Urinary Excretion of Human Epidermal Growth Factor in Premature Infants Requiring Assisted Ventilation over the First Week of Life

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27-34 weeks, birth weight 900-2,600 g, 1-min Apgar score 1-5; 3 had prior intubation before to assess their 5-min Apgar score, while in the remaining 3 this value ranged from 5 to 6). The remaining 6 newborns (group B) were put in oxygen tents for 7 days (gestational age 31-34 weeks, birth weight 1,600-2,170 g, 1-min Apgar score 3-6 and 5-

Dear Sir,

Human epidermal growth factor (hEGF), a 53-amino-acid polypeptide with a molecular mass of about 6,045-6,200 D [1], is synthesized in the kidney by the distal convolute tubules and the thick ascending loop of Henle [2]. hEGF can be measured in numerous body fluids, including saliva, pancreatic juice, sperm, amniotic fluid and urine. Previous reports have shown that in newborns, urinary hEGF excretion is related to development and maturation, depending on renal function [3, 4]. Urinary hEGF excretion, moreover, increases linearly with gestational age [5].

We studied urinary hEGF excretion over the first week of life in 12 premature infants with severe respiratory distress syndrome (RDS), in order to ascertain whether there is a relationship between the severity of renal damage from neonatal asphyxia, defined as a 1-min Apgar score of less than 6, and the urinary hEGF concentration. Immediately after birth, the neonates, who required assisted ventilation, were admitted to the Neonatal Care Unit at the Pediatric Department of the University of Verona. In 1 case delivery was spontaneous, and in the remaining 11 cesarian section had been performed. None of the newborns had congenital abnormalities, such as heart, renal or chromosomal disorders. Informed consent was obtained from all the patient's parents. Six newborns (group A) were put on mechanical ventilation for 7 days (gestational age, assessed according to Dubowitz et al. [6],

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Beginning of assisted ventilation

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3 4 5 6

Time (days after birth)

Fig. 1. Variations of urinary hEGF levels, expressed as mean values, during the first 7 days of assisted ventilation on two groups of asphyxiated preterm newborns. O = Group A (mechanical ventilation); · = group B (oxygen tent).

min Apgar score 7-8). Twelve-hour urine samples were collected every day from birth up to the 7th day of life using a bladder catheter in group A and a sterile bag in group B. Sediment-free urine samples were immediately frozen at -20 °C until analyzed. Quantitative estimation of hEGF was made using a radioimmunological (RIA) method

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(DSL reactivities, Webster, USA); analytical sensitivity was 1 µg/l [7]. The urinary creatinine concentration was measured by an enzymatic method (Ektachem assay, Johnson & Johnson) [8]. Also blood urea nitrogen levels were assessed using an enzymatic method (Ektachem assay). Urinary hEGF levels were normalized to creatinine excretion, in order to reduce the intra- and intervariability, as suggested elsewhere [9]. In the course of treatment, urinary hEGF excretion progressively decreased in group A, while it gradually increased in group B. After the first day of assisted ventilation, the mean values of hEGF in groups A and B were 4.44 ± 2.94 and 3.92 ± 2.44 µg/mmol creatinine respectively (39.3 ± 26.0 and 34.7 ± 21.6 µg/g creatinine). On the 5th day of therapy, the mean values were 2.67 ± 0.84 µg/mmol creatinine in group A (23.7 ± 7.4 µg/g creatinine) and 6.25 ± 1.82 µg/mmol creatinine in group B (55.3 ± 16.1 µg/g creatinine). Finally, on the 7th day the mean values in groups A and B were 0.77 ± 0.03 and 6.83 ± 3.40 µg/mmol creatinine (6.9 ± 0.4 and 60.4 ± 30.1 µg/g creatinine). The Mann-Whitney test was used for the statistical comparison: significant differences were found between findings in the two groups from the 5th day up to the 7th day of therapy ($p < 0.05$). After the first day of life, the mean values of blood

urea nitrogen were 2.61 mmol/l (15.7 mg/dl) in group A and 4.81 mmol/l (29 mg/dl) in group B. No statistically significant difference was found between blood urea nitrogen values of the two groups up to the 7th day of treatment. Figure 1 shows mean urinary hEGF levels in both groups over the first week of life.

hEGF is one of the most important known proximal tubule cell mitogens, and the kidney seems to play an active role in its urinary excretion [10]. It has been reported that in healthy full-term infants urinary hEGF excretion progressively increases in the first week of life while in healthy preterm babies it appears stable [11]. These observations support the hypothesis that urinary variations in hEGF are closely related to tubular renal function. In our study, the group of neonates with endotracheal intubation (group A) had significantly lower urinary hEGF levels than the nonintubated group (group B). It is therefore reasonable to assume that RDS and its treatment may influence the biological production of hEGF by tubular cells. It is, in fact, well

known that prolonged asphyxia and artificial respiration can play a nephrotoxic role, and they might inhibit or even stop the renal production of hEGF.

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