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Selective Increments of Superior Mesenteric Artery Blood Flow by Dopamine Administration in the Pig

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Summary. **Circulatory responses in major branches of the superior mesenteric artery were examined after dopamine (DA) administration into the jugular vein in anesthetized pigs. DA at 10 μg/kg/min for 2 min produced an increase in superior mesenteric arterial blood flow (SMAF) and jejunal arterial blood flow (JAF) without any change in right colic arterial blood flow (RCAF), ileocolic arterial blood flow (ICAF) or systemic arterial blood pressure (SAP). The SMAF and JAF response tended to be dose dependent when the dose of DA ranged from 5 to 20 μg/kg/min. A significant increase in RCAF was induced when the dose of DA was increased to 20 μg/kg/min, but no change in ICAF was seen. Liver and kidney function scores were unchanged after the DA injection.**

These findings suggest that DA is active in increasing superior mesenteric arterial blood flow, but the action of DA is differential at the major branch level.

Key words—dopamine, blood flow, mesenteric circulation, intestine, pig.

INTRODUCTION

It has been shown that exogenously administered dopamine (DA) increases superior mesenteric arterial blood flow by dilating the mesenteric vascular wall through the activation of dopamine receptors.[1-4] Dopamine receptors are widely distributed in the mesenteric artery, including its branches,[5-7] but the contribution of dopamine receptors to the blood flow has not yet been examined at the branch level. On the other hand, although the superior mesenteric artery supplies blood to the intestine through the major branches of the artery, the branches carrying blood to the small and large intestines are different.[8,9]

This experiment was designed to investigate whether DA influences blood flow control in the major branches of the superior mesenteric artery in pigs.

MATERIALS AND METHODS

Animals

Six Landrace-White-Duroc pigs weighing 22-25 kg were used. They were housed individually (12:12 h light dark cycle) with lights on at 6:00 h. They were fed a standard diet (Spurt G, Nihon Nosan, Yokohama) with free access to tap water.

Anesthesia and maintenance

The animals were anesthetized through an endotracheal tube with a mixture of 1.0% halothane and 1.0 L/min oxygen, and were allowed to breathe mechanically on a closed air circuit (Acoma Med Products, Tokyo). The anal temperature was maintained at 36.0 ±1.0℃ with a heating pad (UH-CHW-II, Junkan, Saitama). Analysis of gas in the blood with an analyzer (ABL-30, Radiometer, Copenhagen) was necessary in order to maintain adequate ventilation.[10] The blood gas conditions during the experiment are summarized in Table 1.

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Chemical analysis

Blood samples were cooled with ice immediately after collection and centrifuged at 2,200 rpm for 20 min. Then the separated plasma was stored at -20℃ until measurement of the following parameters of liver and kidney functions with an autoanalyzer (Hitachi-736, Hitachi, Tokyo)[10]: total protein (TP, Biuret method), albumin (Alb, Bromcresol green method), glucose (Glc, glucose oxidase method), total bilirubin (TB, azobilirubin method), glutamic pyruvic transaminase (GPT, Ultraviolet method), alkaline phosphatase (Alp, Bessey-Lowry method), and creatinine (Cre, Jaffe method).

Blood electrolyte analysis

The electrolyte concentration in the blood was measured with an analyzer (EML-100, Radiometer, Copenhangen).

Table 1. Blood gas parameters before (I) and 12 min after (II) DA 10 μg/kg/min injection

	I	II
Temp (°C)	37.0±0.1	37.0±0.1
pH	7.388±0.021	7.379±0.015
Pco_2 (mmHg)	42.4±8.6	42.1±3.8
Po_2 (mmHg)	202.4±5.6	205.7±5.7
HCO_3 (mmol/L)	27.9±0.9	27.8±0.8
TCO_2 (mmol/L)	27.4±0.9	28.8±1.2
BE (mmol/L)	7.2±2.3	7.4±2.5

Values are the mean ± SEM (n=6).

