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FETO-NEONATAL HORMONOLOGY IN PREMATURE DELIVERY

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SUMMARY

The adrenal of the newborn infant is morphologically and functionally similar to the fetal one, and so the study of steroid excretion at birth can provide some information about fetal adrenal activity. We have studied (GLC Mass spectrometry) the behaviour of some 16 oxidated steroids: 16α-hydroxy-dehydroepiandrosterone (16α-OH-DHA); 16β-hydroxy-dehydroepiandrosterone (16β-OH-DHA); 16-oxo-androstenediol (16-oxo-A); 16α-estriol (16α-OH-E_3) in maternal urine, amniotic fluid, fetal plasma (cord blood) and urine of newborn infants, in pregnancies with premature delivery.

Our results are as follows: 1. During pregnancy (mother's urine) 16-oxidated steroids, particularly estriol, are not significantly lower than normal; 2. In amniotic fluid all the steroid values are significantly reduced; 3. Fetal plasma values are significantly reduced, except for 16-oxo-A and 16β-OH DHA; 4. In the urine of newborns, both those born at term or those of the same gestational age from planned deliveries, all the 16-oxidated steroid values are significantly diminished.

The evidence of normal values of 16-oxidated steroids in the mother would indicate that the decrease in the fetuses occurs just before labour. On the other hand, fetal plasma cortisol in premature delivery without maternal complications shows similar values to those found in spontaneous deliveries at term. So it is possible that these two events play some role in determining the initiation of premature labour.

It is generally accepted that the hormonal biology of the newborn infant, at least during the first hours of extrauterine life, with regard to some steroid groups, can be considered as a model of the fetal one [1–2]. In this way the study of steroid plasma levels, their excretion at birth and shortly afterward can provide information concerning fetal endocrine activities [3–4].

It is also well known that the amount of C-21 and C-19 5-ene-3β OH-16-substituted steroids (with OH or O) can indicate the occurrence of important metabolic and biosynthetic steps taking place, above all, in the fetus, and that 16α-estriol is commonly employed as a means of indicating fetal condition [5–7].

Table 1. Method outline

Enzymatic hydrolysis
Ethyl-acetate extraction
Solvolysis
Thin-layer chromatography
Elution and derivatives formation (TMSi-ethers)
Gas liquid chromatography
Mass spectrometry

Using gas liquid chromatography and mass spectrometry (Table 1) (8–10) we have studied the pattern of some 16-OH and oxo-steroids such as 16α-hydroxy-pregnenolone (16α OH-P), 16α and β-hydroxy-dehydroepiandrosterone (16α and β OH-DHA), 16 oxo-androstenediol (16-oxo-A), 16α-estriol (16α OH-E_3) in maternal urine, amniotic fluid, fetal plasma (cord blood) and urine of the newborn at birth in cases of apparent normal pregnancies followed by premature delivery.

Our results are as follows: 1. In the mother's urine, 16-substituted steroid levels and particularly the estriol curve trend during pregnancy, up until premature delivery, do not appear to be significantly lower than normal (Table 2). 2. In the amniotic fluid, at the moment of premature delivery, all the steroid values are significantly reduced (Table 3). 3. Fetal plasma values (in premature delivery) are significantly reduced, except 16-oxo-A and 16β OH-DHA (Table 4). 4. In the urine of the premature newborn at birth, all the 16-oxydated steroid values are more significantly diminished than at term newborn infants (Table 5). On the contrary, premature infants with the same gestational age but born after planned

Table 2. 16-Substituted steroids in mother urine (St./Creatinine). Mean values and statistical comparison

	16α OH-DHA	16 oxo-A 16β OH-DHA	16α OH-P	16α OH-E_3
Normals (13)	1.75	38.19	n.d.	10.24
Premature delivery (10)	1.44	22.75	n.d.	9.95
t	0.71	2.89	—	0.11
p	<0.50	<0.01	—	<0.95

Table 3. 16-Substituted steroids in amniotic fluid (μg/litre). Mean values and statistical comparison

	16α OH-DHA	16 oxo-A 16β OH-DHA	16α OH-P	16α OH-E_3
Normals (10)	470.07	909.04	191.64	748.90
Premature delivery (10)	33.87	479.65	54.19	421.43
t	2.955	2.059	2.893	1.972
p	<0.01	<0.10	<0.02	<0.10

