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

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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
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 Jañowitz, 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 delayed, 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

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