The effect of secretin on duodenogastric reflux in vagotomised dogs

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Summary

An experimental study investigated the effect of secretin on duodenogastric reflux in vagotomised dogs. The amount of reflux was estimated by measuring the concentrations of bile phospholipids in the gastric contents. Secretin infusion increased bile reflux into the stomach and promoted the production of lysolecithin from lecithin.

In a recent experimental study we investigated the effect of secretin on duodenogastric reflux in dogs with an intact stomach. It was found that secretin increased bile reflux and promoted the production of lysolecithin from lecithin. The concentration of bile phospholipids in the stomach was 7.7 ± 1.6 mg/dl during basal fasting conditions and 37.4 ± 5.4 mg/dl during secretin stimulation (P < 0.01). The ratio of lecithin to lysolecithin was 3.855 ± 0.519 during basal fasting conditions and 2.161 ± 0.372 during secretin infusion (P < 0.01). In the present study, using exactly the same techniques, an attempt was made to investigate the effect of secretin on duodenogastric reflux in dogs with truncal vagotomy and pyloroplasty (TV + P).

Materials and methods

Four mongrel dogs trained to stand quietly in a Pavlov stand were used and each one acted as its own control. Under general anaesthesia a TV + P was performed and at the same time a Hollander test. The dogs were allowed a period of 2 - 3 weeks to recover before any tests were concluded. Bile reflux was assessed on many separate occasions in each dog in the following way: the animal was starved of food but not water for 16 hours before any scheduled test. On the day of the test the dog was put in a Pavlov stand with no restraint or sedation. The cap of the stomach was removed and the lumen was cleaned of any food remnants. A 10-minute interval was allowed and then a urine bag containing 0.1 g of ethylene diamine tetra-acetic acid (EDTA) was connected to the cannula. EDTA at high concentrations (more than 0.1 ml) prevents the in vitro formation of lysolecithin from lecithin. The gastric contents were collected over a 6-hour period. Two aliquots were taken and stored at -20°C. Immediately after the collection the same procedure was performed during secretin infusion. The infusion was carried out continuously via a Harvard pump at a rate of 1 U/kg/h. Each dog was subjected to a number of tests. The period between two consecutive tests ranged from 5 to 10 days. The collected gastric contents were randomly analysed for lecithin and lysolecithin. These phospholipids were extracted and separated by means of thin-layer chromatography, and their concentration was estimated by phosphorus determination. The efficiency of the technique was estimated by application and recovery of known quantities of pure lecithin and lysolecithin, to both low and high concentrations. The loss was 11.9 ± 0.9% for lecithin and 9.9 ± 0.8% for lysolecithin. The total concentration of these two phospholipids was used as an index of the amount of bile reflux into the stomach. The paired t-test was used for the analysis of the results.

Results

All 4 dogs remained healthy during the experiments. The only complication was minor skin sepsis around the gastrostomy cannula. A total of 60 tests were performed (30 under basal fasting conditions and 30 during secretin infusion).

Secretin increased bile reflux into the stomach and promoted the synthesis of lysolecithin. The concentration of bile phospholipids in the gastric contents under basal fasting conditions was 16.4 ± 10.3 mg/dl and under secretin infusion it was 58.9 ± 10 mg/dl (P < 0.01). The ratio lecithin/lysolecithin was 5.16 ± 0.17 during basal fasting conditions and 1.72 ± 0.29 during secretin stimulation (P < 0.01). It was interesting to observe that within a few minutes of the commencement of secretin infusion, the colour of the collected gastric contents changed abruptly to bright yellow. This bile-stained secretion persisted throughout the test.

The amount of bile reflux and the ratio lecithin/lysolecithin varied from dog to dog and from time to time in the same dog, although the variation between any two dogs was not significant.

