MATERNAL AND UMBILICAL CORD PLASMA NORADRENALINE CONCENTRATIONS DURING LABOUR WITH AND WITHOUT SEGMENTAL EXTRADURAL ANALGESIA, AND DURING CAESAREAN SECTION

R. JOUPPILA, J. PUOLAKKA, A. KAUPPILA AND J. VUORI

SUMMARY
Serial measurements of maternal and umbilical cord plasma noradrenaline concentrations were obtained in 10 patients undergoing normal vaginal delivery with segmental extradural analgesia, in 10 patients undergoing normal vaginal delivery without extradural analgesia, and in 12 patients undergoing elective Caesarean section under general anaesthesia. Maternal noradrenaline concentrations increased significantly during delivery in all three groups, the peak concentrations occurring at delivery. However, the increase in the maternal noradrenaline concentration during delivery in the extradural group was lower than in the non-extradural group (P<0.05). Umbilical venous and arterial concentrations of noradrenaline were lower after Caesarean section than after vaginal delivery. However, extradural analgesia did not affect the fetal noradrenaline concentrations. Since noradrenaline is probably required for the adaptation of the newborn to extrauterine life, the unaltered fetal response may be beneficial.

Maternal plasma catecholamine concentrations are increased during vaginal delivery, especially in prolonged and painful labours (Lederman et al., 1978). Although this is a normal reaction to stress, the increase in noradrenaline concentration may produce maternal vasoconstriction and thus impair utero-placental blood flow (Shnider et al., 1979) and this may, in turn, put the fetus at risk.

Extradural analgesia relieves pain during labour and modifies the maternal stress response. The secretion of cortisol and free fatty acids is reduced (Jouppila et al., 1976; Maltau, Andersen and Skredi, 1975) and the secretion of maternal prolactin is increased (Jouppila et al., 1980), the secretion of prolactin being controlled by noradrenaline (Fournier, Desjardins and Friesen, 1974).

The effects of delivery, and extradural analgesia, on maternal and fetal noradrenaline concentrations have been determined by measuring the maternal plasma noradrenaline concentration at different stages during vaginal delivery with and without extradural analgesia. In addition, values obtained in patients undergoing Caesarean section have been included for comparison.

PATIENTS AND METHODS
Thirty-two parturients with uncomplicated pregnancies at term (38–42 weeks) were studied. Twenty had spontaneous vaginal delivery, and 12 an elective Caesarean section under general anaesthesia.

In the vaginal delivery group, 10 mothers received extradural analgesia to a level of T10–12 for pain relief during the first stage of labour (extradural group). Analgesia was initiated when the cervix was dilated at least 3 cm (mean 3.4 cm). A single dose of 4 ml (20 mg) of 0.5% bupivacaine was administered to six patients; the other four received one additional dose of 0.5% bupivacaine.

Three parturients in the other group of 10 patients (non-extradural group) undergoing vaginal delivery received pethidine 50 mg i.m. for pain relief. Seven women did not require any pharmacological agent for the relief of pain. There were no differences in the mean age, parity and the length of labour between these two groups.

General anaesthesia for Caesarean section was preceded by atropine 0.5 mg i.v. and 3 min of pre-oxygenation. Anaesthesia was induced with thiopentone 4 mg kg⁻¹. Suxamethonium 100 mg was administered and, after intubation of the trachea, anaesthesia was maintained with 50% nitrous oxide in oxygen until delivery.

Blood samples for the assay of noradrenaline were obtained in the vaginal delivery groups at a cervical dilatation of 3 cm (before extradural blockade), a cervical dilatation of 6–8 cm, and immediately after delivery. In the Caesarean section group the blood samples were taken before the induction of anaes-
Maternal plasma concentrations of noradrenaline (ng ml$^{-1}$) in the different groups (mean ± SEM)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cervix 3 cm</th>
<th>Cervix 6-8 cm</th>
<th>Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before induction</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery: extradural</td>
<td>0.173 ± 0.013 [P &lt; 0.05]</td>
<td>0.188 ± 0.025 [P &lt; 0.05]</td>
<td>0.233 ± 0.029 [P &lt; 0.01]</td>
</tr>
<tr>
<td>Vaginal delivery: non-extradural</td>
<td>0.227 ± 0.018 n.s.</td>
<td>0.313 ± 0.048 n.s.</td>
<td>0.413 ± 0.057 [P &lt; 0.01]</td>
</tr>
<tr>
<td>Caesarean section: general anaesth.</td>
<td>0.204 ± 0.024</td>
<td>0.238 ± 0.027</td>
<td>0.322 ± 0.067</td>
</tr>
</tbody>
</table>

Umbilical venous and arterial blood samples were taken before cord clamping in the vaginal delivery groups, and from the clamped cord in the Caesarean section group. The blood samples were centrifuged immediately in chilled heparinized tubes. Perchloric acid was added to precipitate the proteins and the plasma frozen. Noradrenaline concentration was measured by a radio-enzymatic method described in detail by Lake, Ziegler and Kopin (1976). The sensitivity of this method was within 0.02 ng in 1 ml of plasma. Duplicate assays were determined on one sample; the intra-assay variation was less than 10%.

