The Relationship Between Adverse Events and the Administration of Fluids, Medications, and Blood Products Through an Umbilical Arterial Catheter in Neonates

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Abstract

The field of neonatology lacks adequate research to support or oppose the use of umbilical arterial catheters (UACs) for the administration of most fluids, medications, and blood products. There are recognized risks of having a UAC in place. However, it is unknown whether or not these risks increase with specific infusions. The purpose of this research was to identify and explain any relationships between adverse events and the infusion of fluids, medications, and blood products through UACs. The data collection process included a retrospective chart review of 104 infants in a 12-bed level two neonatal intensive care unit who had a UAC placed. Medical records were examined for the number of indwelling catheter days, the size and position of the catheter, the composition and rate of infusates, and any complications possibly related to UAC use. Researchers examined the significance of any associations between adverse events and infusates and evaluated those relationships for practical significance. Relationships that could not be attributed to additional factors included: packed red blood cell transfusions and secondary port occlusion ($p = .0259$), furosemide and hypertension ($p = .0108$), and caffeine and hypertension ($p = .0367$). Further investigation into the safety of specific infusates is warranted. However, based on the results of this study the authors concluded that adverse outcomes are often not the result of infusions through the line as much as the presence of the UAC itself, and it may not be necessary to completely avoid UAC infusions. In fact, decreasing the pain and risks associated with obtaining additional intravascular access and preserving peripheral vessels for later use may improve neonatal outcomes.

The Relationship Between Adverse Events and the Administration of Fluids, Medications, and Blood Products Through an Umbilical Arterial Catheter in Neonates

Umbilical arterial catheters (UACs) have been common practice in the care of critically ill neonates for 40 years (Caeton & Goetzman, 1985; Marsh, King, Barrett, & Fonkalsrud, 1975; Oppenheimer, Carroll, Garth, & Parker, 1982; Smith & Dills, 2003). However, inconsistencies exist from one hospital to another regarding which infusates are safe to administer through UACs. There is limited research on the topic of side effects caused by the infusion of specific fluids, medications, and blood products. As a result, many providers limit the use of UACs to laboratory tests and blood pressure monitoring. Still others continue liberal use of UACs, without appreciable side effects.

Lack of an evidence-based practice standard may lead to negative effects for patients of the Neonatal Intensive Care Unit (NICU). Neonates in units that practice liberal use of UACs may be suffering undetected short or long-term effects from certain UAC infusates. On the other hand, infants in units that avoid UAC infusions may be enduring the effects of unnecessary intravascular access attempts and the potential risks associated with additional indwelling catheters.

Background and Significance

Current Practice

Although not frequently researched, UACs are still regularly used in NICUs today. However, significant variations exist between institutions regarding which specific fluids and medications are considered to be safe for UAC infusion (Smith & Dills, 2003). In a study by Smith and Dills (2003) medication administration through UACs was found to be

common practice in 37% of NICUs surveyed, and 39% reported using UACs for administering medications only in life-threatening situations. Only 5% of the surveyed NICUs addressed questions regarding what principles their UAC practices were based on, with none of the NICUs reporting research evidence as the basis of their decisions (Smith & Dills, 2003). Current literature is lacking adequate research to support or oppose the use of UACs for the administration of most fluids, medications, and blood products.

Motives for Re-examining UAC Practices

Central venous catheters are difficult to place and carry many risks (Anderson, Leonard, Braner, Lai, & Tegtmeyer, 2008). It also may be challenging to access fragile peripheral vessels, especially in preterm infants (Anderson et al., 2008). Additionally, the pain associated with such procedures will likely affect long-term outcomes for NICU patients (McClain & Kain, 2005). These noxious stimuli can result in negative developmental changes for preterm neonates who are in a period of rapid growth and development (Mountcastle, 2010).

Simons et al. (2003) reviewed daily data regarding the frequency of painful procedures for 151 NICU patients, which included multiple failed attempts at peripheral vascular access. They reported unsuccessful catheter attempts in 30.9% of peripheral intravenous catheters, 45.6% of central venous catheters, and 37.5% of peripheral arterial catheters. According to Simons et al. NICU patients may endure up to 14 painful procedures each day, with most occurring on the day of admission. They also concluded that there is a decrease in the number of venipunctures and heel sticks for those infants with arterial lines present. Mountcastle (2010) suggests that evaluating and changing

umbilical line practices can reduce the number of peripheral punctures and therefore improve outcomes for this population.

