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Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine

Marjan Jahangiri FRCS
Senior House Officer

J W P Bradley FRCS
Consultant Surgeon

A P Jayatunga FRCS
Senior Registrar

C H Dark FRCA
Consultant Anaesthetist

Departments of Surgery and Anaesthesia, The Hillingdon Hospital, Uxbridge, Middlesex

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Phantom limb pain may appear in up to 85% of patients after amputation. There is no effective treatment. Perioperative epidural infusion of morphine and bupivacaine, alone or in combination, is effective in preventing phantom limb pain in patients with pre-existing limb pain. Serious side-effects, however, make them difficult to manage on a general ward. Clonidine has been shown to be an effective postoperative analgesia when applied epidurally. To mitigate the potentially serious side-effects of all these drugs, we have studied their combined efficiency in preventing phantom limb pain in a prospective controlled study of 24 patients undergoing lower limb amputation. In the study group ($n=13$), an epidural infusion containing bupivacaine 75 mg, clonidine 150 μg and diamorphine 5 mg in 60 ml normal saline was given at 1–4 ml/h 24–48 h preoperatively and maintained for at least 3 days postoperatively. The control group ($n=11$) received on-demand opioid analgesia. Pain was assessed by visual analogue scale at 7 days, 6 months and 1 year. At 1 year follow-up, one patient in the study group and eight patients in the control group had phantom pain ($P<0.002$) and two patients in the study group *versus* eight patients in the control group had phantom limb sensation ($P<0.05$). There was no significant improvement in stump pain.

We conclude that perioperative epidural infusion of diamorphine, clonidine and bupivacaine is safe and effective in reducing the incidence of phantom pain after amputation.

Correspondence to: Miss Marjan Jahangiri, Department of Cardiothoracic Surgery, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE

Phantom limb pain may occur in up to 85% of patients after amputation *(1,2)*. It has been demonstrated that perioperative epidural infusion of morphine and bupivacaine is effective in preventing phantom limb pain *(3)*. In addition, it has been shown that epidural clonidine is an effective postoperative analgesic, but with significant side-effects of sedation and hypotension *(4)*. The correlation noted previously between preoperative pain and phantom limb pain *(5)* led us to examine the effect of perioperative pain control on postoperative phantom limb pain. Our experience of using morphine and bupivacaine alone has been that they produce respiratory depression and hypotension and, therefore, make management on a general surgical ward difficult. In an attempt to mitigate the potentially serious side-effects of all these drugs, we set out to study their combined efficiency in preventing phantom limb pain.

Materials and methods

This was a prospective study of 24 patients who underwent lower limb amputation at The Hillingdon Hospital from October 1990 to April 1992. Informed consent was obtained from all patients and approval from the Ethical Committee of the Hillingdon Health Authority was granted.

There were 11 patients (M : F; 8 : 3) in the control group with an average age of 67.8 years (range 38–80 years) and 13 patients (M : F; 10 : 3) in the study group with an average age of 65 years (range 44–81 years). Two patients in the study group died in the follow-up period, one of a relapse episode of chronic lymphocytic leukaemia and the other of chronic renal failure within 6 weeks of operation.

In the study group, seven patients had peripheral vascular disease, three had diabetes mellitus and one had an infected ulcer resistant to conservative management. Eight patients had below-knee amputations and three had above-knee amputations. Of the eleven patients, three had a previous amputation at least 2 years before the date of this presentation.

In the control group, six patients had peripheral vascular disease, four had diabetes mellitus, and one patient had a failed embolectomy. Seven patients had below-knee amputations and four had above-knee amputations.

All patients had pain preoperatively. Exclusion criteria included anticoagulation, presence of local infection and previous lumbar spinal surgery. In the study group, a tunnelled lumbar epidural catheter was placed using an aseptic technique. This was placed under local anaesthesia at least 24 h preoperatively, except in one patient in whom it was placed 5 h preoperatively. An infusion of diamorphine 5 mg, bupivacaine 75 mg and clonidine 150 μg made up to 60 ml volume with sterile 0.9% NaCl was set up. This was run at an initial rate of 2.5 ml/h and then adjusted to individual needs to abolish preoperative pain. All patients received general anaesthesia in addition to their epidural anaesthesia. Epidural infusions continued for 72 h postoperatively, except in two patients who experienced severe postoperative pain when the infusion was withdrawn at 72 h. After starting the epidural infusion, blood pressure was monitored half-hourly for 4 h and then 4 hourly and respiratory rate was monitored hourly for 24 h. Pain was assessed by visual analogue scale on a score of 1–10 preoperatively and then at 7 days, 6 months and 1 year postoperatively, and it was considered significant when the score was $\geqslant 3$. Three categories of pain were assessed: phantom limb pain, phantom limb sensation and stump pain.

