Acid–base state of cerebrospinal fluid during pregnancy and its effect on spread of spinal anaesthesia

Y. HIRABAYASHI, R. SHIMIZU, K. SAITO, H. FUKUDA AND T. IGARASHI

Summary
To assess the possible relationship between changes in acid–base state of cerebrospinal fluid (CSF) and enhanced spread of spinal anaesthesia during pregnancy, we have measured CSF pH, carbon dioxide tension (P\textsubscript{CO\textsubscript{2}}) and HCO\textsubscript{3}– values in 73 women undergoing spinal anaesthesia with hyperbaric amethocaine 8 mg. Patients were allocated to one of four groups according to gestational period: non-pregnant group (n = 13), first trimester group (8–13 weeks, n = 19), second trimester group (14–26 weeks, n = 11) and third trimester group (27–39 weeks, n = 30). The pH of the CSF was greater in the second and third trimester groups than in the non-pregnant group. CSF P\textsubscript{CO\textsubscript{2}} decreased by 0.53–0.8 kPa throughout pregnancy. CSF HCO\textsubscript{3}– was decreased throughout pregnancy. Overall, no clinically significant correlation was found between maximum cephalad spread of analgesia and CSF pH, P\textsubscript{CO\textsubscript{2}} or HCO\textsubscript{3}–. We conclude that pregnancy-induced changes in acid–base state of CSF have little effect on the spread of spinal anaesthesia, although there is a clinically different spread of spinal anaesthesia between non-pregnant and pregnant states. (Br. J. Anaesth. 1996;77:352–355)

Key words

The spread of regional anaesthesia is reported to be enhanced in pregnant compared with non-pregnant women\textsuperscript{1–5}. Mechanical\textsuperscript{6–8} and hormonal\textsuperscript{9–11} changes have been implicated as possible factors for pregnancy-induced enhancement of regional anaesthesia. In addition, acid–base changes during pregnancy have been suggested to affect spread of extradural anaesthesia\textsuperscript{5}.

Cerebrospinal fluid (CSF) is in contact with the spinal cord and spinal nerve roots, and changes in acid–base state of CSF during pregnancy may therefore affect spread of spinal anaesthesia. Although many investigators reported acid–base state of arterial blood during pregnancy\textsuperscript{12–16}, there are few studies which have dealt with acid–base state of CSF in pregnant women. The purpose of this study was to see if changes in acid–base state of CSF correlated with enhanced spread of spinal anaesthesia during pregnancy.

Patients and methods
The study was approved by the Hospital Ethics Committee and informed consent was obtained from all patients. We studied 13 non-pregnant and 60 pregnant women. All patients, ASA I–II, had no major health problems and no contraindications to spinal anaesthesia. Patients were allocated to one of four groups according to gestational period: non-pregnant group (n = 13), first trimester group (8–13 weeks, n = 19), second trimester group (14–26 weeks, n = 11) and third trimester group (27–39 weeks, n = 30). Operative procedures included arthroscopic operation on the knee (n = 13) in the non-pregnant group; procedures for cervical incompetency in the first (n = 19) and second (n = 11) trimester groups; and procedures for cervical incompetency (n = 6) and Caesarean section (n = 24) in the third trimester group.

None of the patients was premedicated. Patients were placed in the lateral position on a horizontal operating table. Under aseptic conditions, lumbar puncture was performed at the L3–4 interspace with a 25-gauge Quincke needle using a median approach. The needle was inserted with its bevel orientated parallel to the dural fibres and then rotated 90° to direct the bevel cephalad. To determine acid–base state of CSF, 1 ml of CSF was withdrawn just before administration of the drug. CSF pH, carbon dioxide tension (P\textsubscript{CO\textsubscript{2}}) and HCO\textsubscript{3}– were measured using a blood-gas analyser (178 pH/blood gas analyser, Ciba Corning Diagnostics, Boston, MA, USA) within 5 min. Amethocaine 8 mg in 2 ml of 10% glucose was given over 40 s. Lumbar puncture and sampling were performed by one anaesthetist who was unaware of the patient’s group assignment, although he knew the type of surgery and abdominal girth. Immediately after spinal injection, patients were turned gently to the supine horizontal position. No attempt was made to influence the level of sensory block by manipulating the operating table. Patients undergoing procedures for cervical incompetency were placed gently in the horizontal lithotomy position, 30 min after spinal injection. Left uterine displacement was applied.

