SYSTEMIC FENTANYL ENHANCES THE SPREAD OF SPINAL ANALGESIA PRODUCED BY LIGNOCAINE

A. FASSOULAKI, C. SARANTOPOULOS AND S. CHONDRELI

SUMMARY
Seventy-one patients undergoing transurethral prostatectomy under spinal anaesthesia were allocated randomly to one of four groups: fentanyl-naloxone (F-Nal), fentanyl-normal saline (F-NS), normal saline-naloxone (NS-Nal), and normal saline-normal saline (NS-NS) group. Twenty minutes after subarachnoid injection of hyperbaric lignocaine 100 mg, we tested the level of spinal analgesia (pinprick sensation) and administered i.v. either fentanyl 100 μg (F-Nal and F-NS groups) or normal saline 2 ml (NS-Nal and NS-NS groups). Ten minutes later, we assessed the new levels of analgesia and administered i.v. either naloxone 0.4 mg (F-Nal and NS-Nal groups) or normal saline 1 ml (F-NS and NS-NS groups). The level of sensory block was reassessed 10 min after the naloxone or normal saline treatment. Ten minutes after i.v. administration of fentanyl or normal saline, the level of analgesia increased in the F-Nal and F-NS groups by 3.98 and 3.78 cm, respectively, and differed significantly compared with the NS-Nal and NS-NS groups (both P < 0.07). Forty minutes after spinal block, the decrease in analgesia in the F-Nal group (3.97 cm) differed significantly from that in the other groups (P < 0.01). Systemic fentanyl enhanced the spread of analgesia. This enhancement was antagonized by naloxone.

KEY WORDS

For certain procedures, spinal anaesthesia may be preferred in the elderly [1]. While administering small doses of fentanyl to patients undergoing surgery under spinal anaesthesia, we observed central spread of sensory analgesia and, occasionally, pain relief after operation by the time the lignocaine block was expected to regress. The present study was designed to evaluate the effect of low doses of systemic fentanyl on the level of spinal analgesia produced by intrathecal lignocaine. The effect of naloxone after administration of either fentanyl or normal saline was investigated also.

PATIENTS AND METHODS
The study was approved by the Local Ethics Committee and informed consent was obtained from all patients.

Seventy-one unpremedicated patients undergoing transurethral resection of prostate (TURP) under spinal anaesthesia were allocated randomly to one of four groups: i.v. fentanyl-naloxone (group F-Nal); i.v. fentanyl-normal saline (group F-NS); i.v. normal saline-naloxone (group NS-Nal); i.v. normal saline-normal saline (group NS-NS). Patients who were receiving tranquillisers and analgesics before operation, or patients with CNS disorders, were excluded from the study.

On arrival of the patient in the operating room, a cannula was inserted into a suitable vein and Ringer Lactate solution administered i.v. Arterial pressure, ECG, heart rate and oxygen saturation were monitored. Oxygen was administered via a Ventimask designed to deliver 35% oxygen.

With the patient in the left lateral position and after subcutaneous infiltration with 2% lignocaine, 5% (100 mg) hyperbaric lignocaine (Xylocaine, Astra, S.G. 1030-1035) 2 ml was...
TABLE I. Patient characteristics (mean (range or SD))

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<tr>
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<th>Fentanyl–naloxone</th>
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<th>Normal saline–naloxone</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>68.9 (58–80)</td>
<td>70.7 (62–80)</td>
<td>72.5 (62–87)</td>
<td>72.0 (66–85)</td>
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<tr>
<td>Weight (kg)</td>
<td>65.7 (10.4)</td>
<td>72.5 (12.5)</td>
<td>73.9 (13.1)</td>
<td>73.4 (9.3)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166 (7)</td>
<td>167 (5)</td>
<td>167 (10)</td>
<td>170 (7)</td>
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</table>

TABLE II. Changes to pinprick sensation (mean (SD)) in each group of patients 30 and 40 min after spinal anaesthesia. P < 0.01: ** vs normal saline–naloxone and normal saline–normal saline groups; †† vs fentanyl–normal saline, normal saline–naloxone and normal saline–normal saline groups

<table>
<thead>
<tr>
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<th>Fentanyl–naloxone</th>
<th>Fentanyl–normal saline</th>
<th>Normal saline–naloxone</th>
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<tr>
<td></td>
<td>(n = 18)</td>
<td>(n = 18)</td>
<td>(n = 17)</td>
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<td>30 min</td>
<td>3.98 (0.87)**</td>
<td>3.78 (0.94)**</td>
<td>-0.17 (0.23)</td>
<td>-0.26 (0.73)</td>
</tr>
<tr>
<td>40 min</td>
<td>-3.97 (0.92)††</td>
<td>-0.41 (0.40)</td>
<td>-0.81 (0.95)</td>
<td>-0.79 (0.80)</td>
</tr>
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injected intrathecally at the L3–4 interspace. All patients remained in the left lateral position for 1 min, after which they were placed in the lithotomy position.

