Prostaglandin F_{1a} and prostaglandin E_2 plasma levels after transvaginal cervical cerclage

N. VITORATOS - D. HASSIAKOS - C. LOURIDAS
G. LIMURIS - P. A. ZOURLAS

Summary: Plasma prostaglandin metabolites, prostaglandin F_{1a} (PGF_{1a}) and prostaglandin E_2 (PGE_2) were measured in a serial set of maternal serum samples by radioimmunoassay after elective transvaginal cervical cerclage (Shirodkar) in 18 patients early in the 2nd trimester (14-15 weeks of gestation) for a history of cervical incompetence. Eight patients received progesterone preoperatively as a myometrial suppressant. The basal PGF_{1a} and PGE_2 were 134.0 ± 25.9 pg/ml and 14.9 ± 1.8 pg/ml, respectively. A gradual rise in both metabolites was observed within 1 hour after the operation (206.81 ± 48.3 pg/ml and 16.7 ± 1.6 pg/ml, respectively, $p > .05$), peaking at 6 hours (265.4 ± 51.8 pg/ml, $p < .01$ and 25.9 ± 4.9 pg/ml, $p < .05$), and falling to basal levels within 24 hours (136.7 ± 26.5 pg/ml and 14.0 ± 1.2 pg/ml, respectively, $p > .05$). The increase in PGF_{1a} was proportionately greater than PGE_2 metabolite ($r = 0.838$, $p < .001$). No differences were found in prostaglandin levels amongst patients who received progesterone as compared to the non-recipients for all the time intervals studied ($p < .05$).

Our findings, further suggest that a temporary increase in prostaglandin production occurs following cervical cerclage, but its role remains unclear.

Key words: Prostaglandin; Cervical cerclage.

INTRODUCTION

It is well-established that rapid increases in plasma concentrations of prostaglandin metabolites occur in pregnant women near term after vaginal examination and amniotomy ([1]). A similar rise in plasma prostaglandin levels have been reported following cervical cerclage (transvaginal or transabdominal), however controversy still exists ([2, 3, 4, 5]). As circulating prostaglandin metabolites are potent myometrial stimulants, the increase in uterine activity noted following cerclage may be attributed to raised prostaglandin levels ([6]). Although, the most common prostaglandin metabolites assayed following cervical cerclage are prostaglandin F_{2a} and prostaglandin E_2, no data exists to our knowledge with regard to the concentrations of 6-

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2nd Department of Obstetrics and Gynecology, Areteion Hospital, University of Athens, Athens (Greece)

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keto prostaglandin F_{1a} (PGF_{1a}), the stable metabolite of prostacyclin.

This study was undertaken to define the fluctuations in prostaglandin metabolites in maternal peripheral plasma which occur following elective transvaginal cervical cerclage for a history of cervical incompetence.

The prostaglandins assayed were prostaglandin F_{1a} (PGF_{1a}) and prostaglandin E_2 (PGE_2).

MATERIALS AND METHODS

The study population consisted of 18 patients (mean age 28±3.2 years) undergoing transvaginal cervical cerclage for a history of cervical incompetence at the Areteion Hospital, University of Athens between December 1987 and January 1990. In all patients cervical cerclage was performed electively at the 14th-15th week of gestation, for a history of previous mid-trimester spontaneous abortion, or premature delivery. All patients had hysterosalpingography and/or ultrasonography performed prior to this gestation indicative of cervical incompetence. Cervical cerclage was performed transvaginally by the Shirodkar technique using a double ended mersilene ribbon as described elsewhere ([7, 8]). The procedure was carried out under general anaesthesia and completed within 5 - 10 minutes. Postoperatively, patients were kept on bedrest for 24 hours, and were followed throughout the pregnancy. Hydroxyprogesterone hexanoate (Proluton Depo, Schering, FRG) was given in 8 patients as a myometrial suppressant 12 hours preoperatively (250 mg intramuscularly).

Maternal blood samples were collected via an indwelling catheter in the antecubital vein before the start of cerclage, and at intervals of 1 hour, 6 hours, 12 hours, and 24 hours thereafter. Blood samples were collected in pre-chilled polypropylene test tubes coated with 4.5 mM EDTA and indomethacin, at concentrations up to 10 ng/ml. The plasma fraction was separated by centrifugation at 1500 g and 10° C within 20 minutes of collection, and stored at −70° C until analysis. The concentrations of 6-keto prostaglandin F_{1a} and 11-deoxy-13, 14-dihydro-15-keto-11, 16-cyclo prostaglandin E_2 in plasma samples were assayed by established radioimmunoassay techniques [Du Pont de Nemours (Deutschland), W. Germany] ([4]). The intraassay and interassay coefficients of variation ranged from 4.5-10.6 % and 8.3-14.0 %, respectively. The sensitivity ranged from 0.15-1.0 pg/ml.

