Effect of nimodipine on regression of spinal analgesia

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Summary
We have investigated the effect of infusion of nimodipine on the spread of spinal anaesthesia in 50 patients undergoing transurethral procedures. Patients were allocated randomly to receive during operation continuous infusion of nimodipine 10 ml h⁻¹ (group N, n=25) or normal saline (group C, n=25) in a double-blind manner. All patients received hyperbaric lidocaine 100 mg (5% in 8% dextrose) intrathecally and were then placed in the lithotomy position. Twenty minutes after intrathecal injection the level of spinal analgesia was tested with a pressure palpator and a baseline was established. Assessments were repeated 5, 10 and 15 min thereafter. Five minutes after establishing baseline, mean regression of sensory analgesia did not differ between groups. Analgesia had regressed by 1.3 (SD 1.4) and 1.0 (1.9) cm, respectively. After 10 min, sensory block in group N regressed by 1.7 (1.7) cm and in group C by 1.5 (1.6) cm. After 15 min these values were 1.1 (1.7) cm and 2.2 (1.9) cm, respectively (P<0.035). Similar results were found after normalizing the changes by dividing the change by patient height. (Br. J. Anaesth. 1998; 81: 358–360).

Keywords: anaesthetic techniques, subarachnoid; anaesthetics local, lidocaine; calcium channel block, nimodipine

Previous studies have shown that systemic opioids and inhalation of 50% nitrous oxide enhance the level or delay regression of subarachnoid analgesia.¹⁻⁴ Calcium is involved in endogenous regulation of pain sensitivity and substances with calcium channel blocking effect have antinociceptive properties.⁵

We have investigated the effect of continuous infusion of nimodipine on the level of spinal analgesia produced by hyperbaric lidocaine.

Patients and methods
After obtaining approval from the Ethics Committee and informed patient consent, we studied 50 male patients, ASA II–III, undergoing elective transurethral prostatectomy or transurethral resection of bladder papillomas. Exclusion criteria were central nervous system disorders, intake of analgesics or drugs which may interact with analgesics, and hearing impairment. Patients were visited the day before surgery and the procedure of assessing the level of spinal analgesia was explained. Premedication was not given.

In the operating room, patients were allocated randomly to receive nimodipine (n=25) or normal saline (control group, n=25) in a double-blind manner. ECG, heart rate, arterial pressure (oscillotonometer) and ŠP₀₂ were monitored. Two peripheral 17-gauge i.v cannuæ were inserted, one to administer Ringer’s lactated solution and the other connected to an infusion pump (DSP, Johnson and Johnson) to administer normal saline or nimodipine 10 ml h⁻¹ (1 ml=0.2 mg). Infusion of nimodipine or normal saline was started before subarachnoid injection of lidocaine.

After local infiltration of the skin with 2% lidocaine, hyperbaric lidocaine 100 mg (2 ml of 5% lidocaine in 8% dextrose) was injected into the subarachnoid space. All lumbar punctures were performed in the L3–4 interspace using a 25-gauge Whitacre needle and with the patient lying in the left lateral position. Surgery and assessments of level of spinal analgesia were performed with the patient in the lithotomy position.

Twenty minutes after subarachnoid injection the level of sensory block was assessed from a caudad to a cephalad direction using a pressure palpator (Pressure FEELER 650 g Sedatelec, Chemin des Muriers, F-69540 Irigny, France).² A baseline level of block was determined 20 min after subarachnoid injection of lidocaine because at that time maximal spread of spinal anaesthesia is usually obtained.⁶ Four points lying on the left posterior, middle and anterior axillary lines, and on the line 4–5 cm medial to the left anterior axillary line at which patients responded to the palpator were located and marked as the baseline of sensory block. The procedure of establishing baseline and assessing the changes in spinal analgesia has been described elsewhere.¹⁻⁴ Sensory block was assessed in each group 5, 10 and 15 min after establishing baseline. Systolic (SAP) and diastolic (DAP) arterial pressures, and heart rate (HR) were recorded before and immediately after spinal anaesthesia, when baseline sensory block was established, and 5, 10 and 15 min thereafter. Nimodipine or normal saline was prepared by

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an anaesthetist who was not involved in administering anaesthesia or assessing the level of spinal analgesia. Thirty-five minutes after subarachnoid injection of lidocaine and 15 min after establishing baseline, when measurements were completed, infusion of nimodipine or normal saline was discontinued.