Twenty minutes after the intrathecal injection, the level of analgesia was assessed by a blinded observer. Pinprick sensation was assessed using a 21-gauge needle in a cephalad to caudad direction. To assess the level of analgesia, we defined four points on the posterior, middle and anterior axillary lines of the left abdominal wall, and on the line 5 cm medial to the anterior axillary line, above which patients experienced sensation to pinprick. Changes in the level of spinal analgesia were measured in cm because of difficulty in locating dermatomes in patients in the lithotomy position.

After the spread of spinal analgesia was assessed, 2 ml of a solution of either fentanyl 100 μg (groups F–Nal and F–NS) or normal saline was administered i.v. Changes to pinprick sensation were noted 10 min later (30 min after intrathecal injection) and either naloxone 1 ml (0.4 mg) (groups F–Nal and NS–Nal) or normal saline 1 ml (groups F–NS and NS–NS) was injected i.v. Ten minutes later (40 min after the intrathecal injection), the level of analgesia was reassessed.

The level of analgesia defined 20 min after subarachnoid injection of lignocaine was taken as the baseline level and changes in the level following either fentanyl or normal saline administration were measured in cm. This level was then redefined as zero and the changes after administration of either naloxone or normal saline were measured. The overall change in the level of sensory block in each group of patients at 30 and 40 min after spinal anaesthesia was calculated by averaging the changes observed in the height of each of the four points lying on the predetermined lines.

A factorial analysis of variance with repeated measures design was used for comparisons of changes in levels of analgesia between groups. When a statistically significant difference was found, Scheffé’s method was applied to evaluate comparisons between individual groups.

RESULTS

The four groups were similar in age, weight and height (table I).

A significant difference between the groups in changes to pinprick sensation was found 10 min after the i.v. administration of either fentanyl or normal saline ($F = 175.5$ with 3,67 d.f. and $P < 0.01$). The F–Nal and F–NS groups reported a similar mean increase in cephalad spread of sensory analgesia (table II). This increase corresponded to 1.5 spinal segments and differed significantly compared with the changes reported by patients in the NS–Nal and NS–NS groups. No significant changes occurred in the NS–Nal or NS–NS groups (table II).

Ten minutes after i.v. administration of either naloxone or normal saline, changes in spinal
analgesia to pinprick were significantly different between groups (\( F = 77.1 \) with 3,67 d.f. and \( P < 0.01 \)). Groups F-NS, NS-Nal and NS-NS reported minor decreases. In the F-Nal group, administration of naloxone resulted in a mean reduction in the level of analgesia of 3.97 cm (table II). This decrease was significant compared with the decreases in the three other groups (\( P < 0.01 \)).

DISCUSSION

The results of the present study show that fentanyl, administered i.v., increased the cephalad spread of sensory analgesia produced by intrathecal lignocaine. This effect was antagonized by naloxone. After the systemic administration of normal saline, naloxone had no effect on the spread of spinal analgesia.

The mechanism of this interaction between systemic fentanyl and intrathecal lignocaine administration is not clear. Systemic fentanyl may affect the intrathecally injected lignocaine indirectly by altering spinal cord blood flow. Systemic morphine has been shown to decrease spinal blood flow [2]. This may reduce absorption of local anaesthetic, increasing the duration rather than the spread of sensory block. However, it is obvious from the NS—Nal and NS—NS groups that the fixation of hyperbaric lignocaine in spinal regions was complete by 20 min. Therefore, changes in spinal cord flow is not likely to affect the spread of sensory block.

The spread of analgesia which followed administration of fentanyl did not occur in the NS—Nal and NS—NS groups. This eliminates the possibility of continued mixing or non-fixation of the lignocaine in the subarachnoid space.

Neither intrathecal morphine 0.2–0.4 mg [3], nor extradural fentanyl [4, 5], modify the analgesic block produced by intrathecal or extradural bupivacaine, respectively. However, the onset and duration of effect of i.v. alfentanil differed significantly compared with alfentanil administered intrathecally [6].

It is conceivable that subclinical analgesia above the level of complete analgesia produced by subarachnoid lignocaine might be potentiated and become clinically detectable by small doses of systemic fentanyl. However, this mechanism is unlikely, because of the low dose of fentanyl administered.

Opioid receptors may act also at supraspinal sites, altering pain processing at supraspinal level or modulating spinal function [7]. Fentanyl may act in a manner similar to morphine and disinhibit the off-cell, a class of neurone in the rostral ventromedial medulla. These off-cells are involved in pain modulation and their disinhibition by morphine contributes to the analgesic effect of this drug [8].

From our data, it is not possible to distinguish between a change in spinal level and a change in the patient’s perception of pain. Assessment of temperature block might be helpful in resolving this issue, but our patients, although co-operative in determining pinprick sensation, were not willing to co-operate in temperature testing.

To our knowledge, neither the interaction of systemic fentanyl and intrathecal lignocaine nor its antagonism by naloxone has been reported previously. Our findings may possess clinical importance, as low doses of systemic fentanyl have a potential role in enhancing spinal analgesia.

REFERENCES