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Respiratory Distress Syndrome: Steroid and Peptide Hormone Levels in Maternal Venous Blood and the Umbilical Vein and Artery

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The concentration of steroid and peptide hormones in the development of the respiratory distress syndrome of the newborn has been investigated. Serum progesterone, dehydroandrostenedione sulphate (DHAS) oestradiol, oestriol, cortisol, prolactin and human placental lactogen (HPL) concentrations were measured by radioimmune assay (RIA) in samples obtained from the maternal vein and the premature newborn's umbilical artery and vein. The results were grouped according to gestational age into two groups, 28—32 and 33—36 weeks. Serum cortisol level was lower in maternal blood and both the umbilical vein and artery if the newborn subsequently developed RDS. No deviations from healthy values were encountered with any other hormone. These observations and data in the literature suggest that maturation of the fetal lung is influenced not only by maternal glucocorticoid secretion but also by the activity of the fetal adrenal cortex.

Hormonal factors may play a part in the maturation of fetal pulmonary tissue [1, 6, 10]. Data for humans are controversial. Increased incidence of the respiratory distress syndrome (RDS) has been encountered in infants with a depressed level of prolactin and cortisol in mixed umbilical blood [8]; no difference in DHAS and cortisol concentrations, accompanied by depressed prolactin levels were found in another study [7] while again other authors observed no differences in these hormone levels [12]. Oestrogen [6, 13] and corticosteroid [10] treatment has been put forward for the prevention of RDS.

The fact that the hormone levels were measured in mixed cord blood may obscure the fetus' own endocrine activity. There are hardly any data comparing maternal and fetal hormone levels. Therefore, we performed simultaneous measurements in the venous blood of the mother and samples removed separately from the umbilical vein and artery of the newborn infant. We attempted to study the activity of all endocrine organs with a proven or probable role in the hormonal system of the mother-feto-placented unit: prolactin reflects pituitary activity, progesterone and HPL are secreted by the placenta, the level of DHAS and cortisol throws light on adrenocortical activity and oestradiol and oestriol concentrations are related to the funcion of the feto-placental unit.

TABLE I

Clinical grouping

	n	Gestational age, weeks	RDS	No RDS
Group I	33	28—32	17	16
Group II	40	33—36	5	35
All	73		22	51

TABLE II

Distribution of the 1671 hormone assays in serum

Hormone	Maternal venous blood	Cord blood	
		venous	arterial
Progresterone	114	72	57
DHAS	115	72	66
Oestradiol	114	73	60
Oestriol	114	72	60
Cortisol	114	73	60
Prolactin	110	72	58
HPL	107	57	31
Total:	1671		

TABLE III

Summary of RIA methods used in the study

Hormone	Intraassay variation per cent	Interassay coefficient,	Method	Reagents
Progesterone	7.8	12.5	Aso et al	WHO, London
Oestradiol	4.6	9.1	Aso et al	WHO, London
Oestriol	7.5	8.4	Aso et al	WHO, London
Cortisol	5.7	10.2	Aso et al	WHO, London
DHAS	7.2	14.5	Buster and Adam	Sterantin Kit
Prolactin	6.8	11.2	Buster and Adam	Sterantin Kit
HPL	9.8	9.0	Mohari and Kocsár	National FJC Research Centre for Radiobiology and Nuclear Medicine, Budapest

Material and Methods

A total of 73 mothers giving birth to premature infants weighing 1001—2500 g between the 28th and 36th week of pregnancy participated in the study (Table I). The diagnosis of RDS was based on clinical and radiological signs. Mother-infant pairs with premature rupture of membranes, receiving corticosteroid prophylaxis to prevent RDS or intrauterine growth retardation were excluded from the study.

The blood samples for hormone measurements were taken from the cubital vein of the mother, and separately from the umbilical vein and artery, immediately after birth of the fetus, before birth of the placenta.