Statistical analysis was carried out using the student's t-test and linear regression analysis where indicated.

RESULTS

The plasma levels of PGF_{1a} and PGE_2 assayed before and after the operation of cervical cerclage in all patients are depicted in Figures 1 and 2. The overall pattern in serum PGF_{1a} and PGE_2 (mean ± SE) are illustrated in Figures 3 and 4. Both preoperative plasma levels of PGF_{1a} and PGE_2 began to rise within 1 hour after commencement of the operation (from 134.0 ± 25.9 pg/ml to 206.8 ± 48.3 pg/ml and from 14.9 ± 1.8 pg/ml to 16.7 ± 1.6 pg/ml, $p > .05$, respectively). The maximum increase was observed at 6 hours (265.4 ± 51.8 pg/ml, $p < .01$ and 25.9 ± 4.9 pg/ml, $p < .05$, respectively). A gradual decrease was noted thereafter with the concentrations reaching their preoperative levels within 24 hours (136.7 ± 26.5 pg/ml and 14.0 ± 1.2 pg/ml, $p > .05$, respectively). Using linear regression analysis the correlation coefficient (r) between plasma PGF_{1a} and PGE_2 values was 0.838, $p < .001$). In the 8 patients who received progesterone prior to the cerclage, the serum prostaglandin levels of both PGF_{1a} and PGE_2 were not significantly different when compared to those who did not receive progesterone, for all time intervals studied ($p > .05$).

With regard to the fetal outcome, all patients delivered after 37 weeks of gestation following removal of the cerclage ribbon with good fetal outcome, except for one patient (6%) who delivered at 26 weeks resulting in neonatal death.

DISCUSSION

A number of investigators have reported an increase in prostaglandin production following transvaginal cervical cerclage early in the 2nd trimester of pregnancy ([2, 4, 5]). Our results demonstrate

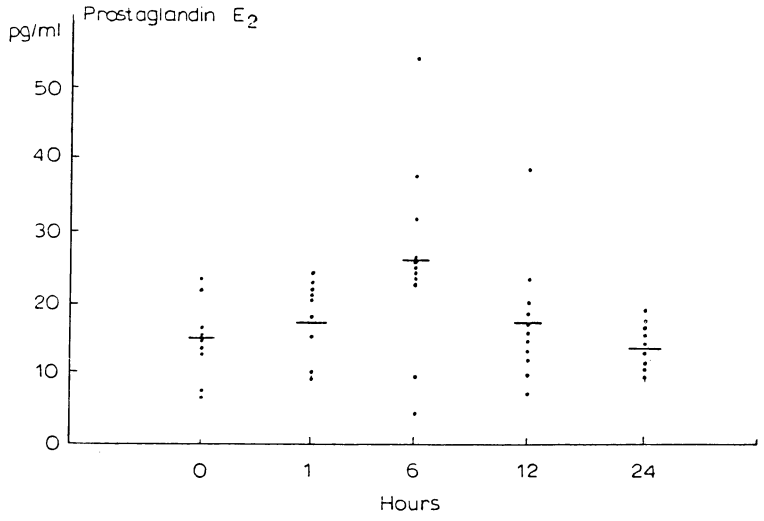

Fig. 1.

that cervical cerclage is associated with a rapid rise in circulating prostaglandin PGF_{1a} and PGE_2 concentrations within 1 hour after commencement of the operation. This rise in our patients was persistent and reached a maximum at 6 hours ($p < .01$). Plasma concentrations of PGF_{1a} and PGE_2, thereafter declined and attained basal (preoperative) levels 24 hours after the operation. Further, the changes in PGF_{1a} and PGE_2 levels after cervical cerclage paralleled one another, although the rise in plasma PGF_{1a} was proportionately greater than that of PGE_2.

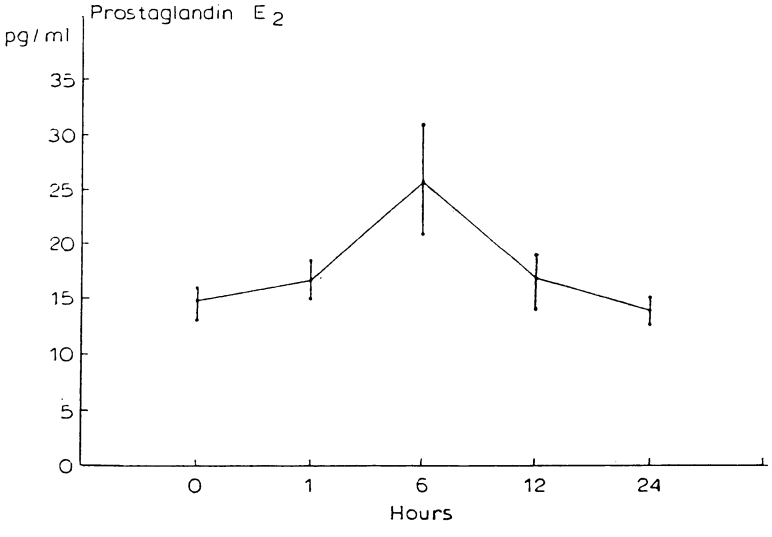

Fig. 2.

