Maternal prostaglandin levels after vaginal examination in twin pregnancy

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Summary

Plasma 13,14-dihydro-15-keto-prostaglandin F₂₀₈ (PGFM) levels were measured in patients with twin pregnancies in some of whom the cervix was dilated and effaced. Significant rises in PGFM values were observed 5 and 10 minutes after vaginal examination in those patients who had a negative cervical score; these changes were abolished by prophylactic oral use of the β-sympathomimetic drug fenoterol (Berotec; Boehringer Ingelheim). Patients who went into labour within 72 hours of examination had a greater percentage rise in PGFM levels than those in whom the onset of labour was delayed. Beta-sympathomimetic drugs such as fenoterol may be of value in preventing prostaglandin release and delaying the onset of labour.

Multiple pregnancy is associated with a high perinatal mortality rate due to preterm labour, and the mean period of gestation at onset of labour is shorter in twin than in singleton pregnancies. This high preterm delivery rate remains a problem, as there has been little success in reducing it in modern obstetrics. The value of bed rest, Shirodkar sutures and β-sympathomimetic drugs remains unproved. Observations at the King Edward VIII Hospital, Durban, have suggested that regular assessment of the cervix in the antenatal period is of value in predicting the onset of labour (and hence the mother's admission to hospital) in twin pregnancies. Because vaginal examination has been shown to release prostaglandins into the maternal peripheral circulation, however, these circumstances could add to the danger of inducing preterm labour in a group already at risk. To establish whether such added risk does in fact exist, circulating levels of 13,14-dihydro-15-keto-prostaglandin F₂₀₈ (PGFM), a metabolite of prostaglandin F₂₀₈, were measured under controlled conditions in patients with multiple pregnancies before and after vaginal examination.

Patients and methods

All patients in the study were seen in the multiple pregnancy clinic at the King Edward VIII Hospital, Durban, during the last trimester of pregnancy and gave informed consent to participation in the trial. Routine antenatal management included an assessment of the state of the cervix and assignment of a 'cervical score' (defined as the length of the cervix from the internal os minus the dilatation in centimetres). Patients with a zero or negative score (between 0 and -3) before the 37th week of gestation were admitted to the antenatal ward for bed rest and were allocated to the following groups: group A — patients with twin pregnancies and a negative score, who were treated by bed rest alone; group B — patients with twin pregnancies and a negative score who were given oral fenoterol (Berotec; Boehringer Ingelheim) 5 mg 4-hourly as prophylaxis against preterm labour (medication was commenced on admission and all patients had received regular therapy for at least 24 hours before examination); group C (the reference group) — patients with a normal cervical score (+1 - +3) and in whom the duration of pregnancy was < 37 weeks, who were admitted to hospital with bed rest as the sole treatment.

Vaginal examination and taking of blood samples. None of the patients allocated to the three groups had experienced any episodes of preterm labour during their present pregnancies and no vaginal examination was performed during the 24 hours preceding the study. Vaginal examination was performed on each patient after admission in order to assess the length, dilation and consistency of the cervix and the height of the head above the pelvic brim and obtain a clinical estimation of the pelvic dimensions. The examination was timed to last exactly 30 seconds and was performed by one of two investigators (R. J. N. or R. M.). Blood samples were obtained before and 5 and 10 minutes after the procedure. Samples were collected in ice-cold tubes containing ethylenediamine tetra-acetic acid with aspirin and spun immediately at 4°C at 2000 g; the plasma was separated and frozen at -20°C.

Estimation of PGFM. PGFM levels were determined by radio-immunoassay after extraction of 4 ml of plasma with cyclohexane-acetic acid (1:3 v/v) and chromatography on silicic acid microcolumns, eluting with benzene:ethylacetate:methanol (60:40:20 v/v). Samples were assayed using tritiated PGFM (Radiochemical Centre, Amersham, UK) and highly specific antibody raised against PGFM-BSA. Within- and between-assay coefficients of variation were less than 15%. Gestational age was assessed by the menstrual history, early ultrasonography and clinical assessment of the neonates. There were no significant differences in mean gestational age at the time of examination between the three groups (group A = 34.3 ± 1.5 weeks; group B = 34.7 ± 1.4 weeks; group C = 36.5 ± 1.8 weeks). All the babies had a 5-minute Apgar score of > 7, and there were no perinatal deaths.

Statistics. Student’s t test was used and a significance level of 0.05 chosen.

Results

The mean PGFM levels in maternal peripheral blood following vaginal examination are shown in Table I. There were no significant differences in basal PGFM values between the three groups. Patients in group A (negative cervical score, no drug therapy) showed a significant rise in prostaglandin levels over the basal
values at 5 and 10 minutes. This elevation was abolished in group B by the administration of fenoterol. Patients with a positive cervical score (group C) did not show a change in prostaglandin values after vaginal examination.

Group A was subdivided into patients who went into labour within 72 hours of the vaginal examination (N = 6) and those in whom labour started after 72 hours (N = 8). The percentage rise in PGFM levels was significantly greater at 10 minutes in the former group (< 72 hours — 115.7%; ≥ 72 hours — 49.2%; P < 0.05), indicating a heightened sensitivity to vaginal examination in patients about to go into labour. The mean interval between examination and delivery was shorter in group A patients than in those on fenoterol or with a positive cervical score (group A — 10.3 days; group B — 19.4 days; group C — 13.6 days).

Discussion

Prostaglandins derived from the fetoplacental tissues are clearly implicated in the myometrial contractions of parturition and are known to be released after amniotomy,7,8 cervical stimulation9 and vaginal examination after 37 weeks’ gestation.4 The findings in this study demonstrate that preterm dilation of the cervix together with a vaginal examination causes a marked rise in maternal PGFM levels and an increased propensity to preterm delivery. The mechanism for this is not clear but appears to be related to an increased ability of the decidual tissues to manufacture and release prostaglandins together with increased exposure of the fetal membranes to the vaginal environment. These membranes are rich in arachidonic acid-containing phospholipids as well as phospholipase A₂ and readily release the precursors for the ‘two’ series of prostaglandins. Alternatively, oxytocin could be released after vaginal examination and this could cause contraction of the uterus and elevation of PGFM values. The results in this study suggest that fenoterol, a β-sympathomimetic drug which raises myometrial cyclic adenosine monophosphate levels and causes uterine quiescence, blocks the release or synthesis of prostaglandins from the uterine tissues.

The benefits of β-sympathomimetic drugs in the prophylaxis of preterm labour have been widely debated.5 The results of our study indicate that β-sympathomimetic drugs are warranted in the particular high-risk situation of multiple pregnancy and a negative cervical score. The rise in PGFM values after vaginal examination is blunted and gestation may be prolonged. However, in a previous study of patients with low-risk twin pregnancies in an outpatient clinic we were unable to demonstrate prolongation of pregnancy with low-dose prophylactic fenoterol.10

The use of routine cervical assessment in multiple pregnancy is debatable. It has been promoted in an attempt to predict the incidence of preterm labour and because it assists admission policy in a situation of antenatal inpatient bed shortage.3 This must be balanced against the potential hazards of infection, preterm labour and rupture of the membranes. Although the vaginal examination in this study was more prolonged and invasive than would be necessary on a routine visit and was not associated with palpable uterine contractions, caution should be exercised when the cervix is dilated. Routine administration of prophylactic β-sympathomimetic drugs before vaginal examination of these patients should be considered.

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REFERENCES