The goal of this scholarly project was to compare various practices of fluid, medication, and blood product infusion through UACs. Researchers investigated the incidence of adverse events in neonates with indwelling UACs and studied the relationship between those adverse events and the infusion of fluids, medications, and blood products.

Conceptual Framework

To assist in the organization of this study, a conceptual framework was created that helps to explain the relationship of the concepts involved (see Appendix A). This model incorporates factors that, when combined with UAC use, may contribute to adverse events in the immediate newborn period and lead to long-term effects. Based on information found in the literature, the framework guided the researcher in establishing a list of the possible contributing factors and resulting symptoms for examination in order to explore possible associations.

In addition to guiding the organization of the study, the model provided a frame of reference for interpretation of the research data. Access to the visual guide prompted evaluation of long-term effects that could be attributed to the possible contributing factors. The model also provided a standpoint for determining whether or not the short-term effects occur more often in neonates with UACs that are being influenced by the possible contributing factors.

Review of Literature

Over 200 journal articles were examined for pertinence to fluid, medication, and blood product administration issues in the neonatal patient. Twenty articles were selected

for a literature review and synthesis. Research on this topic is limited and a great number of the available resources were published many years ago.

Hypothesized Risks of UAC Infusions

The frequency and severity of adverse effects, from administering medications through UACs, is not well published. According to Smith and Dills (2003) the negative effects, which create contention for neonatal providers, include thrombosis, embolism, vasospasm, blood vessel perforation, hemorrhage, infection, and hypertension. These complications can be categorized as thromboembolic, mechanical or vasospastic, infectious, and miscellaneous (Caeton & Goetzman, 1985).

Thromboembolic complications. In the neonatal population, around 90% of thrombi are the result of vascular access devices (Greenway, Massicotte, & Monagle, 2004). Vessel wall endothelial damage may trigger the coagulation cascade and lead to thrombus formation, and this response may be heightened in sick neonates (Coleman et al., 2004; Nash, 2006). Umbilical arterial infusions of hypertonic solutions and alkaline medications have also been associated with thrombosis formation in many of 100 reviewed cases of gluteoperineal necrosis (Ramasethu, 2008). However, some of these cases occurred when only heparinized saline was being infused through a correctly positioned UAC (Ramasethu, 2008). Arterial thrombi may be common but are not often clinically evident in neonates, which causes many to remain undiagnosed (Adelman & Morrell, 2000; Caeton & Goetzman, 1985). It is estimated that a mere one to three percent of cases are symptomatic (Revel-Vilk & Ergaz, 2011). Neonates with symptomatic thrombosis, related to the presence of a UAC, often present with dysfunction of the organ distal to the blockage.

The presence of thrombi in the renal arteries may cause decreased blood flow to the kidneys and lead to hypertension and renal failure (Greenway et al., 2004). A thromboembolism may also travel to the limbs, occluding blood flow and causing ischemia of peripheral tissue (Greenway et al., 2004). Necrotizing Enterocolitis (NEC) and other intestinal pathology are also thought to be associated with the presence of UACs (Havranek, Johanboeke, Madramootoo, & Carver, 2007; Kosloske, 1984; Nash, 2006). One possible reason for this association is that UAC related thrombi occlude superior mesenteric artery (SMA) blood flow (Greenway et al., 2004; Havranek et al., 2007). Although controversial, another thought is that the physical presence of the UAC catheter partially blocks blood flow to the SMA (Havranek et al., 2007). However, Havranek et al. (2007) conducted a study that showed no statistically significant difference between SMA blood flow velocity before and after UAC removal.

Mechanical and vasospastic complications. In addition to obstructing blood flow and damaging vessel endothelial cells, umbilical catheters may lead to vessel perforation. Complete arterial perforation may occur and result in hemorrhage (Caeton & Goetzman, 1985).

Another concern for arterial catheters is the reality that vasospasm can occur by various mechanisms. Vasospasm may be the result of introducing a catheter into the artery or infusing vasotoxic agents (Caeton & Goetzman, 1985). However, due to blood flow differences, vessel injury from irritating solutions is more likely to occur in a peripheral vein than in the arterial circulation (Marsh et al., 1975).

