Ascorbic acid and tyrosine metabolism in preterm and small-for-dates infants

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Mohanram, M., and Kumar, A. (1975). *Archives of Disease in Childhood*, **50**, 235. **Ascorbic acid and tyrosine metabolism in preterm and small-for-dates infants.** Ascorbic acid levels in plasma and leucocytes and urinary excretion of tyrosyl derivatives (TD) were determined in 11 normal, 18 preterm, and 4 small-for-dates infants.

Concentrations of ascorbic acid in both plasma and leucocytes were found to be similar in the 3 groups. There was no difference in the basal levels of TD between normal and small-for-dates infants, but preterms showed higher basal excretion of TD than the other two groups. After protein load the excretion of TD was higher than the basal level in preterms. It was concluded that the altered metabolism of tyrosine observed in preterms is not the result of poor ascorbic acid status; and that tyrosine metabolism is influenced by the period of gestation rather than the body weight of the infant.

It has been reported that scorbutic subjects given a load of L-tyrosine excrete large amounts of tyrosine and its metabolites—a defect that is eliminated by administration of ascorbic acid (Rogers and Gardner, 1949a, b; Morris, Harpur, and Goldbloom, 1950; Huisman and Jonxis, 1957; Mohanram and Reddy, 1974). A transient defect in tyrosine oxidation has also been commonly observed in preterm infants fed on high protein diets (Levine, Marples, and Gordon, 1939; Levine, Gordon, and Marples, 1941; Matthews and Partington, 1964; Rizzardini and Abeliuk, 1971; Prasad, Sinha, and Sen, 1972). Rizzardini and Abeliuk (1971) showed that both plasma and urinary tyrosine levels were markedly increased when high protein diets were given to infants of gestational age below 38 weeks. However, it is not clear whether this abnormality observed in preterm infants is due to altered ascorbic acid status. A study was therefore undertaken to determine the levels of ascorbic acid in leucocytes, which is now accepted as a reliable index of ascorbic acid nutritional status, and urinary excretion of tyrosyl derivatives (TD) in normal, preterm, and small-for-dates infants.

Materials and methods

Eleven normal term infants with body weights more than 2400 g, 4 small-for-dates infants (term infants with body weights < 2400 g), and 18 preterm infants were studied. The gestational ages of the 18 preterm infants ranged from 28 to 34 weeks. Samples of blood and random samples of urine were collected from all the infants within 48 hours of birth. For the first 24 hours after birth all the infants were fed 5% glucose solution orally and thereafter the normal and small-for-dates infants were started on breast milk. In the case of preterms, expressed breast milk was fed orally until they were able to suckle. Levels of ascorbic acid in plasma and leucocytes, and urinary excretion of creatinine and TD were determined. The infants were then fed 4 g/kg milk protein. Random samples of urine were again collected at 24 and 48 hours and the levels of creatinine and TD were determined.

Plasma ascorbic acid was estimated by the method of Roe and Kuether (1943), and the content of ascorbic acid in leucocyte by the method of Denson and Bowers (1961). Excretion of TD in urine was measured by the method of Medes (1932). The compounds measured by this method include tyrosine, *p*-hydroxyphenylpyruvic acid and *p*-hydroxyphenyl-lactic acid. Urinary excretion of creatinine was measured by the procedure of Clark and Thompson (1949). Urinary levels of TD were expressed in relation to creatinine excretion.

Comparison of mean values between groups was made using Student's 't' test, while the effect of load was evaluated using paired 't' test.

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TABLE

Urinary excretion of tyrosyl derivatives (TD) (mean $\pm$ SD and range) in normal, small-for-dates, and preterm infants

	No. of subjects	Body weight (g)	Ascorbic acid levels in		Basal excretion of TD (mg TD/mg creatinine)	Excretion of TD after load (mg TD/mg creatinine)
			Plasma (mg/100 ml)	Leucocytes (μ g/ 10^8 cells)		
Normal infants	11	$\dagger 2824 \pm 363.2$ (2400-3310)	0.23 ± 0.202 (0.10-0.69)	8.8 ± 2.78 (4.6-13.0)	$*0.23 \pm 0.079$ (0.115-0.355)	0.32 ± 0.142 (0.160-0.535)
Small-for-dates infants	4	2035 ± 259.4 (1800-2340)	0.37 ± 0.218 (0.10-0.60)	8.5 ± 3.44 (5.0-11.9)	0.17 ± 0.020 (0.166-0.208)	0.30 ± 0.088 (0.169-0.406)
Preterm infants	18	$\dagger 1550 \pm 267.71$ (1040-1940)	0.43 ± 0.483 (0.10-1.61)	10.4 ± 3.65 (4.6-18.8)	$*0.49 \pm 0.267$ (0.12-1.08)	1.40 ± 1.42 (0.38-4.18)

*P < 0.02.

$\dagger$ P < 0.001.

Results

Results of the study are shown in the Table. The mean body weight of preterms ($1550 \text{ g} \pm 267.7$ SD) was lower than that of normal infants ($2824 \text{ g} \pm 363.2$, P < 0.001). There were, however, no differences in the concentrations of ascorbic acid in plasma and leucocytes between the 3 groups of infants. A considerable variation in basal excretion of TD was observed in all the infants studied, and there was no correlation between urinary levels of TD on the one hand and ascorbic acid content in either plasma or leucocytes on the other.

The mean basal levels of TD were not different between normal term infants and small-for-dates infants, but in preterms the basal excretion was higher than in the other 2 groups of infants (P < 0.02). After protein load the excretion increased in all 3 groups, but the preterm infants showed a higher excretion of TD (P < 0.01).

Discussion

These data indicate defective tyrosine metabolism in preterm infants. Increased tyrosyluria observed in these infants confirm the findings reported earlier by other workers (Levine *et al.*, 1939, 1941; Rizzardini and Abeliuk, 1971; Prasad *et al.*, 1972). The altered tyrosine metabolism in preterms has been attributed to ascorbic acid deficiency, since the defect could be removed by administration of ascorbic acid (Levine *et al.*, 1939, 1941). The evidence from this study, however, shows that there was no deficiency of ascorbic acid in preterm infants, levels of ascorbic acid in leucocytes being no different from those in normal infants. Furthermore there was no correlation between levels of the vitamin and excretion of TD. We

therefore conclude that tyrosyluria in preterms cannot be due to deficiency of ascorbic acid.

Kretchmer *et al.* (1956) showed that the liver of preterm infants had little or no activity of tyrosine oxidizing enzymes, and *in vitro* addition of ascorbic acid had no effect on the enzyme activity. The defective tyrosine metabolism in preterms can therefore be attributed to incomplete development of the enzymatic system necessary for tyrosine oxidation.

Although birthweights were low in both preterm and small-for-dates infants, the above defect was exhibited only by preterm infants. This finding suggests that the defect in tyrosine metabolism is related to period of gestation and not to birthweight.

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