MATERNAL SERUM DEHYDROEPIANDROSTERONE SULFATE LEVELS AND THE EFFICIENCY OF LABOR

M. Modares Gilani[1], *N. Peikari*[2], *S. Ziai*[2] *and B. Faghihzadeh*[2]

1) Department of Obstetrics and Gynecology, Vali-e-asr Hospital, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

2) Department of Midwifery, Tarbiat Moddares University, Tehran, Iran

Abstract - To evaluate the maternal serum dehydroepiandrosterone (DHEA) sulfate levels as a factor influencing labor "efficiency" at term and unsuccessful labor induction. This is a prospective study. In this study the mean (± standard error) maternal serum DHEA sulfate levels of 90 singleton pregnant women in 3 groups with spontaneous labor, need for augmentation and need for induction were compared. Pregnancies complicated by diabetes mellitus, hypertension, fetal growth restriction, tobacco consumption, corticosteroid use or chorioamnionitis were excluded. Bishop score of all cases was less than 5. Serum DHEA sulfate levels were measured by radioimmunoassay. Dehydroepiandrosterone sulfate levels and other obstetric variables were correlated retrospectively with the clinically determined requirements of oxytocin augmentation of labor, and the outcome of each induction attempt. The t-test, Variance analysis Kruskal - Wallis test, Mann-Whitney test, Chi-square (χ^2) distribution, linear correlation and regression were used for statistical analysis. $P < 0.05$ was considered statistically significant. This study showed that the mean (± standard error) maternal serum DHEA sulfate level was not significantly higher in women who progressed spontaneously through labor ($n = 30$) than in those who required augmentation ($n = 30$) (60.78 ± 4.22 versus 70.38 ± 5.84). No significant difference was found between the mean DHEA sulfate levels of spontaneous labor group ($n = 30$) and cases who had prolonged latent phase ($n = 21$) (66.78 ± 4.22 versus 67.02 ± 7.13) or prolonged active phase disorders ($n = 9$) (60.78 ± 4.22 µg/dl versus 78.22 ± 10.23 µg/dl $p = 0.25$).

This study showed that the mean maternal serum DEHA sulfate level was significantly higher in women with spontaneous labor ($n = 30$) than in those who needed induction ($n = 30$) (60.78 ± 4.22 µg/dl versus 39.49 ± 4.56 µg/dl, respectively; $p = 0.0001$). In the group who needed induction, the mean DHEA sulfate level was significantly higher in women who progressed to active labor ($n = 18$) than in whom attempts were unsuccessful ($n = 12$). (48.83 ± 6.48 µg/dl versus 26.96 ± 5.10, respectively $p = 0.035$). In the group who were induced, the main cause of C/S was failure of labor progression (77.8%).

The mean DHEA level was significantly higher in women with spontaneous labor ($n = 28$) than in those requiring cesarean delivery ($n = 7$) (61.01 ± 4.22 µg/dl versus 24.67 ± 7.06, respectively; $p = 0.001$).

The maternal serum DHEA sulfate level did not correlate significantly with cervical Bishop score on admission ($r = 0.02$, $p = 0.78$). DHEA sulfate may be an important factor in successful labor induction, and in efficient labor.

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Key Words: Maternal serum dehydroepiandrosterone (DHEA) sulfate, labor

INTRODUCTION

Dehydropiandroterone (DHEA) sulfate is a weak androgenic steroid produced by the adrenal cortex of both the pregnant woman and her fetus. Its role as an intermediary hormone in the fetoplacental production of androstenedione, testosterone, estrone, and estradiol has been well documented (1). The results of maternal third trimester parenteral DHEA sulfate administration have also been investigated. One study (2) evaluated the metabolism of this steroid as a measure of placental function and fetal well - being, and subsequent reports (3,5) noted the effectiveness of exogenous DHEA sulfate on cervical ripening and labor. Providing support for a direct effect, binding sites for DHEA sulfate have been identified on the plasma membranes of human cervical fibroblasts (6).

Although the effects of antepartum DHEA sulfate administration have been reported, the intrapartum relationships of endogenous DHEA sulfate have also been assessed (4). The objective of this study was to test the hypothesis that the maternal serum DHEA sulfate level is a factor influencing labor "efficiency" at term. More specifically, the study was designed to determine whether serum DHEA sulfate levels of women progressing without augmentation of labor differ significantly from those requiring pharmacologic augmentation or induction of labor.

