Minimum local analgesic concentration of extradural bupivacaine increases with progression of labour

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Summary

We have used the technique of double-blind sequential allocation to quantify the minimum local analgesic concentration (MLAC) of extradural bupivacaine for women in early (median cervical dilatation 2 cm) and late (median cervical dilatation 5 cm) labour. The first bolus was 20 ml of the bupivacaine test solution. The concentration was determined by the response of the previous woman to a higher or lower concentration of bupivacaine according to up and down sequential allocation. Efficacy was assessed using a 100-mm visual analogue pain score (VAPS). The test solution had to achieve a VAPS of 10 mm or less to be judged effective. In early labour, the MLAC of bupivacaine was 0.048% w/v (95% confidence intervals (CI) 0.037–0.058% w/v), and 0.140% w/v (95% CI 0.132–0.150% w/v) in the late group. The MLAC of bupivacaine in late labour was greater by a factor of 2.9 (95% CI 2.7–3.2) compared with the MLAC in early labour (P < 0.0001, 95% CI difference 0.08–0.11). We conclude that advancing labour requires an increased concentration of extradural bupivacaine for pain relief. (Br. J. Anaesth. 1998; 80: 11–13)

Keywords: pregnancy; analgesia, obstetric; analgesic techniques, extradural; anaesthetics, local, bupivacaine

Bupivacaine is used widely to provide extradural pain relief in labour in a wide range of doses, concentrations and volumes. The paucity of data on the dose–response relationships of extradural analgesics in labour has led to the development of a benchmark for extradural local anaesthetics, the minimum local analgesic concentration (MLAC). This is defined as the effective concentration in 50% of women in the first stage of labour (EC50).1

The impact of advancing cervical dilatation on the MLAC has never been assessed, and we sought to take advantage of differing obstetric policies within a single maternity unit. Because one obstetric team discouraged extradural pain relief in early labour, two groups of women, one in early labour and one in late labour with minimal overlap with regard to cervical dilatation, were created. Our aim was to measure and compare the MLAC of bupivacaine at different stages of labour in these two groups of women.

Patients and methods

Our hospital Ethics Committee approved this double-blind sequential allocation study. After obtaining informed consent, we studied 61 women, ASA I or II, with singleton pregnancies and vertex presentation, requesting extradural pain relief in the first stage of labour. We excluded women who had received opioid or sedative drugs. Use of transcutaneous electrical nerve stimulators and Entonox before extradural request was not regarded as a need to exclude.

The extradural technique was standardized. I.v. Ringer’s solution was infused via a forearm cannula. The extradural space was found, either at L2–3 or L3–4 interspace, in the sitting position. Loss of resistance to saline was used to identify the extradural space, limiting the injection to 2 ml in order to minimize dilution of local anaesthetic. The extradural catheter was advanced 3 cm into the space and then aspirated. For the purpose of the study, the test dose was omitted.

The first administration of bupivacaine was from a freshly prepared syringe containing 20 ml of test solution given over 5 min; bupivacaine was diluted with 0.9% w/v saline to achieve the desired concentration at room temperature.

We recruited two groups of 30 women each. Each group was comprised of women from a single obstetric team, one in early and one in late labour, creating two groups with different ranges of cervical dilatation at the time of extradural insertion. The diagnosis of labour was confirmed by the obstetric team before extradural request. Entry into the study required an initial visual analogue pain score (VAPS) greater than 30 mm.

The first woman in each group received 0.1% w/v bupivacaine, in common with the starting point of an earlier study.2 Thereafter, the concentration of the test solution in each individual syringe was determined by the response of the previous patient to the test dose was omitted.

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ASSessment

Efficacy of the first dose was assessed using a 100-mm VAPS. The side presented to the woman in labour portrayed faces depicting happiness (0) to misery (100) in five stages. A movable cursor...
provided a numerical selection on the rear of the scale. Observations were made at 0, 15, 30 and 60 min after injection of the first bolus containing study solution. Three outcomes were possible.

**Effective**

This required that the VAPS decreased to 10 mm or less at the height of contraction, within 60 min, and indicated the end of the study and directed a decrement of 0.01% w/v bupivacaine for the next woman.

**Ineffective**

This followed failure of the VAPS to reach 10 mm within 60 min of the test solution. If at 30 min the woman claimed satisfactory analgesia despite not reaching the VAPS target of 10 mm, the study period was extended to a possible maximum of 60 min. At 30 min, after failing to reach the VAPS target, rescue analgesia consisting of 0.25% w/v bupivacaine 12 ml was offered. After this, a reduction in VAPS to 10 mm or less indicated the end of the study and directed a 0.01% w/v bupivacaine increment for the next woman.

**Repeat**

Failure to achieve a VAPS of 10 mm after the rescue bolus implied a technical failure, and directed that the same concentration be repeated for the next woman.