Perhaps the most frequently reported factor related to arterial vasospasm is catheter position. Yet, the available literature is somewhat inconsistent with regards to

determining the correct position of UAC catheters. Many providers will consider a catheter tip between thoracic vertebrae six to ten (T6-T10) to be in an acceptable high-lying position. A catheter tip positioned at the level of lumbar vertebrae three to four (L3-L4) is typically considered low-lying. Historically, the standard of care typically consisted of using low-lying UACs (Oppenheimer et al., 1982). However, a fact that remains consistent among the more recent literature is that the incidence of vascular compromise is decreased with higher UAC placement (Nash, 2006; Ramasethu, 2008; Revel-Vilk & Ergaz, 2011). According to Smith and Dills (2003) the incidence rate of low-lying UAC complications is 78%, compared to 39% for those in a high position. Nash (2006) reported that a Cochrane Collaboration review led to the recommendation of the exclusive use of high-positioned UAC catheters.

Infectious complications. As with most procedures in the immune-compromised neonatal population, the placement and use of UACs increases infection risks (Anderson et al., 2008; Caeton & Goetzman, 1985; Furdon, Horgan, Bradshaw, & Clark, 2006; Nash, 2006; Ramasethu, 2008; Smith & Dills, 2003). Along with the possibility of contamination during insertion, bacteria can be introduced through a catheter anytime it is accessed. Once the access site becomes colonized, the infectious agent migrates into the bloodstream (Furdon et al., 2006). There is a five-fold increase in the incidence of catheter related sepsis when the catheter is manipulated an average of 3.2 times per day (Furdon et al., 2006).

Miscellaneous complications. Accessing UACs for blood sampling poses additional risks, other than introducing infection. In a study by Jackson et al. (2004) significant hemolysis occurred when a hypotonic solution and placental red blood cells (RBC)s were in stagnant contact for 60 seconds. Hemolysis also occurs when dextrose and

RBCs are inertly mixed, such as would occur in the waste syringe during a UAC blood draw (Jackson et al., 2004).

Specific agents. Most of the available literature describes complications that arise from the mechanics of having a UAC in place. However, research relating to the arterial effects of specific infusates is scarce.

As mentioned above, arterial vasospasm can result from the introduction of vasotoxic substances (Caeton & Goetzman, 1985). In a survey with 130 NICU respondents, six reported the occurrence of vasospasm in at least one patient after the administration of dopamine through an umbilical venous catheter (UVC) or UAC (Smith & Dills, 2003). Three reported vasospasm associated with UAC administration of dobutamine and two reported the same effect from sodium bicarbonate (Smith & Dills, 2003). The only other problem to be reported by more than one NICU was blanching, which occurred in two NICUs after dopamine was infused through an umbilical line (Smith & Dills, 2003).

One source mentioned a significant increase in proteinuria, hematuria, and thrombosis when ampicillin and/or gentamicin were infused through a UAC (Book & Herbst, 1980). This may be due to inadequate mixing of the medication into the blood stream and higher concentrations streaming into aortic branches leading to end organ damage (Book & Herbst, 1980). In a study by Book & Herbst (1980) high concentrations of dextrose, ampicillin, and sodium bicarbonate were found to cause intestinal lesions when rapidly injected into the mesenteric arteries of rabbits. Infusion of these medications through low-lying UACs, with the catheter tip just above the mesenteric arteries, is more likely to be the cause of intestinal problems (Kosloske, 1984).

Total parenteral nutrition (TPN) is another agent that seems to be of concern for providers when making decisions about UAC use. Endothelial damage can occur, and lead to thrombosis, with the use of long-term TPN therapy (Revel-Vilk & Ergaz, 2011). However, Kanarek, Kuznicki, and Blair (1991) found no significant difference when comparing the incidence of complications between UACs and central venous catheters in regards to TPN infusion. That study, which was conducted over 20 years ago, concluded that infusion of TPN through an umbilical artery is an acceptable practice that may decrease the need for immediate additional vascular access (Kanarek et al., 1991).

Methods

Data collection began after approval was obtained from the Department of Clinical Studies at the local facility. The data collection process consisted of a retrospective chart review of infants with UACs placed during 2011-2013 in a 12-bed level two NICU in the Upper Midwest region of the United States. A convenience sample of 104 infants was used. Exclusion criteria included those infants who were transferred to another facility during the first day of life. Researchers examined available data from electronic medical records through February 2014. Therefore, some infants were followed as long as three years post NICU discharge. Researchers did not have interaction with the subjects, and gathered information was kept private with all patient identifiers removed.

For the purpose of this study, fluids were grouped according to the type and additive. However, information detailing the amounts of each additive was available to the researchers when further evaluation was necessary. Lipid infusions were classified as medications instead of fluids, because they did not contain heparin and did not run

continuously for 24-hour periods. Information regarding the dose and rate of each medication was available, but not differentiated in statistical analysis of the data.

