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The Effect of Assisted Ventilation on Creatinine Clearance and Hormonal Control of Electrolyte Balance in Very Low Birth Weight Infants[1]

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ABSTRACT. Because renal function and electrolyte balance are commonly altered in premature infants, particularly those requiring ventilatory support, we studied the influence of assisted ventilation on renal electrolyte and water excretion in infants with birth weights less than 1501 g during the 2 days after birth. Twenty-two infants receiving assisted ventilation, either as intermittent mandatory ventilation or nasal continuous positive airway pressure, were compared with 21 spontaneously ventilating infants of similar birthweight and gestational age. Mean (and SEM) creatinine clearance was lower ($p < 0.05$) in the assisted ventilation group on day 1 (2.9 ± 0.4 *versus* 4.1 ± 0.4 ml/min/1.73 m^2) and on day 2 (4.1 ± 1.0 *versus* 6.8 ± 0.8 ml/min/1.73 m^2, $p = 0.05$), and there was a correlation between creatinine clearance and mean blood pressure in both groups. Mean urine vasopressin was higher in the assisted ventilation group on the first day (360 ± 86 *versus* 123 ± 30 pg/mg creatinine; $p < 0.02$) and correlated with higher urine osmolality. There were no differences in urine volume, in osmolar or free water clearances, or in the intake and urine excretion of sodium, potassium, and chloride. Plasma renin activity, urine aldosterone, and urine prostaglandin E_2 were similar in both groups on both days. Neither the mode of assisted ventilation nor the cause of respiratory failure appeared to affect these results. (*Pediatr Res* 20: 447–452, 1986)

Abbreviations

PEEP, positive end-expired pressure
NCPAP, nasal continuous positive airway pressure
IMV, intermittent mandatory ventilation
PRA, plasma renin activity
PGE_2, prostaglandin E_2
AV, assisted ventilation
SV, spontaneous ventilation
BP, blood pressure
Ccr, endogenous creatinine clearance
HMD, hyaline membrane disease
GFR, glomerular filtration rate

Renal function and electrolyte balance are commonly altered in sick premature infants. Both decreased urine volume (1, 2) and natriuresis (3–5) have been described in inadequately controlled studies. Glomerular filtration rate has been reported to be decreased (6), normal (4, 7) or even increased (3) in infants acutely ill with hyaline membrane disease. Although many or all of the infants in these studies received assisted ventilation with PEEP, none of the studies specifically examined the possible role of such therapy in producing the observed renal dysfunction.

Assisted ventilation using PEEP alters renal function in adult man (8–10) and experimental animals (11–13). Urine volume, urine sodium excretion, and glomerular filtration rate are decreased consistently, while changes in osmolar and free water clearances are less consistent. Whereas some investigators have related observed changes to increased secretion of vasopressin, renin, and aldosterone, others believe that reduced cardiac output and/or systemic blood pressure are more likely responsible. The present study was designed to test the hypothesis that disorders of renal electrolyte and water excretion commonly seen in sick very low birthweight infants are related to use of PEEP. Also we proposed that these changes are mediated through PEEP-induced hormonal changes. We studied two groups of infants, one breathing spontaneously and the other receiving assisted ventilation, either as NCPAP or IMV. We measured urine sodium, potassium, and chloride; osmolar and free water excretion; and endogenous creatinine clearance during the first 2 days after birth. Effects on plasma renin activity, aldosterone, vasopressin, and prostaglandin E_2, and of systemic blood pressure, on these variables also were examined.

PATIENTS AND METHODS

Study population and experimental protocol. We studied infants weighing 1500 g or less at birth admitted to the University of Alabama at Birmingham Regional Newborn Intensive Care Unit. The project was approved by the Institutional Review Board for Human Use and written, informed parental consent was obtained in each case. All infants weighing 1500 g or less and admitted within 12 h of birth were eligible for enrollment. They were excluded for any of the following reasons; maternal hypertension or renal disease; pneumothorax; use of volume expansion, sodium bicarbonate infusion for severe metabolic acidemia, inotropic agents, diuretics, prostaglandin synthetase inhibitors, or exchange blood transfusion. Further, all infants had cranial ultrasound examinations within the time of the study, and those who had grade III or IV intraventricular hemorrhage (14) were excluded from analysis.

