

PROXIMAL - DISTAL GRADIENT OF MEMBRANE pH IN THE RAT
ALIMENTARY CANAL UNDER NORMAL CONDITIONS AND AT
VARIOUS TIMES AFTER BILATERAL TRUNCAL VAGOTOMY

A. Yu. Tsibulevskii and A. P. Éttinger

UDC 616.833.191-089.85-092.9-07:616.
33-008.821-074

KEY WORDS: alimentary canal; membrane pH; gradient; vagotomy.

Vagal denervation of the stomach is nowadays widely used (separately and in conjunction with other procedures) in the surgical treatment of duodenal ulcers. This operation can produce a lasting decrease in acid secretion in the stomach and it thus provides a method of acting on the most important stage in the pathogenesis of this disease, namely, the peptic factor [1, 5, 10, 11]. However, it must be remembered that truncal vagotomy affects not only the stomach, but also other portions of the digestive system and, in particular, the intestine. This problem has not yet been sufficiently widely reflected in the literature. There are only isolated reports dealing mainly with a morphological and functional analysis of the state of the duodenum and jejunum under these conditions [8, 13]. Meanwhile investigation of the various aspects of the effect of division of the vagus nerves on the digestive system and, in particular, on the membrane pH profile of the gastrointestinal tract is of definite theoretical and practical importance: on the one hand, to obtain a deeper understanding of the mechanism of homeostasis of this important physiological parameter, and on the other hand to predict the consequences of operations accompanied by vagotomy. The study of the dynamics of the change in membrane pH at different times after vagotomy in order to detect critical phases in the state of the digestive system after the operation is particularly interesting. On the basis of these considerations it was decided to study the character of the membrane pH profile in different parts of the subdiaphragmatic portion of the alimentary canal after bilateral truncal vagotomy.

EXPERIMENTAL METHOD

Experiments were carried out on 80 noninbred male albino rats weighing 150-180 g. Bilateral subdiaphragmatic truncal vagotomy was performed on 50 animals and the rest served as the control. Under urethane anesthesia (intraperitoneal injection in a dose of 150 mg/100 g) the membrane pH was measured in the body of the stomach, the duodenum, jejunum (middle portion), ileum (terminal portion), cecum, and rectum 1, 3, 7, 14, 30, 60, and 220 days after the operation and after starvation for 24 h. A thin pH-probe and pH-meter (the pH-340) were used for the measurements, by Linar's method [4]. To determine the pH in the stomach the probe was introduced per os, and to determine pH in the rectum, the probe was introduced per rectum (to a depth of 3-5 cm); in all other cases the probe was applied to the required region through an opening made at a distance of 5-7 cm from the measuring point. To describe the membrane pH gradients in the alimentary canal quantitatively, we used a coefficient E, the ratio of the membrane pH of the proximal portion to the corresponding value in the distal portion, between which the gradient was determined. The results of the measurements were subjected to statistical analysis by R. B. Strelkov's method.

EXPERIMENTAL RESULTS

The results (Table 1) showed that a proximal-distal membrane pH gradient exists in intact rats deprived of food for 24 h. One day after vagotomy, although the general character of the membrane pH profile of the gastrointestinal tract still remained, there was a very small increase in pH in the stomach, the pH drop was reversed in the ileum-cecum sector ($E = 1.01 \pm 0.29$ compared with 0.91 ± 0.004 in the control), and a certain fall of pH occurred in the cecum and rectum. Since these changes did not differ statistically signifi-

Department of Histology and Embryology, Faculty of Internal Medicine, and Laboratory of Gastroenterology, Central Research Laboratory, N. I. Pirogov Second Moscow Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. Kh. Vasilenko.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 91, No. 1, pp. 26-28, January, 1981. Original article submitted February 18, 1980.

TABLE 1. Membrane pH in Different Parts of the Alimentary Canal of Intact and Vagotomized Rats

Group of animals	Time after vagotomy, days	Stomach	Duodenum	Jejunum	Ileum	Cecum	Rectum
Intact (control)	—	5,52±0,06	7,85±0,04	8,08±0,05	8,93±0,05	9,81±0,08	8,71±0,06
Undergoing mock operation	Initial value	5,15±0,26	7,40±0,08	8,31±0,06	8,37±0,09	8,44±0,12	8,62±0,16
	1	6,48±0,34	7,90±0,13	8,07±0,10	8,99±0,53	8,90±0,31	8,03±1,34
	3	6,10±0,35	7,54±0,34	7,83±0,14	8,38±0,18*	8,98±0,29	7,93±0,30
Vagotomized	7	7,59±0,14*	7,56±0,08*	7,91±0,06	8,40±0,09*	9,12±0,11*	8,46±0,11
	14	5,72±0,83	7,82±0,19	8,13±0,11	8,45±0,09*	9,19±0,22	7,84±0,45
	30	6,32±0,33	7,59±0,04	7,75±0,07	8,38±0,08	9,06±0,09*	8,47±0,08
	60	6,85±0,42*	8,00±0,16	8,32±0,18	8,93±0,21	9,97±0,18	9,00±0,21
	220	6,81±0,29*	8,03±0,11	8,17±0,11	9,18±0,07	9,90±0,07	9,10±0,24

*Statistically significant differences from control (at $P < 0.05$).