For statistical analysis, Fisher's exact test was used.

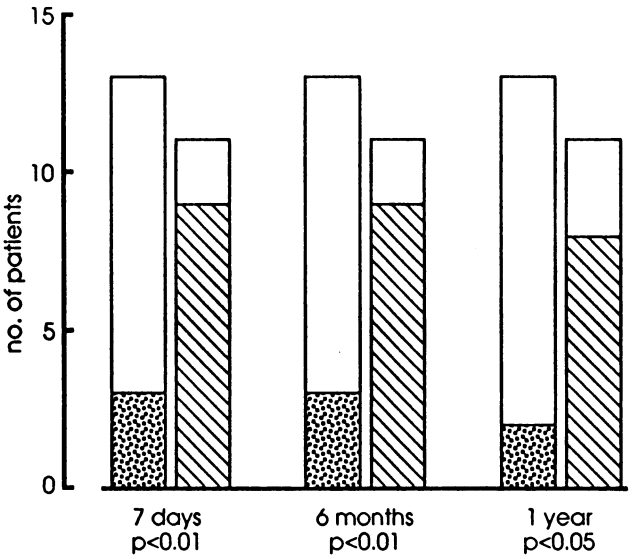

Figure 2. Incidence of phantom limb.

Results

Phantom pain (Fig. 1)

At 7 days postoperatively, three patients in the study group and nine patients in the control group had phantom pain ($P < 0.01$). At 6 months follow-up, one patient in the study group and eight in the control group had phantom pain ($P < 0.002$). The incidence at 1 year follow-up remained the same.

Phantom limb (Fig. 2)

At 7 days postoperatively, three patients in the study group and nine patients in the control group had phantom limb sensation ($P < 0.01$). The incidence remained the same at 6 months follow-up. At 1 year, two patients in the

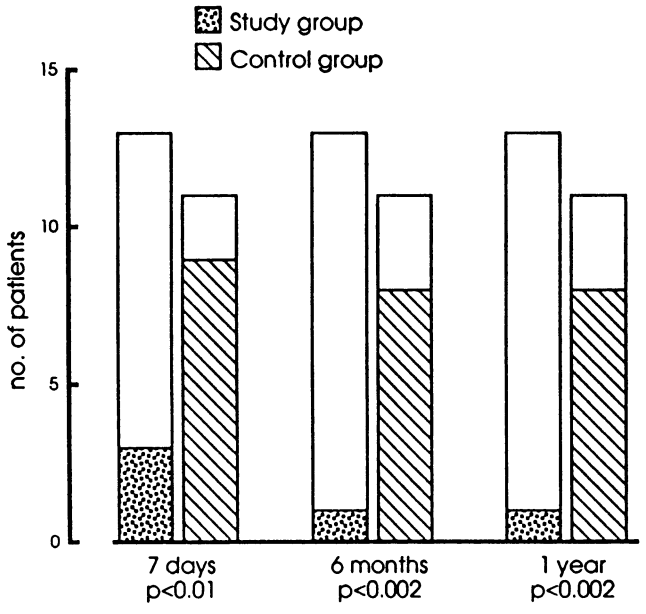

Figure 1. Incidence of phantom pain.

