

The role of steroid hormones in cervical ripening

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Summary: Dehydroepiandrosterone sulphate (DHEA-S), estradiol (E_2), estriol (E_3), progesterone (P_4) and cortisol (F) maternal plasma concentrations were determined using enzyme or fluoroimmunoassays in 28 healthy pregnant women prior to the induction of labour, performed for various reasons, in order to evaluate their impact on cervical ripening. Mean maternal and gestational ages were 24.7 ± 3.6 years and 39.1 ± 1.9 weeks, respectively, and the gravidity ranged from 0-4. The subjects were divided according to cervical maturity into Group A ($n=13$, Bishop scores >4) and Group B ($n=15$, Bishop scores <4).

There were no statistically significant differences observed between the two groups as to concentrations of oestradiol, oestriol, progesterone and cortisol. However, significantly higher concentrations of DHEA-S were found in group A compared to group B (1335 ± 885 ng/ml and 558.2 ± 191.4 ng/ml, respectively), ($p < 0.001$).

In conclusion, the high DHEA-S concentrations in maternal plasma may play an important role in pregnancy by producing favourable cervical conditions for delivery or by triggering the labour itself.

Key words: Steroids; Cervix; Ripening.

INTRODUCTION

The endocrine activity of the feto-placental unit is remarkably altered during the last weeks of normal pregnancies. It has been proved that these functional changes of fetal adrenal glands play an important role in fetal lung maturation and the initiation of labour in many mammalian species (¹⁻⁵).

Fetal adrenal weight increases rapidly after the 34th week and despite the reco-

gnized importance of fetal adrenal function in pregnancy homeostasis, the regulation of steroidogenesis is not well defined. It has been shown that corticosteroid concentrations in fetal blood and 17β -estradiol and estriol maternal circulation levels increase approximately during the 36th week of gestation and this estrogen surge has been attributed to the increased production of DHEA-S by the fetal adrenal gland (⁵⁻⁷). However, it has been shown that estrogen and consequently DHEA-S promote cervical softening and may be associated with the ability to induce labor (⁸⁻¹²).

The present investigation was undertaken in order to evaluate the maternal plasma circulating levels of DHEA-S, estradiol, estriol, progesterone and cortisol in 3rd trimester pregnancies and to investi-

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Table 1. — *Type of assays, performance characteristics and trade names.*

Hormone	Type of assay	Sensitivity	Precision		Accuracy recovery %	Trade name
			intra-assay (CV%)	inter-assay CV%		
E ₃	FPIA (competitive)	10 ng/ml	3.5	5.5	97 ± 5	T _{DX} - Estriol Abbot Lab IL - USA
F	FPIA (competitive)	4.5 ng/ml	5.1	7.0	101 ± 4	T _{DX} ^R - Cortisol Abbot Lab IL - USA
P ₄	FIA (competitive)	0.3 ng/ml	7.5	8.0	95 ± 6	DELFI A - Progesterone Pharmacia - LKB FINLAND
DHEA-S	EIA (competitive)	10 ng/ml	8.6	12.4	94 ± 4	DHEA - S - Immunosystem Sibar Diagnostici Perugia, ITALY
E ₂	FIA (competitive)	10 pg/ml	7.0	7.3	98 ± 6	DELFI A - Estradiol Pharmacia - LKB FINLAND

gate the role of these hormones in the initiation of labour and cervical maturity process.

MATERIAL AND METHODS

A total of 28 pregnant women with uncomplicated pregnancies who attended the 2nd Department of Obstetrics and Gynecology at the Areteion Hospital, were studied. The mean maternal and gestational age was 24.7 ± 3.6 years (ranging from 21-30) and 39.1 ± 1.9 weeks (ranging from 38-42), respectively, and the gravidity ranged from 0 to 4.

The women underwent induction of labour for various reasons including chronic hypertension, pregnancy induced hypertension, as well as postdatism. The patients were divided into Groups A and B according to their Bishop scores. Group A consisted of 13 women whose Bishop scores were >4 , and Group B consisted of 15 women with Bishop scores of <4 . Dilatation, effacement, consistency, position of the cervix and station of the presenting part were determined vaginally throughout the study by the same two obstetricians. The gestational age was determined using the first day of the last menstrual cycle and confirmed by ultrasonography.

Prior to induction of labour 7-8 cc of peripheral venous blood were obtained. The samples were immediately centrifuged and the removed

plasma which stored at -20°C until assayed for DHEA-S, E₂, E₃, P₄ and cortisol (F). The assay procedures used included enzyme immuno-assay (EIA), fluorescence polarization immunoassay (FPIA, TDX system) or fluoroimmuno-assay (FIA) with commercially available kits. The type of assay, their specific performance characteristics and the trade names are given in Table 1.

Statistical analysis was performed using two tailed paired t-test. Differences were considered to be significant at $p < 0.05$.

