilatory response in the buccal segment of the rabbit facial vein may be related to its location in the wall of the cheek. They reported that morphological studies showed no features that would distinguish this part of the vein from portions on either side that contracted in response to stimulation, suggesting that the facial vein has unusual functional properties but not morphologically specific structures. Tsuru and Negita (3) also reported in the canine facial vein ring preparation that beta-adrenoceptors predominate over alpha-adrenoceptors in a moderately precontracted state with PGF2α. Mellander et al. (2) reported that the characteristics of the buccal ring segment of the human facial vein are basically similar to the ones described for the rabbit facial vein, and the isolated vein developed a maintained intrinsic myogenic tone in response to passive stretch and was supplied with alpha- and beta-adrenoceptors. Facial vein specimens showed a reversal into neural beta-adrenergic dilation after alpha-adrenergic blockade, although the human external jugular vein was devoid of intrinsic tone and beta-adrenoceptors in the same experiments. Thus, they proposed that a beta-adrenergic neuroeffector mechanism in superficial ramifications of the facial vein in man might be involved in the emotional blushing reaction (2). In the present study, although the reason why the isolated facial vein has strong intrinsic tone is not clear, it may be possibly due to the high perfusion pressure (20–35 mmHg), intrinsic characteristics of this vessel or other specific mechanisms.

Winquist and Bevan (7) proposed that the buccal segment of the rabbit facial vein acts as a temperature-sensitive sphincter whose tone changes significantly with the temperature of the blood draining the nasal turbinates, showing that intrinsic myogenic tone in the ring preparation of the rabbit facial vein is exquisitely sensitive to small changes in temperature in the range of 33°C to 44°C. Tsuru and Negita (3) considered that the coronary artery and the facial vein seem to share common characteristics, because certain segments of the coronary artery in the dog and monkey have been shown to relax in response to sympathetic nerve stimulation and exogenous NE. However, our previous report (8) demonstrated that NE consistently induced only a vasoconstriction with no significant vasodilation in the simian coronary artery, differing from the canine coronary artery, by use of the cannula inserting method. This method allowed us to study the vascular responses in several kinds of non-preconstricted veins such as isolated, perfused simian and canine femoral veins (9), simian metacarpal vein (10) and canine pulmonary vein (6). However, we did not observe any vasodilatory response to NE in these veins. Therefore, we consider that simian facial veins are indeed unusual among vascular tissues including even those of the coronary vasculature.

In the present study, it was demonstrated that in the isolated simian facial vein NE consistently produced vasodilations in the non-preconstricted condition, indicating that this vein has predominant beta-adrenoceptors and sparse alpha1-adrenoceptors. The buccal
A segment of the facial vein of the rabbit was reported to be a unique exception since it exhibited a pronounced intrinsic myogenic tone in vitro (1). Therefore, it seems that facial veins have common characteristics in several species.

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