Prevention of urinary retention with phenoxybenzamine during epidural morphine

Since the first reports by Wang and Behar and others the use of epidural and intrathecal opiates for pain relief has become widely accepted. The most common and distressing complication of this mode of analgesia is acute urinary retention, which occurs in 3%¹ to 100%² of patients. We studied the postoperative urinary complications in a group of patients who underwent elective caesarean section under epidural anaesthesia and who received epidural morphine for postoperative pain relief. In addition, the efficacy of the alpha adrenergic blocking agent phenoxybenzamine (Dibenyline) in alleviating postoperative micturition difficulties and urinary retention was investigated.

Methods and results

After giving informed consent, 60 patients aged 23-42 years were divided at random into two equal groups. All were injected with 20 ml bupivacaine 0.5% via a Tuohy needle inserted epidurally into the L1-2 or L2-3 interspace. An indwelling catheter was then placed caudally. At the end of surgery a single dose of 4 mg morphine hydrochloride diluted in 10 ml isotonic saline without preservative was injected through the epidural catheter for postoperative analgesia. In addition, the 30 patients in group 2 received four oral doses of 10 mg phenoxybenzamine 24 and two hours before and eight and 16 hours after surgery. Except for the epidural morphine no opiates were given to either group. A non-narcotic drug (1000 mg dipyrone intramuscularly or by mouth), however, was dispensed freely on request. The same amount of postoperative fluid (2.5-3.0 l Hartman's solution) was administered to both groups. The patients were closely observed for 48 hours. Medical staff did not know which of the patients had been given phenoxybenzamine. Difficulty in micturition, volumes of the first two voidings after operation, the time intervals between the end of surgery and first micturition, urinary tract infection, and urinary retention were noted. For this investigation we designated "urinary retention" as discomfort and sensation of a full bladder or a palpable distended bladder. In such instances the patient was encouraged to void. If urine was not passed spontaneously after one hour the bladder was catheterised.

From the volumes of the two initial urine voidings and the time interval between the end of the operation and first micturition phenoxybenzamine clearly alleviated or prevented difficulties in micturition and urinary retention (table). In group 1, 26 patients complained of difficulty in micturition, whereas in group 2 only two patients did so. The overall rate of urinary retention diminished from 46.6% (14 patients) in group 1 to 10% (three patients) in group 2, while the need for bladder catheterisation decreased from 53.3% (16 patients) to 10% (three patients). Urinary tract infections occurred in three patients in group 1 and in none of the patients in group 2. Oral phenoxybenzamine given during epidural analgesia was not associated with hypotension or with any other untoward effect.

Comment

The nervous control of the urinary bladder is complex and the exact role of the sympathetic system in normal micturition is difficult to define. It has been suggested³ that bladder overdistension as occurs during regional anaesthesia enhances alpha adrenergic sympathetic activity, thereby increasing the closure pressure of the urethral sphincter, which, in turn, leads to difficulty in micturition. The same chain of reactions is caused by the stress of anaesthesia and surgery owing to the increased secretion of adrenaline. Under these circumstances administration of an alpha adrenergic blocking agent should diminish effectively the difficulty in micturition.³

The exact mechanism of epidural morphine in causing urinary retention is not known. It may be due to the effect on the tone of the internal urethral sphincter,¹ to the influence of the parasympathetic outflow from the sacral cord,⁴ or to a local anaesthetic effect on bladder innervation. According to Petersen *et al.*,⁵ the effect of morphine on the urinary bladder is peripheral, and this was supported by other workers.²

Postoperative urinary complications in the two groups of patients studied

Group	Mean (SD) volume of first voiding (ml)	Mean (SD) volume of second voiding (ml)	Mean (SD) delay to first voiding (hours)	No (%) of patients with difficulty in micturition	No (%) of patients with urinary retention	No (%) of patients with catheterisation	No (%) of patients with urinary infection
1 (n = 30)	250.0 (155.9)	237.5 (114.7)	9.7 (2.9)	26 (86.6)	14 (46.6)	16 (53.3)	3 (10.0)
2 (n = 30)*	478.3 (186.6)	416.6 (179.8)	5.3 (1.5)	2 (6.6)	3 (10.0)	3 (10.0)	0
p Value	<0.01	<0.01	<0.01				

*Given phenoxybenzamine in addition to epidural morphine.

Most of our patients benefited from phenoxybenzamine. We therefore recommend it as an effective and safe drug for alleviating or preventing urinary complications in patients receiving epidural morphine for pain relief.

¹ Magora F, Olshwang D, Emierl D, *et al.* Observations on extradural morphine analgesia in various pain conditions. *Br J Anaesth* 1980;52:247-52.

² Weddel SJ, Ritter RR. Serum levels following epidural administration of morphine and correlation with relief of postsurgical pain. *Anesthesiology* 1981;54:210-4.

³ Caine M, Pfau A, Perlberg S. The use of alpha adrenergic blockers in benign prostatic obstruction. *Br J Urol* 1976;48:255-63.