Table 4. 16-Substituted steroids in cord plasma (μg/litre). Mean values and statistical comparison

	16α OH-DHA	16 oxo-A 16β OH-DHA	16α OH-P	16α OH-E_3
Normals (22)	2869	4465	1027	1064
Premature delivery (17)	1052	3943	471	548
t	5.541	0.938	3.826	4.636
p	<0.001	<0.40	<0.001	<0.001

Table 5. 16-Substituted steroids in newborn urine (St/Creatinine). Mean values and statistical comparison

	16α OH-DHA	16 oxo-A 16β OH-DHA	16α OH-P	16α OH-E_3
Normals (6)	99.75	96.86	21.88	18.39
Spontaneous premature delivery (31–37 W.) (15)	15.52	18.63	14.73	4.62
t	2.935	3.013	0.846	4.825
p	<0.01	<0.01	<0.50	<0.001
Planned premature delivery (31–37 W.) (4)	63.17	52.59	61.00	16.51
t	2.102	2.227	2.299	2.207
p	<0.10	<0.05	<0.05	<0.05

premature delivery (C.S.) show significantly higher steroid values, which are more similar to those of AGA full-term babies, than those found in premature infants.

Therefore we have found that the following possibilities exist regarding the ratio of mother/newborn estriol values: (1) Term delivery: ratio E_3/C mother/newborn infant: 1,91; (2) Premature delivery (spontaneous): ratio E_3/C mother/newborn infant: 4,31; (3) Premature delivery (planned-without labour): ratio E_3/C mother/newborn infant: 1,47. The evidence of normal values of 16-substituted steroids in the mother's urine during pregnancy, up until premature delivery, would indicate that the lowering of fetal steroid values could occur just before labour. On the other hand, fetal plasma cortisol in premature delivery without maternal complications shows similar values to those which we have found in spontaneous deliveries of due termination [11].

Therefore it would be possible to suppose that, in determining premature delivery, the fetus itself does not play a totally passive role.

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REFERENCES

1. Cleary R. E. and Pion R.: Relationship of C-19 steroid excretion in the newborn to maternal urinary estriol. *Am. J. Obstet. Gynec.* **104** (1969) 166–171.
2. Shackleton C. H., Gustafsson J. A. and Mitchell F. L.: Steroids in newborns and infants. *Acta endocr., Copenh.* **74** (1973) 157–167.
3. Cleary R. E., Depp R. and Pion R.: Relation of C-19 steroid sulfates in cord plasma to maternal urinary estriol. *Am. J. Obstet. Gynec.* **106** (1970) 534–539.
4. Reynolds J. W.: Excretion of 16α-hydroxysteroids by premature infants. *J. clin. Endocr. Metab.* **26** (1966) 1251–1256.
5. Reynolds J. W. and Mirkin B. L.: Urinary steroid levels in newborn infants with intra-uterine growth retardation. *J. clin. Endocr. Metab.* **36** (1973) 576–581.
6. Salvadori B.: *Trattato di Semeiotrica Fetale.* Piccin, Padova. Vol. 1 (1974).
7. Salvadori B., Merialdi A., Benassi L. and Pini L.: 16-Substituted steroids in fetal and neonatal life. *J. steroid Biochem.* **6** (1975) xxxii.
8. Cleary R. E. and Pion R.: Urinary excretion of 16α-hydroxydehydroepiandrosterone and 16-ketoandrostendiol during the early neonatal period. *J. clin. Endocr. Metab.* **28** (1968) 372–378.
9. Shackleton C. H. and Mitchell F. L.: The measurement of 3β-hydroxy-5-ene-steroids in human fetal blood, amniotic fluid, infant urine and adult urine. *Steroids* **10** (1967) 359–385.
10. Schindler A. E., Friedrich E., Barth R., Sparke H. and Wuchter J.: Steroid profiles in amniotic fluid, cord plasma and newborn urine. In *Hormonal Investigations in Human Pregnancy* (Edited by R. Scholler). Sepe, Paris (1974) 603–613.
11. Salvadori B., Merialdi A., Vadora E., Coppola F., Benassi L., Armanetti M., Calestani V. and Bacchi A.: Premature delivery: fetal-neonatal hormonology. *III Congr. Gyn. Obst. of Danubian Countries.* Beograd, 11–14 May (1975).