Gastrointestinal and Mesenteric Hemodynamic Patterns in Neurogenic Hypertensive Rabbits

By Natalie Alexander and Vincent DeQuattro

ABSTRACT
Patterns of blood flow and vascular resistance in the component tissues of the splanchnic region of sinoaortic denervated (SAD) hypertensive rabbits were compared with those of normotensive sham-operated rabbits using previously described methods. SAD rabbits with high total splanchnic resistance showed significant elevations in resistance in all parts of the gastrointestinal tract and mesentery, but the magnitude of the changes compared with values for sham-operated rabbits varied from one area to another, ranging from increases of 34% in the cecum-appendix to 77% in the stomach and jejunum. Blood flow was reduced 22-42% in some areas and less in others. An aboral gradient of mean blood flow was found between and within the small and large intestines in both groups. Intestinal flow pattern differences were found in individual rabbits. We concluded that activation of the sympathetic nervous system by sinoaortic denervation exerted a variable, unpredictable degree of vasoconstrictor tone on different parts of the splanchnic bed which reflected the net result of vascular smooth muscle response to neurogenic and local regulatory factors.

KEY WORDS sympathetic nervous system and hypertension stomach blood flow in hypertension splanchnic regional blood flow aboral blood flow gradient intestinal blood flow in hypertension

In rabbits with neurogenic hypertension induced by sinoaortic denervation (SAD), the synthesis of norepinephrine in the superior mesenteric and the small mesenteric blood vessels (1) and the splanchnic vascular resistance (2) are both increased. To determine whether the resistance and flow changes induced by SAD are distributed uniformly and are of equal magnitude throughout the splanchnic region, we examined the various components that make up total splanchnic tissue, i.e., stomach, small and large intestines, spleen, pancreas, and several types of adipose tissue.

Methods
The procedures used to measure arterial blood pressure, cardiac output, and regional distribution of cardiac output in the unanesthetized rabbit have been described in detail earlier (2). The surgical technique used to achieve SAD has also been presented previously (3).

Splanchnic tissues were handled in the following manner. Ligatures were tied in various locations along the gastrointestinal tract, the stomach and the intestines were then cut away from the mesentery, and the entire gastrointestinal tract was removed from the abdomen. The stomach, duodenum, jejunum, ileum, cecum-appendix, ascending colon, and transverse descending colon were cut apart at the ligatures. The stomach and the cecum-appendix were opened, and their contents were scraped off the mucosa. The contents of the small and large intestines were pressed from the isolated segments. Since the lumen contents weighed about three times more than the tissues themselves and contained considerable amounts of isotope, the total radioactivity of each part of the gastrointestinal tract was taken as the sum of counts found in the tissue and the lumen contents of that tissue (4).

Mesentery was removed from the abdominal cavity and treated separately from gastrointestinal tract organs. The total mesentery included the omentum, the spleen, and the pancreas. The latter consists of streaks of glandular tissue scattered in the mesoduodenum and cannot be totally removed from the mesentery in the rabbit.

Rabbits were not fasted for these studies, because even 4 days of fasting does not empty the stomach and the cecum. Consecutive experiments were carried out on the same day on a SAD and a sham-operated rabbit. Most of the rabbits included in this report were used for studies of systemic and regional hemodynamic patterns up to 30 days after surgery (2). Rabbits studied 31-43 days after surgery were added in the present study.

Results
Table 1 lists the normal tissue weights of gastrointestinal tract organs and mesentery and the distribution (percent) of cardiac output to them. The values were obtained from 13 sham-operated...
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TABLE 1

Tissue Weights and Percent of Cardiac Output to Gastrointestinal Tract Organs and Mesentery of 13 Sham-Operated Rabbits

