PLASMA CORTISOL CONCENTRATIONS DURING CAESAREAN SECTION

Y. NAMBA, J. B. SMITH, G. S. FOX AND J. R. G. CHALLIS

SUMMARY

The effects of extradural and general anaesthesia on the adrenocortical response to elective or emergency Caesarean section were studied in 72 patients. Maternal plasma concentrations of cortisol were measured before surgery, at delivery, and 30 and 60 min after skin incision. Umbilical vein and artery plasma cortisol concentrations at delivery were determined also. Maternal plasma cortisol concentrations in patients receiving extradural anaesthesia did not change significantly from control at any of the time intervals. In the general anaesthesia group concentrations were significantly increased from control, at 30 and 60 min after skin incision for elective Caesarean sections, and at 60 min after skin incision during emergency surgery. There were no significant differences between the mean umbilical vein and artery plasma cortisol concentrations compared within or between extradural or general anaesthesia groups. Extradural anaesthesia, in contrast to general anaesthesia, decreases the adrenocortical response to Caesarean section surgery by blocking afferent neurogenic pathways from the surgical site. The method of anaesthesia does not influence the fetal cortisol response.

The endocrine and metabolic response to surgery is associated with an increase in the secretion of catabolic hormones, for example cortisol, glucagon and catecholamines. Insulin and testosterone, both anabolic hormones, are inhibited during this response (Thorén, 1974). Recently, during intra-abdominal surgery, extradural anaesthesia, in contrast to general anaesthesia, has been shown to modify or abolish the endocrine changes by blocking afferent neurogenic pathways from the surgical site (Lush et al., 1972; Engquist et al., 1977; Madsen et al., 1977). During labour, the progressive increase in plasma cortisol concentrations in patients receiving parenteral analgesics is minimized by extradural analgesia (Buchan, Milne and Browning, 1973).

At present, no data exist describing the adrenocortical response during Caesarean section with either extradural or general anaesthesia. We measured maternal plasma concentrations of cortisol at intervals during elective and emergency Caesarean section. Umbilical vein and artery cortisol concentrations at delivery were determined also.

PATIENTS AND METHODS

Four groups of patients were studied (table I). For elective surgery, 24 patients received extradural anaesthesia and 25 general anaesthesia, according to their choice. These two groups were comparable in age and weight and no patient was taking any medication or had evidence of systemic disease or complications of pregnancy. Fetal gestational age was 38 weeks or greater and all presentations were cephalic as determined by ultrasonography.

Ten patients undergoing emergency surgery received extradural anaesthesia and 13 general anaesthesia. The indications for emergency surgery were failure of labour to progress satisfactorily or persistent pathological fetal heart rate patterns, or both.

An infusion of physiological salt solution was started through a large-bore i.v. catheter in all four groups of patients on arrival at the operating room. After institution of extradural anaesthesia and during preparation for general anaesthesia, the patients were in the supine position with left lateral tilt (wedge under the right hip). They were maintained in this position until delivery of the baby and clamping of the umbilical cord.

Patients were premedicated with atropine 0.4 mg i.m. and antacid 30 ml orally.

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Extradural anaesthesia for elective Caesarean section was managed in the manner described previously (Fox et al., 1979). Sixteen to 20 ml of lignocaine hydrochloride 2% with adrenaline 1: 200 000 was injected to produce sensory blockade to T4 or T5. Associated hypotension, not responsive to fluid load and left uterine displacement was treated with ephedrine i.v. 5-10 mg i.v. Extradural anaesthesia in the emergency group was achieved by injection of lignocaine 2% with adrenaline 1: 200 000 through an extradural catheter previously placed for control of pain during labour in three patients, and started de novo in seven patients. All patients breathed a high inspired oxygen concentration delivered by facemask for at least 10 min before delivery.

