THE EFFECT OF CHOLECYSTECTOMY ON DUODENOGASTRIC REFLUX

AN EXPERIMENTAL STUDY

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For ELIZABETH

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ABSTRACT

An experimental study was designed to investigate the possible relationship between cholecystectomy and subsequent bile reflux into the stomach under various conditions. Bile reflux was examined after cholecystectomy alone, after truncal vagotomy and pyloroplasty with and without cholecystectomy, and after highly selective vagotomy with and without cholecystectomy. The effect of secretin on bile reflux, alone and under the above conditions was also studied.

Bile reflux is an intermittent phenomenon varying markedly from time to time in the same experimental animal, even during one test. In order to obtain a more meaningful picture, reflux was measured over continuous 6-hour periods. Furthermore, each test was carried out on a number of occasions on each animal. The sum of the concentration of lecithin and lysolecithin in the gastric contents was used as an index of the amount of bile reflux. Lysolecithin is a cytotoxic agent produced from lecithin in the duodenum. Because the ratio of lecithin to lysolecithin in the duodenum varies markedly from time to time and depends on the experimental conditions (eg. vagotomy or secretin infusion), use of only one of these phospholipids as an index of the amount of bile reflux could be misleading. For this reason the total concentration of both phospholipids was used as an index of the amount of bile reflux. Gastric contents were obtained by means of a permanent gastrostomy cannula. By using this technique bile reflux could

be measured over long periods of time. Radioactive biliary markers were considered unsuitable because of certain problems: firstly, excretion of the markers by the liver is completed in about 1 hour, therefore they cannot be used to study reflux over long periods of time. Secondly, there is always some retention of the marker in the gall bladder, therefore the estimated amount of bile reflux before cholecystectomy cannot be compared with that after cholecystectomy.

Histological assessment of the gastric mucosa was carried out at the beginning of the experiments, at the time of cholecystectomy, and at the end of the experiments.

Cholecystectomy alone was found to promote bile reflux into the stomach. This change is probably the result of the continuous flow of bile into the duodenum which follows cholecystectomy. Other possible explanations are discussed. In 3 of the dogs the increased reflux persisted until they were sacrificed, 6 months after cholecystectomy. However, on a further 2 dogs the change was temporary, lasting for about 2 months after cholecystectomy and thereafter returning to pre-cholecystectomy levels. Overall, in 5 dogs the post-cholecystectomy bile reflux was significantly higher than that before cholecystectomy (35 tests before cholecystectomy, 80 tests after cholecystectomy, $p < 0,01$). By the end of the experiments 2 dogs in whom increased bile reflux had persisted for 6 months had developed foveolar hyperplasia of the gastric mucosa. Foveolar hyperplasia is considered to be a marker of bile reflux.

Truncal vagotomy and pyloroplasty alone were not invariably associated with increased bile reflux. In 3 of the 4 dogs with truncal vagotomy and pyloroplasty the amount of bile reflux was not significantly different from that in dogs with an intact stomach. When cholecystectomy was added to the truncal vagotomy and pyloroplasty all dogs had persistently increased bile reflux. This reflux was not significantly higher than in dogs with only a cholecystectomy. These experimental findings lend support to the suggestion that the pylorus might not play a major role in preventing duodeno-gastric reflux. However, this statement is made with some reservation because in the present study pyloroplasty was combined with vagotomy, therefore factors other than pyloroplasty may have interfered with reflux. The ratio of lecithin to lysolecithin in dogs with truncal vagotomy and pyloroplasty was significantly more in favour of lecithin than that in dogs with intact vagi and an intact pylorus. This was so, both before and after cholecystectomy. It seems that truncal vagotomy inhibits the production of lysolecithin from lecithin. Pathophysiologically, this is important because lysolecithin is a cytotoxic agent injurious to gastric mucosa. Two of the dogs had developed histological gastritis by the end of the experiments.

The amount of bile reflux in dogs after HSV was not significantly different from that seen in dogs with an intact stomach; nor was it different from dogs with TV+P in 3 out of 4 cases. Even when cholecystectomy was added to HSV, bile reflux did not increase as

in cholecystectomized dogs with an intact stomach or truncal vagotomy and pyloroplasty. It seems that highly selective vagotomy may actually prevent reflux. After highly selective vagotomy the receptive relaxation of the gastric fundus is lost, resulting in increased intragastric pressures. This high pressure, combined with an intact antro-pyloro-duodenal segment, may tend to prevent reflux or empty any refluxed material faster, before mixing with gastric contents can occur. Highly selective vagotomy seems to inhibit lysolecithin production, both before and after cholecystectomy. None of the dogs with highly selective vagotomy developed any mucosal abnormalities by the end of the experiments.

Secretin is a gastrointestinal hormone which might affect bile reflux by affecting bile flow into the duodenum and by changing the antroduodenal motility. Secretin (Boots) stimulation consistently and significantly promoted bile reflux into the stomach, in all groups of dogs, before and after choelcystectomy. The amount of bile reflux during secretin stimulation in dogs with truncal vagotomy and pyloroplasty was significantly higher than in dogs with an intact stomach or with highly selective vagotomy. The increased bile reflux after secretin stimulation could be the result of changes of pressures across the pylorus.

Secretin promoted lysolecithin production in all groups of dogs, both before and after cholecystectomy. This change could be due to the fact that secretin increases the flow of hepatic bile

into the duodenum, promotes the secretion of pancreatic enzymes, and increases the pH of duodenal contents. These are factors which favour lysolecithin formation.

While recognizing the danger of extrapolation of experimental studies to the human situation, the present experimental findings lend support to the suggestion that in some cases of the so-called post-cholecystectomy syndrome seen in human subjects, the cause could be gastritis caused by abnormal amounts of bile refluxing into the stomach. The therapeutic implication is that in appropriate cases, substances such as cholestyramine which bind bile salts may be beneficial. Again in appropriate cases, a surgical procedure designed to prevent reflux, could be considered.

The results in this study support the view that cholecystectomy combined with truncal vagotomy and pyloroplasty is associated with more reflux than that which occurs after TV+P alone. However, cholecystectomy combined with truncal vagotomy and pyloroplasty was not associated with more reflux than after cholecystectomy alone.

Highly selective vagotomy might be the operation of choice for peptic ulcer, especially when a cholecystectomy has to be carried out for co-existing biliary pathology.

Further investigations are needed to examine the relationship between bile reflux and the post-cholecystectomy syndrome in the human subject, and the possible beneficial effect that HSV may have in the management of the syndrome.

LIST OF ABBREVIATIONS

D/G reflux	=	duodeno-gastric reflux
TV+P	=	truncal vagotomy with pyloroplasty
HSV	=	highly selective vagotomy
CCK	=	cholecystokinin
EDTA	=	ethylenediaminetetracetic acid
TLC	=	thin layer chromatography
DU	=	duodenal ulcer
Total phos.	=	total phospholipids

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DECLARATION

This thesis is the original work of Demetrios Demetriades. Neither the substance or any part of this thesis has been submitted in the past or is to be submitted for a degree in any other university.

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