2013

NICU Sodium Administration to Extremely Low Birth Weight Infants: Relationships with Recommendations and Growth

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NICU SODIUM ADMINISTRATION TO EXTREMELY LOW BIRTH WEIGHT INFANTS: RELATIONSHIPS WITH RECOMMENDATIONS AND GROWTH

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

IN

NUTRITION AND FOOD SCIENCE

UNIVERSITY OF RHODE ISLAND

2013

MASTER OF SCIENCE THESIS

OF

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2013

ABSTRACT

Title: NICU sodium administration to extremely low birth weight infants: Relationships with recommendations and growth.

Objectives. To determine the amount of sodium being administered in the Neonatal Intensive Care Unit (NICU) from all sources including parenteral and enteral nutrition, medications, and intravenous solutions to extremely low birth weight (ELBW) infants -- those weighing less than or equal to 1000 grams. It was hypothesized that there are variable amounts of sodium given, but those amounts are not adequate when compared to the recommendation of the American Academy of Pediatrics (AAP) (3-5 mEq/kg/d).

Study design. The study design was a retrospective chart review of surviving ELBW infants admitted to and discharged from the Women and Infants' Hospital (WIH) NICU in Providence, Rhode Island from January 2009 through June 2011 who were not enrolled in the NICU protein study. Information on birth weight, gestational age, length of stay, growth velocity, average protein and calorie intake per kilogram, and average sodium intake per kilogram received from all sources was collected for eleven different time points.

Results. Seventy ELBW infants met the criteria for inclusion in this retrospective chart review. Comparisons of the time points showed the highest amount of sodium per kilogram to be given at Day of Life 14 (4.52 mEq/kg) and only twenty-eight infants (40%) received the minimum amount recommended by the AAP (3-5 mEq/kg) all time points were compared. When analyzed from week 2-12 (week at which true growth occurs), only eight infants (11 %) of the infants

received adequate amounts. When growth velocity was compared with amount of sodium received (using 3 mEq/kg as cutoff), more growth was seen in the group given lower amounts of average sodium with the all-time points set (12.01±1.5 g/kg/day vs. 10.93±2.64 g/kg/day, p=0.034) and the same was true in the weeks 2-12 data set but no statistical significance was seen (p=0.84).

Conclusions. ELBW infants are receiving large amounts of inadvertent sodium from medications and intravenous solutions. During weeks one and two of life, 88% and nearly 50% (respectively) of the sodium intake came from medications or intravenous solutions. Even with the inadvertent amounts of sodium, most of the infants received suboptimal intakes of sodium compared to recommendations by the American Academy of Pediatrics (3-5 mEq/kg). Growth velocity was compared with different levels of sodium (<3 mEq/kg vs ≥3 mEq/kg). More growth was seen in the group with the lower average sodium than those receiving the higher amount of sodium. This could be explained by the morbidity level of these infants. When growth rate of the infants who had no morbidities was compared to those infants with one or more morbidities, greater growth rates were seen in the group with no morbidities (12.80±1.3 g/kg/day vs. 10.66±2.11, p=0.001).

ACKNOWLEDGMENTS

I would like to thank my advisor, Kathleen Melanson for all her help throughout this thesis process. She provided unlimited guidance and patience with what seemed to be multiple obstacles. I would also like to thank the rest of my committee members -- Debra Erickson-Owens, Alison Tovar, and Geoffrey Greene – for their support. My appreciation should also be extended to Dr. Abbot Laptook at Women and Infants' Hospital who inspired this endeavor and to Leslie McKinley MS RD for helping me navigate through the extremely low birth weight infant database. Last, but not least, I would like to thank my husband (Terry Kelly), my daughters (Erica and Mackenzie), and the rest of my family and friends for their continued encouragement during this sometimes trying endeavor.

PREFACE

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CHAPTER 1

INTRODUCTION

Over the last ten years, changes in nutrition practices have improved growth in extremely low birth weight (ELBW) infants (≤1000 grams) (1). The American Academy of Pediatrics recommends a postnatal growth rate that approximates that of a fetus of the same postconceptional age (≥15 g/kg/d) (2). Changes in nutrition practices include earlier parenteral nutrition, earlier enteral feeds, continuous feeds, protein fortification of human milk, and the development of feeding intolerance algorithms. Hanson et al. compared growth pre- and post-implementation of nutrition practice changes and found a decrease in extrauterine growth restriction (weight that is less than or equal to 10th percentile) from 57% (pre-implementation) to 28% (post-implementation) (3). Thiele et al. showed that 73% of these infants grew at or above fetal rates and had less extrauterine growth restriction (EUGR) compared to those 10 years prior (1).

While attention has focused on increasing protein and calorie amounts to avoid growth failure (1,4,5,6), sodium and its requirements for optimal growth has not been thoroughly investigated even though hyponatremia (defined as a serum sodium concentration less than 135 mg/dL) is very common in the NICU and has been implicated as a reason for EUGR (3,7). Sodium is needed for maintenance of extracellular fluid volume, bone mineralization, protein

synthesis, and the transport of glucose across cell membranes (8). As a growth factor, sodium is important because it stimulates protein synthesis and increases cell mass and, as a result, inadequate sodium intake could lead to growth failure (8), and chronic sodium depletion has been found in many conditions related to failure to thrive (9). Modi suggests that if energy intake is adequate, poor growth may be associated with sodium depletion even if serum sodium concentrations are within normal limits (7).

Experimental evidence in both humans and animals suggests that sodium depletion may in itself be responsible for poor growth (10). The mechanism whereby sodium promotes growth is not completely understood, but it is hypothesized that the sodium/hydrogen antiporter system is a likely possibility (9). The plasma membrane sodium-hydrogen exchanger plays a physiological role in the regulation of intracellular pH and the control of cell growth and proliferation and most likely does not function optimally with sodium deficiency (11).

Wassner and Gallagher investigated sodium deficiency with subsequent supplementation of sodium chloride in young rats and found improved growth in the rats that were given sodium supplementation (12,13). Vanpee et al. and Al-Dahhan et al. conducted studies on preterm infants, giving extra sodium to infants between day of life four through fourteen and did see improved growth in those that received sodium supplementation, even after the sodium had been discontinued (14,15).

Even when an infant is receiving adequate energy but continues with poor growth, chronic sodium depletion may be to blame. There have been documented sodium deficiencies due to ileostomies, cystic fibrosis and various congenital deformities. Wassner and Kulin gave sodium supplementation to one boy status post colon resection that was experiencing growth failure and saw a positive relationship between sodium intake and linear growth (10). Bower et al. provided sodium supplementation to eleven infants who experienced metabolic abnormalities caused by ileostomy fluid losses and found a direct relationship between ileostomy output and the sodium intake required for growth (0.13 mEq/kg/d of sodium for every ml/kg/d of ileostomy input) (16). Sacher et al. saw similar findings in the retrospective follow up of 30 neonates with ileostomies (17). In infants with cystic fibrosis, Coates et al. found that none of the ten infants in his study required more calories than their estimated needs when their diet was sodium supplemented.

Recommendations by the AAP (1985) for sodium are based on Zeigler et al.'s factorial method as there are limited studies regarding the optimal amount of sodium needed for premature infants to promote growth. The factorial method provides guidelines for all macronutrients and micronutrients and is based on daily tissue increment, dermal loss, urine loss, intestinal absorption to determine amounts required. For the 800-1200 g infant (26-28 weeks' gestation), 3.5 mEq/kg of sodium is recommended (2). Current recommendations have not altered from Ziegler's original work and are presented as a range of sodium

intake (3-5 mEq/kg/d) for infants less than 1000 g from either enteral or parenteral nutrition (18).

The present study quantified total sodium intakes of 70 ELBW infants admitted to the Neonatal Intensive Care Unit (NICU) at Women and Infants' Hospital from January 1, 2009 through June 30, 2011 and compared values to recommended sodium intakes.

Descriptive analyses and correlations were conducted on variables including growth velocity, gender, birth weight, total number of morbidities, nadir serum sodium value, zenith serum sodium value, average calories, average protein and average sodium (mean and standard deviation). Multiple linear regressions were done based on correlations with growth velocity as the dependent variable.

RESEARCH QUESTIONS

Primary: What are the average amounts of sodium being administered to extremely low birth weight infants in the Neonatal Intensive Care Unit at Women and Infants' Hospital, Providence, Rhode Island?

Secondary: 1) Are adequate amounts of sodium being given based on the recommendations of the American Academy of Pediatrics? 2) Is there a correlation between average sodium intakes and growth velocity?

CHAPTER 2

REVIEW OF LITERATURE

Nutrition practices have improved growth rates over the last ten years in premature infants (1,4,5,6). Despite these improvements, postnatal growth restriction of extremely low birth weight (ELBW) infants is quite common (4). In a network cohort study, Ehrankranz found that the majority of ELBW infants were discharged at weights less than the 10th percentile of expected intrauterine growth and at 18-22 months' corrected age, 50% remained below the 10th percentile (5). There was also an association between poor weight and neurodevelopment impairment found in this study.

Hanson, et al. compared growth pre- and post-implementation of a nutrition practice change (3). These changes included earlier parenteral nutrition, earlier enteral feeds, continuous feeds, protein fortification of human milk, and the development of a feeding intolerance algorithm. With the new guidelines, they found a decrease in extrauterine growth restriction (weight less than or equal to 10th percentile) from 57% (pre-implementation) to 28% (post-implementation) and there was no difference between the groups with regard to NEC, IVH, or death rates (3).

