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Postnatal changes in blood spot 17-hydroxyprogesterone level in healthy preterm and full-term neonates

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Blood spot 17OH-P concentrations were determined in 14 healthy premature (mean birthweight 1439 g, mean gestational age 30 weeks) and full-term newborn infants (mean birthweight 3532 g, mean gestational age 39.2 weeks) during the first five weeks of life to provide reference data for infants with various gestational and postnatal ages.

It was demonstrated that with advancing age there was an abrupt fall in 17OH-P from 296.2 ± 84.1 nmol/l on the first day to 101.2 ± 19.5 nmol/l on the 7th day ($p < 0.001$) and 75.7 ± 8.7 nmol/l ($p < 0.05$) on the 14th day in premature infants. In full-term neonates its initial value is much lower (90.1 ± 12.5 nmol/l) and its fall during the first week is much less pronounced (51.5 ± 6.5 nmol/l, $p < 0.01$). Comparing the postnatal changes in 17OH-P in the two groups it proved to be significantly higher in premature than in full-term infants at all ages except for the 4th week.

When blood spot 17OH-P values were studied as a function of gestational age at the age of 5 days a significant inverse relationship was found between the two parameters.

It is assumed that in addition to placental 17OH-P production and perinatal stress, renal salt wasting may also account for the long lasting elevation of 17OH-P plasma level seen in premature infants.

Measurements of plasma 17-hydroxyprogesterone (17OH-P) concentrations have been proposed to screen newborn infants for congenital adrenal hyperplasia due to 21-hydroxylase deficiency [7, 8, 12, 13, 16]. It has recently become apparent, however, that plasma 17OH-P level may be elevated in neonates without adrenal disorders. Gestational age, postnatal age and the infants' condition has been demonstrated to be major determinants of plasma 17OH-P levels during the neonatal period [5, 6, 11, 18, 23].

In view of the wide range of postnatal age and maturity of infants whose blood samples are sent for 17OH-P determination we thougt it is essential to carry out a longitudinal study in a group of healthy preterm and term neonates to provide reference data for newborn infants with various gestational and postnatal ages.

Materials and Methods

14 healthy preterm and 12 full-term neonates were selected for the study. Their birthweight ranged from 1150 to 1950 g

(mean: 1439 g) and from 2680 to 4630 g (mean: 3532 g), respectively. The corresponding mean gestational ages were 30 weeks (range: 27—34 weeks) and 39.2 weeks (range: 37—41 weeks).

Perinatal history did not reveal toxemia of pregnancy and the mothers were not treated with steroids, beta-mimetic drugs or diuretics. There were no clinical or laboratory signs of acute or chronic fetal distress.

All infants were delivered vaginally after an uncomplicated labour and remained well during the entire neonatal period. Clinical examinations and laboratory data did not show cardiopulmonary distress, impaired renal function, perinatal infection or electrolyte imbalance. Human milk was given to all infants included in the study.

For 17OH-P determinations blood was taken by heel prick and dried on filter paper on the 1st, 3rd and 5th days and later on weekly up to the 5th week of life. Care was taken to collect blood samples at the same time of the day to overcome diurnal variation [20].

Measurements were made by direct RIA method as described by Sólyom et al [19].

For statistical analysis paired and unpaired Student's *t*-test was applied, correlation coefficient and regression equation was also calculated.

The study was approved by a local ethical committee and informed parental consent was obtained for blood sampling.

Results

The relationship of blood spot 17OH-P concentration to gestational age at postnatal age of 5 days is shown in Fig. 1. It can be seen that with increasing maturity there is a progressive decline in blood spot 17OH-P level indicating that at this age gestational factors are still responsible for the elevated hormone levels seen in premature infants (r: -0.607 $p < <0.001$).

Figure 2 demonstrates the postnatal changes in 17OH-P levels in preterm and full-term neonates during the first five weeks of life. On the first day about four times higher 17OH-P level was measured in the preterm than in the full-term group. With advancing age it falls abruptly from 296.2 ± 84.1 nmol/l on the first

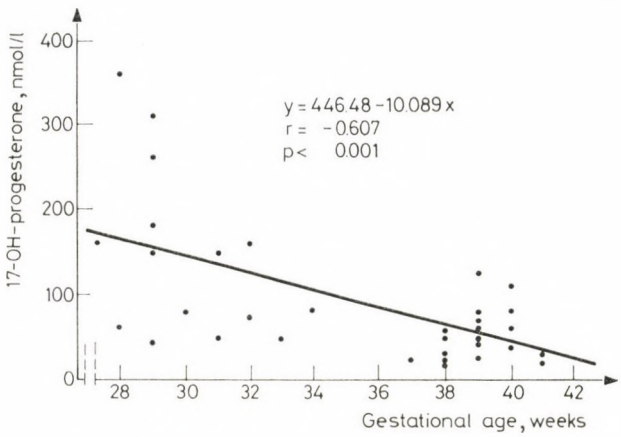

Fig. 1. The relationship of blood spot 17OH-P level to gestational age in healthy newborn infants at age of 5 days