MATERIALS AND MEHTODS

In this prospective study, the mean maternal serum DHEA sulfate level of 90 pregnant women in 3 groups with spontaneous labor, need for augmentation and need for induction was compared. The study was restricted to 90 Iranian women from 18 to 35 years of age, higher than 150 cm, with singleton cephalic pregnancies from 37 to 42 weeks of gestational age and Bishop score less than 5, to eliminate potential bias due to physiologic variations in DHEA sulfate and labor occuring with such factors. After having obtained verbal consent, approximately 90% of potential subjects granted informed consent for participation. Pregnancies complicated by diabetes mellitus, hypertension, fetal growth restiction, or tobacco use were excluded because of potential placental insufficiency and altered DHEA sulfate metabolism.

Pregnancies complicated by chorioamnionitis or maternal corticosteroid use were excluded because of their respective clinical associations with hypotonic contraction patterns and depressed adrenal function.

On admission of women to the labor and delivery unit in active labor, or for induction of labor, samples were collected from 90 women fulfilling inclusion criteria and serum was stored at -20°C until analyzed. Cesarean delivery for nonreassuring intrapartum fetal testing, Intra-uterine growth retardation, fetal distress, birth weight over 4000g or vaginal bleeding further resulted in exclusion of five patients from the analysis.

Following standard guidelines set by ACOG (7) oxytocin was initiated on identification of a hypotonic uterine contraction pattern in combination with lack of progressive cervical dilatation and in women who needed induction.

Using the definition of Watson and co-workers (8), an induction attempt was termed "successful" if the patient reached the active phase of labor as demonstrated by a change in the slope of cervical dilatation.

Maternal serum DHEA sulfate levels were measured by radioimmunoassay (RIA) with commerical kits obtained from Kavoshyar corporation. Each sample was assayed twice, with the reported DHEA sulfate level being an average of the two determinations.

Serum DHEA sulfate levels and other obstetric variables, such as maternal age, parity, gestational age, cervical dilatation, Bishop scores on admission, and birth weight, were correlated retrospectively with the clinicaly determined requirement for pharmacologic augmentation of labor and the need to induce labor. Serum DHEA sulfate levels were then correlated with the success or failure of an induction attempt.

The t-test, Variance analysis, Kruskal-Wallis test, Mann-Whitney test, Chi-square (χ^2) distribution, linear correlatoin and regression were used for statistical analysis. $P < 0.05$ was considered statistically significant.

For the purpose of this study, vaginal delivery without the need for oxytocin augmentation was considered an evidence for "efficient" labor, and an induction attempt was termed "successful" if the patient reached the active phase of labor.

RESULTS

With the exception of cervical dilatation on admission, and birthweight, no significant demographic differences were identified between the 3 groups (Table 1).

Table 1. Characteristics of the study population

	Spontaneous progression (n = 30)	Oxytocin augmentation (n = 30)	Oxytocin induction (n = 30)	P
Maternal age (Y)	24.06 ± 0.71	23.90 ± 0.70	25.50 ± 0.74	NS
Maternal height (cm)	161.60 ± 1.01	159.23 ± 0.86	159.66 ± 0.97	NS
Gravidity (n)	1.60 ± 0.15	1.63 ± 0.14	1.80 ± 0.17	NS
Parity (n)	0.53 ± 0.14	0.46 ± 0.11	0.56 ± 0.14	NS
Bishop score	3.70 ± 0.10	3.40 ± 0.14	2.76 ± 0.18	0.0003
Birth weight (g)	3202.33 ± 58.89	3315.33 ± 94.94	3488.66 ± 75.38	0.03

NS : non significant

Data are presented as mean ± standard error

Compared to women with successful induction attempts, women with unsuccessful attempts had significantly lower perinduction Bishop scores. No other statistically demographic differences were identified between these 2 groups.

The mean (± standard error) DHEA sulfate level was significantly higher in women progressing spontaneously than in those requiring induction of labor (60.78 ± 4.22 μg/dl versus 39.49 ± 4.56 μg/dl respectively P = 0.0001) (Fig. 1).

Maternal serum DHEA sulfate level was significantly higher in women with successful induction than in women with unsuccessful "attempt" (48.83 ±

6.48 μg/dl versus 26.96 ± 5.10 μg/dl, respectively; P = 0.03).

No significant difference was found between the mean DHEA sulfate level of spontaneous labor group (n = 30) and cases who had prolonged latent phase (n = 21) (60.78 ± 4.22 μg/dl versus 67.02 ± 7.13 μg/dl) or prolonged active phase disorders (n = 9) (60.78 ± 4.22 μg/dl) versus 78.22 ± 10.23 μg/dl P = 0.25).