In a retrospective study of 88 ELBW infants with bronchopulmonary dysplasia (BPD), Thiele et al. showed that 73% of these infants grew at or above fetal rates and had less extrauterine growth restriction (EUGR) compared to those 10 years prior (1). New strategies included early parenteral amino acid

administration closer to 3 g/kg/day, earlier initiation of enteral feedings, and fortification of human milk (19).

EUGR refers to the concept that preterm infants develop a severe nutritional deficit during the first weeks after birth (20). It has been shown to correlate negatively with neurodevelopmental milestones at 18 and 24 months' corrected age (3,5,21). Because of this concern, a primary goal in the NICU is maintaining adequate growth (≥15 g/kg/day) (20). Complicating this goal are common morbidities of premature infants including patent ductus arteriosus (PDA), which is a delay in closure of ductus between aorta and pulmonary artery; bronchopulmonary dysplasia (BPD) or chronic lung disease of prematurity (CLD), which is a chronic pulmonary condition; necrotizing enterocolitis (NEC) which is characterized by abdominal distension, bilious aspirates and/or bloody stools; and intraventricular hemorrhage (IVH) which is an intracranial bleed ranging from mild to severe (22,23).

The AAP recommends a postnatal growth rate that approximates that of a fetus of the same postconceptional age (≥15 g/kg/d) (2). Premature infants with morbidities tend to grow more slowly than those without morbidities (4). This is because sick infants' feeds are interrupted more often, yet they have increased metabolic needs (20). Premature infants with inadequate sodium intake and inadequate sodium retention also tend to grow more slowly than those with adequate sodium intake and retention (22).

More attention has been given to increasing and optimizing macronutrients (protein and calories) (1,4,5,6), and sodium is not typically

examined in most large scale studies of growth in premature infants. When an infant is meeting their energy needs but continues with poor growth, chronic sodium depletion may be to blame even with normal or low normal serum sodium concentration (22). Chronic sodium deficiency has been associated with poor skeletal and tissue growth (22).

Renal function

Kidneys in newborn infants have a limited capacity to excrete urine and conserve sodium (7,22). This function occurs in the nephron which is the basic structural and functional unit of the kidney. Development or growth of the kidney (nephrogenesis) continues until 36 weeks gestation (24). Because of this, preterm infants are likely to have a reduced number of nephrons and therefore a decreased glomerular filtration rate (25). After extracellular volume contraction occurs, the preterm infant is vulnerable to sodium depletion secondary to immature sodium reabsorption (25).

Diuresis

Preterm infants less than 26 weeks' gestation are approximately 80-90% water (7). After birth, there is a sudden efflux of fluid from the intracellular fluid (ICF) compartment to the extracellular fluid compartment (ECF) (22,26). The ECF consists mainly of water and sodium and with this increase in the ECF, the neonatal kidneys are flooded, resulting in salt and water diuresis by two to three days which amounts to weight loss of between 10-15% of birth weight during the first 5 days of life (26), and this percentage could even be as high as 20% (25). There is an inverse relationship between birth weight and weight loss percentage

during diuresis (26). Failure to lose this fluid could result in overhydration and possibly lead to PDA and CLD (23).

Adverse effects

Adverse effects of excess sodium administration can be seen in the first few days of life and can increase the risk of hypernatremia (serum sodium >150 mg/dL) especially if fluids are limited. In a retrospective study of infants less than 27 weeks' gestation, nearly 70% of hypernatremic infants developed CLD, PDA and IVH (23). After diuresis, though, ELBW infants are at risk for chronic sodium depletion, and an intake of at least 4 mEq/kg/day is required (7).

Sodium is an important nutrient for preterm infants and is needed for maintenance of extracellular fluid volume, bone mineralization, protein synthesis, and the transport of glucose across cell membranes (8). As a growth factor, sodium is important because it stimulates protein synthesis and increases cell mass (9). As a result, inadequate sodium intake could lead to growth failure (8). Chronic sodium depletion may be found in many conditions related to failure to thrive (9).

Hyponatremia (defined as a serum sodium concentration less than 135 mg/dL) is not always seen as the primary reason for growth restriction, but it is very common in the NICU and has been implicated as a reason for EUGR (3,7). Modi suggests that if energy intake is adequate, poor growth may be associated with sodium depletion even if serum sodium concentrations are within normal limits (7). Experimental evidence in both humans and animals suggests that sodium depletion may in itself be responsible for poor growth (10).

Sodium requirements

Sodium requirements vary on day of life. Because of the prediuretic status of the baby, on day of life 0, a negative sodium balance is desired and only 0-1 mEq/kg/day of sodium is recommended (7). For the transition period (extracellular water contraction and weight loss) on days 1-5 of life, 2-5 mEq/kg/day of sodium are recommended (30). According to the AAP (18), current recommendations for the growing low birth weight infant are 3-5 mEq of sodium, which was first calculated by the reference fetus of Ziegler et al (6), although up to 7 mEq may be needed for babies experiencing late hyponatremia (27). Goals may be underestimated because net gastrointestinal absorption of enteral feeds is approximately 70% (26). Further complicating this goal is that very preterm infants have lower intestinal absorption of sodium or higher urinary losses than estimated (28).

Some institutions give 4-6 mEq/kg/day of sodium on the second or third day of life (DOL) regardless of clinical status (29). Hartnoll et al. and Al-Dahhan et al. recommended delaying sodium supplementation until DOL 4-5 or until 6% weight loss occurs to allow for fluid contraction (28,30). Bhatia recommends no additional sodium until serum sodium is <130 mg/dL, then starting with 2-3 mEq/kg/day (31).

Animal Studies

Wassner studied the effect of supplementing sodium-deficient young rats. Both the experimental and control groups received similar diets and distilled water for 2-3 weeks but the experimental group received 37 mEq of sodium

chloride. The control group gained just 45% and 70% of weight and length, respectively, compared to the experimental group suggesting growth failure with sodium deficiency (12).

Gallagher et al. also studied diet-induced sodium deficiency and measured the lung growth of young rats after undergoing left pneumonectomy (13). As above, experimental and control groups were fed similar diets and distilled water, but the control group received 37 mEq of sodium chloride. After the 7 days, somatic growth was measured as well as lung mass, and it was shown that the sodium-deficient rats grew more slowly than the rats in the experimental group (13).

Infant Studies

As mentioned earlier, there is concern that early sodium supplementation could delay diuresis and therefore further increase expansion of extracellular compartment which, in turn, could affect the lungs and heart. Early sodium administration could be possibly harmful and should be avoided until diuresis occurs (7). Hartnoll et al. (2000) studied oxygen dependency and timing of sodium supplementation. Twenty-four preterm infants of 25-30 weeks' gestational age (weight range 745-1560 g) received sodium supplementation (sodium chloride) before six percent of birth weight was lost (experimental group), and delayed sodium supplementation in twenty-two infants (weight range 420-1570 g) until 6% body weight was lost (control group) (30). The delayed sodium group had a large maximum weight loss than the early group (16.1% vs. 11.4%, p=0.02) but they saw no significant differences in time to

regain birth weight, weight at 36 weeks, nor six months of postmenstrual age. There was also a significant difference in oxygen requirement at seven days with 35% of delayed group on room air compared with only 9% of early group on room air. They concluded that delaying sodium supplementation until 6% of birth weight is lost is beneficial for lungs and did not compromise growth (30).

Elstgeest et al. retrospectively compared two cohorts of infants <28 weeks who received either early TPN administration or late TPN administration (29). Due to a change in clinical practices, TPN was either started on day of life 0 or 1 at 60-80 ml/kg (early TPN) or day of life three at 80-120 ml/kg (late TPN). The early TPN group also received electrolytes within the first day of life. They saw no statistically significant differences in sodium levels (141.8±3.8 vs. 141.0±3.7 mEq/L), although loss of body weight was decreased in the early TPN group (-6.0%±7.7 vs. -0.8%±8.0%). They also found a higher weight gain in the early TPN group at day of life 14 and 21, but attributed this to increased protein administration, not sodium.

Vanpee et al. (1995) studied twenty premature infants (gestational age 29-34 weeks) at the Karolinska Hospital in Sweden. Ten of the infants were randomly chosen to receive an additional 4 mEq of sodium chloride per kilogram from day of life 4 to day 14 of life, which amounted to total sodium amounts of 5.0±0.9 mEq Na/kg (14). The non-supplemented group received 1.7±0.6 mEq/kg/day of NaCl. Both groups were studied at one and two weeks of age. No significant differences between the two groups were seen in gestational age, birth weight, and total fluid intake. At one week, the sodium supplemented group was

in positive sodium balance compared to the nonsupplemented group and also had higher sodium balance at two weeks. Weight loss was greater in the control group at one week, and at two weeks, most of the control group had not returned to their birth weights. Even after sodium supplementation was discontinued, the experimental group's growth velocity was greater. Diuresis and water excretion were similar in both groups at week 1 and 2. None of the supplemented babies had serum sodium levels greater than 145 mg/dL suggesting tolerance of increased sodium amounts (14).

Al-Dahhan et al. (1984) conducted a randomized control trial that studied the clinical and biochemical effects of sodium supplementation given to twenty-two otherwise healthy infants between 27-34 weeks' gestational age from day of life 4 to 14 compared with a group of 24 unsupplemented babies (28). Birth weight was regained more quickly in the supplemented infants, and they lost less weight postnatally, and their improved weight gain (g/kg/day) continued even after supplementation was discontinued. Unsupplemented infants also experienced a significantly greater incidence of hyponatremia compared with the supplemented group. No edema, hypernatremia, or evidence of circulatory overload was seen. There was no significant difference in incidence of PDA, NEC, or IVH (28).