<table>
<thead>
<tr>
<th>Organ</th>
<th>Weight (g)</th>
<th>Flow fraction* (%)</th>
</tr>
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<tbody>
<tr>
<td>Stomach</td>
<td>22.8 ± 1.7</td>
<td>2.7 ± 0.3</td>
</tr>
<tr>
<td>Duodenum</td>
<td>8.8 ± 1.7</td>
<td>1.8 ± 0.4</td>
</tr>
<tr>
<td>Jejunum</td>
<td>6.0 ± 1.6</td>
<td>1.2 ± 0.4</td>
</tr>
<tr>
<td>Ileum</td>
<td>35.5 ± 4.7</td>
<td>6.2 ± 0.9</td>
</tr>
<tr>
<td>Cecum-appendix</td>
<td>39.8 ± 4.0</td>
<td>4.6 ± 0.8</td>
</tr>
<tr>
<td>Colon Ascending</td>
<td>21.9 ± 3.8</td>
<td>2.2 ± 0.5</td>
</tr>
<tr>
<td>Transverse descending</td>
<td>15.0 ± 4.0</td>
<td>1.3 ± 0.4</td>
</tr>
<tr>
<td>Mesentery*</td>
<td>41.3 ± 11.0</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
<td>Total</td>
<td>191.0 ± 4.1</td>
<td>21.7 ± 0.5</td>
</tr>
</tbody>
</table>

Values are means ± SD; the average postoperative time of study was 26 days.

* Fraction of total body counts multiplied by 100 equals the percent of cardiac output.

† Includes the spleen, pancreas, and omentum.

rabbits when their body weights had returned to or above preoperative levels and their hemodynamic values (2) were similar to those for normal unanesthetized rabbits reported by others (5).

The hemodynamic basis of the hypertension beginning 3 days after SAD was high total peripheral vascular resistance (TPR) in most of the rabbits; in a few, high cardiac output maintained the hypertension (2). Except where specifically noted, regional splanchnic data were obtained from a group of nine SAD rabbits with high TPR. Their systemic and total splanchnic hemodynamic characteristics compared with those of the sham-operated group were, respectively, cardiac output 203 ± 14 and 227 ± 20 ml/min kg⁻¹ (-10%, P = ns), mean arterial blood pressure 105 ± 14 and 81 ± 6 mm Hg (+30%, P < 0.01), splanchnic blood flow 71 ± 6 and 81 ± 10 ml/min 100 g⁻¹ (-14%, P < 0.02), and splanchnic resistance 1.5 ± 0.03 and 1.01 ± 0.017 mm Hg/(ml/min 100 g⁻¹) (+47%, P < 0.001).

Figure 1 shows that the large increase in total splanchnic resistance among SAD rabbits was the result of a significant increase in the resistance of all component tissues of the splanchnic bed. The magnitude of the increase compared with values from sham-operated rabbits was, however, variable from region to region. The stomach and jejunum had the largest increases, 77% and 64%, respectively, above values for sham-operated rabbits, and the cecum-appendix and ascending colon showed the smallest increases, 34% and 35%, respectively.

Although total splanchnic blood flow was only 14% lower in SAD rabbits than it was in sham-operated rabbits, spleen, stomach, jejunum and transverse descending colon flows were 20–26% lower. All other differences were less than 15%. Flow values for both groups are shown in Figure 2.

There was a gradient of blood flow in the intestines that was maximum in the duodenum and minimum in the transverse descending colon, i.e., an aboral gradient of blood flow. Mesenteric mean blood flow was lower than that in the transverse descending colon and so followed the gradient. However, the components of the mesentery, the spleen (Fig. 2) and the pancreas (Table 2), had much higher flows; that of the spleen was the same as that of the stomach. The difference in mean blood flow between the terminal small intestine and the beginning of the large intestine, i.e., the ileum and cecum-appendix, was statistically significant as were flow differences within adjacent regions of the large intestine (Fig. 2).

Differences in mean blood flow between adjacent regions of the small intestine did not achieve statistical significance as the result of individual variation in patterns of intestinal flow. This phenomenon is illustrated in Figure 3 where data were grouped according to the duodenal-jejunal flow pattern. Those rabbits of both groups with an aboral gradient between these two regions are considered in the left sections of the figure. Flow was maximum in the duodenum of only 4 of the 13 sham-operated rabbits (38%) and was significantly higher (P < 0.05) than it was in each of the remaining groups of sham-operated rabbits considered in the middle and right sections of Figure 3. The incidence of maximum flow being in the duodenum rose to 7 of 9 (78%) in SAD rabbits; their duodenal flow rate was less (P < 0.01) than that in the 4 sham-operated rabbits with similar aboral patterns (Fig. 3, left). When jejunal flow was 122 ml/min 100 g⁻¹ or less, as it was in 6 of 9 SAD rabbits and 5 of 13 sham-operated rabbits, the gradient between it and the ileum was lost, and ileal flow was the same or higher than flow in the jejunum. In the large intestine of most rabbits, the cecum-appendix had the highest flow rate, although the ascending colon showed the highest rate in a few rabbits of both groups.