The control group consisted of infants who were breathing spontaneously, and included some who required supplemental oxygen. The experimental group consisted of infants receiving assisted ventilation for various reasons, either as NCPAP or IMV. Random allocation to control or experimental groups was not

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considered for ethical reasons. Assisted ventilation was begun or stopped by clinical caretakers using standard criteria and decisions were not influenced by those involved in the study.

A plastic urine-collection bag was applied to the infant's perineum upon enrollment, and the first void was timed and discarded. Urine was collected continuously thereafter (beginning a mean 9 h after birth, range 3–17 h) for 48 h, in six periods of 8 h duration. Urine was removed from the bag, the volume was recorded, and the sample refrigerated as soon as possible after each void. At the end of each 8-h period, or when there was a change in the mode of ventilation (spontaneous *versus* NCPAP *versus* IMV), the crede maneuver was applied to empty the bladder as completely as possible before a new collection period commenced. Only periods in which there was an accurately timed volume of urine of at least 4 h duration were included for analysis. If mode of ventilation was not altered, urine samples were subsequently pooled into two samples representing the 1st and 2nd study days. All samples were stored at −20° C until analysis.

Two blood samples were obtained from each infant, one at a mean 23 h (range 19–27) and the other at a mean 47 h (range 43–53) after birth. These samples were collected to coincide as closely as possible to the midpoint of each 24-h urine collection. Blood was obtained from an indwelling arterial line when present or, alternatively, by venipuncture. Blood for measurement of PRA was placed in a prechilled tube containing 1 mg EDTA; the remainder was placed into a heparinized container. The specimen for PRA was centrifuged at 4° C. All plasma samples not analyzed immediately were stored at −20° C until analysis.

Blood glucose was estimated from heel-stick blood samples using Dextrostix reagent strips read with a reflectance meter; measurements were conducted an average of five times daily. Upper limb blood pressure, determined indirectly by experienced Neonatal Intensive Care Unit nursing personnel using an oscillometric technique, (Dinamap 847 Neonatal Vital Signs Monitor, Critikon, Inc., Tampa, FL) was measured an average of four times daily. The validity of this technique of noninvasive arterial BP measurement in newborn infants, including those born prematurely, has been documented previously (15).

The following data were recorded after daily physical examination and review of appropriate laboratory results and radiographs: cause of respiratory distress; confirmed bacterial infection; occurrence of intraventricular hemorrhage, persistent ductus arteriosus, or necrotizing enterocolitis; site of umbilical artery catheter tip; use of phototherapy; and whether the infant was nursed under a radiant warmer or in a closed-wall incubator.

The infants' charts were reviewed each day and the following data recorded: volume of blood sampled for clinical management; mode of ventilation; arterial blood gas values; inspired oxygen concentration; occurrence of apneic episodes; and, for infants receiving assisted ventilation, peak inspiratory pressure, end-expiratory pressure, and ventilator rate. Parenteral and enteral intakes (including from drugs) or fluid, sodium, potassium and chloride were calculated.

Analytical techniques. Sodium and potassium were measured by flame photometry, chloride by coulometric silver titration, and osmolality by freezing-point depression. True creatinine was measured using a modified Jaffé reaction (16). Urine glucose was measured using a glucose oxidase technique.

Plasma volume was estimated at a mean of 23 h (range 19–27) after birth from the 10-min albumin space, following injection of a mean 0.50 g/kg (range 0.39–0.55) of T-1824 (Evans Blue dye). Plasma samples were analyzed using the double wavelength spectrophotometric technique; blood volume was derived as previously described (17).

Plasma renin activity was measured by radioimmunoassay (18) of angiotensin I generated by incubation of 250 liter plasma at 37° C, pH 7.40 for 30 min. Commercial reagents purchased from New England Nuclear (Boston, MA) were used for the radioimmunoassay and results were expressed as nanograms of angiotensin I per ml/h. Coefficients of variation were 5.1% within assay and 12.8% between assays. The normal mean (± SEM) value in our laboratory for PRA in blood obtained from the umbilical cord artery of nonasphyxiated fullterm infants following uncomplicated pregnancy and spontaneous vaginal delivery is 14.2 ± 2.6 ng/ml/h.