Al-Dahhan et al. (2002) conducted a secondary analysis of previously sodium-supplemented infants (n=37) studying the effects of sodium supplementation on neurodevelopmental outcomes of 10-13 year olds. Some of these adolescents had received sodium supplements on DOL 4-14 while

inpatients in a NICU (15). They found that nine infants in the unsupplemented cohort had had plasma sodium levels of <130 mg/dL compared to four infants in the supplemented group. The supplemented infants performed significantly better in balance and manual dexterity. The supplemented group also had higher verbal intelligence quotients, and significantly different performance and full scale intelligence quotients. Children in the unsupplemented group were also more than likely ($p < 0.07$) than the unsupplemented group to have behavioral disturbances (15).

CASE STUDIES

Several case reports identify a correlation between sodium depletion and poor growth. Wassner and Kulin identified a boy status-post colon resection that occurred at one year of age (10). One month after the surgery, he was admitted with an ileus and his serum sodium level was 119 mEq/L. When seen again at 7 years of age, his weight and height were below the 5th percentile on growth charts. Sodium supplementation was begun and an increase in linear growth was seen. When sodium intake was compared to growth per month, a significant correlation was seen ($p<0.025$) (10).

In a neonates with grade 3 Pierre Robin Sequence (a congenital condition of facial abnormalities, a retrospective chart review was conducted by Skillman et al. on infants born between 2000-2007 at a tertiary center for cleft palate care (32). Twenty-nine infants who required nasogastric or nasopharyngeal intubation were included in the study. After supplementation in 18 of the 21

infants who had low urinary sodium, weight gain improved significantly from 20 to 24 g/day (p=<0.001) (32).

Sodium deficits can also be seen in infants with ileostomies. Excessive sodium loss can occur with ileostomies because of poor or absent colon function (which helps retain fluid and sodium). Bower et al. reviewed the records of eleven infants who were 25 to 38 weeks' gestation who experienced metabolic abnormalities caused by ileostomy fluid losses. All these infants developed total body sodium depletion and metabolic acidosis from ileostomy bicarbonate loss. After sodium supplementation, however, these infants gained weight and a direct relationship was seen between ileostomy output and the sodium intake required for growth (which was calculated as an extra 0.13 mEq/kg/d of sodium for every ml/kg/d of ileostomy input) (16).

Sacher et al. saw similar findings in the retrospective follow up of 30 neonates with ileostomies (17). Because enteral products provide just 2-4 mEq/kg of sodium, a sodium deficiency can amount to 4-6 mEq/kg a day with these patients. After this amount was supplemented in the thirty infants, better growth was seen.

Infants with cystic fibrosis are at higher risk for sodium depletion which can lead to impaired growth. In a study of ten cystic fibrosis patients, weights and plasma/urine sodium were obtained serially (33). The amount of sodium supplementation was determined by fractional excretion of sodium and urinary sodium. Coates et al. found that no infant required more calories than estimated needs when their diet was sodium supplemented.

LATE HYPONATREMIA

Late hyponatremia (low serum sodium levels after two weeks of age) has been observed in very low birth weight infants (birth weight of ≤1500 g) when they received 2-3.5 mEq/kg/day of sodium (34). As these low birth weight infants transition from parenteral to enteral nutrition, sodium intake decreases while sodium requirements increase secondary to their growing more rapidly. This is further complicated by sodium losses during the initial weeks of life secondary to their kidneys' ability to retain sodium (34).

Roy el al. conducted a study of 46 very low birth weight infants between two to six weeks of age (35). The nonsupplemented infants received less than 2 mEq of sodium per kg/day. The supplemented infants received ~3 mEq of sodium/kg/day. Hyponatremia was seen on 54 of 159 occasions in the infants receiving sodium amounts of ≤2 mEq/kg/day.

In a retrospective cohort study in 1996, Kloiber et al. examined data obtained from medical records of VLBW infants admitted to their NICU who experienced late hyponatremia (serum sodium <135 mg/dL between days of life 14-56) (8). There was an association between babies less than 1000 g and late hyponatremia, even though these infants received more sodium than the other infants. This might have suggested a sodium deficiency and the need for increased sodium in these ELBW infants. Because of this, Kloiber et al. estimated sodium requirements of ELBW infants at three to eight mEq/kg/day.

Infants less than 1500 grams are prone to development of hyponatremia which can lead to increased mortality and morbidity (36). Ndwiga et al assigned

56 very low birth weight infants (1000-1500 g) to either an acutely ill group or clinically stable group. The ill infants had persistently low serum sodium (mean of 120 mmol/L) during the first week while the clinically stable infants' sodium levels increased from 127 to 133 mmol/L. At day seven, there was a statistically significant difference in serum sodium levels ($p=0.02$).

Unsupplemented breast milk may not be appropriate for low birth weight infants. Ayisi et al. conducted a sodium supplementation study in 66 healthy infants who weighed between 1001-1500 grams at Kenyatta National Hospital Newborn Unit in Kenya (37). Forty one infants were supplemented with sodium, while the twenty five in the control group were unsupplemented. Serum sodium levels were measured in both groups during the 6-week study period. Feedings were started at 60 ml/kg/day on day 1 and at day 7, 3 mEq/kg/day of sodium was supplemented for a total of 5.95 mEq/kg/day during the 5 consecutive weeks of supplementation, while sodium for the unsupplemented group was 2.75 mEq/kg/day. There was a statistically significant difference in the amount of sodium each group received ($p < 0.01$), although no significant difference was seen in mean serum sodium levels in both groups (140 ± 2 mEq/L vs. 139±+2 mEq/L respectively). Statistically significant differences were seen in weight, length, and head circumference in the group supplemented with sodium compared with the unsupplemented group (37).

MECHANISMS

The mechanism whereby sodium promotes cell growth is not completely understood, but it is hypothesized that the sodium/hydrogen antiporter system which controls the cell interior pH is a likely possibility (9).

The sodium/hydrogen (Na+-H+) exchanger has been documented in the plasma membrane of a wide variety of cell types and is a carrier-mediated Na+-H+ exchange (antiport, countertransport) system that exchanges sodium for hydrogen (11). In the intact cell, the plasma membrane Na+-H+ exchanger controls the extrusion of protons and flux of Na+ into the cell. This process does not need a chemical reaction (such as ATP hydrolysis) but energy is obtained from the Na+ gradient, which is maintained by the active extrusion of Na+ by the Na+,K+- ATPase system. This plasma membrane sodium-hydrogen exchanger plays a physiological role in the regulation of intracellular pH and the control of cell growth and proliferation (11) and most likely does not function optimally with sodium deficiency.

All sodium transporting and regulating systems undergo maturation in the postnatal period. Active sodium transport in all eukaryotic cells is provided by the Na+,K+-ATPase enzyme (25). This transmembrane protein controls the electrochemical sodium and potassium gradient of the cell membrane. Short term regulation of sodium balance is controlled by activity of sodium transporters. Natriuresis is caused when these are down regulated by either atrial natriuretic peptide, dopamine, or diuretics. Sodium retention occurs when these are upregulated by noradrenaline.

CHAPTER 3

METHODOLOGY

A retrospective chart review was conducted after approval by Women and Infants' Hospital and the University of Rhode Island.

Inclusion criteria for the study included birth weight less than or equal to 1000 g and survival past 36 weeks gestational age. Exclusion criteria included expiration prior to 36 weeks, admission into the NICU protein study, and transfer from another facility.

Detailed patient information was extracted from patient medical records and parenteral nutrition software. This information included birth weight, gestational age, length of stay, growth velocity, average protein and calorie intake per kilogram, and average sodium intake per kilogram received from all sources. These sources included enteral and parenteral nutrition, medications, and intravenous solutions. The time points for data extraction included day of life one (1), four (4), seven (7), fourteen (14), twenty-one (21), twenty-eight (28), thirty-five (35), forty-two (42), fifty-six (56), seventy (70) and eighty-four (84).

Presence of the following diagnoses was noted: intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), chronic lung disease (CLD), patent ductus arteriosus (PDA) and were extracted from diagnoses list on the electronic medical record. It has been shown that infants less than 1500 g with

one or more of these morbidities have a slower growth rate than the growth rate of infants who were not diagnosed with any of these morbidities (4).

ELBW Database

At WIH, data from infants less than or equal to 1000 grams are entered into the ELBW database located in Microsoft Access. The purpose of a nutrition database for ELBW infants is to ensure that nutritional goals for this vulnerable group are being met. ELBW infants have high nutritional needs and are at high risk of nutrition-related morbidities such as infection, necrotizing enterocolitis, chronic lung disease, and poor growth. The information recorded includes weight, IV fluids, parenteral nutrition, and enteral nutrition including additives. These data are collected on days of life 1, 4, 7, 14, 21, 28, 35, 42, 56, 70, and 84. Queries are used to determine the total calories, total protein, and total fluids per kilogram at these different time points, and these results were used for this study.

Sodium from Parenteral Nutrition

Parenteral nutrition (PN) is provided to infants from the first or second day of life until transitioned to full enteral feeds. Orders are written by the neonatal nutritionists utilizing Abacus Pharmaceutical Software (Version 2) after review by the interdisciplinary team and are based on laboratory data, diagnoses, and clinical status. A new table was created in the ELBW database to enter sodium intake, and queries were used to calculate sodium in mEq/kg at all the time points. The data abstraction tool that was used to collect this information from Abacus is found in Appendix B.

Sodium from Enteral Nutrition

Information about enteral nutrition was extracted from the queries already created in the ELBW database in Microsoft Access. Different queries were used to calculate the amount of protein, calories, and sodium per kilogram that is contained in the appropriate formula. Formula composition information was obtained from the manufacturers and this information was already in place in the database. Nutrition composition of enteral feeds can be found in Appendix A.

