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Comparison of Fetal Plasma Cortisol Level between Eutrophic and Hypotrophic Newborns

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A B S T R A C T

We tested two groups of singletons born at term: fifty-six eutrophic newborns and 56 hypotrophic subjects. They were selected randomly from all newborns delivered by vaginal route between 8 and 14 hours. Excluded were preeclampsia, diabetes, labours longer than 12 hours and newborns with malformations. Written informed consent was obtained from all women and data were collected before and after labour. Umbilical cord blood samples were obtained immediately following the delivery and plasma cortisol concentrations were measured by radioimmunoassay. The groups did not differ significantly regarding maternal age, parity, gestational age and Apgar score, but birth weight was significant differed ($p<0.001$). In addition, eutrophic newborns had significantly elevated cortisol levels (457.7 nmol/L, 321.8–696.6 nmol/L) compared with hypotrophic newborns (320.5 nmol/L, 215.1–578.7 nmol/L, $p<0.001$). The role of fetal cortisol in intrauterine growth restriction (IUGR) pregnancy and labour is uncertain, but fetal plasma cortisol levels may be lower in IUGR newborns.

Key words: *fetal cortisol, hypotrophic newborns*

Introduction

Activation of adrenal steroidogenesis is critical for maturation of organ systems before birth and appears to contribute to the triggering of parturition[1]. Factors regulating the development of adrenal activity and the hypothalamic-pituitary-adrenal axis have been studied by many researchers elucidating general patterns of increased steroidogenesis near term[2,3]. Specific triggers have been investigated, primarily in singleton gestations, with many appearing to play at least a minor role in this development[2,4–7]. The human fetal adrenal gland secretes cortisol beginning in midgestation[8]. In the fetus, in contrast with the situation in the newborn and in the adult, cortisol may not be solely derived from adrenal secretion. The maternal cortisol concentration is several-fold higher than that of the fetus, but cortisol is extensively metabolized in the placenta; thus the maternal contribution to fetal levels is unclear[8]. In addition, fetal tissues (lung, liver, and brain) could reconvert to cortisol the cortisone derived from placental metabolism of maternal cortisol[8]. In humans, however, the connection of fetal cortisol and intrauterine growth restriction (IUGR) is unknown[7]. Some authors reported that underlying pregnancy complications might influence fetal adrenal steroidogenesis[9–11]. The purpose of this study was to determine whether IUGR has any effect on the level of the fetal plasma cortisol.

Subjects and Methods

This prospective study was conducted at Department of Obstetrics and Gynecology, Clinical Hospital in Split, Croatia, Europe, between May 2001 and May 2003. The hospital ethics committee approved the protocol, and informed consent was obtained from all women. We tested two groups singletons born at term; fifty-six eutrophic newborns and 56 hypotrophic subjects. They were selected randomly from all newborns delivered by vaginal route between 8:00 a.m. and 14:00 p.m.. Excluded were preeclampsia, diabetes, prenatal complications, newborns with malformations and labours longer than 12 hours. None used tobacco, alcohol, or medications other than ferrous sulfate. The study subjects made up two subgroups after delivery; in the first were normal eutro-

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TABLE 1
CHARACTERISTICS OF STUDY POPULATION

	Eutrophic newborns N=56 median (range)	Hypotrophic newborns N=56 median (range)	Statistical significance*
Maternal age (y)	28.1 (21–35)	29.2 (24–34)	ns
Parity	2.1 (0–4)	2.0 (0–3)	ns
Gestational age (wk)	38.8 (37–41)	39.1 (37–41)	ns
Neonatal weight (g)	3612 (3250–3850)	2456 (2100–2750)	p<0.001
Neonatal plasma cortisol concentration (nmol/L)	457.7 (321.8–696.6)	320.5 (215.1–578.7)	p<0.001

*t-test

phic newborns, and in the second were hypotrophic infants. The performance of customised estimated fetal weight centiles in the prediction of neonatal growth restriction was determined for cutoffs at both the 5th and 10th estimated fetal weight customised centiles[12]. Gestational age was calculated from the last menstrual period and confirmed by ultrasonographic assessment before 12 weeks′ gestation. No vasoactive or analgesic drugs were administered to the mother before delivery of the fetus. All women were interviewed. Data were collected before and after labour for maternal age and parity, gestational age, duration of labour, sex, weight and Apgar score of newborns. Blood was taken in tubes from the umbilical vein immediately after delivery of the baby after the cord was clamped and before delivery of the placenta. All samples were centrifuged, separated, and stored at 2–8°C. All samples from each individual were analyzed in the same assay of cortisol (Immunotech, Beckman Coulter Inc, Marseille, France).