Urine aldosterone excretion was measured by radioimmunoassay (19) using commercial reagents purchased from The New England Nuclear Corporation. Free and acid-labile (aldosterone-18-glucuronide) aldosterone were extracted from urine as previously described (Leslie GI, Work J, Ram S, Philips JB, Cassady G, unpublished observations). Mean recovery of ^{3}H-aldosterone tracer from the extraction was 83%. Intraassay coefficient of variation was 5.0% and interassay coefficient of variation was 16.0%. Results are expressed as total aldosterone, which represents the sum of free aldosterone and aldosterone-18-glucuronide. Our normal mean (± SEM) value for urine total aldosterone excretion by full term infants in the 1st day after birth is 2.46 ± 1.22 ng/min/1.73 m^2.

Urine PGE_2 was measured by radioimmunoassay following extraction as previously described (21). Mean extraction recovery of ^{3}H-PGE_2 tracer was 69%. The final PGE_2 concentration was adjusted for loss of ^{3}H-PGE_2 on extraction. Coefficients of variation were 5.0% within assays and 15.0% between assays. The mean (± SEM) PGE_2 excretion in our laboratory for full term infants during the 1st day after birth is 0.32 ± 0.16 ng/min/1.73 m^2.

Urine vasopressin was measured by radioimmunoassay (22). Briefly, rabbit antibody to an arginine vasopressin-bovine thyroglobulin conjugate was produced locally. The antiserum was used at a final dilution of 1:400,000 with an ED50 of 13.6 ± 2.2 pg per assay tube and a least detectable dose of 0.76 ± 0.07 pg per assay tube. Cross reactivities of related peptides, expressed as ED50s were: lysine vasopressin 36 ng; oxytocin—no detectable displacement; desamine-*d*-arginine vasopressin 2.2 ng; 8-arginine vasotocin 7 pg. Synthetic arginine vasopressin and USP arginine vasopressin preparations gave superimposable inhibition curves. The intra- and interassay coefficients of variation were 8.1 and 25.0%, respectively. Mean (± SEM) recovery of exogenous vasopressin added to unextracted urine over a range of 0.5 to 50 pg/ml urine was 96.7 ± 2.4%. Aliquots of various quantities of urine in identical volumes of incubating mixture exhibited parallel lines. Our mean (± SEM) control value of urine vasopressin for normal full term infants during the 1st day after birth is 108 ± 41 pg/mg creatinine.

Clearances were determined using standard formulae, and expressed in relation to body surface area (23).

Statistical analysis. Data are presented as mean ± SEM. Where covariates (BP, Dextrostix, arterial blood gases, ventilator pressures, and rate) were measured more than once in 24 h, the average value during that period was used for statistical analysis. Nonparametric descriptive data were analyzed by χ^2. Because there were no significant differences between the NCPAP and IMV data, these were pooled into one AV group for comparison with the SV group using the 2-sample *t* test. Variables were correlated by the least-squares method, or by using one-way analysis of variance. We considered a p value of 0.05 or less to be statistically significant and did not adjust the level of significance for multiple comparisons even though portions of the data were used for more than one comparison.

RESULTS

Descriptive data. Twenty-one infants were studied during SV and 22 during AV. Six infants were included in both groups because their mode of ventilation was changed during the study. Mean birth weights (1090 ± 45 g for SV *versus* 1040 ± 45 g for AV; p = NS) and gestational ages (29 ± 0.5 wk for SV *versus* 28 ± 0.5 wk for AV; p = NS) of the two groups were similar. There were no significant differences between the groups with respect to mode of delivery, frequency of low Apgar scores, weight loss

from birth to the 2nd day, use of phototherapy, net cumulative deficit of blood removed for clinical care, or urine glucose excretion.

The SV group included 10 infants without respiratory problems, seven who required supplemental oxygen because of retained fetal lung fluid, three with recurrent apnea, and one with HMD. The AV group included nine infants with HMD, six who had a transient need for AV because of either perinatal asphyxia or retained fetal lung fluid, five with recurrent apnea, and two with pneumonia. For those treated with NCPAP, the mean NCPAP level was 4 ± 0.4 cm H_2O. For those who received IMV, mean end-expiratory pressure was 4 ± 0.4 cm H_2O and mean peak inspiratory pressure was 23 ± 0.7 cm H_2O. Mean maximum F_{IO_2} was significantly higher in the AV group on both day 1 (0.53 ± 0.06 *versus* 0.25 ± 0.02; $p < 0.001$) and day 2 (0.51 ± 0.09 *versus* 0.22 ± 0.01; $p < 0.001$). However, there were no significant differences between the groups for mean values of arterial pH, P_{O_2}, or P_{CO_2} on either day.