Sodium from Intravenous Solutions and Medications

At the chosen time points, sodium-containing IV solutions and all medications administered were documented using another data abstraction tool which can be found in Appendix B. The amount in milliliters of each intravenous solution and medication was collected. These values were then entered into the ELBW database in Microsoft Access and queries were used to determine sodium milliequivalents per kilogram.

Information about sodium content of medications was obtained from the manufacturers, from literature, and the pharmacy department at WIH. Several medications are prepared in the pharmacy or at the bedside using normal saline, so even though the medication may not contain sodium, the administered dose will contain sodium because of its preparation. A table depicting the medications, IV solutions and amounts of sodium per 100 ml can be found in Appendix C.

Determining sodium levels from heparin was particularly difficult. Heparin that is added to intravenous solutions is a fraction of the entire bag. Together with Pharmacy, a calculation was used to represent heparin as a percentage of the total bag based on the amount of units/bag. This can also be found on the Medication Sodium List found in Appendix C.

Serum Sodium Values

Serum sodium values that were available at the time points were collected. Because this was a retrospective study, not all infants had serum sodium levels at all the time points. Also collected were the nadir and zenith serum sodium values as well as what day of life they were drawn.

Calculating Growth Velocity

The growth velocity values used in the statistical analysis were calculated for each infant utilizing the two point method (38) which is shown below:

Growth Velocity = W2 - W1 ÷D ÷ W3, where

W2 = Weight at last week measured (g).

W1 = Birth weight (g) divided by

D = The number of weeks (converted to days) that data were collected.

W3 = W2 + W1/2

Z-Scores

At WIH, the Fenton Growth Chart is used as a tool to monitor growth while on the NICU, and this particular version is used for both males and females. This growth chart highlights the 3rd, 10th, 50th, 90th, and 97th percentiles and is in place

in the electronic medical record. Any weight not at the 50th percentile is considered a particular "distance" away from the median – or certain "z-score" away from 50th percentile. For example, using percentiles, an infant could be plotted on the chart and described as weighing less than the 3rd percentile. When using z-scores, the infant's weight is described more precisely as having a z-score of -2.7. Using z scores is another tool to examine growth patterns. Z-scores less than -1.28 are considered growth restricted (3).

Statistical Analyses

All of the data were consolidated into Microsoft Access 2010 (Seattle, WA), allowing extraction of the data from different sources for statistical analyses. Statistical analyses were done using SPSS Version 21 (IBM Corporation, Armonk, NY).

The data were analyzed two ways. First, all data points were used (days of life 1, 4, 7, 14, 21, 28, 35, 42, 56, 70 and 84) and these data underwent analysis using correlations, independent t-tests, and regression. Because in uncomplicated cases, actual growth is not expected until after day of life 14 (2), the data were also analyzed from Week 2 through Week 12 with the same statistical tests.

Growth velocity, birth weight, nadir serum sodium value, zenith serum sodium value, average calories, average protein and average sodium intake were described using standard descriptive statistical methods (mean and standard deviation). Normality for all variables was examined using the Shapiro Wilk test although because the sample size was 70 infants, normality was assumed using

the Central Limit Theorem which states that if sample size is greater than 30, the sample distribution can be safely assumed as normal (39).

Analyses of variance were performed on growth velocity vs. morbidities and average sodium intake for both sets of data (all time points and weeks 2-12). They were also performed on average inadvertent sodium intake and morbidities as well as average calorie intake and morbidities. $P<0.05$ was considered significant.

Pearson correlations were run between average sodium, protein, and calorie intake, gestational age, birth weight and growth velocity at the specific time points as a means of exploring possible relationships. This was used to provide a basis for variables that were entered into a multiple linear regression.

The initial analysis is a description of average sodium, protein, and calorie intake per kilogram from all sources and average weight. Sodium intake averages were compared to recommendations set forth by the American Academy of Pediatrics.

CHAPTER 4

FINDINGS

RESULTS

Study Population

One hundred eighty nine (189) extremely low birth weight infants were admitted to the Neonatal Intensive Care Unit at Women and Infants' Hospital in Providence, Rhode Island from January 1, 2009 through June 30, 2011. Of these, eighteen (18) were transferred from other hospitals, forty two (42) expired prior to week 12 of life, and fifty-eight (58) were enrolled in the NICU protein study, and one (1) was excluded because the electronic medical record was locked by the family and data could not be collected. Seventy ELBW infants satisfied the inclusion criteria for the study. All babies were hospitalized in the NICU through at least 35 days of life. The sample remained essentially stable throughout the first six weeks of life, and three infants were discharged by day 42 (Figure 1).

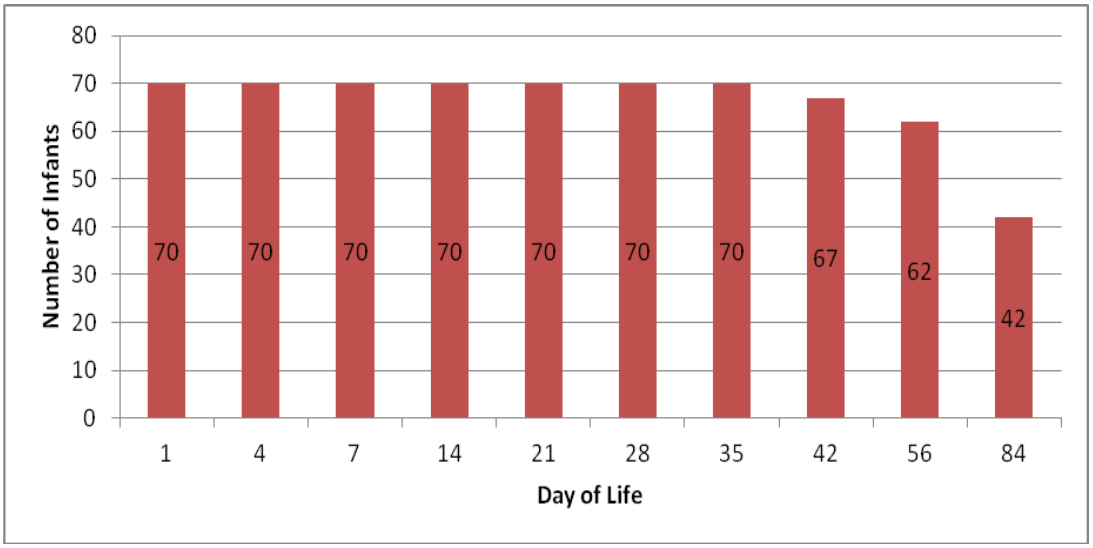

Figure 1. Number of study infants at different time points.

Characteristics of infants enrolled in the study are presented in Table 1 including birth weight, gestational age, length of stay, and gender. Fifteen infants (21%) were considered small for gestational age (SGA) weight -- plotted less than 10% percentile on the Fenton Growth Chart or z score <-1.28 (indicating they were more than 1.28 standard deviations below the population mean). Average calories, sodium, protein and growth velocity for both sets of time points (all time points and week 2-12 time points) can be found in Table 2.

When comparing average sodium intake of the infants at all the time points, the most average sodium per kilogram was given at day 14 (4.52 mEq/kg) (Figure 2). Average sodium, protein, and calories received by the study infants individually can be visualized in Figures 3, 4, and 5.

Available labs for serum sodium (mmol/L) revealed that there were twenty five infants (36%) who experienced hyponatremia (serum sodium <130

mmol/L) and fourteen infants (20%) that experienced hypernatremia (serum sodium >150 mmol/L).

Variable	Mean ± SD or n (%)
Birth Weight (g)	777±151
Gestational Age (weeks)	26.4±2.12
Length of Stay (days)	104±47.4
SGA	15 (21%)
Male	31 (44%)
Female	39 (56%)

Table 1. Descriptive characteristics of infants included in study.

Variable	All Time Points (n=70)		Time Points starting at Week 2 (n=70)	
	Mean	Std Dev	Mean	Std Dev
Avg Calories (cals/kg)	101.5	8.8	116.1	12.2
Avg Sodium (mEq/kg)	2.97	0.69	2.1	0.59
Avg Protein (g/kg)	3.3	0.25	1.8	0.06
Growth Velocity (g/kg/d)	11.58	2.09	10.7	1.8

Table 2. Mean ± standard deviation of average calories, sodium, protein, and growth velocity for both time point sets.

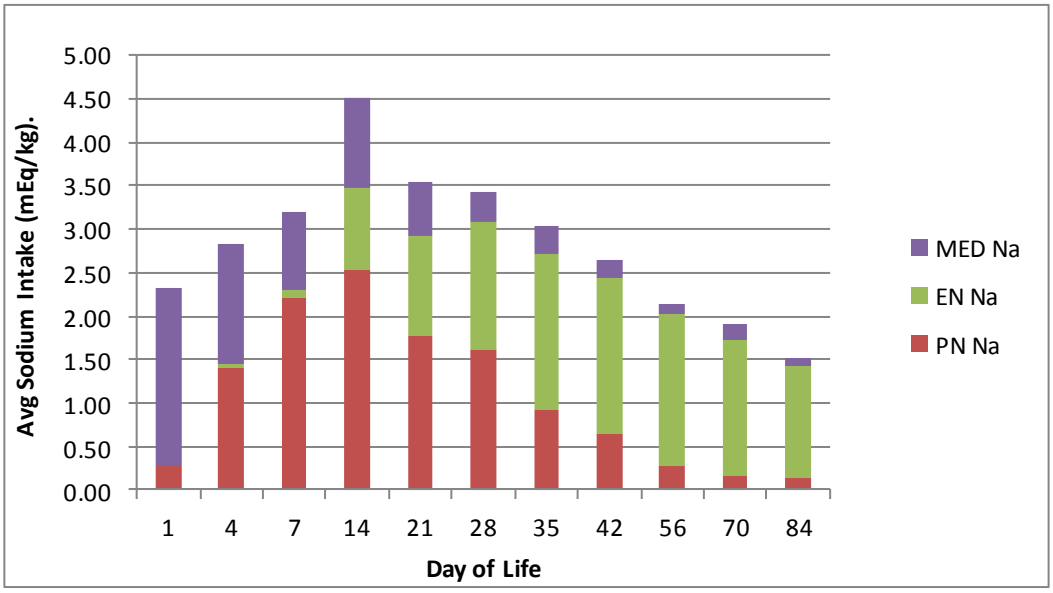

Figure 2. Average sodium intake of all infants (mEq/kg/day) at different time points.