Measuring blood flow

Ultrasonic blood flow meters (Transonic T201, Advance, NY) were utilized to measure the blood flow.[11,12] The probes for blood flow estimation were placed around the superior mesenteric artery, the first jejunal artery, right colic artery, and ileocolic artery. Placement of a probe for a branch was about 2-5 cm distal to the bifurcation of the superior mesenteric artery (Fig. 1). The superior mesenteric arterial blood flow (SMAF), jejunal arterial blood flow (JAF), right colic arterial blood flow (RCAF) and ileocolic arterial blood flow (ICAF) were recorded on a graph with a pen (Biocolor Graph 2G82, Nihon Denki San Ei, Tokyo). The systemic arterial pressure (SAP) was recorded from the carotid artery, using the same equipment.

Test solution

DA (Kyowa Hakko Kogyo Co., Ltd., Tokyo) dissolved in saline was injected into the left side of the jugular vein. The amount used in each test injection was 1.0 ml/min, and was completed in 2 min with an infusion pump. Saline was injected as a control. It was preliminarily observed that the same amount of saline produced no measurable effect on either flow or pressure, mesenteric flow response due to DA was saturated 2 min after injection, and the flow response remained almost the same even when the injection was continued for more than 2 min. Test injections were given at approximately 12-15 min intervals and the dose of DA ranged from 5 to 20 μg/kg/min as in previous experiments.[12]

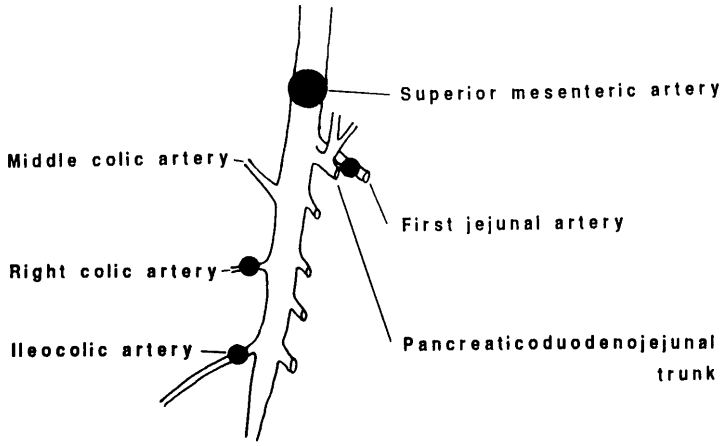

Fig. 1. Schematic presentation of the superior mesenteric artery and its branches. *Closed circles* indicate the placement of the flow probes.

Data analysis

The results were expressed as a percentage of the control value, with each animal serving as its own control. The control value was the value immediately before drug administration. Samples were collected after the first response by each animal to a specific solution. Statistically significant differences were evaluated by one-way ANOVA, and specific values were obtained by Duncan's multiple range test.

Table 2. Systemic and mesenteric circulatory parameters before (I) and 12 min after (II) DA 10 μg/kg/min injection

	I	II
SAP (mmHg)	96.6±4.2	96.0±3.4
SMAF (ml/min)	465.5±13.5	443.0±10.5
JAF (ml/min)	32.4±2.4	33.4±2.4
RCAF (ml/min)	48.0±7.1	45.3±5.6
ICAF (ml/min)	57.1±9.7	58.4±10.1

Values are the mean ± SEM (n=6).

RESULTS

The blood pH and gas tension showed adequate ventilation for the animals (Table 1). It was possible for a considerable number of factors moderating DA action on the vascular musculature to be fixed.[13] Basal levels of SAP and blood flow are shown in Table 2: the order of magnitude in the flow was SMAF, ICAF, RCAF and JAF.

DA 10 μg/kg/min injection increased SMAF (Fig. 2). The increase in SMAF reached its peak approximately 2 min after injection, then returned to the control level within another 2 min (Fig. 3). When SMAF response to DA was analyzed 2 min after injection, the SMAF increase tended to be dose dependent (Fig. 4).

JAF was increased by DA 10 μg/kg/min injection (Figs. 2 and 3). The JAF increase also tended to be dose dependent, and the threshold concentration of DA was higher in the jejunal artery than in the superior mesenteric artery (Fig. 4).