⁴ Yaksh TL. Spinal opiate analgesia: characteristics and principles of action. *Pain* 1981;11:293-346.

⁵ Petersen TK, Husted SE, Rybo L, Schurizek BA, Wernberg M. Urinary retention during IM and extradural morphine analgesia. *Br J Anaesth* 1982;54:1175-7.

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Hadassah University Hospital, Jerusalem, Israel

SAMUEL EVRON, MD, senior in anaesthesia, senior resident in obstetrics and gynaecology

FLORELLA MAGORA, MD, professor of anaesthesiology

ELIAHU SADOVSKY, MD, professor of obstetrics and gynaecology

Correspondence to: Dr Samuel Evron, Department of Obstetrics and Gynaecology, Hadassah University Hospital, PO Box 12000, Jerusalem, Israel 91120.

Resolution of salmonella carriage after duodenoscopic treatment for a common bile duct stone

Less than 3% of patients infected with *Salmonella typhi*, and probably even fewer with other salmonella organisms, become chronic carriers. Most of those who do have gall bladder stones; antibiotic treatment alone is effective in about two thirds of cases. If surgical treatment is indicated (because of occupation or important biliary symptoms), cholecystectomy cures about 85% of patients.¹ We report an apparently unique case of a patient with chronic carriage of an unusual organism (*Salmonella eastbourne*) who was cured by removal of a bile duct stone 18 years after cholecystectomy.

Case report

A 70 year old woman was referred for endoscopic management of recurrent cholestasis attributed to common bile duct stones. She had had a cholecystectomy for gall stones 18 years before (without exploration of the common bile duct) and then remained well until the three years before referral; since then she had required admission on four occasions for recurrent jaundice. Each illness was managed conservatively, the condition resolving over a few days. A stool specimen six months before referral had grown *S eastbourne*, and subsequent cultures remained positive despite the use of gentamicin and cephradine (to which the organism was sensitive) in the management of her biliary disease.

Endoscopic retrograde cholangiography showed a 4×1.5 cm stone in a dilated common bile duct. Duodenoscopic sphincterotomy was performed but an initial attempt to remove the stone was unsuccessful. Culture of stool and bile yielded *S eastbourne*. A nasobiliary catheter was placed to promote drainage² and infuse the duct with mono-octanoin in an attempt to reduce the size of the stone.³

After three days' infusion she developed biliary pain accompanied by

pyrexia. This abated over 48 hours of treatment, which included tobramycin, and repeat endoscopic retrograde cholangiography showed a biliary tree free of stones. She made an uneventful recovery, and subsequently eight consecutive stool samples over a period of three months showed clearance of the salmonella.

Comment

This patient was a chronic carrier of *S eastbourne* despite a cholecystectomy 18 years previously. This appeared to be resistant to appropriate antibiotics until a common bile duct stone was removed. Salmonella carriage was probably perpetuated by biliary stasis analogous to that caused by a stone filled gall bladder.

We thank Dr J Partridge for his help in arranging analysis of stool samples.

¹ Gorbach SL. Infectious diarrhoea. In: Sleisenger MH, Fordtran JS, eds *Gastrointestinal disease*. 3rd ed. Philadelphia: Saunders, 1983:940-4.

² Cotton PB, Williams CB. *Practical gastrointestinal endoscopy*. 2nd ed. Oxford: Blackwell, 1982:90-1.

³ Thistle JL, Carlson GL, Hofmann AF, et al. Monooctanoin, a dissolution agent for retained cholesterol bile duct stones: physical properties and clinical application. *Gastroenterology* 1980;78:1016-22.

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Department of Gastroenterology, Middlesex Hospital, London W1N 8AA

A FORBES, BSC, MRCP, registrar
P B COTTON, MD, FRCP, consultant

Correspondence to: Dr P B Cotton.

Monitoring effects of oral anticoagulants during treatment with heparin

Patients' sensitivities to warfarin vary considerably.¹ Thus it would be useful to identify those who are sensitive to warfarin as early as possible during treatment by monitoring the British corrected ratios before the first dose and daily for the next four days. Because many patients receive heparin by intravenous infusion while they are receiving warfarin we examined the effects of heparin on the British corrected ratio.

Patients, methods, and results

Blood from 25 patients receiving both heparin and warfarin was collected into plastic tubes containing sodium citrate 3.1% (one part to nine parts blood), and the plasma was separated for estimation of clotting times. Heparin activity was measured as the kaolin cephalin clotting time with a platelet substitute (Diagen; Bell and Alton) (control kaolin cephalin clotting time roughly 40 seconds).² Heparin was neutralised by addition of 40 µl protamine sulphate solution (concentration 10 µg/ml) to 1 ml plasma to achieve a final plasma protamine concentration of 0.4 µg/ml. Oral anticoagulant activity was measured by the one stage method of Quick³ with British comparative thromboplastin (control time roughly 12 seconds).

