Measurement of Local Blood Flow of the Intestine by Hydrogen Clearance Method; Experimental Study

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ABSTRACT: Local blood flow of the bowel wall was measured by hydrogen clearance method both in the muscular and submucosal layers in the mongrel dog, separately and concurrently. A platinum wire electrode with a bare tip of 0.5 mm in length and 0.2 mm in diameter was inserted into each layer. About 10 per cent hydrogen gas was inhalated directly through the side hole attached to the endotracheal tube for 1–2 minutes and the obtained clearance curves were plotted on the semi-logarithmic scale, which was almost monoexponential.

The results obtained were as follows:

1) Mean basal perfusion rate of the muscular layer of the intestine was 0.81–0.92 ml/min/gm, whereas that of the submucosal layer was 1.29–1.31 ml/min/gm, respectively. There was little difference of perfusion rates between the small and the large intestine. The results showed good correlationship with those reported by other authors.

2) The effect of vasoactive substances such as vasoconstrictor and vasodilator on the local blood flow in the bowel wall was confirmed.

3) This method is repeatedly applicable for measurement and also renders the information on the distribution of blood flow in the splanchnic area.

KEY WORDS: platinum electrode, hydrogen clearance method, intestinal blood flow, blood flow of the muscular layer, blood flow of the submucosal layer, venous outflow method, vasoactive substances.

INTRODUCTION

The spontaneous and reversible nature observed in some of the episodes of colonic ischemia was first emphasized by Boley and Schwartz in 1963.[2] Thereafter, transient and reversible ischemic lesions of the intestine have been interested by many investigators, particularly in connection with the distribution of the blood flow in the intestinal wall.

Various methods have been developed for the measurement of the blood flow in the tissue. Kety and Schmidt[5] introduced the use of innert gas for this purpose. In 1964, hydrogen clearance method was adapted for the measurement of local blood flow in the myocardium and renal cortex of anesthetized dogs.[1] In this method, the local blood flow was measured with continuous recording in the tissue hydrogen concentration, after direct insertion of the electrode into the tissue.

This study had two purposes, the first being to measure the local blood flow of the bowel wall by the hydrogen clearance method, and the second to make a comparison between this method and direct venous outflow method currently available.

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Materials and Methods

Adult mongrel dogs weighing 12–15 Kg were used without regard to sex. All animals were fasted overnight and anesthetized with Nembutal. A catheter was introduced into femoral or forearm artery to monitor arterial blood pressure and another into the accompanying vein to inject some vasoactive substances. Sufficient and constant ventilation during procedure was provided with endotracheal positive pressure respirator. The modified hydrogen clearance method of Aukland et al.[1] was used for measurement of the local blood flow of the intestinal wall. Hydrogen gas of about 10 per cent concentration was inhalated through the side tube attached to the tracheal cannula for 1–2 minutes. The measuring circuit for hydrogen concentration consisted of a tissue electrode which was connected to Unique Medical PHG 200. The electrode was inserted directly into the bowel wall and the variations in hydrogen concentration after hydrogen gas inhalation were recorded with Ohkura D2R Type M recorder.

The tissue electrode was made from a piece of an epoxide coated platinum of 0.2 mm

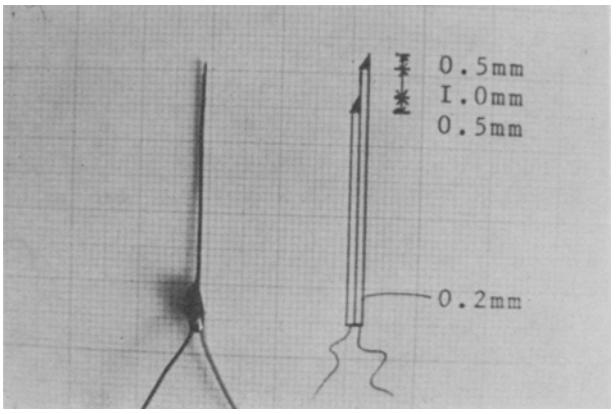

Fig. 1. Double tipped platinum electrode used for measuring the intestinal blood flow.