The results were analysed statistically with Student's t test, and linear regression analyses.

RESULTS

All the labours were uneventful. The first stage of labour was painless in all the 10 parturients receiving extradural analgesia. All 32 babies had Apgar scores of 8 or more at 1 min and 5 min.

In both vaginal delivery groups, maternal plasma noradrenaline concentrations increased during labour, with peak concentrations occurring at delivery (table I). These peak concentrations were higher in the non-extradural ($P < 0.005$) and extradural ($P < 0.05$) groups than their respective baseline concentrations. Baseline concentration was slightly higher in the non-extradural group than in the extradural group ($P < 0.05$). The increase in noradrenaline concentration during labour in the non-extradural group (86 ± 63%) was greater ($P < 0.05$) than that in the extradural group (37 ± 38%) (fig. 1). Consequently, the mean maternal concentration at delivery in the non-extradural group was greater ($P < 0.01$) than in the extradural group.

Before the induction of general anaesthesia (Caesarean section group) the mean maternal noradrenaline concentration was similar to the baseline values in the vaginal delivery groups. During Caesarean section the maternal concentration of noradrenaline increased ($P < 0.05$) and, at delivery, was similar to the values in the non-extradural group, and greater ($P < 0.01$) than the values in the extradural group (table I).

In the vaginal delivery groups the umbilical venous and arterial noradrenaline concentrations were many-fold higher than the maternal concentrations at delivery, while in the Caesarean section group the umbilical arterial noradrenaline concentration was only twice as high as the maternal concentration. Umbilical cord concentrations did not differ between the extradural and the non-extradural groups (table II). Umbilical venous and arterial concentra-
ANALGESIA AND NORADRENALINE IN LABOUR

Vaginal delivery
Vaginal delivery with extradural analgesia
Caesarean section

![Graph showing changes in maternal noradrenaline concentrations](https://academic.oup.com/bja/article-abstract/56/3/251/503256)

Fig. 1. Mean (± SEM) percentage changes of maternal noradrenaline concentrations. *P < 0.05.

...tions of noradrenaline in the non-extradural, and the venous concentration in the extradural group were greater (P < 0.02, P < 0.001; P < 0.05) than the respective concentrations after elective Caesarean section (table II).

DISCUSSION

The maternal plasma concentrations of noradrenaline increase during labour, particularly if the labour is painful and prolonged (Lederman et al., 1978). In the present series, maternal plasma concentrations were similar to those seen in previous studies (Lederman et al., 1977; Falconer and Powles, 1982) and segmental extradural analgesia did not totally prevent the increase in the maternal concentration induced by labour. However, the increase was more pronounced in the non-extradural group. Thus, the present findings suggest that segmental extradural analgesia decreases the maternal response to the stress, although not as strongly as lumbar extradural blockade (Falconer and Powles, 1982). This difference is understandable, since the extent of sympathetic blockade achieved with these various extradural techniques is different. In lumbar extradural analgesia the segments from T10 to S1 are blocked (Falconer and Powles, 1982) whereas, in this study, extradural analgesia affected only the segments from T10 to T12. Thus, the more extensive lumbar extradural blockade might decrease the release of noradrenaline from sympathetic nerve terminals more effectively than segmental extradural blockade.

Acute maternal distress (Shnider et al., 1979) and increased concentrations of maternal noradrenaline (Rosenfeld and West, 1977) have been associated with maternal vasoconstriction and decreases in placental blood flow. The latter can be improved by segmental extradural analgesia and, to a greater extent, by lumbar extradural blockade (Jouppila et al., 1978; Jouppila et al., 1979; Hollmén et al., 1982; Jouppila et al., 1982). Thus, the findings of partial blockade of the maternal noradrenaline response to labour during segmental extradural analgesia, and more effective blockade during lumbar extradural blockade (Falconer and Powles, 1982), are consistent with the changes in placental blood flow observed with these two techniques.

The maternal concentrations of noradrenaline increased also in connection with Caesarean section. This is probably attributable to such factors as tracheal intubation (Shnider and Levinson, 1979) and the stress of the operation. In one previous
the maternal concentration of noradrenaline, at delivery, was similar during Caesarean section and vaginal delivery without extradural analgesia. In this study it was greater in the Caesarean section group than after vaginal delivery with extradural blockade. This suggests that vaginal delivery with extradural blockade is, in this respect, less stressing to the mother than the other types of delivery studied.