Intergroup comparisons. Mean systemic BP was significantly lower in the AV group on the first [37 ± 1 ($n = 21$) *versus* 43 ± 2 ($n = 18$) mm Hg; $p < 0.05$] but not on the 2nd day [42 ± 2 ($n = 9$) *versus* 46 ± 2 ($n = 13$) mm Hg]. At 24 h after birth the mean plasma volume of infants receiving AV (59.0 ± 2.4 ml/kg, $n = 18$) was similar to that of those in the SV group (62.8 ± 2.2 ml/kg, $n = 10$), but their mean blood volume was significantly lower (94.0 ± 2.8 *versus* 106.8 ± 3.7 ml/kg; $p < 0.01$).

Figure 1 shows mean intake, urine excretion and net "balances" for Na, K, and Cl in the two groups. Mean "balances" were positive for each ion in both groups on both days. Mean plasma values for Na, K, Cl, and osmolality were within the range of normal for both groups of infants on both days; and on neither day did the mean value of the AV group differ significantly from that of the SV group for any of the plasma values.

Urine volume, osmolality, and clearance data are presented in Table 1. Mean Ccr was lower in the AV group on both days, and urine osmolality was higher in the AV group on the 1st day. No significant differences were detected between groups for urine volume, Cosm, or CH_2O.

Mean values for PRA and urine excretion of aldosterone, vasopressin, and PGE_2 are presented in Table 2. Statistical analysis was performed on logarithmically transformed data to normalize the distributions. Urine vasopressin excretion was signif-

Table 1. *The influence of AV on urine volume and osmolality, Ccr, osmolar clearance (Cosm) and free-water clearance (CH_2O)**

Measurement		Management: SV	Management: AV
Urine volume (ml/min/1.73 m^2)	Day 1	0.47 ± 0.06 (18)	0.41 ± 0.06 (22)
	Day 2	0.51 ± 0.05 (17)	0.44 ± 0.08 (10)
Urine osmolality (mOsmol/kg)	Day 1	196 ± 14 (18)	265 ± 29 (22)†
	Day 2	274 ± 30 (17)	327 ± 42 (10)
Ccr (ml/min/1.73 m^2)	Day 1	4.1 ± 0.4 (18)	2.9 ± 0.4 (22)‡
	Day 2	6.8 ± 0.8 (17)	4.1 ± 1.0 (10)§
Cosm (ml/min/1.73 m^2)	Day 1	0.31 ± 0.05 (18)	0.32 ± 0.04 (22)
	Day 2	0.45 ± 0.07 (17)	0.47 ± 0.11 (10)
CH_2O (ml/min/1.73 m^2)	Day 1	+0.16 ± 0.03 (18)	+0.09 ± 0.04 (22)
	Day 2	+0.06 ± 0.06 (17)	−0.03 ± 0.06 (10)

* Data are means ± SEM (n).
† $p < 0.025$
‡ $p < 0.05$
§ $p = 0.05$.
} compared with spontaneous ventilation.