Data was not analyzed for those patients with congenital renal disease or neurological problems of known etiology, since the diagnoses were known to be unrelated to UAC placement or infusions. Medical problems and diagnoses documented by a Neonatologist or other healthcare professional were included. The vasospasm category included documented dusky or blanched extremities. Difficulty digesting enteral feedings was a documented medical problem that incorporated increased gastric residuals and vomiting. The category labeled as NEC suspicion included all work-ups to rule out NEC and treatments for possible NEC until disproven. Acquired renal issues included elevated blood urea nitrogen and creatinine levels and decreased urine output, as documented by a healthcare provider in the EMR problems and diagnoses lists. The IVH category was comprised of five Grade I, one Grade III, and one Grade IV, diagnosed by cranial ultrasound. Included in the neurological diagnoses of unknown etiology were cerebral cysts with no evidence of hemorrhage, choroid plexus cysts, arachnoid cysts, hydrocephalus, and hearing loss of unknown origin.

Medical diagnoses from the time of birth through the time of data collection were included for the majority of subjects. However, long-term data was unavailable for a limited, but unknown, number of patients who received follow up care in outlying healthcare systems.

Results from the data collection were entered into a *Microsoft Excel* worksheet for the purpose of descriptive and comparative analysis. Descriptive statistics were used to define characteristics of the study population such as birth weight, gestational age at birth,

and number of days with a UAC in place. Nominal data were evaluated for statistical inference using an online tool by *GraphPad Software* (2014). Fisher's two-tailed exact probability scores were calculated to assess possible relationships between umbilical arterial infusions and adverse events, and to determine statistical significance of existing relationships. All statistically significant relationships were further evaluated for practical significance and alternative causal factors.

Results

Subjects ranged from 24 6/7 to 41 6/7 weeks gestational age at birth, with a mean of 35 weeks. The average birth weight of the sample was 2519 grams and birth weights ranged from 761 grams to 5866 grams. The number of UAC days per neonate in this NICU ranged from two to 23, with a median of six days and average of nine days. However, seven neonates were transferred out of the facility with an indwelling UAC, and no follow up data was available regarding total number of UAC days after transfer.

Size 5-French catheters were used in 58 of the infants, 3.5-French catheters in 44 infants, and the remaining two subjects had a 5-French inserted initially then replaced with a 3.5-French. Dual lumen catheters were used in 84 infants, single lumen in 19 infants, and one infant had no documentation of the number of lumens present.

Catheter tip position in relation to the thoracic vertebrae on radiologic studies generally ranged from T6 to T10. However, in nine infants the catheter tip was found to be as high as the level of T5 on at least one X-ray film. In one case, the UAC was used while positioned at a level of T11 to T12. Additionally, low-lying catheters were used without incidence in two of the infants.

Various heparin containing continuous infusions were administered through the catheters. All crystalloid maintenance fluids contained 0.5 units/mL of heparin, regardless of infusion rate. The most commonly used solutions were TPN, sodium chloride, dextrose, and dextrose with calcium gluconate. See Figure 1 for a complete breakdown of the number of patients receiving each fluid group through the UAC.

The infants in this study received at least one dose each, of anywhere from one to 12 different medications, through the UAC. Ten percent of the neonates received two different medications in the UAC, 27% received three medications, 31% were given four medications, and six different medications were administered to 12% of the study sample (see Figure 2). Ampicillin and gentamicin were the most commonly infused medications, each with 97 infants receiving these medications through the UAC. Some of the more controversial UAC drug administrations included: sodium bicarbonate to six infants, vancomycin to five, phenobarbital to seven, nine patients received indomethacin, and three were given dopamine through the UAC. A complete list of the medications and number of infants receiving each is included in Figure 3.

Packed red blood cell (PRBC) transfusions were administered through the UAC of five infants, fresh frozen plasma and cryoprecipitate were delivered via the UAC to three infants, and one received a platelet transfusion through the UAC. Numerous other blood product transfusions were given through additional documented sites, and there were a small number of transfusions through undocumented routes.

