Effect of diazepam and hyoscine butylbromide on response to secretin and cholecystokinin-pancreozymin in man

J. H. B. SAUNDERS, GUYA MASOERO, AND K. G. WORMSLEY¹

From the Department of Therapeutics, University of Dundee, Dundee

SUMMARY Ten subjects received secretin and cholecystokinin or, in duplicate tests, the two hormones together with either diazepam or diazepam plus hyoscine butylbromide in order to determine whether these drugs, which are often used during retrograde endoscopic cannulation of the pancreatic duct, affect pancreatic and biliary secretion in response to the hormones. Diazepam with hyoscine butylbromide reduced the secretion of trypsin into the duodenum and delayed the appearance of both trypsin and bilirubin in duodenal aspirate. These effects must be taken into account when interpreting pancreatic and biliary responses measured during direct cannulation of the pancreatic duct.

Endoscopic retrograde cannulation of the pancreatic duct has recently been used to measure pancreatic function by collecting the pancreatic juice directly from the pancreatic duct during stimulation with exogenous hormones (Cotton *et al.*, 1974; Gregg *et al.*, 1975; Robberecht *et al.*, 1975). Since sedatives such as diazepam and anticholinergic drugs such as hyoscine butylbromide (Buscopan) are often used during the introduction of the endoscope and ampullary catheter and since anticholinergic drugs have been shown to inhibit the pancreatic secretory response to exogenous stimulant hormones such as secretin and cholecystokinin-pancreozymin (CCK) (Dreiling and Janowitz, 1960; Elmslie *et al.*, 1964; Bock *et al.*, 1968; Schapiro *et al.*, 1968), we have assessed the effect of these drugs on the pancreatic and biliary responses to parenteral secretin plus cholecystokinin.

Methods

Ten patients undergoing study for suspected pancreatic disease underwent duplicate tests, in random order, after obtaining informed consent. Each individual was intubated with a double lumen tube with air vents, under radiological control, so that the duodenal aspiration holes were sited in the descending duodenum and the gastric aspiration

vents in the antrum. Secretin (1 clinical unit/kg-h) and cholecystokinin-pancreozymin (1 Ivy unit/kg-h) were administered for 45 minutes by continuous intravenous infusion in 0.15 mol/l sodium chloride. The hormones had been purchased from the GIH Laboratory, Karolinska Institute, Stockholm, Sweden. On a different day, five subjects received 10 mg diazepam while the other five patients were given 10 mg diazepam plus 20 mg hyoscine butylbromide by intravenous injection immediately before the start of the infusion of hormones. Duodenal aspirate was collected in 15 minute batches and volume recorded. The concentration of bicarbonate was measured by adding a known excess of acid, boiling and backtitrating the residual acid with 0.1 mol/l sodium hydroxide to pH 7. Tryptic activity was measured photometrically, using benzoyl-arginine-p-nitroanilide as substrate. Bilirubin concentration is expressed in terms of icteric index.

Results

Diazepam alone did not significantly affect the total output of bicarbonate, trypsin or bilirubin in response to the hormones (Fig. 1).

Addition of hyoscine butylbromide did not significantly affect the output of bicarbonate but the outputs of trypsin decreased in every subject (Fig. 2). There was a significant delay in attaining peak rates of secretion of trypsin and of bilirubin compared with control after the injection of diazepam plus hyoscine butylbromide during both the

¹Address for communications: KGW, Ninewells Hospital, Dundee DD2 1UB.

Fig. 1 Pancreatic and biliary responses to secretin and cholecystokinin-pancreozymin without and with diazepam. Each pair of points represents results from one individual. C = control; D = with diazepam. The vertical bars indicate mean values of control or diazepam tests. The ordinate represents secretory values during the 45 minute tests. The pairs of columns on the right of the figure indicate the appropriate outputs (control and with diazepam, respectively) during the three successive 15 minute collection periods.

first 15 (Fig. 2) and the first 30 minutes ($P < 0.005$ for trypsin and < 0.05 for bile pigment) after start of stimulation with the continuous infusion of exogenous hormones.

Discussion

The results of the present study indicate that intravenous diazepam or diazepam plus hyoscine butylbromide do not appreciably alter the bicarbonate-secretory response to exogenous hormones in the doses used in the present study. However, as noted previously (Dreiling and Janowitz, 1960; Elmslie *et al.*, 1964; Bock *et al.*, 1968; Schapiro *et al.*, 1968), the administration of an anticholinergic reduced the total output of trypsin in response to the exogenous hormones, albeit only slightly in the dose used. More important, the combination of the diazepam and hyoscine butylbromide significantly de-

Fig. 2 Pancreatic and biliary responses to secretin and cholecystokinin-pancreozymin without and with diazepam plus hyoscine butylbromide.

Significance of symbols as in Fig. 1. x Significant difference between the values represented by the pair of columns of $P < 0.05$, xx $P < 0.02$, xxx $P < 0.01$.

layed, for 30 minutes, both the secretion of enzymes and cholecystokinesis in response to the exogenous hormones. The use of these drugs during endoscopic cannulation of the pancreas will therefore not significantly affect measurement of pancreatic secretory capacity, provided that the collection is carried out for a sufficiently long period to compensate for lag in the secretory response.

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References

- Bock, O. A. A., Bank, S., Marks, I. N., Moshal, M. G., Groll, A., Loxton, A., and Dines, M. (1968). Effect of propantheline bromide and pipenzolate bromide upon exocrine pancreatic secretion. *Gastroenterology*, **55**, 199-203.
- Cotton, P. B., Cremer, M., Robberecht, P., and Christophe, J. (1974). Biochemical studies of pure pancreatic juice obtained by duodenoscopic cannulation of the pancreatic duct in conscious patients. *Gut*, **15**, 838.
- Dreiling, D. A., and Janowitz, H. D. (1960). Inhibitory effect

of new anticholinergics on the basal and secretin-stimulated pancreatic secretion in patients with and without pancreatic disease. *American Journal of Digestive Diseases*, **5**, 639-654.

Elmslie, R. G., White, T. T., and Magee, D. F. (1964). Observation on pancreatic function in eight patients with controlled pancreatic fistulas. *Annals of Surgery*, **160**, 937-949.

Gregg, J., Sipos, T., Sharma, M., Gibbons, G., Whalen, M., and Blackburn, G. (1975). Enzymatic analysis of pure pancreatic juice obtained during the endoscopic cannulation of the main pancreatic duct. *Gastroenterology* **68**, 904.

Robberecht, P., Cremer, M., Vandermers, A., Vandermers-Piret, M.-C., Cotton, P., de Neef, P., and Christophe, J. (1975). Pancreatic secretion of total protein and of three hydrolases collected in healthy subjects via duodenoscopic cannulation. Effects of secretin, pancreozymin and caerulein. *Gastroenterology*, **69**, 374-379.

Schapiro, H., Wruble, L. D., Estes, J. W., Sherman, R., and Britt, L. G. (1968). Anticholinergic drug action on pancreatic exocrine outflow in man and dog. *American Journal of Digestive Diseases*, **13**, 608-614.

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