Changes in Intestinal Net Absorption of a Sodium Chloride Solution Produced by Atropine in Normal and Vagotomized Dogs

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ABSTRACT

TIDBALL, C. S. AND M. E. TIDBALL. Changes in intestinal net absorption of a sodium chloride solution produced by atropine in normal and vagotomized dogs. Am. J. Physiol. 193(1): 25-28. 1958.—Net absorption of 1% NaCl was studied in acute experiments in dogs anesthetized with sodium pentobarbital. In dogs with intact vagi, net absorption was increased by atropine and then decreased below the preatropine level before returning to that level in approximately 1 hour. In dogs with complete bilateral vagotomies, net absorption was increased by atropine and there was no decrease below the preatropine control level; 1 hour following the injection of atropine the net absorption was still significantly elevated. In dogs with vagi intact or sectioned, increased net absorption following atropine is explained, in part if not entirely, by a depression of secretion. That atropine can produce changes in secretion in vagotomized dogs indicates that acetylcholine produced by intrinsic mechanisms is capable of stimulating secretion in the small intestine. In dogs with intact vagi, decreased net absorption following the increased net absorption is believed to be due to a decrease in true absorption. That this decreased net absorption is not observed in the vagotomized dog is evidence that the vagus exerts a stimulatory influence on true absorption.

As early as 1917 atropine had been reported to stop promptly the flow of intestinal secretion produced by rhythmic vagal stimulation (1, 2). The diluting effect observed when hypertonic solutions were placed in the intestinal lumen was found to be increased by pilocarpine and decreased by atropine and therefore was attributed to secretion (3). Rabinovitch (4) studied the absorption of salts and water in unanesthetized dogs with Thiry-Vella fistulas and reported an increase in net absorption following the administration of atropine. This observation was confirmed by Blickenstaff and Lewis (5) who suggested that secretion might play a role in their results but did not specifically investigate this possibility. Nasset and Parry (6) criticized research on intestinal absorption on the basis that changes in secretion had been overlooked as a factor contributing to changes in net absorption. The present study was undertaken to investigate the influence of cholinergic mechanisms on secretion and true absorption and to clarify the role of these processes in changes in net absorption.

METHODS

The test solution in all experiments was 1% NaCl. Absorption was determined for consecutive 10-minute periods. The surgical, sampling and rinsing techniques were the same as those used in a previous study (7). Dogs were anesthetized with sodium pentobarbital, 33 mg/kg intravenously. Loops 30 cm long were established 1-15 cm caudad to the ligament of Treitz, and were isolated from the remainder of the tract by light string ligatures. A multi-perforated 18 French soft rubber catheter was introduced by way of a small slit on the antimesenteric border of the intestine below the caphalad ligature and tied in place. The loop was rinsed with 20 ml of 0.9% NaCl at 37-39°C, after which it was returned to the abdominal cavity. The incision was closed with

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clamps, leaving only the catheter protruding. Thirty-milliliter volumes of test solution were introduced by way of the catheter. After 10 minutes the fluid remaining in the lumen was withdrawn by gentle suction from a syringe. The loop was rinsed once with 20 ml of the test solution and the wash fluid discarded. If the rinse recovery was greater than 20 ml, this additional volume was added to the amount originally withdrawn. The rinse procedure was standardized at 2 minutes. Additional 30-ml volumes of test solution were then introduced and removed in the same manner. In experiments where atropine was used, 1.2 mg of atropine sulfate dissolved in 4 ml of saline were injected subcutaneously. The injection was performed at the midpoint of the last control period so that a maximal effect might be observed in the next period. Total protein was determined by a modification of the Kingsley method (8). Invertase analyses were made by determining the amount of reducing sugar formed after aliquots of the samples were incubated with 1% sucrose solution for 4 hours at 37°C. The sucrose was dissolved in M/15 phosphate buffer and the method of Folin and Wu (9) was used for the final analysis.

RESULTS

The data include net absorption and relative secretion values in milliliters per 10-minute period for normal and vagotomized dogs receiving atropine. The test periods have been grouped under the following headings: initial, control, postatropine and recovery. The post-atropine periods are subdivided into periods during which net absorption was increased above the control level (phase I) and those periods during which net absorption was decreased below the control level (phase II). The mean net absorption and mean relative secretion under each heading are compared with the corresponding means of the control periods. Where statistically significant differences occur the confidence levels, as determined by the t test, are included.

The net absorption of a 1% NaCl solution was studied in eight normal dogs (N) which did not receive atropine. (The term normal is used to distinguish dogs with intact vagi from those in which bilateral vagotomies were performed.) Figure 1 is a graphic representation of the data obtained from dog N-5. After the initial period net absorption remained relatively constant. The net absorption during the initial period for all N dogs was statistically different from that in each of the succeeding seven periods and was therefore excluded from the calculation of the mean net absorption levels. The net absorption did not change significantly from period to period from the second through the seventh period.

The net absorption of a 1% NaCl solution as influenced by atropine was studied in five normal dogs (N-A). After administration of the atropine during the last control period, net absorption increased sharply and remained elevated for two to three 10-minute periods (phase I). It then decreased to a level less than that of the control periods for one to two 10-minute periods (phase II). Following this biphasic change the net absorption returned to the pre-atropinic control level. A typical experiment from the N-A series is illustrated in figure 2.