There was no incidence of blood vessel perforation, hemorrhage, or central line infection in this study sample. Thrombus formation was diagnosed in two of the neonates and three infants had a vasospastic episode. Seven subjects were diagnosed with

intraventricular hemorrhage (IVH): one grade-four IVH, one grade-three, and five grade-one. Six of the infants underwent a workup to rule out NEC during their NICU stay, none of which were confirmed diagnoses. Fourteen of the infants had documented complications with digestion of enteral feeds and four others experienced episodes of hematochezia. Renal and aortic ultrasounds were performed on ten infants. The studies were performed on four infants to evaluate hypertensive episodes, three to investigate recurrent urinary tract infections, two to rule out congenital anomalies associated with cleft palate, and one infant had a series of aortic ultrasounds to re-evaluate a fibrin sheath that was serendipitously found during an echocardiogram. Figure 4 includes a comprehensive graph of the incidence for each of the adverse events included in this study.

All of the documented adverse events and medical diagnoses were compared to each infusate (see Tables 1-12). Renal disease was shown to be associated with UAC infusion of sodium chloride with dextrose and calcium gluconate ($p= .0288$). Difficulty in digesting enteral feeds was positively correlated with ceftazidime ($p= .047$). There was a relationship between hematochezia and ranitidine ($p= .0385$), and UAC platelet infusion ($p= .0385$). Hypertension was associated furosemide ($p= .0108$) and caffeine citrate maintenance infusions ($p= .0367$). Intraventricular hemorrhages occurred more often in those receiving caffeine citrate loads ($p= .0092$) and caffeine citrate maintenance infusions ($p= .0134$). Those infants with secondary UAC port occlusions more frequently received sodium bicarbonate ($p= .0378$), insulin continuous drips ($p= .0028$), and PRBC transfusions ($p= .0259$). Relationships existed between thrombocytopenia and 10% dextrose boluses ($p= .0481$), ranitidine ($p= .0096$), and platelet transfusions ($p= .0096$). Vasospasm occurred more frequently in those receiving ranitidine ($p= .0288$) and platelet transfusions

(p= .0288). There were no statistically significant associations between UAC infusates and oozing at the insertion site, diagnosed thrombus formation, NEC suspicions, or neurological issues of unknown etiology.

Discussion

Due to the multifactorial nature of the etiology behind adverse events in this population, it is difficult to prove a single cause for each event. The most effective method to determine whether administering certain infusates has led to a specific diagnosis is to consider all factors when examining the relationship between infusates and complications.

Line Complications

Occlusion of the secondary UAC port occurred in six infants. However none of those six had documented thrombus formation or other effects related to the occlusion. One occlusion occurred on DOL 16, five days post PRBC transfusion through the line. Another secondary UAC lumen, through which a PRBC transfusion was administered, began flowing sluggishly the following day and occluded two days later. This NICU does not routinely administer a continuous heparinized solution through the secondary UAC ports. Although the stagnancy of the lines should be taken into account, the administration of blood products through the UAC cannot be ruled out as a factor in the secondary lumen occlusions. Avoiding UAC infusion of PRBCs is recommended. If the UAC is the only option, providers should consider adding a continuous infusion of heparinized solution through the secondary port when not in use. The relationship between sodium bicarbonate and line occlusion is weakened by the fact that one patient received a single dose 14 days prior to occlusion, and the other a single dose nine days prior. Secondary port occlusion occurred 13 days after the discontinuation of an insulin drip on one patient, and five days

after a six-day continuous insulin infusion for another patient. Although it is most likely that neither sodium bicarbonate nor insulin drips caused the occlusions in these patients, providers should remain aware of the potential for line occlusion with these medications.

Oozing of blood at the site of insertion was a complication for two of the subjects. However both incidences resolved without further complications and were not likely related to the infusates.

Effects of line positioning, on the relationship between infusates and outcomes, were not examined since the research site primarily uses high-lying positions and the exact position varied within each patient from day to day. One case from this study is worth noting with regard to the effects of line position. An approximately 3,000-gram infant was born between 32-34 weeks gestation to a Type I diabetic mother who was very well controlled throughout the pregnancy. Hypoglycemia was diagnosed and treated in the immediate postnatal period. Glucose, TPN, and medications were infused through a UAC. However, hypoglycemia persisted and worsened over a seven-day period, at which time TPN with 22% dextrose was being administered at 183mL/Kg/day. Providers decided to reposition the UAC from a level of T10 to a low-lying position, under the suspicion that dextrose may have been flowing directly into the celiac artery. Within three days after repositioning the UAC hypoglycemia had resolved and 10% dextrose was infusing at 16mL/Kg/day. The researchers in this study agree with the literature that it is important to place the catheter tip in a position where adequate mixing of infusates with aortal blood flow can occur before delivery into the aortic branches. Zheng et al. (2013) reported the average left ventricular cardiac output of neonates to be above 200 mL/Kg/minute, for term and preterm neonates. This information indicates that blood volume through the

aorta is abundant. Inadequate mixing should not be an issue when the catheter tip is positioned distal to the aortic branches, especially considering the low volumes and rates used in neonates. Knowledge of neonatal physiology needs to be considered when providers are making decisions about what can be infused through a line, especially if the line has migrated or is in a questionable position.