All hormones were determined by RIA, a total of 1671 hormone measurements were carried out (Table II). Progesterone, oestradiol, oestriol, cortisol and prolactin measurements were performed in the Scientific Research Centre for Mother and Infant Health, Ministry of Health, Moscow; DHAS was determined in the 2nd Department of Obstetrics and Gynaecology, Semmelweis University Medical School, Budapest, and HPL in the Frédéric Joliot-Curie Research Centre for Radiobiology Budapest.

Some methodological aspects are presented in Table III.

Mean and standard error of the mean (SEM) values were calculated after logarithmic transformation. First, the eventual effect of gestational age on the hormone levels was investigated by variance analysis. On the basis of its results the study age span was broken down to 28—32 and 33—36 gestational weeks. The hormone levels of mother-infant pairs affected and unaffected by RDS were then compared by the unpaired *t*–test within each gestational age group.

Results

They are summed up in Table IV. As can be read, serum cortisol in the mother and both the umbilical vein and artery were lower in RDS than without it in both gestational age groups. No differences could be detected in any of the remaining hormone levels.

Discussion

Liggins [10] was the first to draw attention to the part of corticosteroids in the pathogenesis of RDS. Our results have confirmed this idea by demonstrating a difference between infants affected and unaffected by RDS only in the serum cortisol level but in none of the other six steroid or peptide hormone levels. Contrary to data of Abdul Karim and Prior [1], other authors [5, 6, 7, 8] found no significant differences in the level of these hormones; this is in accordance with the observation made by Schober et al [12].

An important and hitherto hardly investigated issue is the role of the fetus' own adrenocortical activity in the maturation process of the lung. Beitins et al [3] have shown that 75% of the cortisol content of the fetal serum originates from the fetus itself and only one quarter from the mother. Our own previous data [9] corroborated their findings: there is a significant increase of serum cortisol in the umbilical artery during the period between 28 and 40 weeks of gestation while no similar change could be observed in maternal blood and the umbilical vein. This indicates that there is no change in the mother's adrenocortical secretion during this period while the

TABLE IV

Mean serum hormone values in maternal blood (M), in blood of the umbilical vein (V) and artery (A), broken down by gestational age and presence or absence of RDS

	Gestational age, weeks		No RDS n	No RDS mean	No RDS SEM	RDS n	RDS mean	RDS SEM
DHAS, nmol/l	28—32	M	10	0.99	1.34	15	0.55	1.56 ns
		V	9	1.77	1.36	15	1.36	1.17 ns
		A	8	3.10	1.24	13	2.26	1.14 ns
	33—36	M	26	1.72	1.22	7	0.64	1.32 ns
		V	26	1.92	1.20	7	1.40	1.72 ns
		A	24	2.42	1.20	6	2.97	1.67 ns
Progesterone, nmol/l	28—32	M	10	373.53	1.18	14	439.29	1.17 ns
		V	10	1898.84	1.22	14	2059.05	1.14 ns
		A	7	1021.47	1.37	10	1151.71	1.12 ns
	33—36	M	26	558.36	1.07	7	486.87	1.12 ns
		V	26	2657.13	1.10	7	2482.45	1.29 ns
		A	22	1418.00	1.14	5	1091.74	1.34 ns
Oestradiole, nmol/l	28—32	M	10	29.17	1.29	14	35.95	1.15 ns
		V	10	24.00	1.32	14	20.53	1.16 ns
		A	7	7.67	1.44	10	1.19	1.18 ns
	33—36	M	26	55.59	1.13	7	36.60	1.19 ns
		V	26	35.48	1.15	7	29.76	1.36 ns
		A	22	18.99	1.11	5	12.82	1.13 ns
Oestriol, nmol/l	28—32	M	10	26.84	1.30	14	30.51	1.21 ns
		V	10	220.96	1.32	14	220.30	1.25 ns
		A	7	34.81	1.32	8	69.55	1.27 ns
	33—36	M	26	41.89	1.10	7	37.60	1.08 ns
		V	25	306.13	1.16	7	328.98	1.28 ns
		A	22	205.10	1.15	5	310.05	1.25 ns
Cortisol, nmol/l	28—32	M	10	224.53	1.13	14	143.02	1.16 ns
		V	10	99.78	1.14	14	61.93	1.12 ns
		A	7	74.44	1.21	10	54.49	1.17 ns
	33—36	M	26	208.51	1.11	7	131.11	1.19 ns
		V	26	98.89	1.11	7	68.03	1.26 ns
		A	22	91.29	1.10	5	54.54	1.20 ns
HPL, nmol/l	28—32	M	9	101.09	1.16	14	108.31	1.30 ns
		V	8	5.51	1.50	12	2.00	1.47 ns
		A	7	2.96	1.70	8	1.62	1.48 ns
	33—36	M	25	122.12	1.11	7	153.39	1.26 ns
		V	24	1.86	1.03	6	3.37	1.83 ns
		A	17	1.41	1.24	5	1.90	1.76 ns
Prolactin, mIU/l	28—32	M	9	3304,37	1.42	13	3699.67	1.19 ns
		V	10	3774.41	1.34	13	2430.86	1.17 ns
		A	6	3050.31	1.28	9	1895.05	1.34 ns
	33—36	M	26	4060.25	1.18	7	7840.05	1.43 ns
		V	26	4491.76	1.17	7	6348.67	1.40 ns
		A	22	4954.24	1.16	5	4722.06	1.37 ns