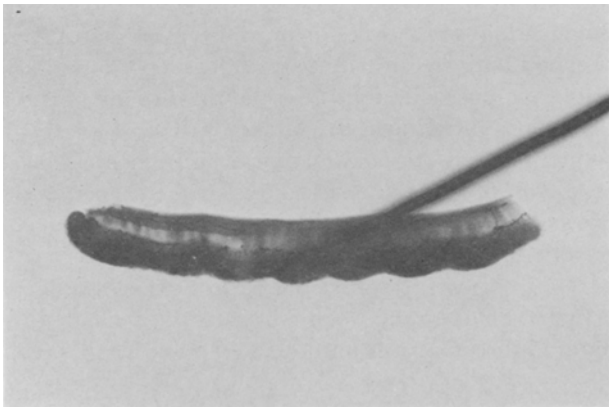

Fig. 2. Softex photograph. Each tip of the electrodes was inserted into the muscular and submucosal layers separately.

in diameter and of 5.0 cm in length. The bare tip was 0.5 mm long and was tapered for easy insertion into the bowel wall. Double tipped electrodes were devised to measure tissue hydrogen concentration both in the muscular and submucosal layers concurrently (Fig. 1). As shown in Fig. 2, each tip of the electrode was inserted into the muscular and submucosal layers separately, the position being confirmed by Softex photographs taken after microbarium injection into the branches of the superior mesenteric artery.

The basal blood flow of the bowel wall was estimated for 47 times in the muscular layer of the small intestine in seven dogs, for 26 times in the submucosal layer in six, for 50 times in the muscular layer of the large intestine in eight, and for 33 times in the submucosal layer in seven.

In separate experiments, the effects of vasoactive substances on the local blood flow in the bowel wall was studied. As a vasoconstrictor drug, 0.01 μg/Kg of Vasopressin was injected into the regional artery of the bowel and the blood flow both in the muscular and submucosal layers was measured. The effect of vasodilator on the local blood flow of the intestine was also studied before and after intraaortic injection of 30 mg of Papaverine hydrochloride.

The local blood flow (F) was calculated from the following formula.

$$F = \lambda \frac{0.693}{T\ 1/2}\ \text{ml/min/gm}$$

where λ is the tissue/blood partition coefficient, defined as 1.0 by Aukland, and T 1/2 is the time in minute for tissue hydrogen concentration to be reduced to half of its numerical value and is readily obtained from the slope of a tissue desaturation curve plotted on a semilogarithmic scale (Fig. 3).

When hydrogen clearance curve showed a biexponential curve, the data were discarded. These cases were encountered in 16 measurements among total of 383 experiments, namely, 11 of 271 measurements in the muscular layer and five of 112 measurements in the submucosal layer, respectively.

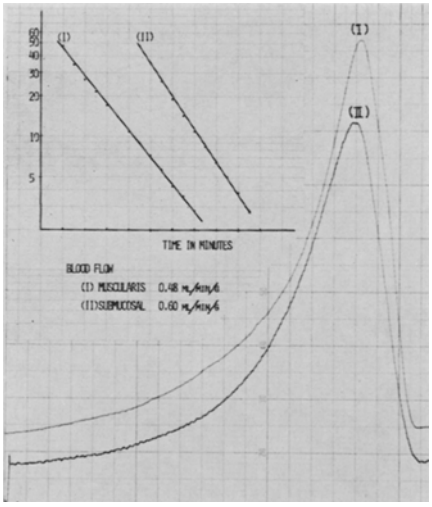

Fig. 3. Typical saturation and hydrogen clearance curve in the canine intestine.

Comparison of the Hydrogen Clearance Method with the Venous Outflow Method

The availability of other methods for estimating the intestinal blood flow lends this organ to validation of a new method of estimating blood flow. This study was carried out to determine if this new technique could estimate local blood flow of the intestine accurately. For this purpose, the results obtained from the hydrogen clearance method were compared with the venous outflow method.

Heparin was given to prevent clotting in the extracorporeal circuit. A 15 cm segment of the small intestine was isolated on a vascular pedicle consisting of the main mesenteric artery and vein. The branch of the superior mesenteric vein coming from this isolated segment was cannulated with a polyethylene catheter of 2–3 mm in internal diameter. In order to avoid the influence of the collateral circulation from the adjacent mesenterium and bowel wall on the local blood flow, the mesenterium was separated, leaving only the arterial supply intact. Intestinal venous blood was drained into a bottle and blood flow was estimated directly by measuring the accumulation of blood for 1 or 2 minutes.