General anaesthesia for both elective and emergency surgery was conducted as follows: Anaesthesia was induced only after the patients were prepared and draped for surgery. The patients were preoxygenated for at least 3 min before induction of anaesthesia. Following tubocurarine 3 mg i.v., a dose of thiopentone 2.5% sufficient to abolish the eyelash reflex was injected. The trachea was intubated after the i.v. injection of suxamethonium. A modified Bain attachment was used and ventilation was controlled to maintain normal maternal carbon dioxide tensions. Anaesthesia was maintained from induction to delivery with nitrous oxide 33% in oxygen, supplemented with halothane 0.5%. Following delivery of the neonate, halothane was discontinued, the nitrous oxide concentration was increased to 66% in oxygen and fentanyl 0.05-0.1 mg i.v. was used to supplement analgesia. An infusion of suxamethonium 0.1% was used throughout surgery to produce adequate neuromuscular blockade.

In all groups, synthetic oxytocin drug 5 u. was injected i.v. after umbilical cord clamping. This was followed by a continuous infusion of oxytocin 10 u. in 500 ml of solution.

Maternal blood samples for measurement of plasma cortisol concentrations were obtained from a vein opposite to that used for the i.v. infusion. Fetal samples were obtained from a doubly clamped segment of umbilical cord. Control venous samples were obtained before induction of general anaesthesia or initiation of extradural blockade. In the patients undergoing emergency surgery with extradural analgesia, the control samples were obtained before augmentation of the block. In all groups further samples were taken at delivery of the baby, and 30 and 60 min after skin incision.

All blood samples were collected in heparinized syringes, centrifuged and the plasma stored at −20 °C until assay. After ethanol 0.5 ml extraction of 0.1 ml of plasma, total plasma cortisol concentrations were measured by radioimmunoassay (Challis et al., 1977). For maternal plasma this assay measured, essentially, unconjugated cortisol. In the fetal circulation, this relationship may not always apply, because of substantial secretion of cortisol sulphate by the fetal adrenal glands (Sharpe-Cageorge et al., 1977) and the probability that maternal unconjugated cortisol contributes after transplacental transfer to the pool of cortisol in the fetal compartment (Challis and Thorburn, 1976). Our measurements of fetal cortisol concentrations are therefore expressed as "total cortisol" and include cortisol sulphate and corticosterone.

The results at each collection interval were expressed as per cent change from control because normal cortisol concentrations exhibit marked circadian fluctuations. Analysis of variance was applied to each group of maternal results. Students' t test for unpaired groups was applied to the fetal results. A P value < 0.05 was considered a significant change.

RESULTS

All deliveries occurred between 08.00 and 15.00 h. Pre-anaesthetic absolute values of maternal plasma cortisol are shown in table I.

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<th>Table I. Study groups and control plasma concentrations (ng ml⁻¹) of cortisol (mean values ± SEM)</th>
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Eight patients in the elective extradural group, but none of the remaining patients, required ephedrine i.v. to correct arterial hypotension. The cortisol concentrations in the ephedrine-treated group were similar to those of the other patients within this group, and therefore all results are reported together.
Maternal plasma cortisol concentrations at delivery and 30 and 60 min after incision during elective surgery are shown in figure 1 as a percentage change from control concentrations (±SEM). The general anaesthesia group had an increase to 121%(±10), 160%(±18) and 148%(±12.7) of the pre-anaesthetic concentration at delivery, 30 and 60 min after incision. In the extradural group the increase was to 125%(±11.5), 133%(±13.8) and 136%(±15.7) of control concentrations at delivery, 30 and 60 min after incision. The concentrations 30 and 60 min after incision in the general anaesthesia group were the only values significantly different from concentrations before anaesthesia in both elective groups.

The per cent change in maternal cortisol concentrations during emergency Caesarean section are shown in figure 2. Minor non-significant fluctuations occurred during extradural anaesthesia. These changes were 99% (±5.8), 102% (±6.3) and 97% (±8.8) at delivery, 30 and 60 min after incision. The changes during general anaesthesia were much greater. These were 127% (±30), 143% (±17) and 179% (±21.5) at delivery, 30 and 60 min, with the value 60 min after incision being significantly different from control.