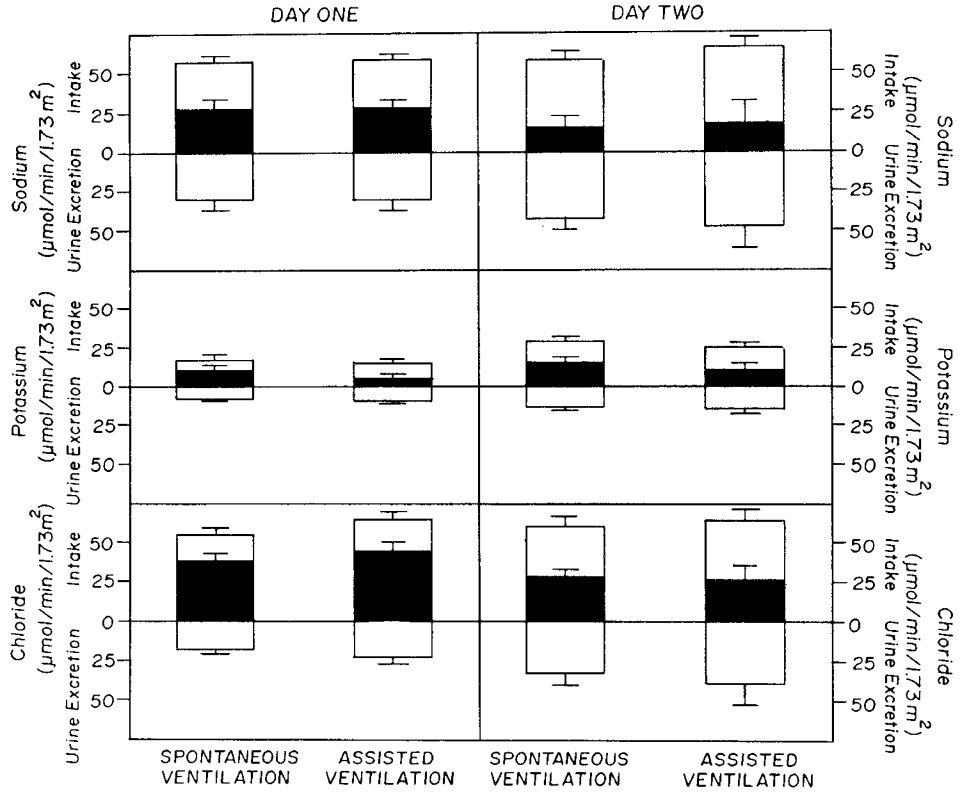

Fig. 1. Lack of influence of AV on intake, urine excretion, and "balance" for sodium, potassium, and chloride in very low birth weight infants during the 2 days after birth. Data are mean ± SEM. There are no significant differences between groups for any of the variables.

icantly higher in the AV group than in the SV group on the 1st, but not the 2nd day. No significant differences between groups were detected for the other hormonal values.

Correlations of variables. The relationship between Ccr and mean BP is shown in Figure 2. One-way analysis of variance indicated that mean BPs below 40 mm Hg were associated with lower values for Ccr. These variables ($n = 61$) also correlated significantly ($r = 0.44$, $p < 0.001$). The formula for the regression line was Ccr = 5.54 ln BP − 16.34. Blood volume at 24 h did not correlate with Ccr.

PRA correlated with urine aldosterone excretion ($r = 0.55$, $p < 0.001$, $n = 36$). The formula for the regression line was log PRA = 0.558 log urine aldosterone − 0.627. No other significant associations among the hormones were detected. Urine vasopressin excretion correlated directly with urine osmolality ($r = 0.63$, $p < 0.001$, $n = 50$). The formula for the regression line was Uosmol = 124 log urine vasopressin − 21. There was an inverse correlation between urine vasopressin and free-water clearance ($n = 50$, $r = -0.59$, $p < 0.0001$). The formula for the regression line was $CH_2O = 0.625 - 0.240$ log urine vasopressin. Neither PRA, urine aldosterone excretion, nor urine PGE_2 excretion correlated significantly with renal excretion of water, total solutes, Na, K, or Cl.

We compared the nine infants receiving AV for hyaline membrane disease with the 13 receiving AV for other reasons using the 2-sample *t* test; there were no significant differences with respect to these variables on either day 1 or 2 of the study. In addition, mean BP was similar in infants with and without HMD.

Table 2. *Mean values for plasma renin activity and urine excretion of vasopressin, aldosterone, and PGE_2**

Plasma measurement		Management SV	Management AV
Plasma renin activity (ng/ml/h)	Day 1	46 ± 14 (9)	92 ± 28 (16)
	Day 2	45 ± 13 (7)	65 ± 13 (8)
Urine vasopressin excretion (pg/mg creatinine)	Day 1	123 ± 30 (13)	360 ± 86 (15)†
	Day 2	313 ± 114 (16)	251 ± 67 (6)
Urine aldosterone excretion (ng/min/1.73 m^2)	Day 1	4.7 ± 2.3 (15)	3.6 ± 1.3 (18)
	Day 2	3.9 ± 1.7 (15)	4.3 ± 1.9 (7)
Urine PGE_2 excretion (pg/min/1.73 m^2)	Day 1	149 ± 52 (15)	99 ± 14 (16)
	Day 2	153 ± 23 (15)	146 ± 30 (7)

* Data are mean ± SEM (*n*).
† $p < 0.02$ compared with SV.