Because the blood flow was influenced by the surgical manipulation, it was necessary to avoid the venous stasis by holding an outflow orifice at the same level of the inferior vena cava. The accumulated blood was pumped back mannually to the femoral vein immediately after measurement.

During direct measurement of venous outflow, the tissue electrodes were placed into

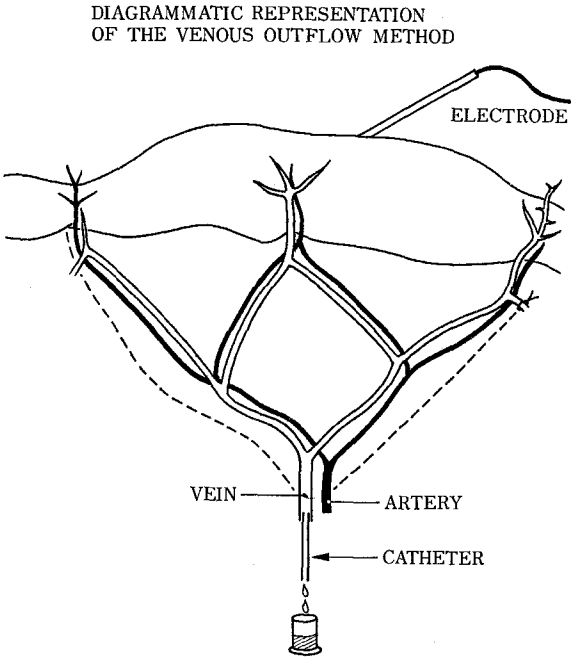

Fig. 4. Simultaneous measurements of the intestinal blood flow by direct and indirect methods.

the antimesenterial portion of the bowel wall at the midst of the prepared segment and the hydrogen clearance was recorded (Fig. 4).

The intestinal segmant was resected after completion of the experiment. Both the muscular and submucosal layers of the intestine were then weighed and were used for calculating venous outflow per gram per minute, and the values obtained were compared with those from hydrogen clearance method. The experiments were carried out for 18 times at 12 intestinal segments in four dogs.

Results

1. Basal Flow

The mean basal perfusion rate was 0.81 ml/min/gm in the muscular layer and 1.31 ml/min/gm in the submucosal layer of the small intestine, and 0.72 ml/min/gm in the muscular layer and 1.29 ml/min/gm in the submucosal layer of the large intestine, respectively (Table 1). The difference in perfusion rate between the muscular and submucosal layer was significant both in the small and large intestine, however, there was little difference in the local blood flow between the small and large intestine.

2. Effects of Vasoconstrictor Drug

Fig. 5 shows the changes in the hydrogen clearance curve and the estimated local blood flow in the bowel wall before and after regional arterial injection of Vasopressin.

Table 1. Comparison of the canine intestinal blood flow measured by different methods

		Authors	Mackie	Delaney	Kiribuchi
Small intestine	Muscularis	0.81±0.24	0.85±0.10	0.72±0.11	0.54±0.05
	Submucosa	1.31±0.38			
Large intestine	Muscularis	0.92±0.23		0.82±0.10	
	Submucosa	1.29±0.37			

ml/min/gm

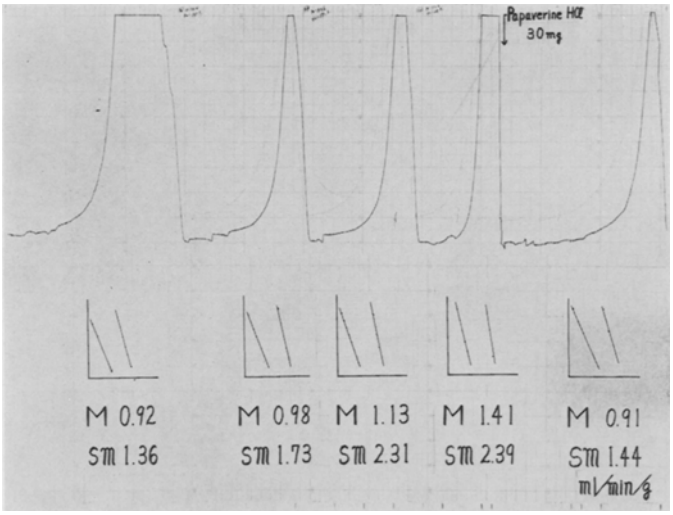

Fig. 5. Effect of Vasopression on the canine intestinal blood flow. Right to Left. M: muscularis, sm: submucosa.