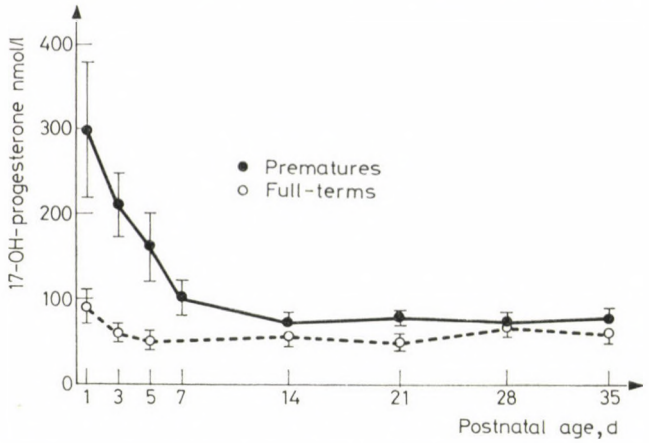

FIG. 2. The postnatal course of blood spot 17OH-P concentrations (mean ± SE) in preterm and full-term neonates during the first five weeks of life

day to 101.2 ± 19.5 nmol/l on 7th day ($p < 0.001$) followed by a moderate, but significant decrease to 75.7 ± ± 8.7 nmol/l by the end of the second week ($p < 0.05$) and it remains practically unchanged during the further period of study. In full-term neonates the initial value is much lower and its fall during the first week is much less pronounced (90.1 ± 12.5 nmol/l on the first versus 51.5 ± 6.5 nmol/l on the fifth day) ($p < 0.01$). After this age period further decrease does not occur in 17OH-P levels over the time period studied.

Comparing blood spot 17OH-P values between the two groups it proved to be significantly higher ($p < 0.001$) in premature infants than in full-term ones at all ages except for the 4th week.

DISCUSSION

Our present study confirmed previous observations that plasma 17OH-P level is higher in preterm than in full-term neonates and it rapidly falls during the immediate neonatal period [5, 6, 8, 11, 18, 23]. On the other hand, this study provided new information demonstrating that the inverse relationship between 17OH-P concentration and gestational age still exists on the fifth day of life. Furthermore, it was also shown that 17OH-P levels in premature infants remain elevated long after the first week of life when compared to those found in full-term neonates.

It is to be noted that the 17OH-P blood spot values measured in this study are substantially higher than those reported by other laboratories. This may be the result of the different, simplified method applied in which after methanol: diethyl ether: ethyl acetate (50: 45: 5) extraction direct RIA was used without chromatographic separation. In this way in addition to 17OH-P cross-reacting steroids — mainly progesterone — were also measured in spite of the high specificity of the antiserum used.

The reason for the high 17OH-P seen after birth is not apparent. Perinatal stress [11, 23] and placental 17OH-P has been proposed to account for the elevated hormone levels [9, 25]. These factors, however, fail to explain the fact that in prematures the response after birth is more pronounced and the 17OH-P elevation is lasting for weeks. Namely, the effect of stress imposed by labor and delivery is over by the end of the first week and placental 17OH-P is also eliminated by that age. It is to be considered, however, that in pregnant women plasma progesterone concentration is the highest at about the 34th week of gestation followed by a marked fall until term [24] and the peak plasma 17OH-P response to short term exogenous adrenocorticotropic hormone stimulation in preterm ill infants has been reported to be signifincantly higher than the response in full-term ill infants [23].

The significant difference in plasma 17OH-P levels between preterm and full-term neonates may be the result of renal salt wasting which has been shown to occur frequently in low birthweight premature infants. It has been repeatedly demonstrated that the rate of renal sodium excretion, in particular, fractional sodium excretion is inversely proportional to the gestational or postconceptional age of the newborns [1, 3, 10, 14, 17, 21].

It is of interest that the function of renin-angiotensin-aldosterone system is excessively activated in premature infants, the increased renal salt excretion therefore does not result from inadequate aldosterone production but rather from renal tubular unresponsiveness to aldosterone [22]. This condition shares some similarities with pseudohypoaldosteronism which is featured by elevated 17OH-P levels [2, 15]. With this observation in line one can assume that renal salt wasting and the subsequent sodium depletion — as a stressful stimulus — may induce adrenocorticotroph hormone secretion, adrenal gland stimulation and enhanced 17OH-P production. This possibility seems to be substantiated by the findings that very low birthweight sick premature infants have considerably greater renal sodium excretion than their healthy matches [4] and their plasma 17OH-P levels were also found to be more elevated [11, 23].

It is of importance that 17OH-P has saltlosing properties, it may contribute, therefore to the further worsening of the salt-depleted state.

In conclusion, the present study provided evidence that during the first 5 weeks of life blood spot 17OH-P level is significantly higher in preterm than in full-term neonates. When newborn infants with various gestational and postnatal age are screened for congenital adrenal hyperplasia these findings should be considered.

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