PLASMA CONCENTRATIONS OF BUPIVACAIN FOLLOWING COMBINED SCIATIC AND FEMORAL 3 IN 1 NERVE BLOCKS IN OPEN KNEE SURGERY

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SUMMARY
We administered combined femoral 3 in 1 and sciatic nerve blocks to provide postoperative pain relief in 22 consecutive patients undergoing elective knee replacement surgery under spinal anaesthesia. The patients were allocated randomly to two groups. In group A (n = 11) the blocks were performed with 0.5% bupivacaine (with adrenaline) 3 mg/kg body weight and in group B (n = 11) 0.5% plain bupivacaine in the same dose was used. Serial plasma concentrations of bupivacaine were measured for up to 2 h and the duration of postoperative analgesia was measured in both groups. No significant differences were found between the two groups. There were no clinical signs or symptoms of bupivacaine toxicity in each group. This study demonstrated that, after combined sciatic and 3 in 1 femoral block, concentrations of bupivacaine associated with toxicity were not reached, even though the dose of bupivacaine administered exceeded the manufacturer’s recommended dose by 50%.

KEY WORDS
Anaesthetics, local: bupivacaine. Anaesthetic techniques: sciatic and femoral 3 in 1 nerve blocks.

In our experience, satisfactory postoperative analgesia following open knee surgery may be achieved using single 3 in 1 femoral and sciatic nerve blocks with 0.5% bupivacaine 3 mg/kg body weight with or without 1:200000 adrenaline. This dose exceeds that of 2 mg kg⁻¹ recommended by the manufacturer, but is less than the 10 mg kg⁻¹ used by Moore [1] in a similar study.

Recommended doses of local anaesthetic drugs depend upon variability of systemic absorption rates which are influenced by such factors as tissue perfusion and the likelihood of inadvertent i.v. injection. Smith [2, 3] showed that peak plasma concentrations of local anaesthetic drugs were greater following perineal and intercostal infiltration than after caudal and extradural injection with the same dose of drug.

Sciatic and femoral 3 in 1 nerve blocks appear to be associated with low rates of absorption. Therefore we have examined bupivacaine concentrations following combined sciatic and femoral 3 in 1 block with either plain 0.5% bupivacaine or 0.5% bupivacaine with adrenaline and related these to the bupivacaine concentrations associated with toxicity. We also recorded the incidence of adverse affects and the duration of analgesia.

PATIENTS AND METHODS
Following Ethics Committee approval, informed consent was obtained from 22 consecutive ASA I–III patients undergoing elective knee replacement surgery. The selected patients did not suffer any known sensitivity to local anaesthetics, have groin or lumbar sepsis, or have any contraindication to lumbar puncture.

Anaesthetic procedure
No premedication was given to the patient. On admission to the anaesthetic room, the patients were allocated randomly to one of two groups. The patient was re-identified and two 14-gauge i.v. cannulae were inserted under local anaesthetic (1% lignocaine). One cannula was used only for...
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Blood sampling. Dextrose saline was infused i.v. via the other cannula at a rate of 100 ml h⁻¹. ECG and non-invasive arterial pressure were monitored from the start of the procedure.

Spinal anaesthesia was performed with the patient in the sitting position using plain 0.5% bupivacaine 3 ml. Five minutes after the spinal block had been performed, the sciatic and femoral 3 in 1 nerve blocks were administered for postoperative pain relief. Group A received 0.5% bupivacaine with adrenaline 1:200000 and group B received plain 0.5% bupivacaine for the peripheral nerve blocks. The nerve blocks were performed with the aid of an insulated 22-gauge, 100-mm pole needle attached to a peripheral nerve stimulator (Neurostim: Hugo Sachs Elektronik Type 220).

The sciatic nerve block was performed using a classical posterior approach in all except five patients (three in group A and two in group B) who had undergone previous hip replacement; in these the anterior approach was used to avoid repositioning an anaesthetized patient with a possible prejudicial effect on the hip prosthesis. The femoral 3 in 1 nerve block was performed as described by Winnie [4]. The total volume of local anaesthetic (3 mg kg⁻¹) was distributed between the sciatic and femoral nerves in a ratio of 1:1.5.

**Blood samples**

Ten-millilitre blood samples were obtained in lithium heparin bottles. The plasma was separated within 4 h and stored at -20 °C until required for analysis. Samples were taken at the time of insertion of the i.v. cannula (t = 0), every 5 min after the peripheral nerve block for the first 30 min and every 15 min thereafter for the next 90 min.