Umbilical vein and artery total cortisol concentrations during elective surgery are shown in table II. There was no difference between the mean venous and arterial concentrations compared with each other or between the extradural or general anaesthesia groups. There was no correlation in either group between maternal and umbilical venous or arterial concentration.

Umbilical cortisol concentrations during emergency sections are not shown because too few results were obtained to allow statistical analysis.
DISCUSSION

The normal metabolic response to surgical stress is shown in figure 3. The hypothalamus receives neurally mediated input from the surgical site. In addition, the hypothalamus receives input from the higher centres which may be psychological in origin, for example, fear or anxiety. In response to these stimuli, the hypothalamus releases corticotropin releasing factor (CRF) which induces the anterior pituitary gland to secrete ACTH. The latter hormone directly affects the adrenal cortex to increase cortisol secretion. A second response to hypothalamic stimulation is increased sympathetic nervous system activity. This in turn causes an increase in the release of catecholamine from the adrenal medulla and increase in the secretion of pancreatic glucagon. Extradural analgesia can play a major role in modifying the stress response by blocking noxious afferent stimuli from the surgical site.

Most reports (Lush et al., 1972; Gordon, Scott and Percy Robb, 1973; Brandt et al., 1976; Madsen et al., 1977) regarding the effects of surgical stress and influence of anaesthesia on the endocrine response are from studies in which extradural anaesthesia has been combined with general anaesthesia. However, Brandt and colleagues (1978) compared the cortisol response to abdominal hysterectomy during general anaesthesia or extradural anaesthesia alone. During general anaesthesia an increase occurred in plasma cortisol concentration which was not seen during extradural anaesthesia.

Chattoraj and his colleagues (1974) reported maternal cortisol concentrations at delivery during Caesarean section following spinal or general anaesthesia. He did not apply statistical analysis to his results, but the mean concentrations of cortisol were greater during general anaesthesia. Buchan, Milne and Browning (1973) demonstrated that maternal cortisol concentrations do not increase when extradural analgesia is given during labour. However, a marked and progressive increase in cortisol concentration is found when narcotic analgesia is utilized for pain relief.

Our present study with Caesarean sections confirms previous reports that extradural analgesia modifies the cortisol response to surgery, while general anaesthesia fails to do so. The percentage changes in maternal cortisol concentrations are remarkably constant at all sampling times within both extradural groups. The small but non-significant increases seen at all time intervals during elective surgery may represent psychological hypothalamic stimulation attributable to surgery in the awake state. During emergency Caesarean section these small increases in cortisol concentration were not seen because stress stimulation was high before control blood sampling, probably because of labour, pain and the decision to perform previously unanticipated surgery. This is substantiated by the greater control cortisol concentrations in the emergency extradural group (table I).

In contrast to extradural anaesthesia, the increases in plasma cortisol concentrations during general anaesthesia achieved statistical significance at 30 and 60 min following skin incision in the elective group and at 60 min in the emergency group. Although an increase in mean plasma cortisol concentration was seen at delivery, the difference from baseline was small because the cortisol response to surgical stimulation takes several minutes to occur. The skin incision to delivery interval ranged from 5 to 9 min and the cortisol response to stress may not be fully developed in all patients at delivery. By 30–60 min the increase in plasma cortisol can be detected easily. This is in agreement with Brandt and co-workers (1978) who also noted significant differences at 30 and 60 min following the start of surgery.

It is unlikely that the change in anaesthetic technique following delivery of the baby influenced the cortisol concentrations because during surgical stimulation, neither thiopentone, halothane, nitrous oxide (Oyama et al., 1971; Oyama,
CAESAREAN SECTION AND PLASMA CORTISOL

1973) or narcotics (Oyama and Takiguchi, 1970) prevent the increase in cortisol concentrations.