British corrected ratios in plasma from patients receiving warfarin alone to which heparin was added in vitro. Numbers in parentheses are the ratios after subsequent neutralisation with protamine sulphate (1.0 µg/ml plasma in cases 1 and 8; 0.4 µg/ml plasma in all other cases)

Case No	Heparin concentration (U/ml)					
	0	0.2	0.4	0.6	0.8	1.0
1	1.2 (1.3)*	1.2 (1.3)*	1.3 (1.3)*	1.3 (1.3)*	1.4 (1.3)	1.5 (1.3)
2	1.2 (1.3)*	1.3 (1.2)*	1.4 (1.2)*	1.5 (1.2)	1.5 (1.2)	1.7 (1.3)
3	1.3 (1.3)*	1.3 (1.3)*	1.3 (1.3)*	1.4 (1.3)	1.5 (1.3)	1.7 (1.3)
4	2.4 (2.5)*	2.3 (2.3)*	2.7 (2.4)	2.8 (2.3)	3.2 (2.4)	3.5 (2.6)
5	2.9 (3.0)*	3.0 (2.8)*	3.2 (2.9)	3.5 (3.1)	3.8 (3.0)	4.4 (3.3)
6	3.4 (3.7)*	3.5 (3.4)*	3.9 (3.5)	4.4 (3.5)	5.3 (3.6)	6.6 (3.9)
7	3.5 (3.7)*	3.6 (3.6)*	3.9 (3.6)	4.3 (3.7)	5.0 (3.7)	6.1 (3.8)
8	3.5 (4.0)*	3.6 (3.9)*	4.0 (3.9)	4.3 (3.8)	4.8 (3.8)	5.6 (3.6)
9	5.4 (5.6)*	5.6 (5.7)	6.2 (5.4)	7.3 (5.5)	8.7 (5.9)	11.2 (6.1)

*Kaolin cephalin clotting time within or below therapeutic range (<2.5 times control).

Plasma was also collected from nine patients receiving warfarin alone. Heparin sulphate was added to achieve plasma heparin concentrations of between 0.1 and 1.0 U/ml. Heparin was neutralised with protamine as described above. The table shows the effect of in vitro addition of heparin on the prothrombin time of plasma from the nine patients, whose initial British corrected ratios were between 1.2 and 5.4. The percentage increase in prothrombin time induced by heparin (1.0 U/ml) was greater the higher the initial British corrected ratio ($r=0.916$, $p<0.001$). In those samples in which the corresponding kaolin cephalin clotting time was within or below the therapeutic range (1.5-2.5 times control) the median maximum percentage increase in British corrected ratio was only 3% (range -4 to +17%).

The table also shows (in parentheses) the British corrected ratios in samples from the nine patients after addition of protamine. Protamine brought the British corrected ratio close to the control value in all samples except at the highest heparin concentration (1.0 U/ml). Addition of protamine (0.4 µg/ml) to the control samples caused only a slight increase in British corrected ratio.

In the 25 patients receiving both heparin and warfarin addition of protamine reduced the British corrected ratio, the percentage reduction being directly related to the initial kaolin cephalin clotting time of the sample ($r=0.756$, $n=25$, $p<0.001$). In those patients whose kaolin cephalin clotting time was in the therapeutic range, however, the median reduction in British corrected ratio was only 4% (range 0-11%).

Comment

At present the recommendation for treatment with warfarin is to give 10 mg daily for three days and measure prothrombin time from the fourth day of treatment.³ Unfortunately, this loading dose regimen results in up to 70% of the patients being outside the range for anticoagulation by the fourth day.⁴ Half may have received too little anticoagulation and the other half too much and, therefore, be at greater risk of haemorrhage.⁴ Patients should, therefore, be monitored daily from the first dose of warfarin and subsequent doses should be tailored according to the British corrected ratio. Presumably this is not recommended at present because concomitant treatment with heparin might affect the British corrected ratio. This only occurs, however, when heparin is given by intravenous bolus; heparin infusions do not substantially interfere with prothrombin time when measured by Thrombotest.⁵ We have shown that this also holds for the British comparative reagent, provided that the kaolin cephalin clotting time is within the therapeutic range. If the kaolin cephalin clotting time is abnormally long the effect of heparin on the British corrected ratio can be neutralised by protamine in vitro. As heparin is normally given now by infusion with adjustment of dose rate according to the kaolin cephalin clotting time, however, neutralisation of samples with protamine should rarely be necessary. If the British corrected ratio is measured daily from the start of treatment with oral anticoagulants patients sensitive to these may be more rapidly identified and their dosages reduced accordingly.

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Departments of Medicine, Haematology, and Thoracic Medicine, Llandough Hospital, Penarth, South Glamorgan

P THOMAS, MB, BS, senior house officer

A FENNERTY, MB, MRCP, registrar

G BACKHOUSE, FIMLS, technician

D P BENTLEY, MRCP, MRCPATH, consultant haematologist

I A CAMPBELL, MD, FRCP, consultant thoracic physician

Department of Pharmacology and Therapeutics, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN

P A ROUTLEDGE, MD, MRCP, consultant physician and senior lecturer in clinical pharmacology

Correspondence to: Dr P A Routledge.