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# Uric acid in a single urine sample from neonates with perinatal hypoxia

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In a referral neonatal intensive care unit, $PaO_2$ values of 40 newborn infants were compared with the serum and urinary uric acid levels. The latter was estimated from the first urine obtained after admission. A significant inverse correlation was found between $PaO_2$ and serum uric acid concentration and between $PaO_2$ and urinary uric acid per creatinine ratio, but no correlation was seen between $PaO_2$ and urinary uric acid concentration.

The urinary uric acid per creatinine ratio was determined on the 1st, 2nd and 5th days of life in 27 normal prematures, 28 hypoxic prematures, 23 normal full-term infants and 25 hypoxic full-term neonates.

Significantly higher values were obtained in both hypoxic groups on the 1st day, and in hypoxic prematures even on the 2nd day.

Although creatinine as a reference substance is regarded as unreliable in the neonatal period, if a single urine sample is only available, determination of the uric acid per creatinine ratio seems to be warranted, since higher values may retrospectively point to hypoxia.

It has been known for long that shock, acute metabolic disturbances and anaerobic conditions may lead to a remarkable increase of serum ammonia and urate levels [1, 2, 3, 11]. It has also been shown that during the first days of life newborn infants with perinatal complications have higher serum and urinary urate concentrations than normal neonates [8, 10, 13]. The increased excretion of uric acid is probably less due to renal retention than to an overproduction of blood oxypurines in consequence of increased nucleotide breakdown associated with hypoxia [13, 17]. This is valid for other end products of purine metabolism, especially for hypoxanthine, the urinary output of which may be useful in estimating perinatal hypoxia retrospectively [5, 7, 9, 15].

All these studies have dealt with urine collections of 0 to 48 or even 0 to 96 hours after birth which is impracticable in most neonatal units, and also the biochemical methods applied are not easily available. This has stimulated us to investigate the correlation to hypoxia of uric acid measured in the first single urine sample obtained after admission to our referral neonatal unit.

## Patients and Methods

The study was carried out in two parts.

I) $PaO_2$, serum and urinary uric acid and creatinine values were determined im-

mediately after admission in 40 neonates weighing more than 1500 g. They were referred to our unit from 8 obstetric departments at the age of 1 to 48 hours because of pathological conditions of various origin. All these variables were disregarded, and only the actual $PaO_2$ values measured at arrival were correlated to the simultaneously determined serum uric acid levels, and to the urinary uric acid values and uric acid per creatinine ratios obtained from the first urine sample obtained after admission.

II) In a total of 103 infants the urinary uric acid per creatinine ratio was determined on the 1st, 2nd and 5th postnatal days. They were grouped according to two criteria.

1) Neonates born before the 37th week of gestation were regarded as premature, those born at or after the completed 37th week were considered full-term infants, irrespective of their birth weight.

2) In our obstetrical department normal control babies were selected on the basis of uncomplicated pregnancy and delivery, and of good condition at birth (Apgar score 8 to 10 at 1 minute) and afterwards. Neonates were regarded as hypoxic when their birth was complicated, Apgar score was 5 or less, when there was a history of any type of resuscitation and/or they required $O_2$-therapy for at least 3 hours.

Based on these criteria the infants were divided into four groups.

1. Control prematures, n = 27,mean gestational age 33.9 weeks, mean birth weight 2027 g.

2. Hypoxic prematures, n = 28, mean gestational age 32.5 weeks, mean birth weight 1890 g.

3. Normal control full-term infants, n = = 23, mean gestational age 39.1 weeks, mean birth weight 3154 g.

4. Hypoxic full-term neonates, n = 25, mean gestational age 39.0 weeks, mean birth weight 3110 g.

## Results

A close inverse correlation was found between $PaO_2$ and plasma uric acid levels determined immediately after admission (Fig. 1). No significant relationship was observed between $PaO_2$ and the uric acid level in the first urine sample but the correlation of $PaO_2$ values to urinary

