inadequate cortisol synthesis secondary to diminished activity of 3β hydroxysteroid dehydrogenase. The concentrations of ACTH and of cortisol observed in the plasma, however, do not support this hypothesis. The persistent rise of the 3β-OH-5-ene steroids might therefore be due to the response of an adrenal cortex, consisting predominantly of DHA secreting fetal zone cells, to the normal ACTH drive required to maintain plasma cortisol concentrations.

It seems most likely that the weak fetal zone androgens are responsible for the virilisation. This cannot be the only cause however because both we (see table) and others 1,2 have observed female preterm infants with raised concentrations of 3β-OH-5-ene steroids, who were not virilised. There may be other factors involved, for example variations in end organ sensitivity, localised conversion of fetal steroids to more potent androgens at the site of action in the genitalia, or high concentrations of circulating free androgens. Another factor may be the degree of immaturity of the preterm infant. Grumbach and Ducharme have pointed out that the virilising effect of an androgen depends on the maturity of the fetus. Androgen exposure between 8-13 weeks' gestation causes labial fusion and clitoromegaly, whereas after this time only hypertrophy of the clitoris is seen. 1 The fact that the most severely affected infant was 24 weeks' gestation may be a manifestation of the different response of the immature fetus to weak androgens. The increasing survival of such immature infants is a recent phenomenon and this may be the reason why clitoromegaly has not been reported before in preterm babies.

We wish to thank Mr W P T Chitty (Organon-Teknika Limited, Cambridge) for donation of the Eurodiagnostics Assay kits for ACTH.

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3 Murphy JF, Boyce BG, Dyas J, Hughes IA. Plasma 17-

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Topical prostaglandin E₂ gel for cervical ripening and closure of the ductus arteriosus in the newborn

R Y T Sung, J A Yin, E P L Loong, T F Fok, J Lau

Abstract

The closure time of the ductus arteriosus was investigated in 29 full term babies born vaginally after induction with prostaglandin E₂ and in 22 controls. Serial Doppler echocardiography studies showed a significantly prolonged closure time in babies induced by prostaglandin E₂. Whether the difference is related to changes in fetal prostaglandin E₂ concentration remains to be established.

Patients and methods

Fifty one babies born at full term by vaginal delivery were studied. Twenty nine babies (mean (SD) gestational age 39.86 (1.66) weeks) were born to mothers who had received a 3 mg prostaglandin E₂ pessary (Upjohn) to ripen the cervix before induction of labour. Twenty two babies (mean (SD) gestational age 39.82 (1.14) weeks) whose mothers did not receive prostaglandin E₂ acted as controls.

DETERMINATION OF DUCTAL CLOSURE TIME

Serial Doppler echocardiography studies were done with an Aloka SSD-280S ultrasound scanner within 12 hours of birth, then twice daily at intervals of about 12 hours until ductal shunting could no longer be detected. 4

MEASUREMENT OF MATERNAL AND CORD PROSTAGLANDIN E₂ CONCENTRATIONS

Cord blood was drawn from the umbilical vein immediately after clamping and cutting of the cord, and before placental separation. Paired maternal venous blood samples were collected at the same time. The samples were then transferred into prechilled polypropylene tubes containing EDTA and indomethacin, and cen...
Concentrations of prostaglandin E2 in maternal and cord blood in patients treated with prostaglandin E2 and controls

<table>
<thead>
<tr>
<th>Group treated with prostaglandin E2</th>
<th>Control group</th>
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<tbody>
<tr>
<td><strong>No of samples</strong></td>
<td><strong>Mean (SD) concentration (pg/ml)</strong></td>
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<tr>
<td>Maternal blood</td>
<td>23</td>
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<tr>
<td>Cord blood</td>
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<td>Cord blood</td>
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There was no significant difference between the groups.

Concentrations in the treated group were similar, being 3246 g (range 2500–4200) and 3317 g (range 2150–4500), respectively. The mean time interval between application of the gel and delivery was 13 hours (range 3 to 28).

Results

Mean birth weights of the treatment and control groups were similar, being 3246 g (range 2500–4200) and 3317 g (range 2150–4500), respectively. The mean time interval between application of the gel and delivery was 13 hours (range 3 to 28).

CLOSURE TIME OF THE DUCTUS ARTERIOSUS

In the treated group half of the ductus arteriosuses closed at 28 hours compared with 15 hours in the controls. The difference was significant (p<0.05).

PROSTAGLANDIN E2 CONCENTRATIONS IN BLOOD

The results are shown in the table. There were no significant differences in the concentrations of prostaglandin E2 between the control and treatment groups either in maternal or cord blood. No correlation between the maternal and cord blood concentrations was seen in the control group, but a significant correlation was noted in the treatment group (r²=0.39, p=0.03).

Multiple logistic regression analysis showed that birth weight and cord blood prostaglandin E2 concentration are not significant variables when predicting whether the closure time of the ductus arteriosus would be shorter or longer than 24 hours (p values 0.06 and 0.21, respectively).

Discussion

The results of this study show that there was delay in closure time of the ductus arteriosus in newborn babies whose mothers had had prostaglandin E2 pessaries for ripening of the cervix before the onset of labour. No clinical problems resulted, however. Whether delayed ductal closure also occurs in premature babies whose mothers are given prostaglandin E2 deserves further investigation, especially as patent ductus arteriosus causes so many problems in preterm babies.

Maternal and cord blood concentrations of prostaglandin E2 were, unexpectedly, not significantly higher in the treated group, but this might be because of the time that the blood was sampled. It has been reported that after vaginal administration of 3 mg prostaglandin E2 in patients during weeks 9–14 of pregnancy, peak plasma concentrations of between 3500 and 10 000 pg/ml were observed three to six hours after the start of treatment; these returned to normal after 10 hours. Whether the same dose of prostaglandin E2 given to pregnant women at full term results in similar plasma concentrations is unknown. The low maternal and cord blood concentrations in our study, however, may be related to the interval between application of the gel and delivery (about 13 hours).

Repeated maternal and fetal blood sampling at a predetermined time after the prostaglandin E2 has been given may shed light on the relation between maternal and fetal blood concentrations.

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