Evaluation of Outcomes

Increased infection risk related to frequently accessing the UAC did not prove to be an issue in this study. There were no central line infections despite the number of times the UACs were accessed for medication administration. Diligent care of the access site and aseptic technique are as effective for preventing the spread of infection as limiting the use of UACs for medication administration.

Since there was no incidence of vessel perforation or hemorrhage in this study, there is no data to link specific infusates to these complications. However vessel perforation and hemorrhage are likely the result of the presence of a line, not necessarily the solution being infused. Similarly, arterial thrombus formation was not significantly related to any of the infusates in this study, which is an indication that thrombi are also likely a result of the mere presence of a catheter in the artery.

Vasospasm. Although there was a significant relationship between vasospasm and ranitidine, there was only one patient in this study who received ranitidine through the UAC. This infant had been receiving intermittent Ranitidine doses one to two times per day through the UAC. After three days the infant experienced an episode of vasospasm, which resolved with repositioning of the UAC catheter. The infant continued to receive one to three doses of Ranitidine per day in the same site without further complications. This

explanation is consistent with literature relating arterial vasospasm and catheter position. However, with a subset of only one patient, there is not enough data to discount ranitidine as a vasotoxic agent and cause of vasospasm in this case. Therefore, ranitidine should be considered vasotoxic until proven otherwise. The issue of a small sample size also prevents researchers from disproving an association between platelets and vasospasm.

The results of this research varied from the literature with regards to an association between dopamine and vasospasm. None of the subjects receiving sodium bicarbonate or dopamine experienced vasospasm or blanching. The Fisher's two-tailed probability score comparing dopamine and vasospasms was p=1 in this test, indicating no relationship between the two variables. Dobutamine was not infused in the UAC for any of the 104 subjects; therefore data is not available to evaluate a possible relationship with vasospasm.

Intraventricular Hemorrhage. The association between caffeine citrate and IVH is a prime example of the value of assessing for practical significance. When evaluating the three patients with IVH who had received caffeine citrate through the UAC, researchers discovered that all three were diagnosed with IVH prior to caffeine citrate treatment. Additionally, the infants were at high risk for IVH based on their gestational age alone, and follow up cranial ultrasounds after the start of caffeine citrate showed no changes in severity.

Gastrointestinal Effects. Two of the three infants who received ceftazidime through the UAC also had difficulty digesting, which indicated a statistically significant association between the two variables. However, the relationship was not practically significant. One infant had difficulty digesting since birth, was placed on ceftazidime on DOL 10, with no change in digestion after the start of the medication. The other infant was

placed on ceftazidime for NEC precautions, due to increased gastric residuals. Therefore, in both cases ceftazidime in the UAC can be ruled out as a cause of slow digestion. The relationships between hematochezia with ranitidine and platelets can also be discounted, as the only patient in the study who received ranitidine and platelets received them after the diagnosis of hematochezia was documented.

Hypertension. The significance of the relationships of hypertension with furosemide and caffeine citrate cannot be disregarded. Typically the sickest neonates are the ones who develop hypertensive issues and the ones usually receiving such medications. However, in this study the mean gestational age (33 6/7 weeks) and birth weight (2554 grams) of those who developed hypertension are similar to the mean gestational age and birth weight of the entire sample population. Since low gestational age and birth weight are often indicators of sicker infants, the similarity between the two groups does not suggest those with hypertension are sicker. Other factors would need to be considered before making such a determination.

Thrombocytopenia. This is another example of the degree to which limited sample size affects association values. Since only one subject was diagnosed with thrombocytopenia, receiving medications not frequently given to the entire population will carry more weight when determining probability significance. This is especially true in this case as the same patient was also the only subject of the study to receive ranitidine and platelets through the UAC. An association between the variables can be disproven in this case, because the platelets and ranitidine were not administered prior to the diagnosis. However, because of the small sample size, the probability of a significant relationship

cannot be confirmed or disproven. Providers need to take into account this possibility when administering platelets and ranitidine through the UAC of a neonate.