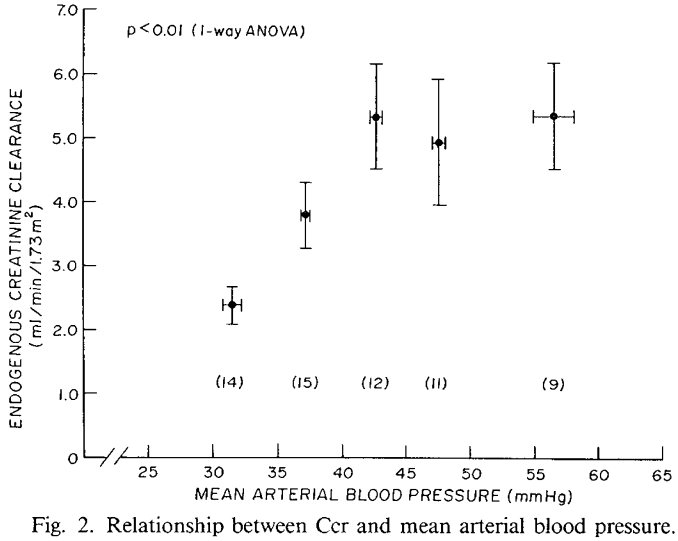

Fig. 2. Relationship between Ccr and mean arterial blood pressure. Data points represent mean ± SEM for creatinine clearance on the Y axis and mean BP on X axis. The number of observations for each data point are shown in parentheses. Creatinine clearance is significantly lower in infants with mean BP < 40 mm Hg [$p < 0.01$, one-way analysis of variance (ANOVA)].

DISCUSSION

This is the first study to specifically examine the influence of AV on neonatal renal function. Unlike previous studies of sick newborns, we excluded infants with potential confounding disorders and cointerventions such as intraventricular hemorrhage, pneumothorax, and volume expansion. We found use of AV, regardless of the indication for its use, to be associated with lower mean Ccr and higher mean values for urine vasopressin and osmolality, findings which may be explained by the lower mean BP of the infants receiving AV. Ventilation with PEEP previously has been shown to produce similar effects in controlled studies in other models.

Our control and experimental groups were matched as closely as possible within the limits of ethical reason. However, since infants were not randomly allocated to SV or AV but rather AV was used when clinically indicated, the group who received AV might be considered to have been "sicker" than those who were spontaneously ventilating. This, in addition to or rather than AV itself, could have influenced the variables measured. On the other hand, both groups included infants with similar diagnoses, and not all infants receiving AV had primary lung disease. In fact, the "sickest" infants, *i.e.* those with potentially confounding disorders and cointerventions which had been identified *a priori*, were excluded from analysis.

We found AV to be associated with a lower Ccr, regardless of the indication for its use; mean values in the AV group were between 60 and 70% of SV means on both days. Our study design does not allow us to prove that AV per se actually caused the lower Ccr in these infants. However, these findings are very similar to those of controlled studies in both adult man and experimental animals, in which PEEP ventilation caused mean values for GFR to decrease to between 50 and 75% of mean control values (10–13). Previous conflicting data from sick newborns (3–7) most likely result from the influence of variables such as hypoxemia, AV, and volume expansion. The present study suggests that AV, per se, is associated with a decrease in GFR in premature infants as it is in more mature individuals.

The lower Ccr of those receiving AV was significantly related to their lower mean BP. This is consistent with the hypothesis that the effects of AV on renal function are mediated through a PEEP-induced decrease in cardiac output resulting in lower values for mean BP (or pulse pressure) and renal blood flow (9, 11, 24). Although decreased pulmonary compliance might be expected to offer some protection from such PEEP-induced changes, this did not appear to be the case in our group of infants receiving AV, since values for mean BP and Ccr in those with HMD were just as low as values in infants who did not have HMD and who would be expected to have normal pulmonary compliance.

It is particularly interesting to note that mean BP and Ccr were related nonlinearly, suggesting the phenomenon of autoregulation of GFR, even though none of our infants was hypotensive according to published normal BP values (25). Whereas there was little variation in mean Ccr values when mean BP was between 40 and 65 mm Hg, values for Ccr were significantly lower when mean BP was less than 40 mm Hg. While autoregulation of GFR previously has been documented in puppies (26), we are not aware of similar data for human newborns.

Abnormalities of plasma electrolytes are common in sick premature infants (4). While we did not observe hyponatremia, both hypernatremia and hyperkalemia were common, as were high plasma values for chloride and osmolality. The frequency of hypernatremia in the AV group was about half of that in the SV group, possibly because of the unmeasured free-water intake from airway humidification in the former infants.