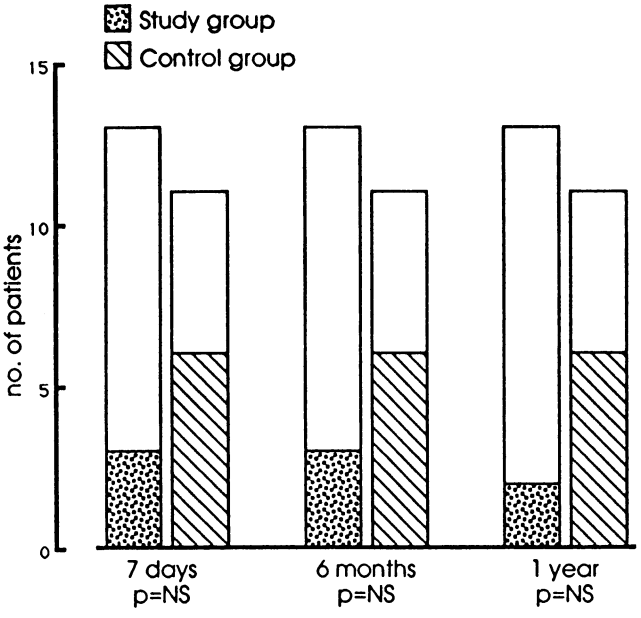

Figure 3. Incidence of stump pain.

study group and eight in the control group had phantom limb sensation ($P < 0.05$).

Stump pain (Fig. 3)

At 7 days and 6 months postoperatively, three patients in the study group and six patients in the control group had stump pain (P=NS). At 1 year follow-up, two patients in the study group and six in the control group had stump pain (P=NS).

The three patients who had previous amputations stated that they noticed a major difference in their pain and phantom limb sensation. They all had significant phantom limb pain after their first operation.

In the study group, two patients developed urinary retention, requiring catheterisation for 4 days postoperatively, and two patients developed faecal incontinence which settled 2 days postoperatively.

Discussion

This study shows that the epidural infusion of diamorphine, clonidine and bupivacaine in the cases described above is effective in preventing phantom limb pain and phantom limb sensation. The mechanism is uncertain and probably complex, accounted for by changes in the activity and neurochemistry of the cerebral cortex, peripheral neurones and spinal cord.

The purpose of the study was to establish a safer epidural infusion regimen for use on general surgical wards.

Clonidine is an α_2-adrenergic agonist which produces analgesia via a non-opioid receptor. Analgesia is accompanied by sedation and hypotension. The addition of morphine and bupivacaine did not cause respiratory depression or hypotension. There was, however, an incidence of minor side-effects in the study group. Two patients developed urinary retention, a known side-effect of epidural morphine and bupivacaine. A further two patients developed faecal incontinence, presumably related to bupivacaine-mediated reduction in anal sphincter tone.

In a similar study it has been shown that epidural blockade with bupivacaine and morphine is effective in controlling phantom limb pain in the first year after operation *(3)*. However, there is no mention of the well-known risks of respiratory depression and hypotension.

We found no significant improvement in stump pain. Stump pain is thought to arise from the peripheral nervous system, possibly the sprouts of regenerating nerve fibres *(6)*. It is sometimes treated by surgical excision of the neuromas in the stump, injection of local anaesthetics or with oral agents. Its mechanism does not appear to be modified by epidural infusion.

Our study suggests that preoperative epidural infusion of morphine, bupivacaine and clonidine significantly reduces the incidence of phantom limb pain and phantom limb sensation and is safe for use on general surgical wards with a low incidence of minor side-effects.

References

1 Krebs B, Jensen TS, Kromer K, Neilsen J, Jorgensen HS. Phantom limb phenomena in amputees 7 years after limb amputation. *Pain Suppl 2* 1984; S85.

2 Sherman RA, Sherman CJ. Prevalence and characteristics of chronic phantom limb pain among American veterans. *Am J Phys Med* 1983; **62**: 227–38.

3 Bach S, Noreng MF, Tjellden NU. Phantom limb pain in amputees during the first 12 months following limb amputation, after preoperative lumbar epidural blockade. *Pain* 1988; **33**: 297–301.

4 Bonnet F, Boico O, Rostaing S, Loriferne JF, Saada M. Clonidine induced analgesia on postoperative patients: epidural versus intramuscular administration. *Anesthesiology* 1990; **72**: 423–7.

5 Jensen TS, Krebs B, Neilsen J, Rasmussen P. Phantom limb, phantom pain and stump pain in amputees during the first six months following limb amputation. *Pain* 1983; **17**: 243–56.

6 Siegried J, Simmerman M. Preface I. In: J Siegfried, M Zimmerman, eds. *Phantom and Stump Pain*. Berlin: Springer-Verlag, 1991; 5–7.

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