Renal Functions of Low Birth Weight Infants during the First Two Months of Life

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Summary

A postnatal contraction of extracellular fluid occurs in low birth weight infants. Patterns of postnatal renal maturation were assessed with the assumption that changes in body composition were mediated in part by the developing kidney. Twenty-two appropriate for gestational age, low birth weight infants (birth weight mean = 1380 g, gestational age mean 31 weeks) were studied between 12 hr and 61 days of age to evaluate simultaneously glomerular and tubular functional maturation. Since most low birth weight infants have respiratory morbidities (respiratory distress followed by chronic lung disease), the infants were grouped into: *group I* (13 infants), transient or absent respiratory morbidities; and *group II* (9 infants), persistent and severe respiratory morbidities. Sodium excretion decreased with postnatal age in both groups. Sodium intake did not vary with postnatal age. The percentage of fractional sodium excretion was inversely related to postnatal age. Creatinine clearance correlated directly with postnatal age in both groups. Increased sodium excretion and percentage of fractional sodium excretion in the first 10 days of life may reflect extracellular fluid solute losses through the kidney. The premature kidney matured in a balanced fashion and persistent respiratory morbidities did not alter this pattern.

Speculation

The kidney of low birth weight infants probably plays an important role in the regulation of body fluid during the first week of life. The adjustment in renal tubular handling of sodium with greater sodium loss in the first days reflects its compensation to fit the demand of greater sodium excretion from the contraction of the extracellular fluid compartment. In an infant with a stable circulatory status, the presence of respiratory complications did not influence this adjustment process.

During the first week of life, a rapid contraction of extracellular fluid occurs (7). It has also been estimated that the contraction of the extracellular fluid in low birth weight infants is significantly greater in comparison to the full term infants on the basis of a larger fluid compartment in the former. This difference will result in the disposal of a larger quantity of the extracellular fluid through the kidney of the low birth weight infant during the first week of life. It is therefore expected that the sodium excretion in the low birth weight infant would also be higher, reflecting the excretion and disposal of the isotonic extracellular fluid. Siegel and Oh (11) have shown previously that during the first 48 hr of life, the fractional sodium excretion is inversely related to gestational age. This data would suggest that the developing kidney may play a role in the regulation of sodium balance in the face of changing body composition in infants of different levels of maturity. Our hypothesis is as follows: In low birth weight infants (28-33 weeks of gestation), is the renal handling of sodium consistent with the previously reported changes in body

composition during the first week? If so, do chronic respiratory complications have any influence on the renal adaptation?

MATERIALS AND METHODS

Twenty-two appropriate for gestational age infants (13 males and 9 females) were the subject of this study. The mean gestational age was 31 weeks (range 28-33 weeks) and the mean birth weight was 1380 g (range 1000-1928 g). Gestational age was assessed in all infants by the Dubowitz scoring technique within 48 hr of birth (2). Thirty-nine studies (11 serially) were performed between 12 hr and 61 days of age. The mean study weight was 1460 g.

Since very few low birth weight infants are free of respiratory problems, we have classified our study infants into two groups according to the severity of respiratory complication. *Group I* (13 infants) was comprised of those with transient or no respiratory distress and *group II* (9 infants) was comprised of those with more severe respiratory distress followed by chronic pulmonary disease. The duration of oxygen therapy was used as major criteria for classification: in *group I*, the duration of oxygen therapy was 0-6 days with a mean of 3 days and in *group II*, 10-56 days with a mean of 22 days. None of the infants were hypotensive, acidotic, or hypoxic at the time of study. No infant had known renal disease. All infants survived and were well at the time of discharge.

During the study period, therapy and, particularly, fluid and electrolyte management proceeded normally as determined by the physicians caring for the infant. The rate of intravenous fluid was controlled by an infusion pump. Orally fed infants received formula every 3 hr by gavage or nipple. At the time of study 5 infants were receiving intravenous fluids alone, 19 were receiving oral and intravenous fluids, and 15 were receiving oral fluids alone. The mean duration of study was 122 min (range = 76-285 min), at which time, timed urine samples were collected by a pediatric urine collector. The bladder was credé to insure complete emptying of the bladder. One-half milliliter of blood was obtained at midpoint during the urine collection. An aliquot of formula and/or infusate was obtained at the end of the study. Fluid intake was calculated as intravenous and/or formula per unit of time. Sodium intake was calculated on the basis of formula and infusate sodium concentration and total volume of intake per unit of time. Infusate, formula, urine, and serum sodium were measured on a Beckman flame photometer, serum and urinary creatinine by a modified Jaffé method (6). Creatinine clearance and fractional sodium excretion were calculated by the conventional formulas. All clearances were expressed per 1.73 m² body surface area as calculated from a standard nomogram of body length and weight (9).

RESULTS

As shown in Figure 1, the sodium intake did not vary significantly during the first 2 months of life. Figure 2 demonstrates the negative correlation between urinary sodium excretion and post-

Fig. 1. Scattergram showing the pattern of sodium intake (milliequivalents per kg per 24 hr) and postnatal age.