RESULTS

Steroid (mean \pm SD) plasma concentrations of DHEA-S E₂, E₃, P₄ and cortisol for both groups are shown in Table 2 and depicted in Fig. 1. In the analysis of the data there were no statistically significant differences between patient groups comparing the mean maternal and gestational age (25.3 ± 4.6 years and 39.1 ± 0.9 weeks, respectively, for group A and 24.1 ± 3.1 years 39 ± 0.8 weeks for group B). The same was true for the gravidity which ranged from 1-4 for group A (2.1 ± 1.4), whereas it was 0 for group B.

Table 2. — Serum steroid concentrations ($\bar{x} \pm SD$) in ripe and unripe cervixes.

	Oestradiol ng/ml	Oestriol ng/ml	Progesterone ng/ml	Cortisol ng/ml	DHEA-S ng/ml
Group A	62.9 \pm 22.6 a	213.1 \pm 87.2 a	484.2 \pm 282.0 a	314.8 \pm 110.3 a	1335 \pm 855.0 b
Group B	66.5 \pm 23.3	214.1 \pm 8.2	513.6 \pm 139.5	262.7 \pm 61.1	558.2 \pm 191.4

a: $p > 0.05$; b: $p < 0.001$.

There were no statistically significant differences among the two groups for all hormones mean levels observed except for DHEA-S concentrations which were found to be significantly elevated in patients with ripped cervixes (1335 ± 855 ng/ml for group A and 558.2 ± 191.4 ng/ml for group B), ($p < 0.001$).

DISCUSSION

The exact mechanism of the onset of labour is still obscure, but cervical condition (softening and dilatation) constitutes one of the most important and dynamic factors related to human parturition and cervical maturity has been associated with estrogen activity in the maternal

blood circulation^(8, 9, 13). The transformation of maternal and fetal DHEA-S into 17β -estradiol and estriol, its maternal blood concentration during pregnancy, and especially its enhanced level prior to and during labour demonstrates its relationship to cervical maturing and the ability to induce labour^(14, 15). In addition, increased DHEA-S clearance during pregnancy and the fetal contribution to estriol production have been attributed to the placental DHEA-S aromatation into 17β -estradiol and to the 16α -hydroxylation within the maternal compartment⁽¹⁶⁾.

Various authors refer to the use of DHEA-S as a test for evaluation the function of the fetoplacental unit, and it was found that the administration of

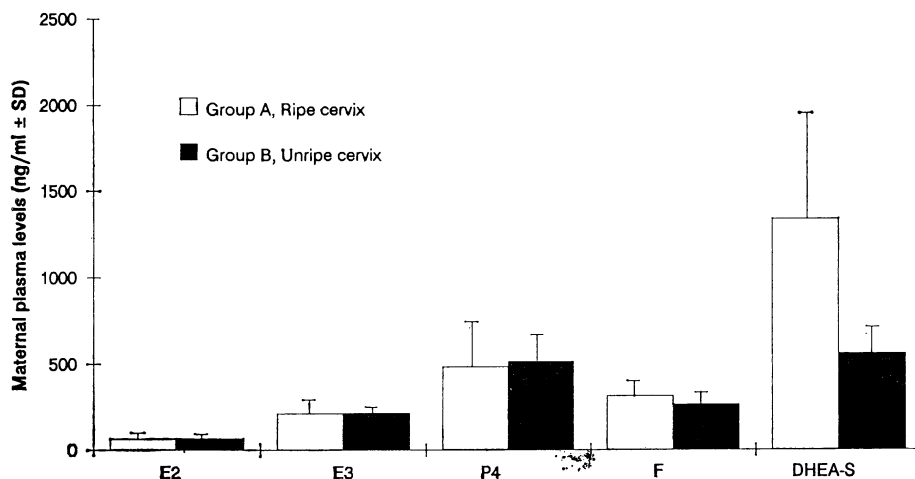


Fig. 1. — Mean \pm SD maternal plasma Dehydroepiandrosterone sulphate (DHEA-S), estradiol (E_2), estriol (E_3), progesterone (P_4) and cortisol (F) concentrations in ripe (group A) and unripe (group B) cervixes.

DHEA-S to pregnant women relaxed the birth canal by increasing the pelvic score and triggering the onset of labour^(8, 9, 17). It has also been mentioned that the total collagenolytic activity as well as 17 β -estradiol serum concentrations were considerably elevated and responsible for cervical ripening in late pregnancy⁽¹⁸⁾.

Our material presented significantly increased maternal serum concentrations of DHEA-S in pregnant women with mature cervixes, these being evaluated according to Bishop scores and the progress of labour induction. These results are in agreement with those of Zuidema *et al.* 1986⁽¹³⁾ who also noted no effect of estradiol, estriol and progesterone maternal plasma concentrations on cervical maturity.

In conclusion, although fetal adrenal steroids seem to participate actively in the initiation of labour in mammals, their role in humans remains uncertain, even though changes of the cervix preceding the initiation of labour are always associated with elevated concentrations of DHEA-S in the maternal circulation.

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