In the present study, as in previous studies (Falconer and Lake, 1982; Irestedt, Lagercrantz and Hjerndahl, 1982; Puolakkka et al., 1983), the umbilical cord blood noradrenaline concentrations, after vaginal delivery, were higher than after Caesarean section. The reason for this might be the mechanical effects on the fetus during vaginal delivery, or fetal hypoxia, which may occur transiently even in normal labour, during contractions, and lead to an increase in the release of fetal catecholamines. The low fetal concentrations of noradrenaline after elective Caesarean section may be at least partly a result of the absence of labour. The similarity of the umbilical cord blood catecholamine concentrations after vaginal delivery and after emergency Caesarean section also lend support to this explanation (Eliot et al., 1980). On the other hand, there is a higher frequency of respiratory distress in infants delivered by Caesarean section than in those delivered vaginally (Usher, Allen and McLean, 1971) and this might be caused by low sympathoadrenal activation after Caesarean section. This phenomenon was also seen in this study and may result in delayed absorption of lung liquid and a decrease in the release of pulmonary surfactants (Usher, Allen and McLean, 1971). Segmental extradural analgesia did not affect the fetal noradrenaline response to the stress of labour. This phenomenon is likely to be beneficial, since the adaptation of the fetus to neonatal life is probably controlled by the fetal catecholamines. For this reason, and because segmental extradural blockade slightly decreased maternal plasma concentration of noradrenaline during labour, it can, in this respect, be regarded as a safe analgesic technique in obstetrics.

REFERENCES


ANALGESIA AND NORADRENALINE IN LABOUR

CONCENTRATIONS PLASMATIQUES DE NORADRENALINE CHEZ LA MERE ET DANS LE SANG DU CORDON AU COURS DU TRAVAIL AVEC ET SANS ANESTHESIE PERIDURALE SEGMENTAIRE ET AU COURS DE LA CESARIENNE

RESUME
Des mesures sériées des concentrations plasmatiques de noradréanaline chez la mère et dans le sang du cordon ont été obtenues chez 10 patientes au cours d'accouchements normaux par voie basse sous analgésie péridurale segmentaire, chez 10 patientes au cours d'accouchements normaux sans analgésie péridurale et chez 12 patientes subissant une césarienne réglée sous anesthésie générale. Les concentrations de noradréanaline augmentaient significativement chez les mères au cours de l'accouchement dans les trois groupes, le maximum de concentration étant obtenu lors de l'expulsion. Cependant, l'augmentation des concentrations maternelles de noradréanaline au cours de l'accouchement était plus faible dans le groupe qui avait bénéficié d'une péridurale que dans l'autre (P> 0,05). Les concentrations de noradréanaline dans le sang artériel et dans le sang veineux ombilical étaient plus basses après césarienne qu'après accouchement par voie basse. Cependant, l'analgésie péridurale n'affectait pas les concentrations de noradréanaline chez le foetus. Dans la mesure où la noradréanaline est probablement nécessaire à l'adaptation du nouveau-né à la vie extra-utérine, l'absence de modification de la réponse foetale est peut-être bénéfique.

NORADRENALINKONZENTRATIONEN IM MUTTERLICHEN PLASMA UND IM NABELSCHNURPLASMA BEI WEHEN MIT UND OHNE SEGMENTALE EXTRADURALE ANALGESIE UND BEI KAIERSCHNITT

ZUSAMMENFASSUNG

CONCENTRACIONES DE NORADRENALINA EN EL PLASMA MATERNAL Y DEL CORDÓN OMBILICAL DURANTE EL PARTO CON Y SIN ANALGESIA EXTRADURAL PARCIAL Y DURANTE LA OPERACION CESAREA

SUMARIO
Se obtuvo mediciones de serie de las concentraciones de noradrenalina en el plasma materno y del cordón umbilical en 10 pacientes con parto vaginal normal y analgesia extradural parcial, en 10 pacientes con parto vaginal normal sin analgesia extradural y en 12 pacientes sometidas a una sección cesárea electiva bajo anestesia general. La concentración de noradrenalina materna aumentó de manera significante durante el parto en los tres grupos, las concentraciones máximas ocurriendo al momento mismo de dar a luz. Sin embargo, el aumento de la concentración de noradrenalina materna durante el parto en el grupo extradural fue más bajo que en el grupo no-extradural (P<0,05). Las concentraciones arteriales y venosas umbilicales de noradrenalina fueron más bajas después de la operación cesárea que después de los partos vaginales. No obstante, la analgesia extradural no afectó las concentraciones fetales de noradrenalina. Puesto que la noradrenalina es probablemente necesaria en vista de la adaptación del recién-nacido a la vida extra-uterina, la respuesta fetal inalterada puede ser ventajosa.