We did not find a correlation between maternal plasma and cord cortisol concentrations. Nor did we find any significant difference in the umbilical artery and umbilical vein concentrations of cortisol as suggested by some (Leong and Murphy, 1976), but not by other authors (Fencl, Osathanondh and Tulchinsky, 1976).

Interpretation of cord cortisol concentrations is difficult, because the steroid may be derived from fetal adrenal secretion or transplacental transfer from the mother (Thorburn and Challis, 1979). However, comparison of umbilical artery concentrations, which are more likely to reflect fetal adrenal production, does not indicate any marked difference in the “stress” response of the neonates to different methods of anaesthesia.

This study demonstrates that extradural analgesia, as compared with general anaesthesia, reduces the maternal cortisol stress response during Caesarean section. However, the technique of anaesthesia does not appear to influence the stress response in the fetus.

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REFERENCES


CONCENTRATIONS DE CORTISOL DANS LE PLASMA PENDANT UNE OPERATION CESAIENNE

RESUME

On a etudié, sur 72 pacientes, les effets qu’ont les anesthésies extradurales et générales sur la réaction cortico-surrénale à l’opération césarienne d’urgence ou effectuée à froid. On a mesuré les concentrations de cortisol dans le plasma maternel avant l’opération, au moment de l’accouchement, puis 30 min et 60 min après l’incision de la peau. On a également déterminé les concentrations de cortisol qui se trouvaient dans le plasma de la veine et de l’artère ombilicales au moment de l’accouchement. Les concentrations de cortisol dans le plasma maternel des patientes ayant subi une anesthésie extradurale n’ont à aucun moment varié d’une manière significative par rapport aux valeurs témoins. En ce qui concerne le groupe soumis à une anesthésie générale, les concentrations ont augmenté d’une manière significative par rapport aux valeurs témoins, 30 min et 60 min après l’incision de la peau lors des opérations césariennes effectuées à froid, et 60 min après l’incision de la peau lors des opérations d’urgence. Il n’y a eu aucune différence notable entre les concentrations moyennes de cortisol dans le plasma de la veine et de l’artère ombilicales entre les groupes ou parmi les groupes soumis à l’anesthésie générale ou à l’anesthésie extradurale. Contrairement à l’anesthésie générale, l’anesthésie extradurale a fait baisser la réaction cortico-surrénale à l’opération césarienne en bloquant les voies d’accès neurologiques afférentes venant du terrain d’opération. La méthode utilisée pour l’anesthésie n’influence pas la réaction du foetus au cortisol.
PLASMA-CORTISOLKONZENTRATIONEN WÄHREND KAISERSCHNITT

ZUSAMMENFASSUNG


SUMARIO

Se estudiaron en 72 pacientes los efectos de la anestesia general y extradural sobre la respuesta adrenocortical a la operación de cesarea de tipo electivo o de emergencia. Las concentraciones de cortisol en el plasma materno se midieron antes de la operación, durante ésta y a los 30 y 60 min de efectuar la incisión en la piel. También se determinaron durante el parto las concentraciones de cortisol en el plasma de la vena y de la arteria umbilical. Las concentraciones de cortisol en el plasma materno, para aquellas pacientes que recibieron anestesia extradural no cambiaron de forma significativa con relación al grupo de control en ninguno de los intervalos de tiempo. En el grupo de anestesia general, y para las operaciones de cesarea electiva, tuvo lugar un incremento significativo de las concentraciones a los 30 y a los 60 min después de la incisión, y a los 60 min de efectuada la incisión para las operaciones de emergencia. No hubo diferencia significativa entre las concentraciones medias de cortisol en el plasma de la vena y arteria umbilical, en comparación con, ni entre los grupos de anestesia general y extradural. La anestesia extradural, en contraposición a la anestesia general, disminuye la respuesta adrenocortical a las operaciones de Cesarea mediante el bloqueo de las rutas neurogénicas aferentes que parten del emplazamiento quirúrgico. El método utilizado para anestesia no influye la respuesta de cortisol del feto.