Immediately after injection the blood flow decreased significantly both in the muscular and submucosal layers. More than 50 per cent decrease was observed in the former. The pulse rate unchanged, although the blood pressure showed slight elevation. The decrease of the local blood flow induced by Vasopressin continued for about 50 minutes.

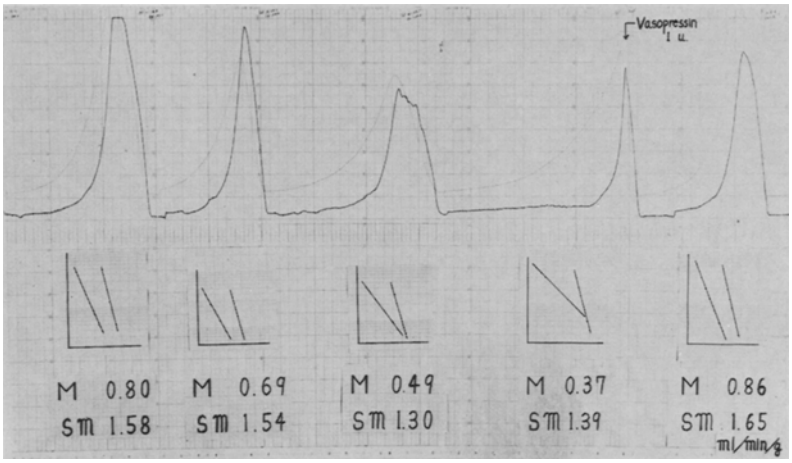

Fig. 6. Effect of Papaverine hydrochloride on the canine intestinal blood flow. Right to Left. M: muscularis, sm: submucosa.

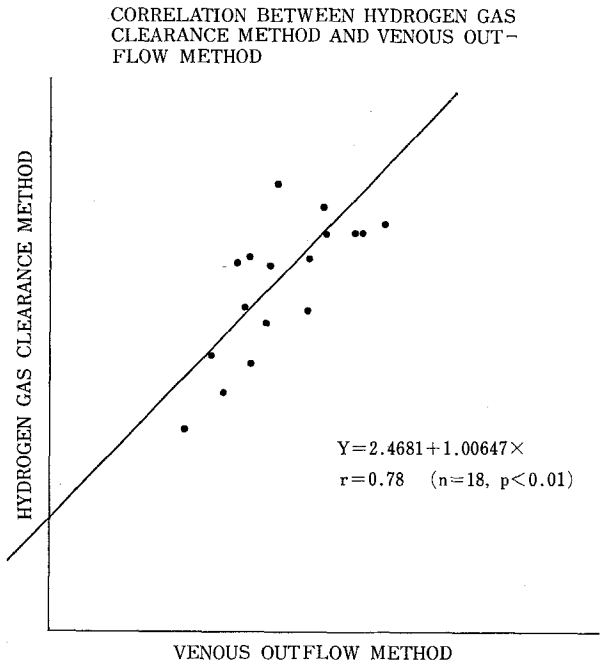

Fig. 7. Comparison between hydrogen gas clearance method and direct venous outflow method.

3. Effects of Vasodilator Drug

Fig. 6 shows the changes in the hydrogen clearance curve and the estimated local blood flow in the large intestine before and after intraaortic administration of Papaverine hydrochloride. Administration of Papaverine induced a marked augmentation of the local blood flow, but the duration of its vasodilating effect was rather short.

4. Comparison with the Venous Outflow Method

Fig. 7 shows the correlation between the hydrogen gas clearance method and the venous outflow method. The correlationship was statistically significant ($p<0.01$), correlation coefficient being 0.78 and recurrent line $Y=2.4681+1.0065X$.

Discussion

Aukland reported that the decay constant of hydrogen gas tissue desaturation as detected by a platinum black electrode was equal to blood flow per unit volume of tissue. Hyman[4] demonstrated that the platinum black enamel electrode system produced a current that was directly proportional to hydrogen partial pressure.

In the present study, we used the electrode of 0.2 mm in diameter. LaMorgese et al.[6] compared the validity of the electrodes with 0.05 mm, 0.25 mm and 0.45 mm in diameter and concluded that the electrode of 0.25 mm in diameter was most reliable and reflected well the changes in the blood flow caused by autoregulatory mechanism of the cerebral circulation.

