Gut, 1986, **27**, 567–569

Effect of modern analgesic drugs (Tramadol, pentazocine, and buprenorphine) on the bile duct sphincter in man

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SUMMARY Modern narcotic analgesic drugs, such as tramadol, pentazocine, and buprenorphine share similarities of molecular structure with morphine which is widely believed to cause spasm of the bile duct sphincter and so impede bile flow. This study assessed the effects of intravenously administered analgesics on bile duct sphincter motor activity measured by ERCP manometry. Ten minutes after pentazocine injection the duration of contractions and baseline pressure of the bile duct sphincter rose from 6·2±0·2 to 8·2±0·27 s and from 5·1±0·6 to 8·8±0·4 mmHg respectively. Tramadol, buprenorphine and saline showed no such effect. These data indicated that the effects of such drugs on bile duct sphincter function can be safely assessed by ERCP manometry and that pentazocine adversely affects the bile duct sphincter, whilst tramadol and buprenorphine do not. We consider therefore that pentazocine is not the premedication of first choice for endoscopic procedures involving the sphincter of Oddi and should also be avoided in patients with pancreatic and biliary disorders.

The bile duct sphincter (sphincter of Oddi) is the smooth muscle component of the choledochoduodenal junction which provides regulation of the bile flow and prevents duodenobiliary reflux. The effects of narcotic analgesic drugs on its function have been assessed indirectly by measuring resistance to flow through a choledochal T-tube, both intraoperatively and postoperatively.[1–3] This approach has the disadvantages of being unphysiological, intraoperative studies are complicated by the use of narcotics during general anaesthesia and postoperative studies of choledochal pressure may introduce artefacts by false raising of sphincter tone in response to artificially raised duct pressures.[2 4]

In contrast. ERCP manometry allows assessment of sphincter of Oddi motility and baseline pressure during routine ERCP[4–6] and can be done in the absence of other interfering medications. Because analgesic drugs are commonly used as premedication for ERCP we have used ERCP manometry to study the effects of morphine-like analgesics (tramadol, pentazocine and buprenorphine) in doses commonly used in clinical practice (one ampule per patient).

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Received for publication 16 August 1985.

Methods

PATIENTS AND STUDY DESIGN

Twenty three patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) for the investigation of possible pancreatic and/or biliary disease were included in the study. Endoscopic manometry was done before ERCP which in all cases was subsequently found to be normal. No patient was found to have gastric or duodenal ulceration, diabetes mellitus, or any other systemic disease and none were alcoholics. Informed consent was obtained from all patients who were divided into four groups:

1 PENTAZOCINE GROUP

It consisted of eight patients, five men and three women, with a mean age of 46 years in whom 30 mg pentazocine was given intravenously.

2 TRAMADOL GROUP

It consisted of five patients, three men and two women, mean age 43 years in whom 50 mg tramadol was administered intravenously.

3 BUPRENORPHINE GROUP
It consisted of five patients, two men and three women, mean age 49 years who received 0·3 mg buprenorphine intravenously.

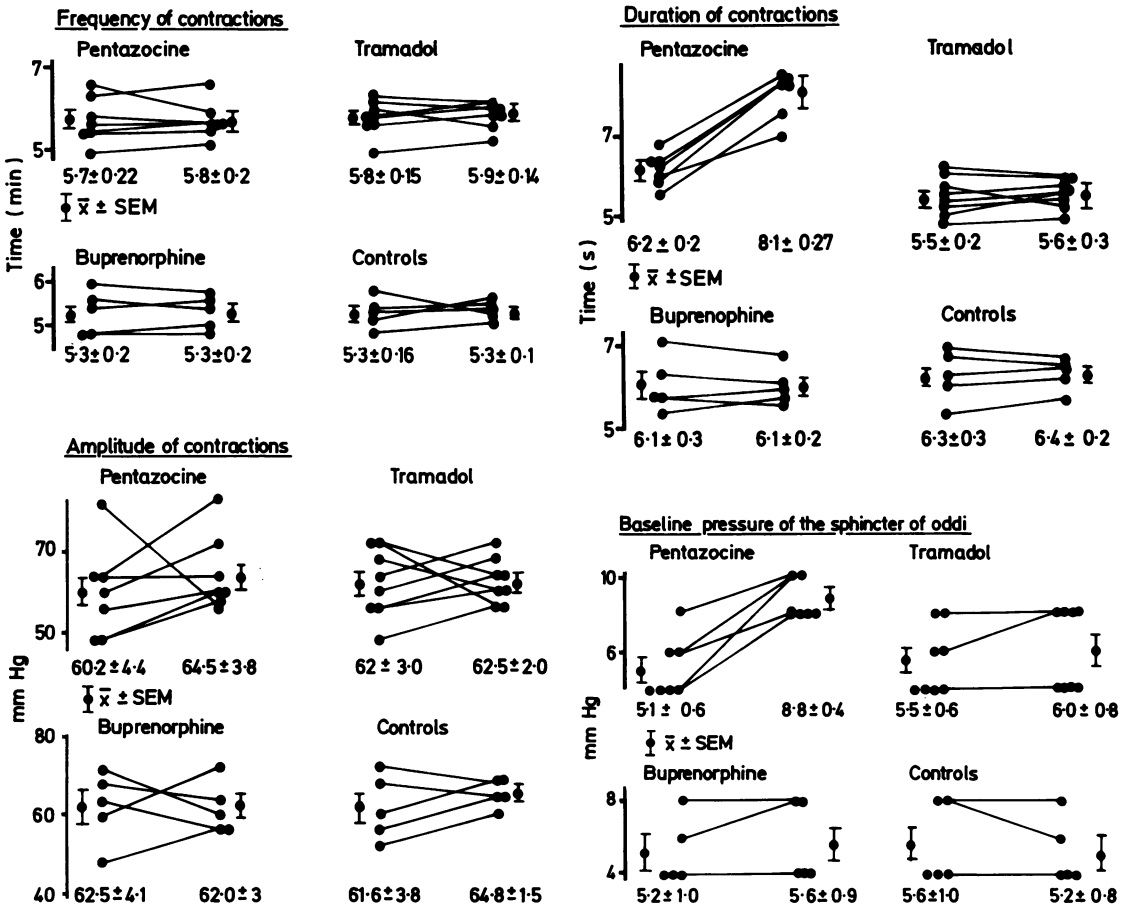
4 CONTROL GROUP
It consisted of five patients, three men and two women, mean age 49 years who received 1 ml 0·9% saline intravenously and served as controls.