Plasma concentrations of bupivacaine were measured using high pressure liquid chromatography, using the technique described by Wieand and Chou [5].

**Patient assessment**

The time taken for return of sensation to the blocked limb (lateral part of thigh for femoral 3 in 1 and plantar surface of foot for sciatic) was noted. The extent of analgesia to pinprick was assessed at 60-min intervals by a trained nurse observer who was blind to patient grouping, and the occurrence of adverse side effects was noted. The time of the patient’s first request for analgesia for pain in the vicinity of the operation was noted.

**RESULTS**

There were no significant differences between the two groups in age and weight. Anaesthesia was uneventful in all patients and there was no evidence of a toxic reaction to the local anaesthetic. The peripheral nerve blocks were successful in all 22 patients. Two patients, however, needed analgesia only 6 h after completion of the operation.

The mean peak plasma concentration of bupivacaine using the plain 0.5% solution was 0.703 (0.09) µg ml⁻¹ and that for the combination of bupivacaine with adrenaline was 0.787 (0.14) µg ml⁻¹ (ns; t = 0.4, P = 0.6). The mean time to peak plasma concentration of bupivacaine was 60 (7) min in the group receiving plain 0.5% bupivacaine (group B) and 63 (7) min in group A (P > 0.05). The bupivacaine concentration–time profiles for the two groups did not differ significantly (analysis of variance with repeated measures: F = 0.11, P = 0.7) (fig. 1).

The time taken for return of sensation was 9 (1) h in group A and 14 (3) h in group B for the femoral distribution and 13 (1) h in group A and
20 (4) h in group B for the sciatic distribution. However, some patients experienced pain at the site of surgery before complete return of sensation in the representative areas tested. The mean time to first analgesia was 15 (2) h in group A and 20 (4) h in group B. The difference was not significant ($t = -1.08, P = 0.29$). No patient reported any untoward effects following the peripheral nerve blocks.

**DISCUSSION**

This study has demonstrated that, after combined sciatic and 3 in 1 femoral block, concentrations of bupivacaine associated with toxicity (> 2 µg ml$^{-1}$) were not reached, even though the dose of bupivacaine administered exceeded the manufacturer’s recommended dose (2 mg kg$^{-1}$) by 50%.

The addition of adrenaline to bupivacaine did not influence significantly the peak plasma concentrations of bupivacaine, time to reach peak concentration, or duration of postoperative analgesia. There were no concentrations in excess of the reported toxic concentration of 2 µg ml$^{-1}$. However, in one patient (weight 87.5 kg) who received bupivacaine with adrenaline for his nerve blocks, the peak plasma concentration of bupivacaine was 2 µg ml$^{-1}$ at 5 min. He did not receive any sedation and exhibited no clinical signs or symptoms of toxicity. The duration of analgesia at the operation site for this patient was 12 h.

Time to first analgesia in both groups of patients was about 17 h. This included five patients who received opioids for pain at a site other than the operated knee, as patients undergoing knee replacement surgery frequently have a polyarticular affliction.

The potential toxicity of local anaesthetic drugs is determined by several factors which include site of injection [6, 7], rate of injection [8], concentration of drug used and the use of vasoconstrictors to reduce systemic absorption [9, 10].

One of the most important factors contributing to the toxicity of local anaesthetic agents is the vascularity of the area into which they are injected [6, 11]. In this study, the time to peak concentration of bupivacaine in both groups was relatively slow (63 min in group A and 60 min in group B).

Reynolds [12] infused bupivacaine i.v. and described toxic symptoms of a minor nature at an arterial concentration of 1.5–2 µg ml$^{-1}$. Jorfeldt and colleagues [13] infused bupivacaine i.v. to a mean arterial concentration of 2 µg ml$^{-1}$ with no neurological or cardiovascular side effects. They suggested that, in man, “the dangerous level” was 4 µg ml$^{-1}$. This value is supported by blood concentrations in patients during convulsions [14]. Toxicity is related, not to the total drug, but to the concentration of the drug which is free and active in the plasma. Bupivacaine has been shown to be highly protein bound, with 90% binding in vivo at concentrations of up to 5 µg ml$^{-1}$ [15].

Although the concentration of bupivacaine was less at 120 min than the peak concentration in all patients, there is a possibility of later increases in the plasma concentration of bupivacaine if top up doses are administered through a catheter in the vicinity of the sciatic and femoral nerves, with the concurrent possibility of side effects.

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**REFERENCES**

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