Comparison of the Effect of Dopamine in Primate Arteries and Veins

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Mechanical responses to dopamine of isolated human and monkey veins were isometrically measured and compared to those of the arteries. Human gastroepiploic and monkey mesenteric veins responded to dopamine with contractions, whereas the arteries in the same region responded with relaxations. Treatment with phentolamine converted the venous contraction to a relaxation, which was not influenced by propranolol but was abolished by droperidol. The relaxation was endothelium-independent and converted to a contraction by SCH23390 but unaltered by domperidone. Dopamine increased the cyclic AMP content in the human veins. Monkey vena cava and portal vein did not respond to dopamine with relaxation even under α-adrenoceptor blockade. It is concluded that primate veins and arteries from the gastric and mesenteric regions respond quite differently to dopamine; the α-adrenoceptor-mediated contraction predominates over the relaxation mediated via D₁-receptor in the veins, and vice versa in the arteries. In monkey large veins, dopamine receptor does not appear to play a functional role. The venoconstrictor action of dopamine, together with actions on myocardium and resistance vessels, would contribute to increasing of the cardiac output. (Hypertens Res 1995; 18 Suppl. 1: S35-S37)

Key Words: primate, venoconstriction, dopamine, D₁ receptor, cyclic AMP

Dopamine, a sympathomimetic amine, is useful in the treatment of shock and heart failure accompanying oliguria and low cardiac output, since dopamine is a positive inotropic agent (1) and promotes renal and mesenteric arteriolar dilatation (2). We have first reported that dopamine-induced relaxations in isolated arteries are not affected by β-adrenoceptor antagonists, atropine, aminophylline and cyclooxygenase inhibitors (3, 4). A variety of dog and monkey arteries (5) in the presence or absence of α-adrenoceptor antagonists respond to dopamine with a relaxation which is selectively inhibited by droperidol (6). However, the responses to dopamine are quite variable in arteries from different locations, those of different sizes and those from different species. Further, although responsiveness to dopamine of a variety of arteries is well established, the effect of dopamine on the venous system is uncertain. In the present study, therefore, responses to dopamine of isolated human and monkey blood vessels were studied by focusing on the comparison between venous and arterial responses.

Human Gastroepiploic Artery and Vein

Gastroepiploic artery branches and vein tributaries were removed from the same regions of the omentum excised during operation for stomach cancer or ulcer. Helical strips of the arteries and veins partially contracted with prostaglandin (PG)F₂α respond to dopamine quite differently; the veins cause dose-dependent contractions, whereas the arteries in the same region relax in response to low concentrations (up to $5 \times 10^{-6}$ mol/l) of the amine (7, 8). Pretreatment with phentolamine converts the vein contraction to a relaxation and potentiates the artery relaxation. The maximal relaxations relative to those caused by $10^{-4}$ mol/l papaverine, a standard drug for relaxation, in the venous and arterial strips pretreated with α-adrenoceptor antagonists do not significantly differ, and the EC₅₀ values are 6.4 and $2.3 \times 10^{-7}$ mol/l, respectively. The relaxations are not influenced by propranolol but suppressed by droperidol in a concentration ($3 \times 10^{-5}$ mol/l) in which the relaxation caused by nitroglycerin is not affected. These findings indicate that contractions caused by dopamine, possibly by activation of α-adrenoceptors, are clearly predominant over relaxations mediated by dopamine receptor activation in the human veins, and vice versa in the arteries. The relaxation of arterial and venous strips is converted to a contraction by SCH23390, a selective D₁-receptor antagonist (9), but not influenced by domperidone, a D₂-receptor antagonist (10).

Further, the relaxations in human gastroepiploic arteries and veins are not endothelium-dependent, nor influenced by treatment with oxyhemoglobin, indicating that the dopamine-induced relaxation is not associated with endothelial cell function, and endogenous nitric oxide is not involved in the relaxation. Dopamine increases cyclic AMP content in the human gastroepiploic veins, as reported in rab-
bit mesenteric arteries (11) and cultured rat mesenteric vascular smooth muscle cells (12). Increase in cellular cyclic AMP associated with stimulation of D1-receptor subtype may participate in the relaxation of human blood vessels. Figure 1 illustrates the mechanism of action of dopamine in human gastroepiploic arteries and veins.

**Monkey Arteries and Veins**

Responses to dopamine of cerebral, coronary, mesenteric, renal and femoral arteries isolated from monkeys are quite different (5); moderate relaxations were obtained in cerebral and mesenteric arteries precontracted with PGF2α, and, in contrast, marked contractions are seen in femoral arteries. relaxations in the cerebral and mesenteric arteries are observed without treatment with α-adrenoceptor antagonists. Various arteries obtained from dogs, cats and rabbits respond to dopamine consistently with contractions (13-16), and relaxations are observed only when the arteries are treated with high concentrations of α-adrenoceptor blockers. The contraction of renal, coronary and femoral arteries by dopamine is reversed to a relaxation by treatment with α-blockers, and the relaxation of cerebral and mesenteric arteries is potentiated by the treatment. These findings suggest that dopamine stimulates α-adrenoceptors to induce contractions and to attenuate relaxations, and the extent of α-adrenoceptor-mediated response differs in various arteries. The magnitude of relaxations caused by dopamine and the EC50 value of dopamine in a variety of monkey arteries under α-blocker treatment differ; relaxations of cerebral, mesenteric, and renal arteries are appreciably greater than those of femoral and coronary arteries. These relaxations are not influenced by propranolol, atropine, cimetidine, aminophylline or aspirin but are markedly suppressed by droperidol as seen in human gastroepiploic arteries.

On the other hand, monkey mesenteric, renal and portal veins and vena cava respond to dopamine with contraction as seen in human gastroepiploic veins. Human saphenous and rabbit portal veins also contract in response to dopamine (17, 18). Contraction of mesenteric and renal veins by dopamine are converted to a relaxation by treatment with α-blockers, magnitude of the relaxation in monkey mesenteric vein (33% of that induced by 10-5 mol/l papaverine) is markedly less than that in the mesenteric artery, but the EC50 values are not appreciably different (4.9 vs. 8.5×10-5 mol/l). α-Adrenoceptor-mediated contractions are markedly greater than relaxations mediated by dopamine receptors in the mesenteric veins, and vice versa in the arteries. Interestingly, vena cava and portal vein respond to dopamine only with contractions which are suppressed but not converted to relaxations even after pretreatment with high concentrations of α-adrenoceptor antagonists. In these large veins, dopamine receptor does not appear to play a functional role.

**Conclusion**

As far as monkey and human veins are concerned, dopamine produced only contractions, whereas human gastroepiploic and monkey mesenteric and cerebral arteries respond to the amine with relaxations. The relaxations mediated by dopamine receptors, possibly D1 subtype, are less in the veins than in the arteries. Dopamine in low doses decreases peripheral vascular resistance and lowers diastolic blood pressure (1) due possibly to vasodilation by stimulation of dopamine receptors. On the contrary, venous tissues in primates seem to respond to dopamine only with contraction, thus decreasing venous capacitance, increasing venous return and increasing cardiac output. Gotoh et al. (19) have estimated the venous return curve in vivo in volunteers by the use of radionuclide and occlusion plethysmography, and they observed an increase in venous return after intravenous infusion of low dose of dopamine. In addition to the action on myocardium, increase by dopamine in preload due to venoconstriction and decrease in afterload due to arterial dilation would contribute to the increased cardiac contractility.
References