The net absorption of a solution of 1% NaCl as influenced by atropine was studied in five dogs in which the vagi were sectioned in the cervical region approximately 1 hour prior to

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A detailed table has been deposited as Document number 5449 with the AD1 Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting $1.25 for photoprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.
the acute intestinal absorption experiment (A V-A), and in five chronically vagotomized dogs. No differences were observed in the pattern of net absorption between the acutely and chronically vagotomized dogs. They are therefore considered as one group (V-A).

In the 10 V-A dogs, injection of atropine was followed by a rise in net absorption (phase I). The increase was of shorter duration (1 to 3 10-min. periods) and of less magnitude than that seen in the N-A group. There was no phase II. In subsequent periods, though the net absorption returned toward the control level, in general it had not reached this level by the end of the experiment (fig. 3). Average net absorption values for the N-A and V-A dogs are illustrated graphically in figure 4, emphasizing the difference in response to atropine.

In order to evaluate changes in secretion occurring at the same time as the changes in net absorption already described, the total protein content of the material recovered from the loops after each 10-minute test period was determined. Since the amount of protein recovered in each period remained constant after the first two, data from these two periods were excluded from the calculation of the average protein secretion for all animals. Protein data are reported in optical density units (O.D.); with the analysis used, 0.09 O.D. is equivalent to 1 mg of 95% pure bovine albumin (Armour's fraction V).

The amount of protein recovered after each period was determined for six of the eight N dogs. The average relative secretion per 10-minute period, as indicated by the protein analyses, was compared with the average net absorption per 10-minute period in the same group. The small changes in net absorption were independent of changes in secretion (fig. 5).

Administration of atropine produced an inhibition of secretion in the dogs of both the N-A and V-A series. The significant decrease in relative secretion was sustained for approximately 1 hour. A summary of the relation between net absorption and relative secretion after atropine administration to normal and vagotomized dogs is represented graphically in figure 6.

**DISCUSSION**

Atropine administration to normal dogs produced a biphasic pattern of net absorption: an increase followed by a decrease. When atropine was given to vagotomized dogs only increased absorption ensued. The second phase of the biphasic response was absent. These results could form the basis for a qualitative difference between the behavior of acutely prepared intestinal loops and chronic fistulas in unanesthetized dogs.

In 21 dogs the total protein content of the material returned from the loops after each 10-minute test period was determined and taken as a relative measure of secretion. The validity of this estimate was strengthened by performing analyses for invertase activity on samples recovered from nine of the same dogs. This specific indicator of secretion and the broad criterion of total protein content failed to show statistical independence indicating that the two methods estimate the same parameter (t0.005, 108 df = 2.86; experimental t = 11.37). It is unlikely that the parameter would be other than secretion. Attempts were made to
collect samples of pure secretion from acutely prepared jejunal loops. The watery portion was so rapidly absorbed that the protein concentration of the remaining fluid was no longer representative of that found in pure secretion. Accordingly the factor relating total protein content to absolute secretion volume could not be determined. However, it was of greater importance to detect changes in secretory rate than to measure absolute secretion volume. Optically density units of protein were therefore used as a relative index of secretion.

The increase in net absorption following atropine administration (phase I) in both normal and vagotomized dogs was paralleled by a decrease in relative secretion. These two processes were not shown to be independent (0.5% confidence level). That atropine was capable of causing an increase in net absorption associated with a decrease in secretion in the vagotomized dog confirms the view that intrinsically produced acetylcholine has a regulatory function in the small intestine. The observations of Youmans et al. (10) concerning regulatory effects of intrinsically produced acetylcholine on intestinal motility may be extended to include a stimulatory effect on intestinal secretion.

The second portion of the biphasic response to atropine in normal dogs was accompanied by relatively little change in the secretory response. Thus the large decrease in net absorption must be explained on the basis of a decrease in true absorption. It is reasonable to interpret that the inhibition of secretion occurs rapidly while inhibition of true absorption occurs at a slower rate, thereby accounting for the biphasic nature of the response. In vagotomized dogs receiving atropine no phase II response occurred. This suggests that increases in true absorption are effected primarily by the vagus and can act independently of changes in secretion. The data also suggest that intrinsic cholinergic fibers are capable of exerting the primary influence in the stimulation of intestinal secretion.

Further evidence for independence of true absorption and relative secretion is gained from examination of data from the normal dogs. After the second test period small changes in net absorption were accompanied by unrelated small changes in secretion.

When both the vagal and intrinsic regulatory mechanisms are intact, the decreased intestinal secretion due to atropine blockade is compensated by a decrease in true absorption. The time required to return the intestine to a state of absorption-secretion balance is ultimately dependent upon the time necessary for vagal recovery. If the vagus has been severed, the effects of atropine blockade remain uncompensated.

It is evident from data reported here that changes in both secretion and true absorption will alter net absorption. The changes are of sufficient magnitude that neither net absorption nor secretion alone can serve as an index of true absorption.

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REFERENCES