**For all women, age, weight, height, gestation, parity, cervical dilatation and use of oxytocin were recorded.**

**STATISTICAL ANALYSIS**

Patient and obstetric data were collected and are presented as mean (SD) and median (interquartile range) as appropriate. The median effective concentration was estimated from the up–down sequences using the formula of Dixon and Massey which enabled MLAC with 95% confidence interval to be derived.3 The data were also subjected to Wilcoxon and Litchfield probit regression analysis as a back-up sensitivity test. Further analyses included Student’s t test, Mann–Whitney U test, Kolmogorov–Smirnoff test for Gaussian distribution and Fisher’s exact test.4 5 All analyses were carried out on two personal computers (Dell Dimension XPS P100c and Zenith Z-Star EX 486DX 50) using the following software: Microsoft Excel 6.0a for Windows, Statistical Package for the Social Sciences (SPSS) 6.1 for Windows, GraphPad Instat 2.05a for DOS and Pharmacologic Calculation System (PCS) 4.2 for DOS. Statistical significance was defined for an overall α error at the 0.05 level. All P values were two-sided.

**Results**

There were no significant differences in characteristics in the groups (table 1).

<table>
<thead>
<tr>
<th></th>
<th>Early (n=30)</th>
<th>Late (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.2 (22–35)</td>
<td>29.3 (23–38)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.5 (63.5)</td>
<td>74.1 (69.5)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166.4 (4.20)</td>
<td>168.3 (4.95)</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>40 (40–41)</td>
<td>40 (40–41)</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Multiparous</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Oxytocin</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Cervix (cm)</td>
<td>2 (2–3)</td>
<td>5 (5–5)</td>
</tr>
<tr>
<td>Initial VAPS (cm)</td>
<td>68 (59–70)</td>
<td>90 (85–94)</td>
</tr>
</tbody>
</table>

Women in late labour had greater dilatation of the cervix (P<0.0001) and higher initial visual analogue pain scores (VAPS) (P<0.0001) than those in early labour reaching the VAPS target of 10 mm, the study period was extended to a possible maximum of 60 min. At 30 min, after failing to reach the VAPS target, rescue analgesia consisting of 0.25% w/v bupivacaine 12 ml was offered. After this, a reduction in VAPS to 10 mm or less indicated the end of the study and directed a 0.01% w/v bupivacaine increment for the next woman.

**Repeat**

Failure to achieve a VAPS of 10 mm after the rescue bolus implied a technical failure, and directed that the same concentration be repeated for the next woman.

For all women, age, weight, height, gestation, parity, cervical dilatation and use of oxytocin were recorded.
late labour was significantly greater than that in early labour by a factor of 2.9 (95% CI 2.7–3.2).

Discussion

We have shown that the MLAC of bupivacaine increased with advancing labour. This implies that when low concentrations of local anaesthetic are used for extradural analgesia in order to achieve motor sparing and perhaps ambulation, the concentration may need to be increased as labour progresses to maintain satisfactory analgesia. Breen and colleagues reported that approximately 50% of women receiving an infusion of 0.04% w/v bupivacaine in combination with fentanyl 1.7 μg ml<sup>–1</sup> and epinephrine 1.7 μg ml<sup>–1</sup> went on to deliver without a change in regimen.<sup>6</sup>

The application of the two obstetric policies was not exact, and there was a minor degree of overlap with regard to cervical dilatation. One woman in late labour had a cervical dilatation of 3 cm; without this the two groups would have been distinct. The double difficulties posed by differing obstetric policies and consumer choice prevented randomization to the groups.

There was a significant difference in the two groups regarding the initial VAPS. This suggests that the obstetric policy was effectively applied to women in late labour who might otherwise have received extradural pain relief earlier.

The use of saline to detect loss of resistance implied that dilution of the test concentration of bupivacaine could have occurred within the extradural space. To minimize this, extradural injection of saline was reduced to a clinically insignificant volume. The alternative to saline would have been air. This was rejected because of a suggestion that pockets of air in the extradural space might obstruct the spread of local anaesthetic.<sup>7</sup>

The role of concentration of local anaesthetic in conduction block is in the production of differential nerve block.<sup>8</sup> The requirement for an increasing concentration as labour progresses prompts speculation that larger fibres are recruited as the cervix opens and the head descends. The term visceral is used to describe the pain of the contracting uterus and the dilating cervix, supplied by sympathetic afferent fibres, which characterizes the first stage of labour. As the presenting part distends and compresses pelvic structures during the second stage, the pain is described as somatic.<sup>9</sup> In reality the distinction between the two is not always clear cut, but it might be reasonable to speculate that at the earliest moment of labour, pain is purely visceral in nature. It might also be worth speculating that first stage pain is predominantly C fibre, with an increasing contribution from Aδ fibres as labour progresses. Our knowledge of spinal opioids, which block C-fibre discharge more effectively than Aδ fibres, and are more useful in the first than in the second stage of labour, supports this hypothesis.<sup>10,11</sup> Such a hypothesis might explain our findings. An alternative explanation is that increasing concentration is required as the frequency of stimulation of individual pain fibres intensifies. This would be unlikely if frequency dependent block occurs in clinical practice. Studies with bupivacaine indicate that increased frequency of stimulation leads to more profound conduction block.<sup>12</sup>

In summary, we found that as labour progressed, there was a significant increase in the requirements for extradural bupivacaine.

References