The total mesentery received about the same fraction of cardiac output as did the duodenum, but it weighed four to five times more (Table 1). In addition to the spleen, other components of the mesentery, namely, the pancreas, the mesenteric...
adipose tissue, and the omental adipose tissue, were studied in a few rabbits of both groups (Table 2). In all three tissues of SAD rabbits, vascular resistance was increased to different degrees. Flow was markedly reduced to the pancreas and the mesenteric adipose tissue, as it was to the spleen; however, flow to the omental adipose tissue was not reduced.

Splanchnic tissues were studied in four SAD rabbits whose basis of hypertension was a 36% average increase in cardiac output; their total splanchnic flow was increased 20% and their splanchnic resistance was increased 12% compared with values for sham-operated rabbits. These changes were the net effect of large flow increases in the ileum (32%, $P < 0.01$) and cecum-appendix (53%, $P < 0.01$), with essentially normal flows elsewhere, and large resistance increases of more than 45% in the stomach and the spleen, with small resistance changes in the remaining areas.

**Discussion**

This study showed that the large increase in total splanchnic resistance found in chronic SAD hypertensive rabbits (2) was the result of increased resistance in all parts of the gastrointestinal tract and the mesentery. The magnitude of increase, however, compared with values for the sham-operated rabbits, varied from one area to another, ranging from 34% in the cecum-appendix to 77% in
the stomach; all increases were statistically significant (Fig. 1). In this same group of SAD rabbits, the largest flow reductions (Fig. 2), 20–26%, were found in the stomach, transverse descending colon, jejunum, and spleen (Fig. 2); from a limited number of observations, the pancreas and the mesenteric adipose tissue had flow reductions of 27–42% (Table 2). Flow was close to normal in other gastrointestinal tract areas and in the omental adipose tissue.

The results indicated that the degree of increased vasoconstrictor tone was unequal in different tissues supplied by the same major artery as well as by different arteries. Thus, in the particular group of SAD rabbits studied in the present paper, liver arterial blood flow was close to the normal value (−15%, P = NS) reported for a larger group of rabbits (2). The stomach and the pancreas showed significant reductions in flow, but resistance was increased 25% more than it was in the liver arterial circulation. All three of these tissues receive all or most of their blood supply through branches of the

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FIGURE 2

Mean blood flow in gastrointestinal tract organs, total mesentery, and spleen of sham-operated and SAD hypertensive rabbits. Abbreviations and P values are the same as they are in Figure 1. The difference in flow rates between successive parts of the intestine within each group's gradient reached the following levels of statistical significance of < 0.1 or better. Sham-operated rabbits: jejunum and ileum P < 0.1, ileum and cecum-appendix P < 0.001, cecum-appendix and ascending colon P < 0.05, ascending colon and transverse descending colon P < 0.05, and transverse descending colon and mesentery P < 0.001. SAD hypertensive rabbits: duodenum and ileum 0.05 > P > 0.02, ileum and cecum-appendix P < 0.001, ascending and transverse descending colon P < 0.01, and transverse descending colon and mesentery P < 0.001.
TABLE 2

Effect of SAD Hypertension on Hemodynamics of the Pancreas and the Mesenteric and Omental Adipose Tissues

<table>
<thead>
<tr>
<th></th>
<th>Sham-operated rabbits (N = 4)</th>
<th>SAD rabbits (N = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Flow (ml/m100 g⁻¹)</td>
<td>Resistance (mm Hg/ml/min 100 g⁻¹)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>38.5 ± 2</td>
<td>2.0 ± 0.2</td>
</tr>
<tr>
<td>Adipose tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenteric*</td>
<td>10.6 ± 4</td>
<td>8.2 ± 3.0</td>
</tr>
<tr>
<td>Omental</td>
<td>8.6 ± 3</td>
<td>9.6 ± 3.0</td>
</tr>
</tbody>
</table>

Values are means ± sd. The SAD group had a 16% lower cardiac output (P < ns) and a 30% higher mean arterial blood pressure (P < 0.01) than did the sham-operated group.