ENDOSCOPIC MANOMETRY
After a 12 hour fasting period and standard premedication with 10–15 mg diazepam, previously shown by Nebel[7] and in our own pilot study not to affect sphincter of Oddi motility, duodenoscopy was carried out and the bile duct cannulated before undertaking endoscopic manometry according to the technique that was recently described.[5] Manometric examination was done in all patients before and 10 minutes after intravenous administration of the test drug or saline.

STATISTICAL ANALYSIS
Values are reported as mean ± standard error and individual data are given in the Figures. The values obtained before and after drug administration are compared by the Wilcoxon's test.

Results

Initial values recorded for sphincter contraction frequency, contraction amplitude, duration of contractions and baseline pressure were similar in all four groups (Figs 1–4). After pentazocine admini-



Figures 1–4 *Contraction frequency (1), contraction amplitude (2), duration of the contractions (3), and baseline pressure (4) of the bile duct sphincter (sphincter of Oddi) before and after administration of the analgesic drugs and saline (controls) respectively.*

stration the duration of sphincter contractions significantly increased from 6·2±0·2 to 8·2±0·27 s ($p<0·001$, Fig. 3) and the baseline pressure rose from 5·1±0·6 to 8·8±0·4 s ($p<0·001$, Fig. 4). In the other groups administration of tramadol, buprenorphine or saline caused no changes (ns) in sphincter motility parameters nor baseline pressure (Figs 1–4). There were no complications in any patient studied related to endoscopic manometry or the ERCP examination which followed.

Discussion

ERCP manometry allows determination of sphincter of Oddi motility and baseline pressure. Between sphincter contractions baseline pressure provides resistance to bile flow which is in turn determined by the pressure gradient between common bile duct and duodenum.[8] Drugs reducing this baseline pressure, such as nitroglycerine, diminish the resistance of the sphincter to bile flow.[5] In contrast, pentazocine increases baseline pressure and causes longer closing phases of the sphincter by increasing the duration of contractions. These two effects indicate that pentazocine increases sphincter resistance to bile flow. Although not shown in this study, it is likely that similar changes may also take place in the pancreatic sphincter. Nor can we state how long this duration of action lasts. Our results, however, suggest that pentazocine should not be used as premedication for endoscopic diagnostic or therapeutic procedures such as ERCP, endoscopic papillary dilatation[9] and particularly endoscopic medical dilatation of the bile duct sphincter by nitroglycerine.[10] It can therefore not be recommended as analgesic drug of first choice for such procedures or for post-ERCP pain, which is probably induced by papillary spasm.[11]

In our opinion, these data should draw further attention to the effects of drugs commonly used in clinical practice on the sphincter of Oddi and care should be given to the use of analgesics in patients undergoing endoscopic procedures and those suffering from pancreatic and biliary disease.

This study is dedicated to Prof Dr W. Gerok on his 60th birthday. Part of the work has been presented at the meeting of the International Association for the Study of the Liver (IASL) Berne, Switzerland, September 1984. We are very grateful to Dr D L Carr-Locke, Consultant physician, University of Leicester, The Leicester Royal Infirmary, for helping with the manuscript.

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