Effects of Catecholamines on Isolated Canine Facial Veins

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Abstract—The buccal segment of the canine facial vein which was precontracted moderately with prostaglandin F2α relaxed to different extents in response to dopamine (DA), norepinephrine (NE), epinephrine (Epi) and isoproterenol (Isp). Propranolol (10⁻⁶ M) reversed the relaxation responses to contractions. In the presence of an α-adrenoceptor blockade and inhibitors of neuronal and extraneuronal uptakes, the four catecholamines relaxed the vein fully, and the order of pD₂ values was Isp (8.34) > Epi (7.53) = NE (7.50) » DA (5.31). The results indicate that in the canine facial vein, β-adrenoceptors predominate over α-adrenoceptors, and the subtype of β-adrenoceptor may be the β₁-type.

The buccal segment of the rabbit facial vein exhibits uncommon properties in dramatically developing myogenic tone in response to stretch and displaying a β-adrenoceptor-mediated relaxation to sympathetic nerve stimulation (1). Similar characteristics have been observed in the superficial buccal segment of the human facial vein (2). Several possible physiological roles for these segments have been proposed: the facial vein can act as a temperature-sensitive sphincter for cranial thermoregulation in the rabbit (3) and the facial vein in man may be involved in the emotional blushing reaction (2).

In the present study, the effects of catecholamines including norepinephrine (NE), a sympathetic nerve transmitter, epinephrine (Epi), a circulating endogenous β-adrenoceptor agonist (2), as well as isoproterenol (Isp), a most potent β-adrenoceptor agonist, and dopamine (DA), a precursor of NE and Epi, on the canine facial vein were examined to determine the characteristics of the adrenoceptors, in comparison with those on the canine saphenous vein which have been shown to have predominantly the β₂-type of adrenoceptors (4).

Male mongrel dogs, weighing 8–15 kg, were anaesthetized with pentobarbital sodium, either 35 mg/kg, i.v., or 50 mg/kg, i.p. The buccal segment of the facial vein and the lateral saphenous vein (used as a comparison) were isolated and immediately immersed in physiological saline solution. Ring segment preparations of 2 mm and 1.5 mm in length were made for the facial and saphenous veins, respectively. In vitro experiments were carried out as reported previously (5).

Although the facial vein spontaneously exhibited intrinsic tone during the equilibration period of 2 hr after giving a load of 1 g, as described with the rabbit facial vein (1, 3), the developed tone varied from one preparation to another, ranging from 1–1.5 g. Therefore, the effects of catecholamines were tested in a moderately precontracted state with prostaglandin (PG) F2α not only in the saphenous vein but also in the facial vein at concentrations of 3×10⁻⁷–10⁻⁶ M in the former and 1–3×10⁻⁶ M in the latter, in order to observe the relaxation responses more clearly and to match the experimental conditions as much as possible between the two different veins. Thus the obtained precontracted levels were approx. 2 g in the facial vein and 4 g in the saphenous vein. They were in the range between 60 and 75% of the maximum developed tension, which included intrinsic active tone, produced by 10⁻⁵ M PGF2α, 3×10⁻⁵ M methoxamine and 120 mM KCl in the facial vein and in the range between 40 and 60% of the maximum developed tension produced by 10⁻⁴ M NE.
in the saphenous vein.

When pD2 values for β-adrenoceptor-mediated relaxation were obtained, the ancillary agents which eliminate the factors influencing the sensitivity of β-adrenoceptors (6, 7) were contained in the physiological saline solution, i.e., an α-adrenoceptor antagonist, 10⁻⁶ M phentolamine, and inhibitors of neuronal and extraneuronal uptakes, 10⁻⁵ M cocaine and 3×10⁻⁵ M corticosterone, respectively (5).

Drugs used were as follows: dopamine hydrochloride (Sigma), (-)-norepinephrine bitartrate (Sigma), (-)-epinephrine bitartrate (Sigma), (-)-isoproterenol hydrochloride (Sigma), α-(3,4,5-trimethoxyphenethylaminomethyl)-3,4-dihydroxybenzylalcohol hydrochloride (T-1583, Tanabe), procaterol hydrochloride (Otsuka), (±)-propranolol hydrochloride (Sigma), phentolamine mesylate (Ciba-Geigy), prostaglandin F₂α (Prostalmon, Ono), cocaine hydrochloride (Takeda), corticosterone (Sigma), and papaverine hydrochloride (Tokyo Kasei). All data are given as the mean±S.E. from 6-8 experiments and compared using Student's t-test, P<0.05 being taken as the limit of significance.

All four catecholamines relaxed the facial vein precontracted moderately with PGF₂α to different extents (Fig. 1). The mean maximum relaxations expressed as decreases in tension (gram, g) from the precontracted levels (0 g) were Isp, -1.74±0.22; NE, -1.32±0.16; Epi, -0.86±0.16; and DA, -1.06±0.06. Papaverine, 10⁻⁴ M, did not produce a greater relaxation than Isp-induced relaxation. A β-adrenoceptor antagonist, propranolol 10⁻⁶ M, abolished these relaxation responses and reversed to contractions, showing that the relaxation response was mediated by β-adrenoceptors.

All four catecholamines produced maximum relaxation similar to the extent of that produced by 10⁻⁴ M papaverine in the presence of ancillary agents, i.e., an α-adrenoceptor antagonist, and inhibitors of neuronal and extraneuronal uptakes. As shown in Fig. 2, the order of potency for the relaxation response (mean pD2 value±S.E. in parentheses) was Isp (8.34±0.11) > Epi (7.53±0.14) = NE (7.50±0.10) ≫ DA (5.31±0.11).