Evaluation of Infusates

Aside from the secondary lumen occlusions, documented adverse events for those infants receiving blood products through the UAC can be explained. One infant was diagnosed with IVH but the diagnosis arose prior to blood product transfusion. Two infants experienced slow digestion, but did not worsen after the UAC was used for blood product administration. An infant who received two PRBC transfusions through the UAC on DOL 14 presented with hypertension eight days later. Renal ultrasound on this neonate revealed elevated resistive indices but no blood clots were discovered. The hypertension was medically managed and resolved, with the infant having two weeks of stable blood pressures off medications prior to discharge.

Concerns from the literature regarding TPN infusions did not prove to be valid in this study. There was no significant relationship between TPN and thrombi from endothelial damage. It can be concluded that TPN infusion through UACs is not detrimental to the wellbeing of term and preterm neonates. This information should be taken into account when making decisions regarding obtaining additional intravascular access for infants requiring UACs for blood sampling. The risks of administering TPN through a UAC should be weighed against the risks associated with painful procedures and the introduction of infection when attempting to gain additional access.

The findings in this study are inconsistent with available literature with regards to the effects of many medications. Ampicillin and Gentamicin infusions through the UACs did not increase the incidence of proteinuria, hematuria, or thrombosis. In fact there were no

reported cases of proteinuria or hematuria in this study, and the incidence of thrombus formation was only two percent in the sample population. Additionally, the few patients who did not receive either Ampicillin or Gentamicin via the UAC did not experience a decrease in the rate of digestion difficulties, hematochezia, or NEC suspicion.

Subjects in this study who received vecuronium, acyclovir, alprostadil, and fentanyl through the UAC had no related adverse effects. Additionally, many diagnoses noted with the use of other infusates can be attributed to various factors.

Another medication that many providers are hesitant to infuse through the UAC is dopamine. Of the three patients in this study who received dopamine, one had thrombus formation no other complications were noted. Dopamine was administered to this infant on DOL 2 & 3. Peripheral and arterial blood pressures remained similar to each other during and following dopamine infusion. An echocardiogram was performed at five weeks of age to rule out coarctation of the aorta, due to slightly differentiated blood pressures in the right arm and left leg. A fibrin sheath was discovered, extending from the diaphragm to the aortic bifurcation. The main renal arteries and superior mesenteric arteries remained well perfused. Blood pressures returned to normal and the infant remained asymptomatic until complete resolution of the clot at 14 months of life. Treatment consisted of low molecular weight heparin therapy, with a change to aspirin therapy during the five weeks prior to resolution. Other risk factors for this infant included birth weight less than 1,500 grams, gestational age at birth less than 29 completed weeks, 15 days with the UAC in place, and administration of eight different medications through the line.

Limitations and Recommendations

Although the size of the overall sample population was adequate, the number of infants receiving certain infusates was minimal. Additionally, there were a number of medications not included in the study, simply because they were not administered through the UACs of study participants. Further research on specific medications and blood products is warranted to develop an inclusive list of safe versus unsafe UAC infusates.

Information about diagnoses was dependent on the providers' adequate documentation of findings. Investigation of laboratory values may have been valuable in the discovery of additional adverse outcomes, but was not performed due to time constraints. Additionally, a number of infants were transferred out of the facility. Medical records were not attainable for those subjects from the time they were transferred out until their return to the local healthcare system for post discharge care. Although most infants received follow up care within the studied healthcare system, long-term records were not available for those few patients seeking healthcare outside of the system. A prospective study would be helpful in improving the comprehensiveness of findings documentation, as providers would be impelled to record all observations and diagnoses that could be linked to the study topic. Another benefit of prospective research is an improvement in long-term follow up through continuing communication with primary care providers.

The studied facility reported only a few isolated problems with the accuracy of blood samples from UACs, and indicated that redrawing the samples corrected the inaccuracies in almost all cases. However, an investigation into the effects of various infusates on the accuracy of laboratory values is recommended. Procedures should be

developed and followed to reduce the possibility of blood sample contamination by fluids and medications in the UAC.

Conclusion

Most practices regarding the use of UACs for the administration of fluids, medications, and blood products are not evidence based. This study demonstrated that there may be misconceptions about the dangers of more liberal UAC use. While there are risks associated with UACs, adverse outcomes often were not the result of infusions through the line as much as the presence of the UAC itself. Premature and sick neonates endure pain and stress on a regular basis, most often in the first days of life. If a UAC is necessary for monitoring pressures and obtaining blood samples, the routine administration of fluids and medications through the line may be a way to avoid inflicting unnecessary pain and stress. Providers should consider neonatal physiology and pharmacodynamics of medications, as well as employ common sense, when assessing the risks of infusions through UACs.