RCAF was unaffected by DA 10 μg/kg/min injec-

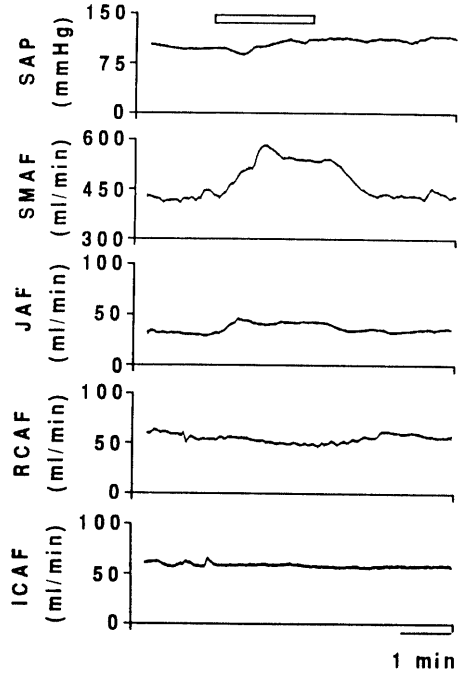

Fig. 2. Effects of jugular injections of DA on SAP, SMAF, JAF, RCAF and ICAF. DA 10 μg/kg/min was given for 2 min. *The bar* shows the time of injection.

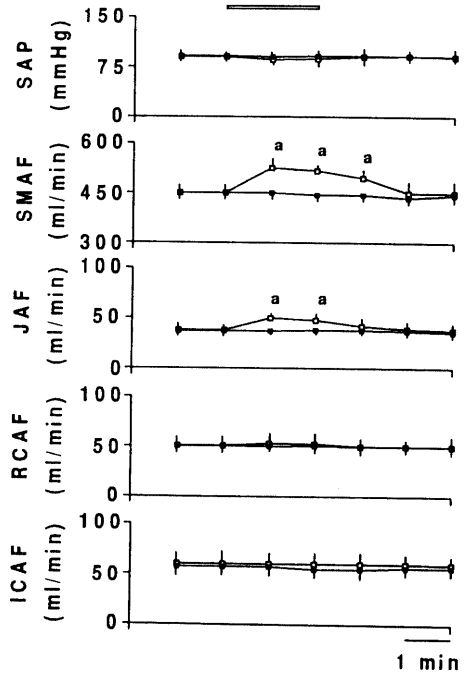

Fig. 3. Time courses for SAP, SMAF, JAF, RCAF and ICAF after DA administration. Jugular injections of DA (□, 10 μg/kg/min) or saline (■) were performed. *The bar* indicates the time of injection. Values are the mean ± SEM (n=6). [a]$p<0.01$ vs ■.

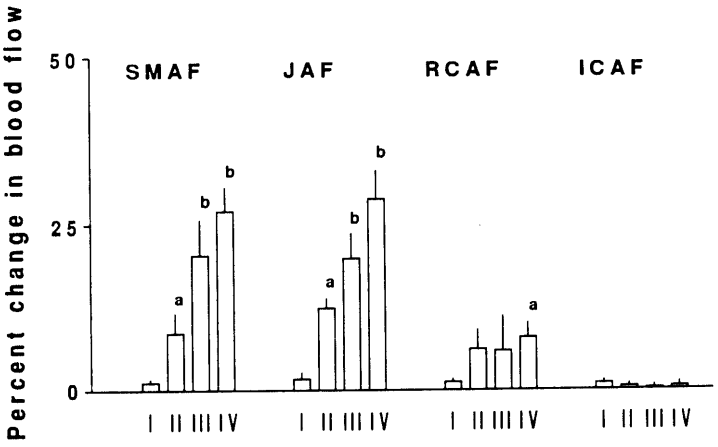

Fig. 4. Percent changes in SMAF, JAF, RCAF and ICAF after DA injection. Three different doses of DA (II, 5 μg/kg/min; III, 10 μg/kg/min; IV, 20 μg/kg/min) were injected into the jugular vein, and blood flows 2 min after injection are shown. Saline was injected as the control (I). Values are the mean ± SEM (n=6). $^{a}p<0.01$ vs I. $^{b}P<0.05$ vs II.

tion (Figs. 2 and 3). A significant increase in RCAF was induced when DA was increased to 20 μg/kg/min (Fig. 4).