Discussion

The techniques used for the collection of gastric contents and the estimation of bile reflux have been extensively discussed previously and no further discussion will take place here. In a recent study we reported that secretin stimulation in dogs with an intact stomach promoted bile reflux. In the present study secretin was again found to increase reflux but significantly more than in dogs with an intact stomach (phospholipid concentrations during secretin infusion: dogs with an intact stomach 37.4 ± 5.4 mg/dl, dogs with TV + P 58.9 ± 10 mg/dl (P < 0.05)). The ratio lecithin/lysolecithin during secretin tests was not significantly different in the two groups (2.16 ± 0.37 for dogs with an intact stomach, 1.72 ± 0.29 for dogs with TV + P (P > 0.05)). Various possible explanations have been offered to explain the increased bile reflux during secretin stimulation: (i) secretin stimulates bile flow into the duodenum and therefore more bile is available for reflux if the local conditions permit; (ii) secretin changes the pressure pattern in the gastroduodenal region, and this may facilitate reflux; and (iii) the secretin used was not highly purified and there is a possibility that certain contaminants, such as cholecystokinin, might have an effect on reflux.

Secretin was found to stimulate the production of lysolecithin from lecithin. Lecithin is the only phospholipid in hepatic bile and is metabolised to lysolecithin by the action of the pancreatic phospholipase A in the presence of trypsin and taurocholic acid. This reaction takes place in the duodenum and upper
jejenum. Secretin increases the flow of hepatic bile into the duodenum, promotes the secretion of pancreatic enzymes, including trypsin, and increases the pH of the duodenal contents. These factors would favor the production of lysolecithin.

Lysolecithin is a known cytotoxic substance which has been implicated in the pathogenesis of chronic gastritis and ulcer. The possible clinical significance of the present findings remains to be shown.

Regarding the observation that secretin stimulation in dogs with TV + P was associated with higher concentrations of bile phospholipids in the gastric contents than in dogs with an intact stomach, there are two possible explanations: (i) secretin decreases the intraluminal pressure of both the stomach and duodenum; destruction of the pyloric sphincter by means of a pyloroplasty might result in even higher bile reflux into the stomach; and (ii) it is possible that the higher concentrations of bile phospholipids in the group of dogs with TV + P might be the result of less dilution of the refluxed material since TV decreases the amount of gastric secretion. This hypothesis is supported by the findings that the mean volume of collected gastric contents during secretin stimulation was only 33.9 ± 2.3 ml in vagotomised dogs compared with 64 ± 5.9 ml in dogs with an intact stomach (P < 0.01). The smaller volumes of gastric contents in vagotomised dogs might also be due to a rapid emptying of gastric fluids because of the vagotomy. However, if this was the case any refluxed material should be evacuated too and therefore the bile concentration in the stomach should not be increased.

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REFERENCES


Cholecystectomy with highly selective vagotomy — the effect on bile reflux

An experimental study

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Summary

An experimental study investigated the effect of highly selective vagotomy (HSV) alone and HSV combined with cholecystectomy on bile reflux into the stomach. The amount of reflux was estimated by measuring the concentration of bile phospholipids in the stomach. Neither HSV alone nor HSV combined with cholecystectomy was associated with increased reflux. In fact HSV seems to prevent reflux and inhibit the production of lysolecithin, which is injurious to the gastric mucosa.

In previous studies it was shown that cholecystectomy in normal dogs and in dogs with truncal vagotomy and pyloroplasty (TV + P) was associated with increased bile reflux into the stomach. In the present study, using the same techniques, the effects of highly selective vagotomy (HSV) alone and HSV combined with cholecystectomy on bile reflux were studied.

Material and methods

Four mongrel dogs underwent HSV and a modified gastrostomy cannula was inserted 8 cm proximal to the pylorus and close to the greater curvature of the stomach. Muscular biopsies of the greater and lesser curvature of the gastric fundus and the antrum were taken. The animals were allowed 2 weeks to recover from the operation. A Hollander test was then performed to assess the adequacy of vagotomy. Bile reflux tests were repeatedly performed in each dog after deprivation of food but not water for 16 hours before any scheduled test. Dogs were put in a Pavlov stand without any restraint or sedation, and the cannula was cleaned of any food remnants. After 10 minutes a bag containing ethylene diamine tetra-acetic acid (EDTA) powder 0.1 g was connected to the cannula. EDTA at concentrations of more than 0.1 mM inhibits the \textit{in vitro} production of lysolecithin from lecithin. The