Most investigators have found urine Na excretion to be higher and Na balance to be more negative in sick premature infants than in controls (3–5), although fractional Na excretion was not influenced by HMD in one study (7). In these earlier studies, however, the Na intake of sick infants was often high, mostly parenteral and usually included Na bicarbonate, whereas controls usually had a lower, predominantly enteral Na intake. Such factors, as well as differences in gestational ages (4) and use of volume expansion (5) and drugs such as digoxin (3) make interpretation of these studies difficult. By contrast, studies of adult man and experimental animals in which conditions were more controlled, consistently demonstrated a relative salt retention with intermittent positive pressure ventilation (8–13); results with NCPAP were more variable (8, 10, 11, 13). In the present study total Na intakes were very similar in our two groups of infants, predominantly as parenteral NaCl. AV, either as NCPAP or IMV, failed to alter urine excretion or balance for Na, K, or Cl. Also there was no difference between infants with HMD and those receiving AV for other reasons. Probably there was no salt retention in our infants receiving AV because of the premature infant's limited ability to conserve Na in early postnatal life (27).

Others have reported urine volume to be decreased in association with AV in adult men (8–10) and experimental animals (11–13), and also in association with severe respiratory distress in newborn infants (2). It is likely that baroreceptor-stimulated vasopressin release is responsible for the decreased urine volume with AV (8, 9, 13, 24). Since severe hypoxemia also can stimulate vasopressin secretion (28), vasopressin also may have contributed to the decrease in urine volume of infants in earlier neonatal studies. The lack of decrease in urine volume associated with AV in our study could be explained either by an inability to produce vasopressin or by decreased sensitivity of the distal nephron to vasopressin. Since mean urine vasopressin was significantly higher in our AV group on the 1st day, these infants are clearly able to produce vasopressin, and the stimulus for increased vasopressin secretion is most likely baroreceptor-mediated, since mean BP was significantly lower in the AV group on the 1st day but not the 2nd day, paralleling the alterations in urinary vasopressin excretion. The alternate hypothesis of decreased distal nephron sensitivity to vasopressin is supported by previous data from a fetal sheep model (29). In addition, we have preliminary data suggesting that full term infants respond more rapidly and more predictably to endogenous vasopressin than did the current study infants (Leslie GI, Philips JB, Work J, Cassady G, unpublished observations). The apparent decrease in renal sensitivity to vasopressin in the AV group on day 1 could reflect, in part, competitive inhibition of the renal vasopressin receptor by another antidiuretic agent known to be secreted by the newborn infant pineal gland, namely, vasotocin. Vasotocin has been found in fetal sheep plasma (30). Because of the nearly 50% cross-reaction of vasotocin on the present vasopressin radioimmunoassay system, we are not able to differentiate between these possible explanations.

There are a number of hemodynamic changes associated with the use of AV which can potentially stimulate the renin-angiotensin-aldosterone system (8, 24). While some studies have found an increase in vasopressin levels (24), others have not (7, 10). Mean PRA in our AV group was 50% higher than that of the SV group on the 1st day, but individual values overlapped considerably and mean values were similar in both groups on the 2nd day. There was no clear increase in aldosterone excretion with AV on either day. Since electrolyte balance was not altered by AV in our study, we cannot assess the possible role of the renin-angiotensin-aldosterone system in the development of electrolyte imbalance by very low birth weight infants during AV from our results.

Renal PGE_2 may be important for maintenance of renal blood flow and may interact with the renin-angiotensin-aldosterone system and vasopressin to influence renal excretion of Na and water, although its true physiological role remains uncertain. Although urine PGE_2 excretion was lower in a group of premature with HMD than in those without on the 1st postnatal day (31), this finding was not correlated with renal solute or water excretion. In our study neither mode of ventilation nor diagnosis influenced urine PGE_2 excretion. Furthermore, urine PGE_2 did not correlate with any measure of electrolyte balance or with levels of the other hormones. Therefore we cannot implicate, PGE_2 in the changes in renal function which were associated with AV in this study.

In summary, we conclude from our data that AV, per se, alters renal function in premature infants as it does in more mature individuals. Developmental immaturity in distal renal tubular hormone-responsiveness might explain the lack of effect of AV on renal electrolyte and water excretion.

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