n: number of cases
s: significant ($p<0.01$)
ns: non-significant

fetal adrenal cortex exhibits increasing activity.

Our data draw attention to the importance of depressed serum cortisol levels. They also suggest that, in addition to the maternal adrenal cortex, the fetus' own adrenocortical activity has a marked influence on fetal lung maturation.

References

1. Abdul-Karim RW, Prior JT: The influence of oestrogens on the lung vasculature of the premature rabbit neonate. J Reprod Med 2: 140, 1969.
2. Aso T, Guerro R, Cekan S, Diczfalusy E: A rapid 5 hour RIA of progesterone and oestradiol in human plasma. Clin Endocr 4: 173, 1975.
3. Beitins IZ, Bayard F, Anges IG, Kowarski A, Migeon CJ: The metabolic clearence rate blood production, interconversion and transplacental passage of cortisol and cortisone in pregnancy near term. Pediatr Res 7: 509, 1973
4. Buster JE, Abraham GE: RIA of plasma DHAS. Analyt Letters 5: 543, 1972
5. Conly PW, LeMaire JW, Monkus EF, Cleveland WW: Plasma estriol concentration in infants with the respiratory distress syndrome. Fetal Neonat Med 83: 851
6. Diczkey RP, Robertson AF: Newborn estrogen excretion: its relationship to sex, birth-weight and maternal complications of IRDS. Am J Obstet Gynecol 104: 551, 1969.
7. Gluckman PD, Ballard PL, Kaplan SL, Liggins GC, Grumbach MM: Prolactin in umbilical cord blood and the respiratory distress syndrome. J. Pediatr 93: 1011, 1978
8. Hauth JC, Parker FC, MacDonald CP, Porter JC, Johnston JM: A role of fetal prolactin in lung maturation. Obstet. Gynecol 51: 81, 1978
9. Hercz P: Quantitative changes in steroid and peptide hormones in the maternal — fetoplacental system between 28–40 weeks of pregnancy. Acta Med Sci. Hung. 42: 29, 1985
10. Liggins GC, Howie RN: A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics 50: 515, 1972
11. Mohari K, Kocsár L, Kutas V: HCS (HPL) labelling with 125-iodine isotope and application in RIA. Eur J Nuclear Med 2: 125, 1979
12. Schober E, Simbrunner G, Salzer H, Husslein P, Spona J: The relationship of prolactin in cord blood, gestational age and respiratory compliance after birth in newborn infants. J Perinat Med 10: 23, 1982
13. Shanklin DR: Pathogenesis and treatment of experimental hyaline membrane disease. Proc Soc Pediatr Res. 135, 1964

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