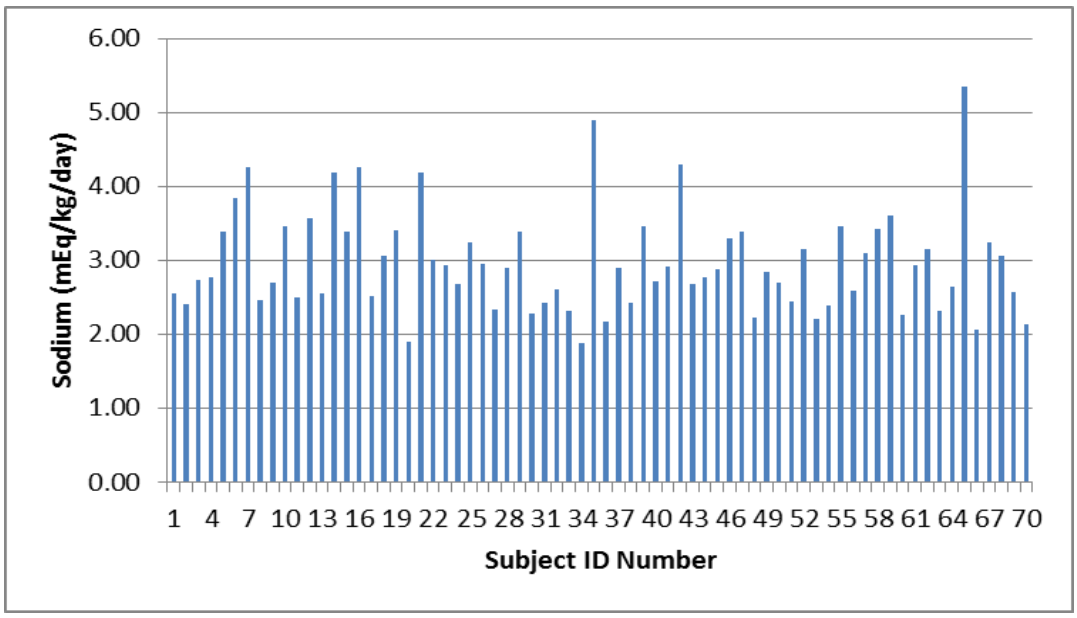

Figure 3. Individual average sodium intake (mEq/kg/d) of study infants.

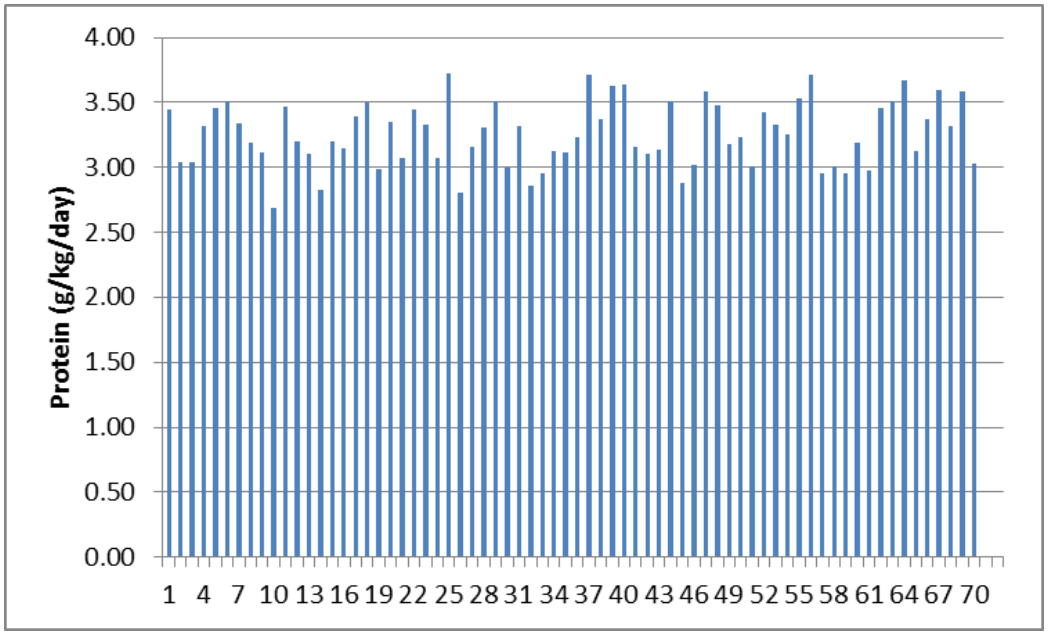

Figure 4. Individual average protein intake (g/kg/d) of study infants.

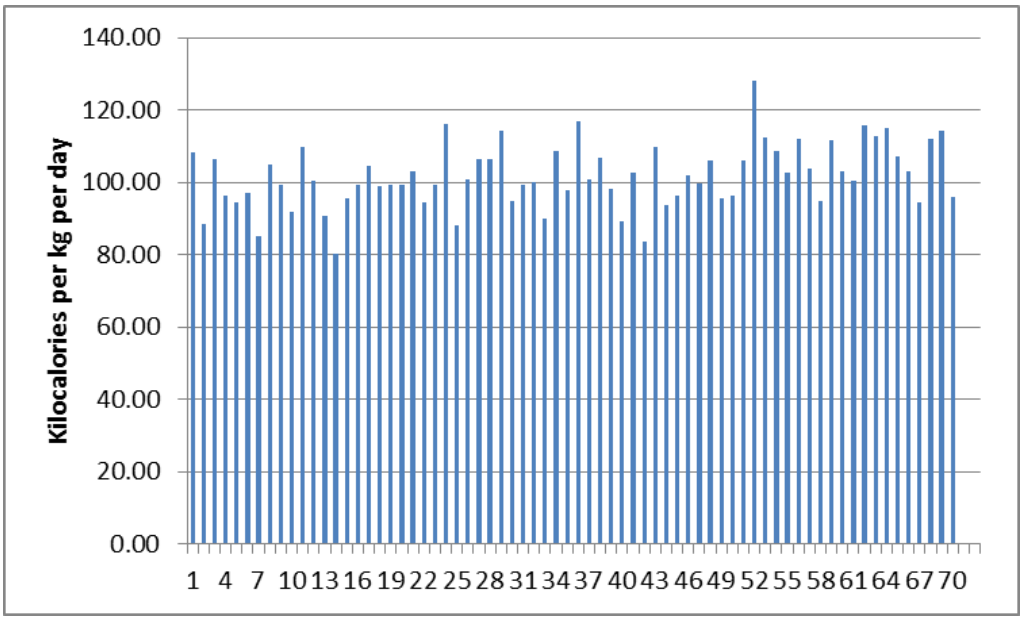

Figure 5. Individual average calorie intake (kcal/kg/d) of study infants.

Growth Velocity vs. Sodium Group

Growth velocities (g/kg/d) were compared between those infants receiving ≥3 mEq/kg of sodium and those receiving <3 mEq/kg of sodium using an analysis of variance with both sets of data (all time points and weeks 2-12). In the all-time point set, 42 infants (60%) received an average of less than 3 mEq/kg of sodium and had a mean growth velocity of 12.01± 1.5 g/kg/day. Twenty-eight infants (40%) received an average sodium intake of ≥3 g/kg/day and had a mean growth velocity of 10.93±2.64 g/kg/day. There was a significant difference found between the two groups (p=0.034) (Figure 6). When time points from only weeks 2-12 were included, 62 infants (89%) received an average sodium intake of <3 mEq/kg and only eight infants (11%) received an average sodium intake of ≥3 g/kg/day. No statistical significance was seen between groups (p=0.8376).