cantly from those in animals undergoing a mock operation at the same time, in all probability they should be regarded as the result of a nonspecific reaction of the digestive system to the operation. On the third day after the operation the ileocecal membrane pH gradient was restored ($E = 0.93 \pm 0.02$), but the membrane pH in the ileum was lower than in the control. Seven days after vagotomy the structure of the pH profile of the alimentary tract was altered even more. For instance, as a result of the increase in the pH of the stomach and its decrease in the duodenum, the gastroduodenal membrane pH gradient became equalized ($E = 1.004 \pm 0.02$ compared with 0.070 ± 0.005 in the control) and the absolute values of membrane pH in the ileum and cecum decreased despite preservation of the local physiological gradient. At the same time there was a tendency toward normalization of the membrane pH in the rectum. The character of the proximal-distal gradient and the absolute values of membrane pH in the gastrointestinal tract of the vagotomized rats 14 days after the operation were indistinguishable on the whole from the corresponding values in intact animals. However, the membrane pH in the ileum was significantly reduced; in addition, a tendency was found for the pH in the cecum and rectum to fall. Thirty days after vagotomy, while the general structure of the pH profile of the alimentary canal was unchanged, an increase in membrane pH was observed in the stomach, together with a decrease in its value in the cecum. In the later stages after the operation (60 and 220 days) an increase in the membrane pH was found in the stomach; since at the same time a tendency was observed for the membrane pH in the duodenum to rise, the physiological gradient between these portions of the digestive tract showed no appreciable change ($E = 0.86 \pm 0.03$ after 60 days and $E = 0.85 \pm 0.03$ for 220 days). The values of the membrane pH in other parts of the gastrointestinal tract of the vagotomized rats did not differ significantly from the control.

A proximal-distal membrane pH gradient thus exists in the alimentary canal of intact rats and is characterized by two well-marked local pH drops: between the stomach and duodenum — from acid to weakly alkaline, and between the ileum and cecum — from moderately alkaline to alkaline. In the early stages after the operation (1 and 7 days, but not 3 days) vagotomy leads to disappearance of these physiological gradients: the gastroduodenal after 7 days and the ileocecal after 1 day. In the later stages the membrane pH gradients are restored and maintained at a constant level sufficiently quickly, although the absolute values of membrane pH in the regions of the alimentary tract forming the gradient (or in only one region, in this case, the stomach) may vary. The critical time after vagotomy is evidently 7 days, for in this period changes in membrane pH are observed simultaneously in several components of the alimentary canal (stomach, duodenum, ileum, and cecum) and the gastroduodenal gradient is reversed. After 14 days a temporary and relative normalization of the membrane pH profile of the gastrointestinal tract takes place. In the later stages its structure again becomes reorganized, but the changes in membrane pH in this period are confined to the stomach. The wave-like character of the changes in membrane pH in the alimentary canal after vagotomy coincides with the dynamics of changes in many other functional and structural parameters of the digestive organs under these conditions [2, 3], and it evidently reflects a general rule governing the development of the denervation syndrome in time. With regard to the strictness of homeostasis of the membrane pH after vagotomy, the regions of the gastrointestinal tract studied in these experiments can be arranged in the following order: jejunum, rectum, ileum, cecum, duodenum, and stomach. It is a noteworthy fact that the membrane pH is maintained most strictly in the jejunum, an organ with a high density of nerve fibers of vagal origin, in which considerable changes in membrane pH would be expected after vagotomy. This "disparity" can be explained, in our opinion,

by the fact that the pH in the juxtamural layers of the jejunal contents is one of the most important physiological constants for this organ [6, 7], and many mechanisms (including some which are not nervous in nature) take part in its maintenance, thereby ensuring the constancy of its level in various pathological states. The distal portions of the alimentary canal evidently do not have such precise regulation, and although the relative contribution of the vagus nerves to their parasympathetic innervation is not so great, vagotomy, as stated above, leads to marked changes in their membrane pH profile. It is very probable that the diarrhea, which is a leading manifestation of the postvagotomy syndrome [9, 12], is connected in a definite manner with the changes discovered in the membrane pH profile of the large intestine.

Changes in the membrane pH profile discovered in the gastrointestinal tract after vagotomy thus reflect a general functional reorganization of the alimentary canal under these conditions, a matter of undoubted importance for the organization of its activity at the new level of its function.

LITERATURE CITED

1. I. M. Grigorovskii, *Khirurgiya*, No. 8, 135 (1978).
2. Yu. K. Eletsii, in: *Regulation of Morphogenesis and Regeneration of the Digestive Glands* [in Russian], Leningrad (1974), pp. 6-8.
3. Yu. K. Eletsii, in: *Cytological Mechanism of Histogenesis* [in Russian], Moscow (1979), pp. 109-119.
4. E. Yu. Linar, *The Acid-Forming Function of the Stomach under Normal and Pathological Conditions* [in Russian], Riga (1968).
5. V. S. Mayat, Yu. M. Pantsyrev, Yu. K. Kvashnin, et al., *Resection of the Stomach and Gastrectomy* [in Russian], Moscow (1975).
6. A. M. Ugolev, *Membrane Digestion* [in Russian], Leningrad (1972).
7. R. O. Faitel'berg, *Absorption in the Gastrointestinal Tract* [in Russian], Moscow (1976).
8. A. Yu. Tsibulevskii and Yu. K. Eletsii, *Byull. Éksp. Biol. Med.*, No. 5, 628 (1976).
9. O. L. Shovskii and S. A. Chernyakevich, in: *The Sequelae of Vagotomy* [in Russian], Moscow (1975), pp. 54-61.
10. I. Johnston, *S. Afr. J. Surg.*, 14, 119 (1976).
11. T. Junginger and H. Pichlmaier, *Dtsch. Med. Wschr.*, 104, 127 (1979).
12. S. Morris, *Postgrad. Med. (Minneapolis)*, 65, 219 (1979).
13. W. Schmid, *Acta Anat. (Basel)*, 104, 36 (1979).