Possible Association of Xanthine Dehydrogenase/Xanthine Oxidase Activity with Nitric Oxide in vivo

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$y = 0.83x + 0.37$, $r = 0.62$, $p < 0.01$

$y = 0.58x + 0.47$, $r = 0.51$, $p < 0.05$

Λ 1.5Π

Λ 1.5-1

0.0 0.5 1.0 1.5
Urinary NOx (mmol/mmol Cr)

0.0 0.5 1.0 1.5
Urinary NOx (mmol/mmol Cr)

Fig. 1. Relationship between urinary UA and NOx in term (a) and preterm infants (b). Significant positive correlations are observed in term and preterm subjects.

Dear Sir,

The final metabolic reactions in purine metabolism involve the oxidation of hypo-xanthine to xanthine and then to uric acid (UA) by the catabolic enzyme xanthine de-hydrogenase/xanthine oxidase (XD/XO) [1]. XD/XO is also a source of production of the oxidants, O₂ and $\frac{5}{8} < \frac{3}{4}$ [1, 2]. The mechanisms responsible for the regulation of XD/ XO in vivo remain largely unknown. Recently, we had the opportunity to obtain some evidence for an association between XD/XO activity and nitric oxide (NO) [3] in vivo.

Our study group consisted of 35 infants aged 1 month; 17(10 boys and 7 girls) were healthy term infants, and 18 (9 of both sex) preterm infants who were born with a gestational age of 24-32 weeks (mean 29) and a birth weight of 808-1,970 g (mean 1,398). All preterm babies developed respiratory distress just after birth requiring ventilatory support and oxygen supply during the first 2-76 days (mean 15) and 3-90 days (mean 22), respectively; 3 of them were still ventilated at the time of study. Spot urine samples were collected in a bag applied to the perineum. UA was measured spectrophotometrically using the uricase-peroxidase-coupled reaction. Nitrite/nitrate anions (NOx), stable end products of NO [3, 4], were determined by the brucine method [5]. Urinary excretion of UA and NOx was expressed as a ratio to the urinary creatinine (Cr)

concentration (by the Jaffe method). Data were presented as means $\pm$ SEM. Correlations between the two parameters were tested using linear regression analysis; statistical significance was set at $p < 0.05$.

Urinary UA levels were 0.93 ± 0.07 and 0.91 ± 0.08 mg/mg Cr in term and preterm infants, respectively. The respective NOx levels were 0.67 ± 0.05 and 0.76 ± 0.07 mmol/mmol Cr. Interestingly, urinary levels of UA and NOx were significantly positively correlated with each other in each group of infants (fig. 1).

Our present results suggest an intriguing, possibly synergistic, relationship between UA and NO production in vivo. The underlying mechanisms of this finding remain highly speculative. The XD/XO activity can be modulated by NO through direct binding of NO to the enzyme iron-sulfur moiety or to its sulfhydryl groups [1, 6]. The enzyme activity might be augmented by NO, since NO decays $\text{O}_2^{\cdot -}$, which is generated by XD/XO and decreases its activity [7]. Activation of some kinds of cytokines may underlie mRNA expression of both XD/XO and NO synthase in vivo [8]. Our finding appears to be the first in vivo evidence for an association of XD/XO activity with NO. Considering that both oxidants (i.e. O_2 and H_2O_2) and NO play significant roles in the pathogenesis of many diseases not only in infants but also in children and adults [1-3], further basic and clinical studies are warranted on this topic.

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