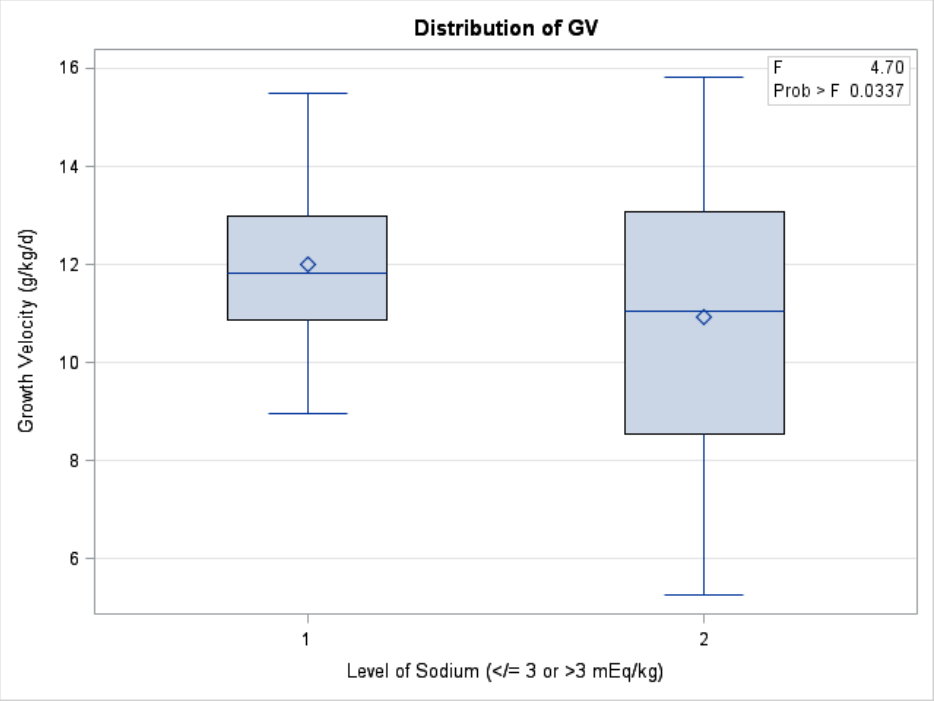

Figure 6. Growth Velocity vs. sodium level [<3 mEq/kg (group 1) or ≥3 mEq/kg (group 2)] all time points.

Average Sodium Intake vs. Morbidities

Thirty infants had no morbidities (43%) and 40 infants (57%) had one or more morbidity. An ANOVA was performed between average sodium intake (mEq/kg/d) and infants with no morbidities and those with one or more morbidities in both time-point sets. In the all-time-point set, there was a significant difference between the amount of sodium received and the number of morbidities [2.7 ±0.51 mEq/kg (none) vs. 3.16±0.75 mEq/kg (1-3 morbidities), p=0.0064] (Figure 7). In the Weeks 2-12 data set, no statistical significance was seen between amount of sodium received no morbidities vs 1-3 morbidities (p=0.61).

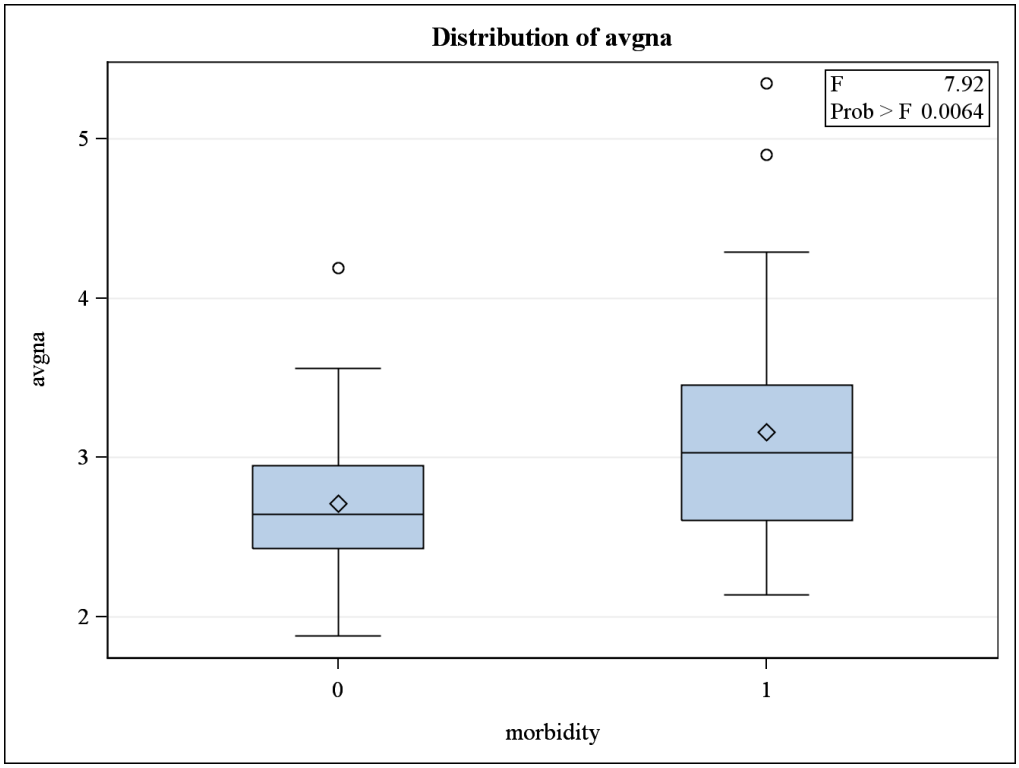

Figure 7. Total number of morbidities vs. average sodium (mEq/kg) all time points. Group 0 = no morbidities; Group 1 = one or more morbidity.

Growth Velocity vs. Number of Morbidities

An ANOVA was performed comparing growth velocity between those infants with no morbidities and those with one or more morbidities. In the all-time-point group, a significant difference was seen between the two groups (12.80±1.3 g/kg/d vs. 10.66±2.11 g/kg/d, p=0.001) (Figure 8). In the 2-12 week time point group, no significant difference was seen (p= 0.0742).

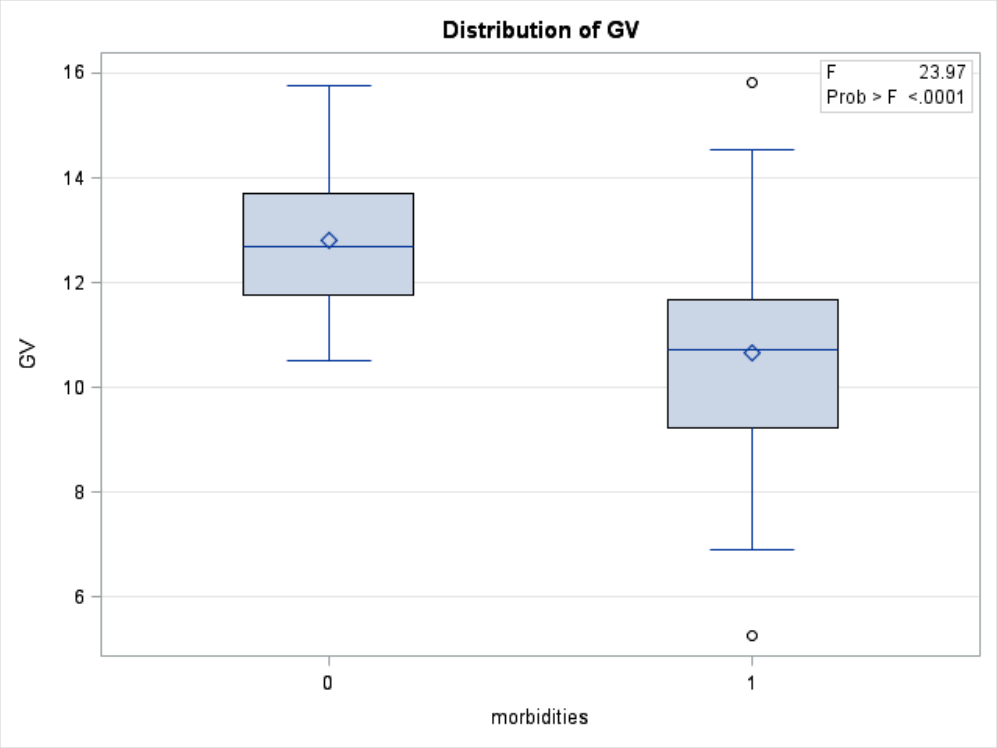

Figure 8. Total number of morbidities vs. growth velocity (all weeks). Group 0 = infants with no morbidities; Group 1 = infants with 1-3 morbidities.

Average Calories Intake vs. Morbidities

Average calorie intake (kcal/kg/d) was compared with two levels of morbidities (none or 1-3) for both time point data sets. In the all-time point group, there was a significant difference between those infants without morbidities compared with those infants with morbidities (104±7.72 kcal/kg/d vs. 99.8±9.2 kcal/kg/d, p=0.036) (Figure 9). In the time point data set from 2-12 weeks, a significant difference was also seen between those infants without morbidities and those infants with one or more morbidity (119.44 kcal/kg/day 113.6 kcal/kg/day, p=0.047) (Figure 10).

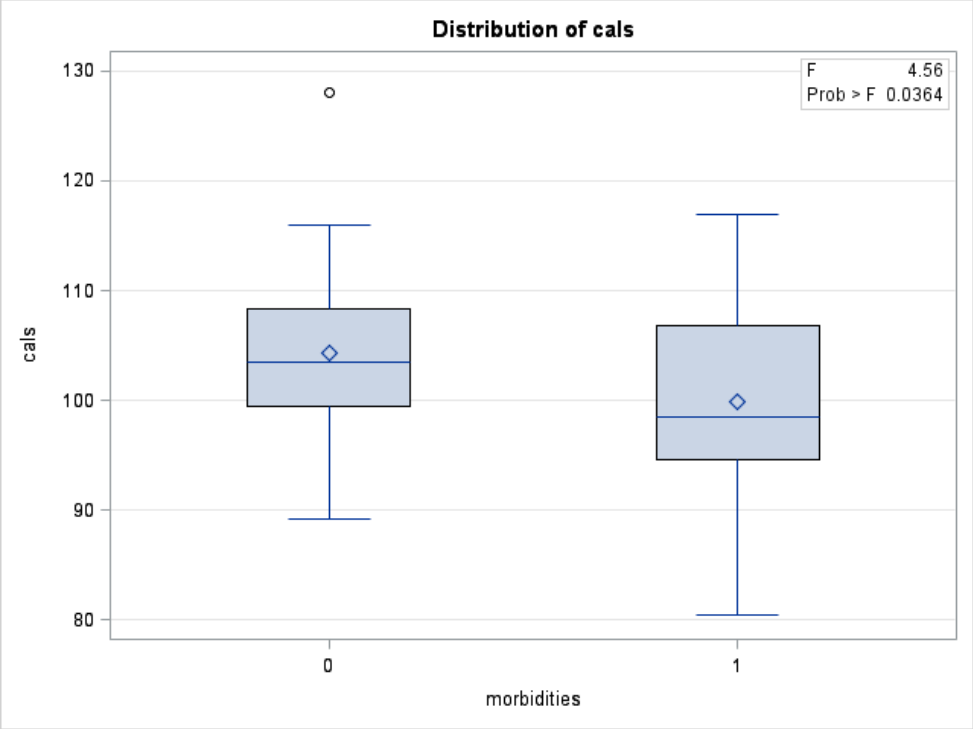

Figure 9 Average Calorie Intake vs. Morbidities for all time points. Group 0 = no morbidities and group 1 = 1 – 3 morbidities.