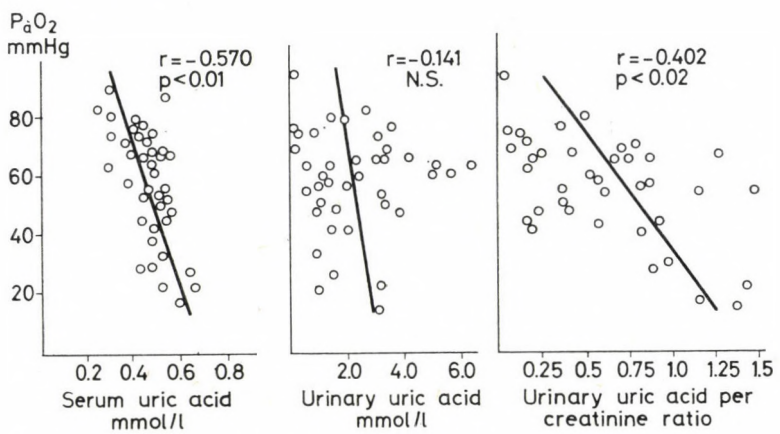


Fig. 1. $PaO_2$, serum uric acid concentration, urinary uric acid level, and uric acid per creatinine ratio in the first urine sample obtained after admission

TABLE I

Urinary uric acid per creatinine ratio in hypoxic and control premature and full-term neonates on the 1st, 2nd and 5th days of life (mean ± S.D.)

| Day | Premature | | | Full-term | | |
|---|---|---|---|---|---|---|
| | Normal control n = 27 | Hypoxic n = 28 | P | Normal control n = 23 | Hypoxic n = 25 | P |
| 1st | 1.40 ± 0.66 | 1.96 ± 0.65 | < 0.02 | 0.80 ± 0.34 | 1.09 ± 0.40 | < 0.05 |
| 2nd | 1.45 ± 0.80 | 1.71 ± 0.70 | < 0.05 | 0.92 ± 0.61 | 1.03 ± 0.56 | N.S. |
| 5th | 0.92 ± 0.48 | 0.88 ± 0.38 | N.S. | 0.54 ± 0.72 | 0.52 ± 0.28 | N.S. |

uric acid per creatinine ratios proved to be significant statistically.

In both premature and full-term neonates the uric acid per creatinine ratio was significantly higher in the hypoxic groups than in the controls on the 1st postnatal day (Table I). In prematures this difference persisted on the 2nd day, but not on the 5th day, and in full-term infants no significant differences were seen after the first 24 hours. In every compaison prematures had higher urinary uric acid per creatinine ratios than full-term infants.

## DISCUSSION

The presents findings provide further evidence for increased uric acid production and excretion in neonates with perinatal hypoxia. The study was not free from different kinds of biases. $PaO_2$, for instrance, is regarded as a barely reliable measure of hypoxia for it is quickly reversible. This is why Saugstad [15] recommented to reckon instead of $PaO_2$ with the less rapidly changing base deficit, but this was not possible in our study, because the majority of the babies received different doses of bicarbonate intravenously before or during transport, which influenced the base deficit much more than the $PaO_2$ level at admission.

It has also been emphasized that the regulation and mechanism of creatinine excretion differ from those of other substances including uric acid [6, 14, 16]. Since there is an increasing creatinine clearance and a relatively constant uric acid output in the neonatal period, the use of creatinine as reference substance is considered unreliable [9, 12, 16].

In addition, our material was rather inhomogeneous. The newborn patients differed in age, nature and severity of perinatal pathology, and a certain subjectivity in the distinction between normal and hypoxic neonates could not be avoided.

All these factors could, however, have acted by diminishing the differences in serum and urinary uric acid values between control and hypoxic infants. Yet, a significant inverse correlation was found between $PaO_2$

and serum uric acid level. Considering the rapid changes in $PaO_2$, measurement of urinary urate concentration reflecting a longer time with or without hypoxia, seemed to be more promising. Actually, the urinary uric acid concentration in itself was irrelevant, but when it was related to creatinine concentration, a significant inverse correlation to perinatal hypoxia was observed. This was confirmed in the second part of the study when higher urinary uric acid per creatinine ratios were found in the hypoxic neonates. This ratio was remarkably higher in prematures than in full-term infants which can be explained by the later onset of creatinine excretion by the immature kidneys. The rapidly increasing creatinine clearance may account for the fact that after the first 24 to 48 hours the originally significant difference between the uric acid per creatinine ratio of normal and hypoxic neonates disappeared.

Nevertheless, in spite of well established physiological observations, the ratio seems to be fairly reliable in the first 24 to 36 hours of life, irrespective of sex, maturity and perinatal pathology. From a practical point of view this means that in a referral neonatal unit, examination of the first urine sample obtained after admission may help in detecting hypoxic episodes. Determination of the uric acid per creatinine ratio is technically simple, quick and inexpensive. At evaluation a high ratio may refer to a previous hypoxia while a low value does not exclude it.

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