We used about 10 per cent hydrogen gas for inhalation, because it had little influence on the arterial gas partial pressure.[9] As to the inhalation, Pasztor et al.[8] reported that the time necessary for stabilization of hydrogen diffusion into tissue depended upon the blood flow rate of the tissues and that the inhalation time ranging from 1 minute to 7 minutes had little influence on the hydrogen clearance curve obtained in the brain tissue. Aukland stated that the effect of recirculation might be kept at a minimum by using a short administration period for the most highly perfused tissues, while a relatively longer period of administration should be used for tissues in the intermediate or low flow range. Our preliminary study showed that inhalation of hydrogen gas through a side hole of the respirator for 1–2 minutes was sufficient for measurement of the local blood flow of the bowel wall.

In our studies, there was little difference in the local blood flow between the small and large intestine. The results were consistent with those obtained by Mackie[7] and by Delaney,[3] the hydrogen clearance method being used in the former and ^{86}Rb clearance method in the latter. However, the volumes of the local blood flow were somewhat higher than those obtained by direct venous outflow method. Aukland noticed that the hydrogen clearance method was best indicated for measurement of blood flow less than 1.5 ml/min /gm and under favourable condition at flows up to 5.0 ml/min/gm.

The main virtue of the hydrogen clearance method is its applicability to repeated measurements. It also provides informations on the distributions of the blood flow in the splanchnic area. Injury to the bowel wall due to insertion of electrodes and influence of arteriovenous fistula in the bowel wall would not be neglegible, however, these do not appear to be a major problem, since reliable measurements of regional blood flow were obtained from the hydrogen clearance curve.

As the treatment for the massive intestinal bleeding, local infusion of Vasopressin has been widely used. However, to our knowledge, the literature reporting the measurement of the local blood flow of the bowel wall after intraarterial administration of such

vasoconstrictors seems very few. In our study, the lowering of the perfusion rate in the bowel wall by vasoconstrictors was confirmed, especially in the muscular layer, lasting for about 50 minutes.

It is also widely accepted that the intraarterial infusion of vasodilators such as Papaverine hydrochloride and Prostaglandin E_1 is effective for the cases with ischemic enterocolitis or non-occlusive bowel ischemia. Our study showed a marked augmentation of the regional blood flow after local administration of the vasodilating drugs.

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References

1. Aukland, K., Bower, B.F. and Berliner, R.W.: Measurement of local blood flow with hydrogen gas, *Circulation Res.* 14: 164–187, 1964.
2. Boley, S.J., Schwartz, S., Lash, J. and Sternhill, V.: Reversible vascular occlusion of the colon, *Surg. Gynec. Obstet.* 116: 53–60, 1963.
3. Delaney, J.P.: Chronic alterations in gastrointestinal blood flow induced by vagotomy, *Surg.* 62: 155–157, 1967.
4. Hyman, E.S.: Linear system for quantitating hydrogen at a platinum electrode, *Circulation Res.* 9: 1093–1097, 1961.
5. Kety, S.S. and Schmidt, C.F.: The determination of cerebral blood flow in man by the use of nitrous oxide in low concentrations, *Am. J. Physiol.* 143: 53–66, 1945.
6. LaMorgese, J., Fein, J.M. and Schulman, K.: Polarographic and microsphere analysis of ultraregional cerebral blood flow rates in the cat. in Harper, A.M., Jennet, W.B., Miller, J.D. and Rowan, J.O.: Blood flow and metabolism in the brain. pp. 7.3–7.8, London, Churchill Livingstone, 1975.
7. Mackie, D.B. and Turner, M.D.: The effect of truncal vagotomy on jejunal and ileal blood flow, *J. Surg. Res.* 11: 356–363, 1971.
8. Pasztor, E., Symon, L., Dorsch, N.W. and Branston, N.M.: The hydrogen clearance method in assessment of blood flow in cortex, white matter and deep nuclei of baboons, *Stroke* 4: 556–567, 1973.
9. Tamura, A., Asano, T., Tak, Y., Manaka, S., Hirakawa, K. and Sano, K.: Measurement of cerebral blood flow with hydrogen clearance method, *Noh to Shinkei (Brain and Nerve)* 30: 47–54, 1978 (in Japanese with English summary).