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to parturients undergoing Caesarean section until the beginning of the operation. A second anaesthetist who was blinded to the CSF data assessed the spread of analgesia bilaterally using pinprick at 5, 10, 15, 20, 30 and 60 min after spinal injection according to a dermatomal chart. If the analgesic level differed on each side, the average value was used for analysis. In 22 of the 73 patients, an aliquot of the CSF sample was provided for progesterone analysis, which has been reported previously11.

Comparisons between the four groups were made by analysis of variance (ANOVA) followed by Fisher’s protected least significant difference test for parametric data, and Kruskal–Wallis followed by Fisher’s protected least significant difference test for non-parametric data. Correlation between indices of acid–base state and maximum cephalad spread of analgesia was analysed using Spearman’s rank correlation coefficient (ρ). P<0.05 was considered significant.

Results
There were no differences in age and height between the four groups (table 1). Median gestational age indicated that patient characteristics in the first trimester group clustered at the end of the range, second trimester group at the beginning of the range and third trimester group at the end of the range. The characteristics of the third trimester patients were similar gestationally to term parturients. Maximum cephalad spread of analgesia was higher in the second and third trimester groups than in the non-pregnant group. Times to maximum cephalad spread did not differ between the four groups (table 2).

CSF pH was greater in the second and third trimester groups than in the non-pregnant group (table 3). CSF pH did not correlate with maximum cephalad spread of analgesia (fig. 1A). CSF PCO2 was decreased by 0.53–0.8 kPa below non-pregnant levels even during the early stages of pregnancy and was maintained at this decreased level for the remainder of the pregnancy (table 3). CSF HCO3− correlated inversely with maximum cephalad spread of analgesia (fig. 1B). CSF HCO3− was decreased throughout pregnancy (table 3). CSF HCO3− correlated inversely with maximum cephalad spread of analgesia (fig. 1C). Overall, although there were significant differences in the changes in CSF pH, PCO2 and HCO3−, changes in median values and ranges were such that these were unlikely to be clinically significant.

Discussion
We have shown that CSF PCO2 began to decrease even in the early stages of pregnancy, and that CSF pH was unchanged during the early stages of pregnancy and then increased for the remainder of the pregnancy. These observations, however, are not surprising. Pregnancy induces an increase in minute ventilation to approximately 50% above non-pregnant levels6. This increase in minute ventilation, beginning early in the first trimester, decreases maternal PaCO2 from 5.33 kPa to approximately 4.0 kPa12–14. Arterial pH, however, remains near normal because of increased renal excretion of HCO3−12–14. The decrease in CSF PCO2 and HCO3− may be a direct result of changing PaCO2 and lower HCO3− levels in arterial blood. Unlike arterial blood, increased CSF pH during the middle and later stages of pregnancy, observed in this study, suggests a partially compensated acid–base change from non-pregnant controls.

Local anaesthetic solution applied to a nerve membrane exists in two forms: the non-ionized base and the ionized cation17. The Henderson–Hasselbalch equation for the equilibrium determines the levels of ionized and non-ionized forms. An increase in pH increases the amount of local anaesthetic in the non-ionized base form, which should enhance the rate of diffusion across the nerve sheath and nerve membrane, resulting in a more rapid onset time of nerve block. In this study, CSF

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**Table 1** Patient characteristics (median [range] or mean (SD)) in the non-pregnant, first trimester, second trimester and third trimester (term) pregnant groups. *P<0.05 vs non-pregnant group

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>13</td>
<td>19</td>
<td>11</td>
<td>30</td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156 (8)</td>
<td>158 (3)</td>
<td>158 (6)</td>
<td>156 (6)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>53 (9)</td>
<td>55 (6)</td>
<td>55 (5)</td>
<td>61 (7)*</td>
</tr>
</tbody>
</table>

**Table 2** Maximum cephalad spread of analgesia and times from spinal injection to maximum spread in the non-pregnant, first trimester, second trimester and third trimester (term) pregnant groups. *P<0.05; ***P<0.001 vs non-pregnant group

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum cephalad spread of analgesia (min)</td>
<td>[T10–T4]</td>
<td>[T11–T2]</td>
<td>[T7.5–T2]</td>
<td>[T5–T2]</td>
</tr>
<tr>
<td>Time to maximum spread</td>
<td>21 (8)</td>
<td>18 (7)</td>
<td>21 (8)</td>
<td>19 (8)</td>
</tr>
</tbody>
</table>