Fig. 2. Scattergram showing the pattern of sodium excretion (milliequivalents per kg per 24 hr) and postnatal age.

natal age in both groups of infants. In Figure 3, sodium intake minus sodium excretion is plotted against the infants' ages. During the first 10 days of postnatal life 8 of 13 infants were in negative sodium balance; beyond 11 days of age, all infants were in positive sodium balance. Figure 4 illustrates the negative correlation between percent fractional sodium excretion and postnatal age. Percentage of fractional sodium was inversely related to postnatal age in both groups. The highest fractional sodium excretion rate occurred in both groups in the first 10 days of life. By 30 days of age, the percentage of fractional sodium excretion had significantly decreased in both groups. As shown in Figure 5, glomerular filtration rate (GFR) (creatinine clearance) was directly related to postnatal age in both groups. Creatinine clearance was lower in infants with respiratory morbidities during the first 10 days of life: group I, creatinine clearance = 14.7 ± 0.9 ml/min/1.73 m² ($n = 7$, mean $\pm$ SEM); group II, creatinine clearance = 7.5 ± 2.6 ml/min/1.73 m² ($n = 6$, mean $\pm$ SEM), $P < 0.05$ by student t -test. Beyond the 11th day, the GFR's of both groups were comparable.

DISCUSSION

The data of Friis-Hansen (3) shows that the extracellular fluid compartment in infants between 28–32 weeks of gestation is approximately 52% of the total body weight (520 ml/kg body weight). The data of Kagan *et al.* (7) demonstrates that the extracellular fluid compartment at 6 days of age in this group of infants is approximately 40% of the total body weight (400 ml/kg body weight). Therefore, during the first week of life, the redistribution and contraction of body fluid of low birth weight infants result in the reduction of 100 ml/kg extracellular fluid. Since the extracellular fluid is isotonic, the reduction of 120 ml/kg body weight in the first week of life would contribute to approximately 15 mEq sodium to the renal solute load during this period of time. With this consideration, the data shown on Figure 2, which demonstrate an average of 1.2 mEq/kg/day net negative sodium loss in the first 10 days of life, are consistent with the reduction of sodium pool as a result of the contraction of extracellular fluid. The higher sodium excretion rate in the

SODIUM INTAKE – SODIUM EXCRETION (mEq/24 hrs)

Fig. 3. Scattergram showing sodium intake minus excretion (milliequivalents per 24 hr) and postnatal age.

% FRACTIONAL SODIUM EXCRETION

Fig. 4. Scattergram showing an inverse correlation between percentage of fractional sodium excretion and postnatal age.

Fig. 5. Scattergram showing a direct correlation between creatinine clearance (milliliters per min per 1.73 m^2) and postnatal age.

kidney as well as the greater fractional sodium excretion in the first week of life probably reflects the functional and developmental characteristic of the kidney to accommodate the fluid and electrolyte homeostasis resulting from the body composition changes, fluid and electrolyte intake, and the influence of hormonal control. Previous data have shown an appropriate aldosterone level for the sodium intake and excretion in low birth weight infants with or without respiratory distress syndrome (10); the results shown in this report demonstrate the appropriate relationship between changes in body composition and functional balance of the glomerular and tubular components for the regulation of the fluid electrolyte homeostasis.

The initial decrease in percentage of fractional sodium excretion probably reflects renal adjustment for handling of sodium in response to body compositional changes. The further decrease of percentage of fractional sodium excretion probably represents the appropriate reduction of fractional sodium excretion (or increment in tubular sodium reabsorption) in the face of increasing GFR (and increment in filtered sodium load) along with less significant contraction of extracellular fluid during this age period as compared to the changes during the first week. By 30 days of age, the percentage of fractional sodium excretion has significantly decreased and creatinine clearance has significantly increased. Glomerular filtration is increasing simultaneously with increasing tubular sodium reabsorption and the premature kidney is maturing in a physiologically balanced fashion.

Controversy exists over the effect of respiratory distress on renal function. Cort (1) demonstrated oliguria, decreased urea clearance, and increased sodium excretion in infants dying of respiratory distress syndrome; Guignard *et al.* (5) showed decreased inulin and *p*-aminohippurate clearances in infants with

respiratory distress syndrome. Siegel *et al.* (10) demonstrated no difference in creatinine clearance, net acid excretion, or serum aldosterone in infants with or without respiratory distress syndrome. It is very likely that the severity of the disease and the cardiorespiratory status of the infants during the study period might have accounted for the discrepancies in these observations. In this report, we found a lower glomerular filtration rate in the infants who were severely ill in the first 10 days of life, but the improvement beyond this period of time proceeded at a rate similar to those with no respiratory complication (4, 8). These data indicate that in the handling of fluid and electrolyte therapy in chronically ill low birth weight infants suffering from chronic respiratory complications, the renal functional status is within the range of normal for the level of maturity and can be relied upon as a compensatory mechanism to maintain normal fluid and electrolyte homeostasis.

CONCLUSION

Postnatal renal maturation was studied in 22 appropriate for gestational age infants. Percentage of fractional sodium excretion and sodium excretion were highest in the first 10 days of life at the time that extracellular fluid contraction occurs. The maturing kidney may in part mediate this phenomena. Percentage of fractional sodium excretion decreased simultaneously with increasing creatinine clearance. Respiratory morbidities did not alter this developmental pattern.

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