Maternal DHEA sulfate levels were not significantly higher in those laboring patients progressing spontaneously compared with those requiring oxytocin augmentation (60.78 ± 4.22 μg/dl versus 70.38 ± 5.84 μg/dl). The mean DHEA sulfate level was significantly higher in women with spontaneous labor than in those requiring cesarean delivery (61.01 ± 4.32 μg/dl versus 24.64 ± 7.06 respectively, P = 0.001) (Fig. 2). No maternal serum DHEA sulfate level, correlated significantly with Bishop score, on admission (r = 0.02 P = 0.78).

There were no statistically significant linear correlations between the natural logarithm of maternal serum DHEA sulfate levels and gestational age (r = -0.06 P = 0.53), or birth weight (r = -0.16 P 0.11), (Table 2).

There was a reverse significant linear correlation between the maternal serum DHEA sulfate levels and maternal age (r = -0.26 P = 0.01) (Table 2).

When DHEA sulfate levels were at or below 60 mg/dl, the odds ratios (ORs) for an unsuccessful induction increased progressively as the maternal serum DHEA sulfate level decreased.

In the above levels of 60 mg/dl, the OR for an unsuccessful induction was not statistically significant.

Table 2. Correlation between the natural logarithm of maternal serum DHEA sulfate levels and demographic factor

Demographic factor	r	p
Gestational age (wk)	-0.0665	0.533
Duration of second stage	0.0075	0.949
Bishop score	0.0288	0.788
Birth weight	-0.1678	0.114
Maternal age (y)	-0.2672	0.011
Duration of active phase	0.1789	0.126
Duration of latent phase	0.0970	0.202

DISCUSSION

In 1991, Granstrom and co-workers (9) reported that insufficient remodeling of uterine connective tissue may contribute to protracted labor. Women with ineffective labor who required oxytoxin administration and subsequent cesarean delivery due to arrest of labor had significantly higher uterine collagen concentration and lower local collagenolytic activity than control women with normal labor progression. The underlying mechanisms responsible for such remodeling have not been elucidated fully. However, DHEA sulphate may be involved, because Mochizuki and Tojo (3) showed that collagenase activity in the uterine cervix increased significantly after repeated intravenous injection of DHEA sulfate into pregnant women at term. The proposed mechanism of DHEA sulfate action was an estrogen-induced activation of collagenolytic activity mediated through placental conversion of DHEA sulfate to 17 β-estradiol.

In contradiction to this theory of estrogen mediated activation of collagenase activity, the addition of estradiol to rabbit uterine cervical cultures has been found to inhibit fibroblast collagenase activity. However, addition of DHEA sulfate to similar cultures resulted in an approximately 60% increase in fibroblast collagenase action (10). With the recent identification of DHEA sulfate binding sites on the plasma membranes of human cervical fibroblasts (6) there is now sufficient evidence to hypothesize a similar mechanism of direct DHEA sulfate action on uterine collagenase activation.

Parenteral administration of DHEA sulfate has been used effectively for cervical ripening and labor induction. The proposed mechanism of action is an activation of total collagenolytic activity, resulting in uterine connective tissue remodeling. Recent animal studies (11) have suggested that DHEA sulfate acts synergistically with interleukin - 8 to increase collagenase clastase, and gelatinase activity while decreasing the cervical collagen content.

The cervical collagenolytic effect of DHEA sulfate may also be mediated thorugh prostaglandin E_2, because its synthesis is enhanced by DHEA sulfate in human cervical tissue (12).

Sufficient uterine connective tissue remodeling is important in allowing normal labor progression.

The present study provides clinical support for the concept that DHEA sulfate increases fibroblast collagenase, hence, efficient labor. Maternal venous DHEA sulfate levels were significantly lower in women requiring induction of labor than in women without this requirement.

Our study provides clinical support for those animal and culture studies, suggesting a role for DHEA sulfate in successful induction of labor in humans. The endogenous preinduction DHEA sulfate levels were significantly lower in patients with unsuccessful inductions than in those with successful inductions.

The level of preinduction maternal serum DHEA sulfate appears to influence the ultimate outcome (success or failure) of an induction attempt (14).

Although one report (13) suggested that maternal DHEA sulfate levels increased at the onset of labor, intrapartum trends in DHEA sulfate following the spontareous onset of labor have not been reported.

The maternal serum DHEA sulfate level is certainly not the sole factor determining the success or failure of an attempted vaginal delivery. The results of a study underscores this fact (15). The average DHEA sulfate level of women requiring cesarean delivery (despite oxytoxin augmentation in all cases) was near that of those progressing spontaneoully to vaginal delivery. But in our study, the maternal serum DHEA sulfate levels of women requiring cesarean delivery was low than those progressing spontaneously to vaginal delivery.

Our findings are consistent with the hypothesis that the maternal serum DHEA sulfate level is an important factor in successful labor induction and in the efficiency of labor at term.

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