**Table 3** CSF pH, PCO2 and HCO3− (median [range]) in the non-pregnant, first trimester, second trimester and third trimester (term) pregnant groups. *P<0.05; **P<0.01; ***P<0.001 vs non-pregnant group

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.30</td>
<td>7.31</td>
<td>7.34*</td>
<td>7.33***</td>
</tr>
<tr>
<td>PCO2 (kPa)</td>
<td>6.30</td>
<td>5.63***</td>
<td>5.45***</td>
<td>5.47***</td>
</tr>
<tr>
<td>HCO3− (mmol/l)</td>
<td>23.3</td>
<td>21.5**</td>
<td>21.8*</td>
<td>21.5**</td>
</tr>
</tbody>
</table>

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pH was greater in the second and third trimester groups than in the non-pregnant group; maximum cephalad spread of analgesia was higher in the former than in the latter group. The increase in CSF pH may, in part, contribute to the observed enhancement of analgesia in the middle and late stages of pregnancy. However, the spinal cord and spinal nerve roots within the dural sac are not covered with sheaths, and thus diffusional delays may have little significance on local anaesthetic action when given directly into the CSF. In this study, CSF pH did not correlate with maximum cephalad spread of analgesia, and times to maximum cephalad spread did not differ between groups. To what degree the change in CSF pH contributed to the observed enhancement of analgesia in the middle and late stages of pregnancy could not be determined.

The presence of carbon dioxide has been reported to enhance both rate and potency of local anaesthetic action. This effect is consistent with the ionized cationic form of local anaesthetics being the more active form. After penetration of the nerve sheath and nerve membrane, the non-ionized drug dissociates into the non-ionized base and the ionized cation. The quantity of each varies with the pH of the axoplasm. Carbon dioxide diffuses rapidly across the membrane and causes lowering of intracellular pH. A lowered pH increases the amount of local anaesthetic in the ionized cationic form, which should act as a potent blocker of sodium channels. The results of this study, however, demonstrated that CSF $P_{\text{CO}_2}$ correlated inversely with maximum cephalad spread of analgesia. The reason for this inverse correlation is unclear. We speculate that enhancement caused by factors other than carbon dioxide may overshadow the effects of carbon dioxide.

A decreased buffering capacity during pregnancy has been suggested to explain enhanced extradural anaesthesia during the first trimester of pregnancy. The decreased buffering capacity may allow the local anaesthetic to remain in a salt form for longer and, therefore, stay longer in the area of injection (extradural space). In this study, CSF HCO$_3$ was found to decrease during pregnancy. The degree of the decrease, however, was small, and hence local anaesthetics injected directly into the CSF might not be affected significantly. In addition, in accordance with the results of a previous study, we failed to demonstrate enhancement of spinal anaesthesia during the first trimester. Unlike extradural anaesthesia, spinal anaesthesia during the first trimester may not be affected by pregnancy-induced decreases in buffering capacity.

In contrast with spinal anaesthesia, alkalinization of local anaesthetics has been investigated in extradural anaesthesia. The investigators disagree about the efficacy of this preparation. Some authors reported faster onset and better quality of sensory and motor blocks. Others have failed to show any clinical advantages of alkalinization over a plain solution. Additional studies are needed to draw definitive conclusions on the onset of extradural anaesthesia with pH-adjusted local anaesthetics.

We showed higher levels of analgesia in pregnant women during the second and third trimesters compared with non-pregnant controls, but did not assess the onset of the block. Therefore, we could not draw any conclusions on the onset of block during pregnancy. However, it is believed that, as a rule, onset of spinal anaesthesia is more rapid during pregnancy. Pregnancy-induced changes, including curvature of the spinal column, soft-tissue anatomy within the spinal canal, and higher progesterone concentrations, have been implicated as possible factors for the enhancement.

![Figure 1](image-url)
A limitation of this study was the position of the patients examined. This study was performed in clinical patients undergoing various types of operation, but not in volunteers who can be kept in a uniform position throughout the observation. Patients undergoing procedures for cervical incompetency were placed in the horizontal lithotomy position, which is thought to decrease the height of spinal block. However, the horizontal lithotomy position has been reported to have little effect on the height of the block. In addition, left uterine displacement was performed in patients undergoing Caesarean section. It could be argued that this manoeuvre might alter the spread of the block but the counter argument would be that in the interest of neonatal well being, the manoeuvre was the best compromise.

References