Data were analyzed with Student *t* test. p<0.05 was considered statistically significant.

Results

Cord blood samples were taken from 53 female and 59 male term newborns. They were fifty-six eutrophic newborns and 56 IUGR subjects. Apgar scores were >8 at 1.5 minutes. All newborns had an uncomplicated neonatal course. All mothers and infants were discharged from hospital in good condition.

Table 1 shows characteristics of mothers and newborns. The groups did not differ significantly regarding maternal age, parity, and gestational age. Birth weight was significant differed between eutrophic (3,612 g, 3,250–3,850 g) and IUGR newborns (2,456 g, 2,100–2,750 g, p<0.001). In addition, eutrophic newborns had significantly elevated plasma cortisol levels (457.7 nmol/Lp 321.8–696.6 nmol/L) compared with IUGR infants (320.5 nmol/Lp 215.1–578.7 nmol/L) (t = 4.381, p<0.001).

Discussion

The adrenal cortex of the human, both in utero and after delivery, produces prodigious quantities of cortisol[11]. The factors that regulate cortisol production are well defined[11,13]. It is known that pregnancies under stress, particularly those pregnancies with intrauterine growth retardation and/or hypertensive disorders have elevated corticotropin-releasing hormone levels[14–18]. Fetal cortisol is crucial to fetal development and neonatal survival. It is well known that the fetal plasma cortisol is an independent predictor of the duration of pregnancy[1,2,6–8]. But the role of fetal cortisol in IUGR pregnancy and labour is unknown[7]. Some authors reported contradictory findings about fetal plasma cortisol in hypotrophic infants. Reis and al. reported that IUGR is associated with an activation of the hypothalamus-pituitary-adrenal axis, reflected by increased fetal plasma concentrations of cortisol[19]. Nieto Diaz et al. reported their findings of lower levels of cortisol in amniotic fluid in IUGR infants[20]. Our results suggest that IUGR is associated with lower cord blood cortisol levels. Our observation most probably reflects the high incidence of antenatal complications in these subjects. Fetal plasma cortisol may be a marker of antepartum risk conditions for IUGR.

In conclusion, fetal plasma cortisol may have some value as a marker of newborn complications. Further studies with a larger number of subjects are necessary to clarify the relationship between fetal cortisol and IUGR.

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USPOREDBA RAZINE FETALNOG SERUMSKOG KORTIZOLA IZMEĐU EUTROFIČNE I HIPOTROFIČNE NOVOROĐENČADI

S A Ž E T A K

Ispitivali smo dvije skupine terminske novorođenčadi iz jednoplodnih trudnoća: 56 eutrofične i 56 hipotrofične djece. Ispitanici su slučajno odabrani između sve djece rođene vaginalno između 8 i 14 sati. Isključene su preeklampsije, dijabetesi, porodi dulji od 12 sati i malformirana novorođenčad. Rodilje su upoznate s istraživanjem, dragovoljno su potpisale pristanak, a podaci su upisivani prije i nakon poroda. Odmah nakon rođenja djeteta uzimani su uzorci krvi iz pupkovine i određivana je razina fetalnog serumskog kortizola. Skupine se nisu razlikovale glede majčine dobi, pariteta, trajanja trudnoće i Apgar skora, ali novorođenačka težina bila je statistički značajno različita ($p<0.001$). Također, eutrofična djeca imala su značajno višu razinu kortizola (457.7 nmol/L, 321.8–696.6 nmol/L) u usporedbi s hipotrofičnom novorođenčadi (320.5 nmol/L, 215.1–578.7 nmol/L) ($p<0.001$). Uloga fetalnog kortizola u trudnoćama sa zastojem rasta je nepoznata, no činjenica je kako fetalni kortizol može biti niži u hipotrofične novorođenčadi.