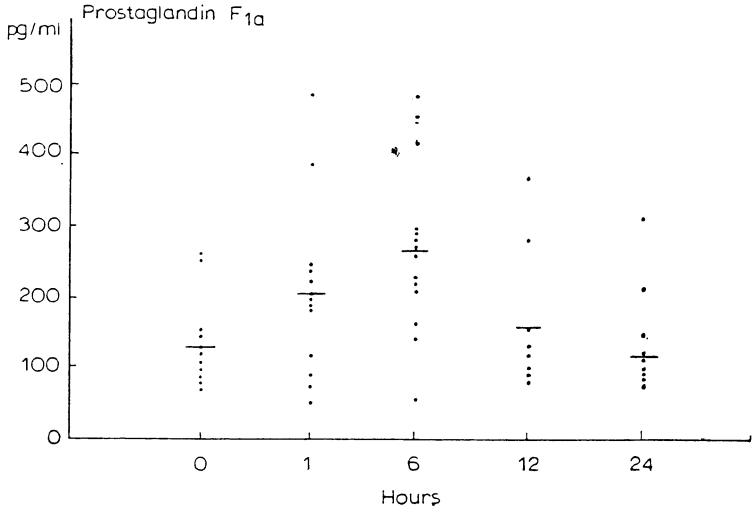

Fig. 3.

Using linear regression analysis, the correlation coefficient between PGF_{1a} and PGE_2 was 0.838 ($p < .001$).

At the present time, the increased release of circulating prostaglandins in response to cerclage remains unexplained, but may be the result of several factors: stimulation of the vagina and cervix and disturbances of the fetal membranes may predispose to augmentation of prostaglandin, release and/or production; prostaglandins are known potent stimulators of uterine activity, and cervical ripening effects, the significant rise of prostaglandin

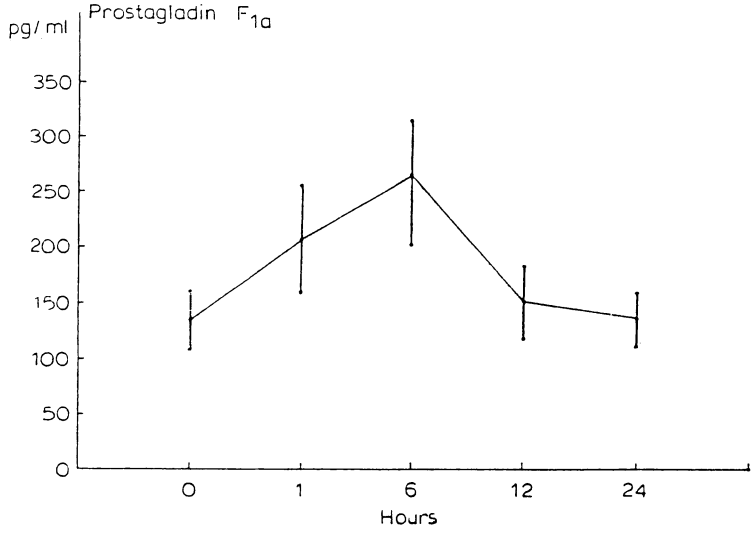

Fig. 4.

concentrations following cerclage may possibly result in an increase in myometrial activity, cervical dilation and effacement, which is not desirable at this stage of pregnancy and further defines the purpose of the operation. Although, PGE_2 has been shown more potent in its uterotonic and cervical ripening effects than other prostaglandins, the role of 6-keto prostaglandin F_{1a} in uterine contractility remains unclear ([6, 9, 10]).

In conclusion, our data do not support the routine use of prophylactic prostaglandin synthase inhibitors for cerclage procedures, as the observed increase in prostaglandin levels were transient and subsided quickly to baseline levels following cerclage. Also, as shown by Novy *et al.* ([4]), the magnitude of the rise in prostaglandin levels did not correlate with gestational age, severity of cervical changes (mild-moderate), or fetal survival, therefore the routine administration of prostaglandin inhibitors is not advocated.

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Address reprint requests to:
N. VITORATOS, M. D.
Areteion Hospital
76 V. Sofias Av.
115 28 Athens (Greece)