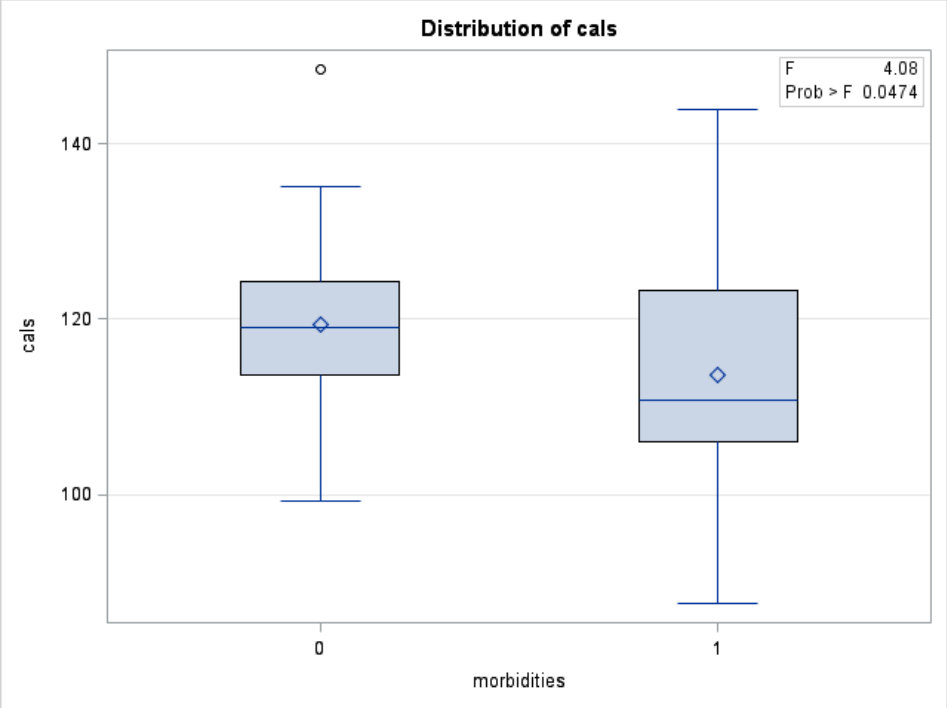

Figure 10 Average Calorie Intake vs. Morbidities for time points weeks 2-12. Group 0 = no morbidities and group 1 = 1 – 3 morbidities.

Average Inadvertent Sodium Intake vs. Morbidities

Average inadvertent sodium intake was compared with the two morbidity sets (no morbidities vs. 1-3 morbidities). The thirty infants without morbidities received 0.39±0.32 mEq/kg/d of sodium via medications and/or intravenous solutions. The other 57% of the infants (1-3 morbidities) received 0.83±0.58 mEq/kg/day of sodium. This revealed a significant difference (p=0.0005). (Figure 11). In the Week 2-12 data set, the thirty infants without morbidities received 0.104±0.22 mEq/kg/d of sodium via medications and/or intravenous solutions. The other 40 infants with 1-3 morbidities received 0.35±0415 mEq/kg/day of sodium. This also revealed a significant difference (p=0.044).

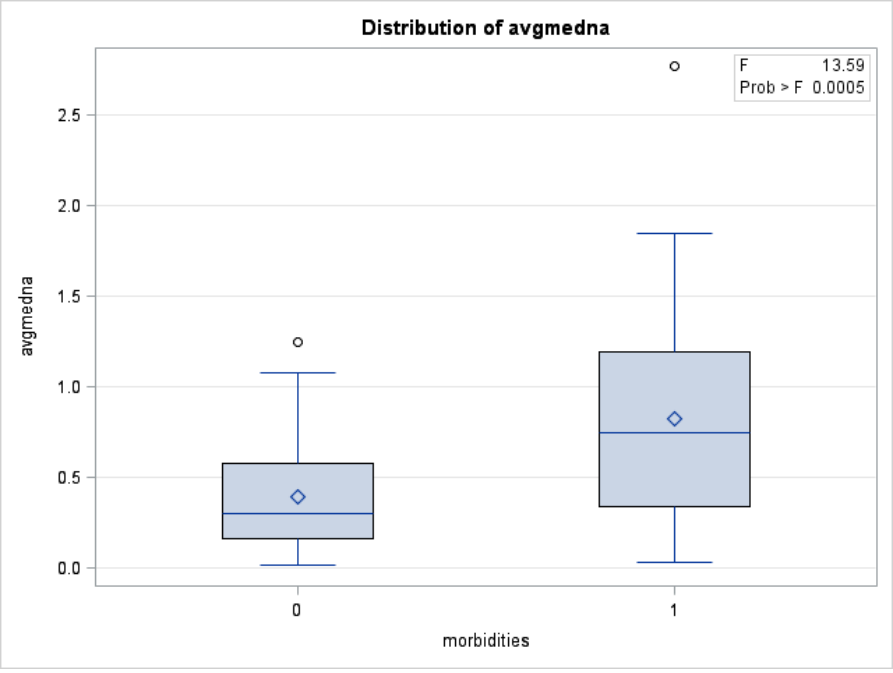

Figure 11 Number of morbidities compared with average inadvertent sodium intake (mEq/kg/d). Group 0 = no morbidities and group 1 = 1 – 3 morbidities.

Pearson Correlations

Pearson correlations were conducted between variables growth velocity; average protein, average sodium, average calories, and birth weight) in the All Time Point data set. Non-significant correlations were seen between growth velocity and average protein (r=-0.010). Moderate correlations and statistical significance were seen between growth velocity and average sodium (r=-0.319; p=0.007); average calories (r=0.399,p=0.001); and birth weight (r=0.332, p=0.005). In the Week 2-12 data set, no significant correlations were seen, thus, no regression analysis was done with this time-point grouping.

Normality

Normality for all variables was examined using the Shapiro Wilk test. Results of this testing is presented in Table 3. While only growth velocity, protein, and calories were considered normally distributed in the all-time point group and only sodium and calories were considered normally distributed in the weeks 2-12 group, normality was assumed for all variables because of the large sample size citing the Central Limit Theorem (39).

Variable	All Time Points		Weeks 2-12	
	Shapiro Wilk	P value	Shapiro Wilk	P value
Growth Velocity	0.98	0.47	0.83	<0.001
Protein	0.98	0.34	0.87	<0.001
Sodium	0.92	0.004	0.97	0.28
Calories	0.99	0.89	0.99	0.97
Birth weight	0.95	0.01	0.95	0.01
Gestational Age	0.92	0.001	0.92	0.001
Length of Stay	0.91	0.001	0.91	0.001

Table 3. Results of the Shapiro Wilk analyses

Regression

A multiple linear regression was used to test if average sodium intake significantly predicted growth velocity. The original model contained growth velocity (dependent variable), average sodium intake (mEq/kg/d), average calorie intake (kcal/kg/d), and average protein intake (g/kg/d). The results of this regression indicated that the three predictors explained 22% of the variance [R^2=0.22, F(3,66)=6.16, p=0.009]. Average protein showed no significance and was removed from the model (Table 4).

The final model included growth velocity (dependent variable), average sodium intake and average calories. The results of this regression indicated that the two predictors explained 20% of the variance [R^2=0.20, F(2,67)=8.71, p=0.004] (Table 5).

Variable	Label	DF	Parameter Estimate	Standard Error	t value	Pr > t
Intercept	Intercept	1	8.08	4.07	1.99	0.05
X1	Avg Protein	1	-0.96	0.94	-1.02	0.31
X2	Avg Sodium	1	-0.702	0.345	-2.03	0.045
X3	Avg Calories	1	0.086	0.027	3.12	0.003

Table 4. Parameter Estimates Original Model

Variable	Label	DF	Parameter Estimate	Standard Error	t value	Pr > t
Intercept	Intercept	1	5.49	3.178	1.73	0.09
X1	Avg Sodium	1	-0.69	0.345	-1.99	0.50
X2	Avg Calories	1	0.0799	0.0268	2.98	0.004

Table 5. Parameter Estimates Final Model.

CHAPTER 5

CONCLUSION

In this retrospective cohort study, it was shown that sodium intake of ELBW infants is suboptimal when compared to the AAP recommendations derived by Zeigler et al's factorial method and the more recent recommendations of the AAP which is 3-5 mEq/kg/d) (2,18). Comparisons of the time points showed the highest amount of sodium per kilogram to be given in the first two weeks of life, and the most was given on day of life 14 (4.52 mEq/kg). This could be related to antibiotics given during that time -- antibiotics that contain large amounts of sodium in their preparation (i.e. ampicillin). Other inadvertent amounts of sodium are administered from arterial lines (which are infused with normal saline), blood products, and resuscitation fluids.