ICAF was unchanged after DA 10 μg/kg/min injection (Figs. 2 and 3). No significant change in ICAF was induced when DA was increased to 20 μg/kg/min (Fig. 4).

SAP was unchanged when DA 10 μg/kg/min was injected (Figs. 2 and 3). A slight decrease in SAP was seen when DA was given at 20 μg/kg/min (data not shown).

Blood chemical scores indicating liver and kidney functions were unchanged after DA 10 μg/kg/min injection. The electrolyte concentrations in the blood were also unaffected by the DA administration (Table 3).

Table 3. Blood chemical parameters before (I) and 12 min after (II) DA 10 μg/kg/min injection

	I	II
TP (g/dl)	5.7±0.1	5.7±0.1
Alb (g/dl)	3.4±0.1	3.4±0.1
Glc (mg/dl)	130±18	129±14
TB (mg/dl)	0.2±0.0	0.2±0.0
GPT (U)	28±2	28±3
Alp (U/l)	281±27	274±24
Cre (mg/dl)	1.2±0.1	1.2±0.1
Na^+ (mEq/l)	138±1	138±1
K^+ (mEq/l)	5.4±0.2	5.4±0.2
Cl^- (mEq/l)	102±1	102±1

Values are the mean ± SEM (n=6).

DISCUSSION

We found that DA enhances blood flow differentially in the major branches of the superior mesenteric artery: DA 10 μg/kg/min injection effectively increased SMAF and JAF but not RCAF or ICAF. This is essentially in keeping with the view that DA increases splanchnic circulation.[1-4]

DA administration is capable of increasing JAF. The action of DA on the jejunal artery wall seemed to be peculiar to DA, because the JAF response tended to be dose dependent.

The mode of DA action on the artery wall has been investigated, and a biphasic change in the superior mesenteric arterial blood flow after DA injection was noted[14,15]: the initial decrease is caused by a contractile effect, and any subsequent rise is due to a direct vasodilator effect on the mesenteric artery. In this study, DA increased blood flow in a monophasic pattern. This could mean that the flow response observed was the result of a vasodilative action.

When DA increases splanchnic blood flow, the action site of DA has been considered to be distributed evenly in the superior mesenteric arterial wall, especially since dopamine receptors are widely identified in the vascular bed,[5-7] but the artery has many branches[8,9] and their contribution to blood flow control was unclear. In the present study, the

threshold concentration of DA effective in the increasing blood flow differed according to the artery branch tested. This may partly hold true for the phenomenon showing that there are regional differences in the effects of DA on vascular tissues;[16] one possible explanation for this is that the DA receptor density in the artery wall is uneven.

Rheologically, basal levels of the blood flow reflect the relative diameter sizes of the arteries examined, and the flow order was SMAF, RCAF, ICAF and JAF (Table 2). However, DA response was prominent in the SMAF and JAF, and the appearance of flow control by DA is not simply correlated with artery size. In connection with this, the two principal functions of the intestines, absorption and secretion, are dependent on an adequate supply of blood.[17,18] As mentioned above, blood flow control by DA was different in the jejunal and colic arteries. DA action on the intestinal blood supply might be determined by the primary function of each intestine.

DA action on SAP changes according to the concentration: at a lower concentration α-action is dominant, while β-action can be present at higher concentration.[19] Also, a lower dosage of DA has been presumed to increase mesenteric blood flow without changes in cardiac output.[20,21] In this study, unfortunately, no record of cardiac output was made, but SAP was unchanged after DA injection. It may well be deduced that the flow response observed is derived from the α-action, although it cannot be denied that systemic vasodilation and cardiac output enhanced by DA caused no change in SAP.

In clinical practice, increasing blood flow in the mesentery can contribute to an improved prognosis for mesenteric disease when the mesentery has been in an ischemic condition.[22,23] Our findings showing that a vasodilative agent for ischemia effectively increased blood flow in the selected arterial branch indicate that such an agent may have an appropriative action site within the mesenteric vascular net. Further study on this point is necessary.

These observations lead us to conclude that DA is effective in increasing superior mesenteric arterial circulation, but the DA action is differentially uneven at the major branch level.

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