As patient height ranged from 155 to 185 cm, we adjusted the loss of level of analgesia (in cm) by dividing by patient height. Patient data, changes in the level of sensory block and haemodynamic changes at the predetermined times between the two groups were compared using the unpaired Student’s t-test.

**Results**

Patient characteristics and volume of solution administered during operation were similar between groups. Mean age, body weight and height were 71 (range 53–85) yr, 72 (SD 14) kg and 166 (SD 10) cm, and 72 (53–88) yr, 73 (13) kg and 166 (7) cm in the nimodipine and control groups, respectively. Mean volumes administered were nimodipine 7.3 (SD 0.9) ml (1.5 mg) and normal saline 7.2 (0.7) ml.

Five minutes after establishing baseline, similar regression of the level of sensory block was found in the nimodipine and control groups. At this point the 95% limits of confidence for the nimodipine group were −1.843 and −0.699, and −1.797 and −0.202 for the control group. Ten minutes after defining baseline, the level of sensory analgesia regressed further in both groups. The 95% limits of confidence were −2.443 to −1.057 and −2.139 to −0.801 in the nimodipine and control groups, respectively. However, at 15 min, regression differed significantly between the two groups, being two-fold greater in the control group (P=0.038); the 95% limits of confidence were −1.853 and −0.446 in the nimodipine group and −3.00 and −1.453 in the control group (table 1).

After adjusting for height, the differences were consistent with the raw data and significant 15 min after baseline (P=0.035) (table 1). SAP, DAP and HR did not differ between groups at any time (table 2).

**Discussion**

This study has shown that i.v. infusion of nimodipine was associated with a delay in regression of sensory block produced by intrathecal injection of lidocaine.

Previous studies have shown that systemic administration of opioids or inhalation of 50% nitrous oxide enhanced the spread of spinal analgesia or delayed its regression.1–4 Opioids and nitrous oxide may alter the pain process at a supraspinal level by disinhibiting neurones in the rostral ventromedial medulla.1,2,7,8 In contrast, tenoxicam, a non-steroid anti-inflammatory analgesic, had no effect on the spread of spinal analgesia.8 This drug has a very low lipophilicity and concentrations in the central nervous system are negligible.

Nifedipine given extradurally in rats has analgesic properties and it has been suggested that the antinociceptive effect is regulated by spinal rather than supraspinal mechanisms.9

Calcium channel antagonists interfere with the action of local anaesthetics. In rats, verapamil given intrathecally potentiated spinal analgesia produced by lidocaine or tetracaine.10 Intrathecal verapamil alone did not produce motor or sensory block but in combination with lidocaine or tetracaine, the block produced was more potent and of longer duration than that produced by the local anaesthetic alone.10 Iwasaki and colleagues demonstrated in rats that local sensory block produced by lidocaine injection at the tail base was potentiated by verapamil, diltiazem and nicardipine in a dose-dependent manner.11

In a laboratory study, Sugiyama and Muteki showed that tetracaine, at concentrations required
for spinal anaesthesia, depressed high and low voltage-activated calcium channels of dorsal root ganglion cells of rat sensory neurones, the most susceptible being the L-type calcium channel. The anaesthetic potencies of local anaesthetics correlate well with their potencies in inhibiting calcium influx via voltage-gated channels. Therefore, inhibition of calcium influx via voltage-gated calcium channels resulting in inhibition of calcium-dependent biochemical processes may contribute to the mechanisms of spinal anaesthesia. Hirota and colleagues studied the effect of procaine, prilocaine, lidocaine, bupivacaine, amyloucaine and R(+) and S(−) ropivacaine on L-type voltage-activated calcium channels in cerebrocortical membranes prepared from rat brains. They found an interaction between local anaesthetic agents and the L-type calcium channel.

In one clinical study, systemic nifedipine potentiated extradural morphine-induced analgesia, but this was accompanied by significant decreases in arterial pressure. In our study, nimodipine did not produce hypotension. However, the lithotomy position after spinal anaesthesia attenuates the decrease in arterial pressure, and this position may have contributed to the haemodynamic stability of our patients.

Our data support the experimental data, suggesting a contribution of voltage-activated calcium channels to nociception process. In our study, the delay in regression of spinal analgesia associated with nimodipine had statistical, but probably not clinical, significance. In contrast with fentanyl or nitrous oxide, administration of nimodipine is not recommended to enhance or delay regression of spinal block.

References

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