While the catecholamines other than Isp contracted the saphenous vein precontracted with 3×10⁻⁷-10⁻⁶ M PGF₂α in the absence of α-adrenoceptor blockade, the vein relaxed in response to all the catecholamines in the presence of ancillary agents including the α-adrenoceptor antagonist. The maximum relaxation responses were as follows (shown as decrease in tension from the initial precontracted level, g): Isp, -3.54±0.36; Epi, -3.72±0.47; NE, -3.21±0.16; DA, -3.96±0.21; PGF₂α, -5.26±0.35; and papaverine, -4.83±0.32.

Fig. 1. Effects of four catecholamines on precontracted canine facial veins. Each point and vertical bar represent the mean and S.E. of 7-8 experiments, respectively. Ordinate: relaxation from the precontracted level (0 g) which includes intrinsic active tone and contraction produced by prostaglandin F₂α (1-3×10⁻⁶ M). Isp, isoproterenol; NE, norepinephrine; Epi, epinephrine; and DA, dopamine.
Fig. 2. Concentration-relaxation response curves for four catecholamines in canine facial veins. The vein was precontracted with prostaglandin F2α, 1–3×10⁻⁶ M, in the presence of 10⁻⁶ M phentolamine, 10⁻⁵ M cocaine and 3×10⁻⁵ M corticosterone. Symbols are the same as in Fig. 1.

0.44; and DA, −1.36±0.19. Only the DA-induced relaxation was significantly smaller than the others, indicating that DA was a partial agonist for the receptor. In contrast, Isp, Epi and NE seemed to be full agonists, since they relaxed the vein as much as 10⁻⁴ M papaverine did. The order of apparent pD₂ values for relaxation was Isp (8.35±0.11) > Epi (7.79±0.12) > NE (7.02±0.10) > DA (6.09±0.17).

The additional experiment with the selective β₁-adrenoceptor agonist, T-1583 (8), and the selective β₂-adrenoceptor agonist, procaterol (9), were made under similar conditions as the above. The pD₂ values of T-1583 in the facial and saphenous veins were 7.66±0.12 and 6.37±0.10, and those of procaterol were 7.29±0.17 and 8.77±0.15, respectively.

The facial vein in the dog shares many characteristics with those in the rabbit (1, 3) and in man (2). Namely, the canine facial vein exhibited intrinsic tone in response to passive stretch and relaxed to NE as well as to other catecholamines both in the spontaneously contracting state and in the additionally precontracted state with PGF₂α. Thus, NE released from the sympathetic nerve terminals as well as circulating Epi, which is generally considered to be the main endogenous β-adrenoceptor agonist under physiological conditions (2), might physiologically relax the canine facial vein. By contrast, the saphenous vein contracted to the catecholamines except Isp in the absence of α-adrenoceptor blockade. These results indicate that populations of α- and β-adrenoceptors in the facial and saphenous veins are quite different. In this regard, the coronary artery and the facial vein seem to share common characteristics. Namely, 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 (10). It has been also suggested that the subtypes of β-adrenoceptors in the coronary artery in the dog (11) and monkey (10) are the β₁-type.

To classify the subtype of β-adrenoceptors in the facial vein, agonisms of catecholamines were compared with those in the saphenous vein which has been shown to have predominantly the β₂-type of adrenoceptors (4). In fact, the potency ratios among Isp, Epi and NE in the saphenous vein were consistent with those observed in tissues abundant with the β₂-type (7). In contrast, the potency ratios in the facial vein were consistent with those observed in the heart (7), suggesting that the responses of the facial vein were mediated via the β₁-type of adrenoceptors.

This suggestion is strengthened by the observation that the facial vein was more sensitive to the selective β₁-adrenoceptor agonist T-1583 and less sensitive to the selective β₂-adrenoceptor agonist procaterol.
than the saphenous vein. It has been reported that the activities of T-1583 on the contractile force of guinea-pig papillary muscle (response to \( \beta_1 \)-receptor) and on the guinea-pig trachea (response to \( \beta_2 \)-receptor) were approx. 1/7 and 1/300 those of Isp, respectively (8). On the other hand, the pD\(_2\) values of procaterol for relaxation of guinea-pig trachea, for the positive chronotropic effect on guinea-pig right atria and for the positive inotropic effect on guinea-pig left atria have been reported as 8.74, 7.86 and 6.59, respectively (9). Therefore, our data and opinion seem to be in good agreement with these reports. In addition, although the experimental conditions were somewhat different from those of Tokudome and Taira (4), similar pD\(_2\) values of Isp, T-1583 and procaterol for the saphenous vein were obtained in the present study, indicating that the ancillary agents used in the present study did not affect the sensitivities to these agonists. However, it seems reasonable to eliminate factors influencing the sensitivity of receptors in this kind of experiment (6, 7).

Although the effects of DA on the cardiovascular system have been shown to be complex (12), DA seemed to relax both the canine facial and saphenous veins mainly through \( \beta \)-adrenoceptors since the relaxation response was abolished by propranolol at the not so high concentration of \( 10^{-6} \) M.

In conclusion, the facial vein in the dog shares many characteristics with those in the rabbit and man, and \( \beta \)-adrenoceptors in the canine facial vein seem to be the \( \beta_1 \)-type.

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References