* Only two SAD values.

celiac artery (6). Both the ileum and the jejunum receive blood through the superior mesenteric artery branches, but jejunal flow was reduced 20% in SAD rabbits compared with a 12% reduction in the ileum. Moreover, resistance in the jejunum was increased 27% more than it was in the ileum.

We have shown that norepinephrine synthesis is increased in splanchnic blood vessels as well as in other organs of SAD rabbits (1, 2). Variability of smooth muscle sensitivity to a given level of sympathetic activity could contribute to the net hemodynamic effect. Colon and mesentery in the conscious cat are the only regions that respond with a significant reduction in blood flow to 90 seconds of hypothalamic stimulation (7). In the present study of the effects of chronic activation of the sympathetic nervous system, the transverse descending colon and the mesentery both had more than a 50% increase in resistance and the colon had a significant reduction in flow.

The celiac artery and its branches were very sensitive to the effects of SAD. In the group of four
SAD hypertensive rabbits with high cardiac output, total splanchnic resistance showed only a 12% increase, but vasoconstrictor tone was high enough in the celiac bed to raise resistance in the stomach and spleen more than 45% above values for sham-operated rabbits. The ileum and cecum, in contrast, had normal resistances; their blood supply is through branches of the superior mesenteric artery. Apparently the degree of vasoconstrictor tone in chronic SAD hypertensive rabbits is highly variable within the splanchnic bed so that, against a raised head of arterial blood pressure, blood flow can be normal, below normal, or even at times above normal in component splanchnic tissues.

Ross (8) has proposed, from findings in acute studies of mesenteric circulation when arterial blood pressure is allowed to rise, that the escape of intestinal vessels from vasoconstriction caused by nerve stimulation may be characteristic of the smooth muscle of particular vessels. The vasculature of the ileum, cecum-appendix, and ascending colon—all supplied by branches of the superior mesenteric artery in the rabbit—seemed to be the least susceptible and that of the stomach, spleen, pancreas, jejunum, and transverse descending colon seemed to be the most susceptible to increased vasoconstrictor effects of chronic sympathetic activation by buffer nerve denervation.

FLOW GRADIENTS

The **Rb method permitted us to determine whether rabbits have a blood flow gradient within the intestinal tract, information not published previously, and whether hypertensive rabbits show a flow pattern the same as that in normotensive rabbits. Normal (sham-operated) rabbits did have an aboral flow gradient between the small and large intestines; the cecum-appendix had a significantly lower flow rate than did the ileum. Neither the fasted dog (9) nor the cat (7) show an aboral gradient between the small and large intestines; rather, colon flow exceeds that of the small intestine. In contrast, the fasted rat (10, 11) does show an aboral gradient as did the unfasted rabbit in the present study. **RbCl was the indicator used in all of these studies. When electromagnetic flow probes were used for flow measurements in the anesthetized dog, an aboral gradient was found between the small and large intestines (12).

Aboral flow gradients are present within both the small and large intestines of dogs, cats, and rats in the above-mentioned studies, as they are in our nonfasted rabbits. Mean flows in the three parts of the small and large intestines did form an aboral gradient, although differences between adjacent parts were not all statistically significant (Fig. 2) because of considerable variation in values among sham-operated rabbits. Only about 33% of the sham-operated rabbits had a duodenal flow higher than their jejunal flow, whereas the incidence increased to 78% at lower absolute flows among hypertensive rabbits (Fig. 3). Moreover, in the latter group as a whole, mean ileal flow was significantly lower than duodenal flow, whereas it was not in sham-operated rabbits (Fig. 2). Thus, chronic activation of the sympathetic nervous system, providing a high level of vasoconstrictor tone, tended to reduce individual variability and increase the incidence of aboral intestinal flow gradients. If the decreasing gradient of blood flow is the result primarily of decreasing energy requirements along the intestinal trace, then even a small reduction in total flow, as was present in hypertensive rabbits, seems to promote closer adherence to the balance between flow distribution and tissue needs.

References

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