Because more sodium, medications, and blood products are given during the first two weeks of life and because real growth occurs after week two (2), the data were also analyzed from week two through twelve. When all time points were compared with the amount recommended by the AAP (3-5mEq/kg), only twenty-eight infants (40%) received the minimum amount. When analyzed from weeks 2-12, only 11% of the infants received the minimum amount recommended.

Both sets of time point data were then split into two groups in order to compare growth velocity with amount of sodium received using 3 mEq/kg as a

cutoff. When comparing data from all the time points, a faster growth rate was seen in the group given lower amounts of average sodium (12.01± 1.5 g/kg/day vs. 10.93±2.64 g/kg/day, p =0.034) and the same was true using weeks 2-12 although not statistically different. One could assume that this is related to these infants having one or more morbidities. When growth rate of the infants who had no morbidities was compared to those infants with one or more morbidities, greater growth rates were seen in the group with no morbidities (12.80±1.3 g/kg/day vs. 10.66±2.11, p=0.001)

Surprisingly, average protein intake did not appear to be correlated to growth velocity in this sample although other studies have supported such a relationship (4,8). It may have been because many of the infants received close to adequate protein amounts (~3 g/kg/d). In the present study, growth velocity seemed to be better explained by caloric intake rather than sodium or protein intake. It is worth noting that growth velocity averaged only 11.58±2.09 g/kg/day (all time points) and 10.7±1/8 (weeks 2-12), which is substantially below the 15 g/kg/day recommended by AAP (2). Furthermore the factorial method of estimating needs assumes 130 calories, and the infants in this study averaged only 101.5±8.8 kcal/kg (all time points) and 116.10±12.2 kcals/kg (weeks 2-12). It is also noteworthy that when comparing z scores from birth to discharge, only 7 of the infants (10%) increased their z score while hospitalized. This further strengthens the thought that there is still additional work to be done to improve growth outcomes.

When exploring gender and growth velocity, there was a statistical

difference seen between gender and growth velocity in the all-time point grouping (p=0.035). Because the NICU at WIH utilizes just one growth chart (Fenton) (40), a decision was made not to control for this in the analyses.

In the final regression model, average sodium was not a predictor of growth velocity, and it appeared that average calorie amount may have been more important in predicting growth velocity.

LIMITATIONS AND STRENGTHS

Because blood draws are kept to a clinically-necessary minimum in the NICU to reduce the need for blood transfusions, serum sodium values were not available on all babies at all-time points in the way needed for a research study about sodium intake. This also assumes that serum sodium levels are the best way to assess sodium balance in preterm infants. Flushes received at the bedside were not counted in this study as they are not documented in the electronic medical record yet registered nurses do this routinely. The strengths of this study included the sample size and consideration of multiple factors that may impact growth velocity in ELBW infants. Examining sodium from all sources across the entire length of stay for these infants also provided valuable clinical information.

FUTURE RESEARCH

It would be useful to approach sodium administration in a randomized controlled study using the approaches established previously such as delaying the administration of sodium until diuresis occurs and serum sodium is less than 130-135 mmol/L in order to prevent fluid overload. After this diuresis, two

study groups could be formed, controlling for morbidities and level of sodium administration. Methods for documenting inadvertent sodium administration should be implemented in order to quantify total sodium throughout the stay ruling out extra sodium as a cause for morbidities experienced by preterm infants.

APPENDICES

Appendix A

Nutrition Composition of Enteral Feeds

		Protein (g)	Iron (mg)	Calcium (mg)	Vit D (IU)	Zinc (mg)	Na (mEq)	K (mEq)
20	**Human Milk$_{20}$ (HM), Mature**	1.54	0.04	41	3	0.18	1.1	2
22	**HM$_{20}$+Similac HMF$_2$** (50mL:1 pkt)	2.1	0.3	115	83	0.8	1.5	2.9
24	**HM$_{20}$+SHMF$_4$** (25mL:1 pkt)	2.5	0.5	177	149	1.4	1.7	3.6
27	**HM$_{20}$+SHMF$_4$+Neo$_3$/EnfaCare$_3$**	2.3	0.6	169/171	140	1.4/1.3	1.7	3.6/3.5
30	**HM$_{20}$+SHMF$_4$+Neo$_6$/Enfa$_6$**	2.5	0.7	163/166	133/134	1.3	1.7	3.6/3.5
24	**HM$_{20}$+Neo$_4$/EnfaCare$_4$**	1.7	0.3	51/54	14	0.4/0.3	1.2	2.3/2.1
27	**HM$_{20}$+Neo$_7$/EnfaCare$_7$**	1.8	0.5	57/61	20	0.4	1.2/1.3	2.4/2.2
30	**HM$_{20}$+Neo$_{10}$/EnfaCare$_{10}$**	1.9	0.6	62/67	25	0.5	1.2/1.3	2.5/2.2
20	**Enfamil Premature Lipil (PE)**	3	1.8	165	240	1.5	2.5	2.5
24	**PE High Protein$_{24}$**	3.5	1.8	165	240	1.5	2.5	2.5
27	**PE High Protein$_{24}$+SC$_{30}$** (1:1)	3.25	1.8	173	195	1.5	2.2	2.9
20, 30	**Similac Spec Care Adv (SC)**	3	1.8	180	150	1.5	1.9	3.3
24	**SC High Protein$_{24}$**	3.3	1.8	180	150	1.5	1.9	3.3
27	**SC High Protein$_{24}$+SC$_{30}$** (1:1)	3.15	1.8	180	150	1.5	1.9	3.3
≤ 30	**EnfaCare**	2.8	1.8	120	70	1.3	1.5	2.7
≤ 30	**NeoSure**	2.8	1.8	105	70	1.2	1.4	3.6
≤ 30	**Enfamil**	2.1	1.8	78	60	1	1.2	2.8
≤ 30	**GoodStart**	2.2	1.5	67	60	0.8	1.2	2.8
≤ 30	**Similac**	2.1	1.8	78	60	0.8	1	2.7
≤ 24	**Alimentum**	2.8	1.8	105	45	0.8	1.9	3
≤ 24	**Nutramigen**	2.8	1.8	94	50	1	2	2.8
≤ 24	**Pregestimil** (50% MCT oil)	2.8	1.8	94	50	1	2	2.8
≤ 24	**Elecare for Infants**	3.1	1.5	116	60	0.8	2	3.9
≤ 24	**Neocate Infant** (33% MCT oil)	3.1	1.9	124	60	1.7	1.6	4
≤ 30	**Nutramigen AA**	2.8	1.8	94	50	1	2	2.8
≤ 30	**EnfaPort** (84% MCT oil)	3.5	1.8	94	50	1	1.3	2.9

Appendix B
Data Abstraction Tools

Sodium from TPN

ID Number:

Day of Life	Date	Amount (mEq)	Serum Sodium
0			
1			
Yesterday			
4			
Yesterday			
7			
Yesterday			
14			
Yesterday			
21			
Yesterday			
28			
Yesterday			
35			
Yesterday			
42			
Yesterday			
56			
Yesterday			
70			
Yesterday			
84			
Yesterday			

Sodium from Medications and Intravenous Solutions

Day of Life	Date	Medication	Amt Rec	Medication	Amt Rec	Medication
0						
1						
4						
7						
14						
21						
28						
35						
42						
56						
70						
84						
Day of Life	**Date**	**Medication**	**Amt Rec**	**Medication**	**Amt Rec**	**Medication**
0						
1						
4						
7						
14						
21						
28						
35						
42						
56						
70						
84						

Appendix C
Sodium Amounts in Medications (41)

Medications that contain zero sodium	Medication	Amount	Medication	Amount
Amlodipine	Omeprazole	200	Furosemide	13.86
Caffeine Citrate	3% NS	51.3	LR, D5	13
Cefepime	Na Bicarbonate	50	LR	13
Chlorothiazide	Aquadek	43	Oxacillin	12.5
Clindamycin	Packed RBC	31.3	Indocin	12.32
Dexamethasone	Platelets	30.5	Midazolam	10
Diuril	Ampicillin	29	cefotaxime	10
Dobutamine	Ceftazidime	21.85	10 mEq Na/100	10
Dopamine	Fresh Frozen Plasma	17.2	8 mEq Na/100	8
Ergocalciferol	Meropenum	15.455	0.45% NS	7.7
Fat Emulsion	Dopamine w/ NaCL 0.9	15.4	4.6 mEq Na/100	4.6
Fentanyl 200 mcg	0.9% NS	15.4	23.4% NaCl	4.003
fentanyl 50 mcg	Plasmanate	15.4	4 mEq Na/100	4
Fentanyl 500 mcg	Saline Flush (0.9%NS)	15.4	Amphoterin B	3.7
Fentanyl bolus	Cosyntropin	15.34	0.225% NS	3.4
FeSO4	Fentanyl w NaCL 0.9%	15.04	Vecuronium 10 mg vial	3
Fluconazole	Metaclopramide	15	2 mEq Na/100	2
Ibuprofen	Hydralazine	14.63	Tylenol	1.74
Inositol	Albumin, 25%	14.5	hydrocortisone	0.3
Intralipid	Phenobarbitol	14.168	Heparin 100 u	0.154
Morphine	Metronidazole	14	Gentamicin	0.054
Polyvisol w/ Iron	Lasix	13.86	Heparin 25 u	0.0385
Potassium Chloride				

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