mouth and he was anaesthetised with alfentanil 100 μg/kg. After injection of vecuronium 6 mg the trachea was intubated and intermittent positive pressure ventilation continued with nitrous oxide and oxygen. As soon as the induction dose of alfentanil had been given an infusion of alfentanil 1 μg/kg/min was begun and continued for two hours. During this period a further 6 mg vecuronium was given in divided doses. Fifty five minutes after discontinuing the alfentanil infusion and after the administration of atropine 1·2 mg and neostigmine 2·5 mg the endotracheal tube was removed. The patient could move all four limbs, was completely coherent and orientated, and remarked spontaneously: "I feel fantastic." Head lift was maintained for 20 seconds. Seventy minutes after stopping the infusion a sudden respiratory arrest occurred. No femoral pulse was palpable. After endotracheal intubation, ventilation with 100% oxygen, and external cardiac massage the femoral pulse was again palpable. Naloxone 0·4 mg was given intravenously and spontaneous respiration returned within three minutes. Twelve lead electrocardiogram and arterial blood gas and plasma potassium and calcium values were all within the normal range. The patient gradually woke up and was extubated, talking and moving all four limbs within 180 minutes of the arrest.

Case 2—A 54 year old woman weighing 64 kg scheduled for vascular decompression of the fifth cranial nerve was premedicated with temazepam 30 mg by mouth. After alfentanil 32·5 μg/kg and thiopentone 200 mg an infusion of alfentanil 7 μg/kg/min was given for 10 minutes and then 1·6 μg/kg/min was given for 110 minutes. Curare 45 mg was used for neuromuscular blockade. Fifty minutes after stopping the infusion and after atropine 1·2 mg and neostigmine 2·5 mg she woke up and was conversing normally, saying that her facial pain was completely cured. Thirteen minutes later she stopped breathing and was immediately reintubated. Spontaneous ventilation returned after naloxone 0·4 mg was given intravenously. The radial pulse remained palpable throughout. Plasma alfentanil concentration at the time of the respiratory arrest was 95 μg/l.

Comment

Respiratory depression is a well recognised complication after administration of opioid analgesics. The interesting feature of these two cases is that both patients had initial rapid, clear recovery from anaesthesia, with sudden respiratory arrest. Furthermore, the plasma alfentanil concentration in the second case was below that which would be expected to cause respiratory arrest. Unfortunately, the plasma alfentanil concentration was not measured in the first patient.

These respiratory arrests are unlikely to be due to second peaks in plasma alfentanil concentration as have been described for fentanyl,[2] since all the available pharmacokinetic data suggest that plasma alfentanil concentrations decline exponentially after stopping administration.[1 3 4] Possibly a decrease in ambient stimulation after transfer to the recovery ward may have been a contributory factor. Possibly also age was relevant in the first patient, as alfentanil elimination is prolonged with increasing age.[4] Other workers have used infusion regimens with higher doses than we in 15 patients without problems with postoperative respiratory depression.[3] Our two cases, however, occurred in a series of 26 patients who had received alfentanil. We therefore recommend that when alfentanil infusions are used, as with other opioids, respiration should be monitored very closely in the initial postoperative period.

Neither the Committee on the Safety of Medicines nor the manufacturers, Janssen Pharmaceutical Ltd, were aware of this potential problem with alfentanil. Nevertheless, since submitting this report we have learnt of a further, similar episode described in a patient in Canada.[5]

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Management of retained biliary calculi: relaxation of sphincter induced by ceruletide

Several non-operative techniques have been reported as effective in the management of retained stones after exploration of the common bile duct. Infusion of saline is of doubtful efficacy and infusion of cholate unreliable.[1] Infusion of glyceryl mono-octanoate via a T tube is effective but induces erosive duodenitis.[2] Other methods of proved efficacy include endoscopic sphincterotomy and extraction of stones, and percutaneous removal via the T tube tract.[3] The first of these requires special skill, which is not available in many hospitals. Extraction via the T tube tract with a catheter that may be guided and a flexible choledochoscope is effective but requires six weeks' delay to allow for maturation of the T tube tract.[4] I describe a simple method of treatment in which maximal relaxation of the sphincter was induced pharmacologically by ceruletide, which allowed large volumes of saline to be infused via the T tube without a deleterious rise in biliary pressure. Ceruletide is the synthetic analogue of caerulein and elicits a powerful cholecystokinetic response with relaxation of the sphincter of Oddi.[5]

Patients, methods, and results

Four patients with retained ductal calculi were treated according to a preset protocol. All had undergone cholecystectomy during the same admission, with exploration of the common bile duct and insertion of an F16 T tube. The residual stones were diagnosed from a T tube cholangiogram obtained usually on the seventh postoperative day. Two patients had a single distal ductal calculus (radiological sizes 0·4 and 0·7 cm), one had two small ductal calculi (0·2 cm), and the fourth had eight calculi of varying size (range 0·2-0·8 cm) in the common bile duct and a long cystic duct remnant. None of the patients had jaundice or any evidence of sepsis.

Ceruletide (Farmitalia) was administered intravenously in a dose of 2 ng/kg/min in saline for one hour with a constant infusion pump. Five minutes after the start of the infusion sterile isotonic saline was infused via a disposable manometry line through the external limb of the T tube at a rate that kept the biliary pressure at 25-30 cm water. The infusions were stopped after one hour and the T tube connected to a bile drainage bag. The amount of saline infused averaged 2·1 (range 1-3) litres. Prophylactic antibiotic treatment was administered as a single intravenous injection of 1 g cefuroxime half an hour to one hour before the procedure. T tube cholangiography was performed before and after the procedure.

In three patients the biliary tree was clear of stones after one treatment. In the patient with multiple calculi six were flushed out by the first treatment but two remained in the cystic duct remnant. These were eliminated when the treatment was repeated a few days later. No cardiovascular side effects were noted during the procedure, but watery diarrhoea occurred in two patients who received more than 2·5 litres of saline via the T tube during the treatment. A mild increase in serum amylase activity was observed in all four patients.

Comment

Administration of ceruletide as a constant infusion allows fairly large volumes of saline to be administered via the T tube without an increase in biliary pressure beyond the physiological maximal hepatic secretory pressure of 28-30 cm water. This permits a short phase of enhanced flushing of the biliary tree, which together with the relaxation of the sphincter induced by ceruletide favours passage of residual calculi smaller than one cm into the gastrointestinal tract. The technique appears to be efficacious and free of serious side effects, and it should be used before more invasive methods currently available for dealing with this problem.

I thank Farmitalia Carlo Erba for supplying ceruletide.

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