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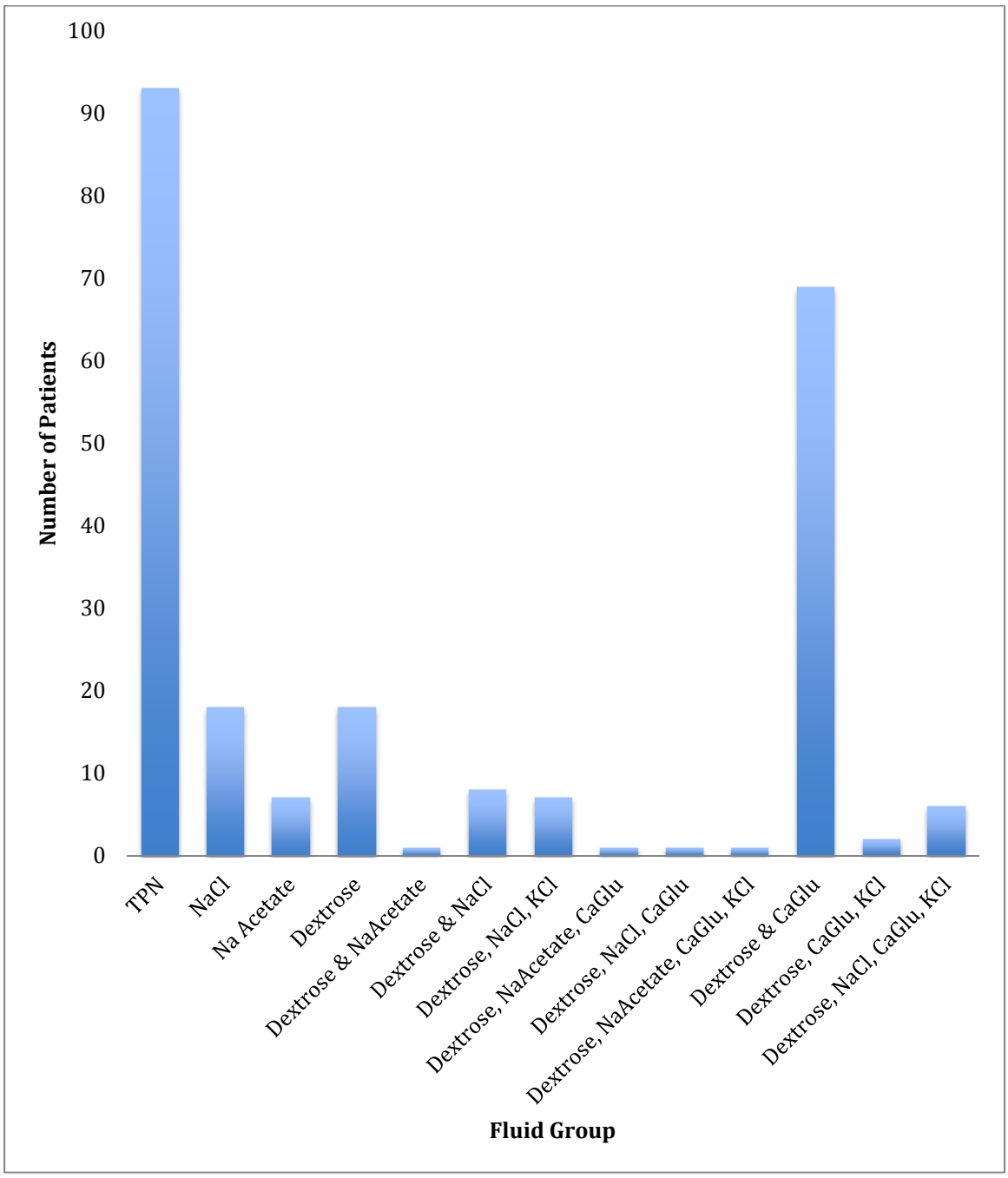

Figure 1. The Number of Patients Receiving Each Fluid Group. TPN= Total Parenteral Nutrition; NaCl= Sodium Chloride; NaAcetate= Sodium Acetate; KCl= Potassium Chloride; CaGlu= Calcium Gluconate

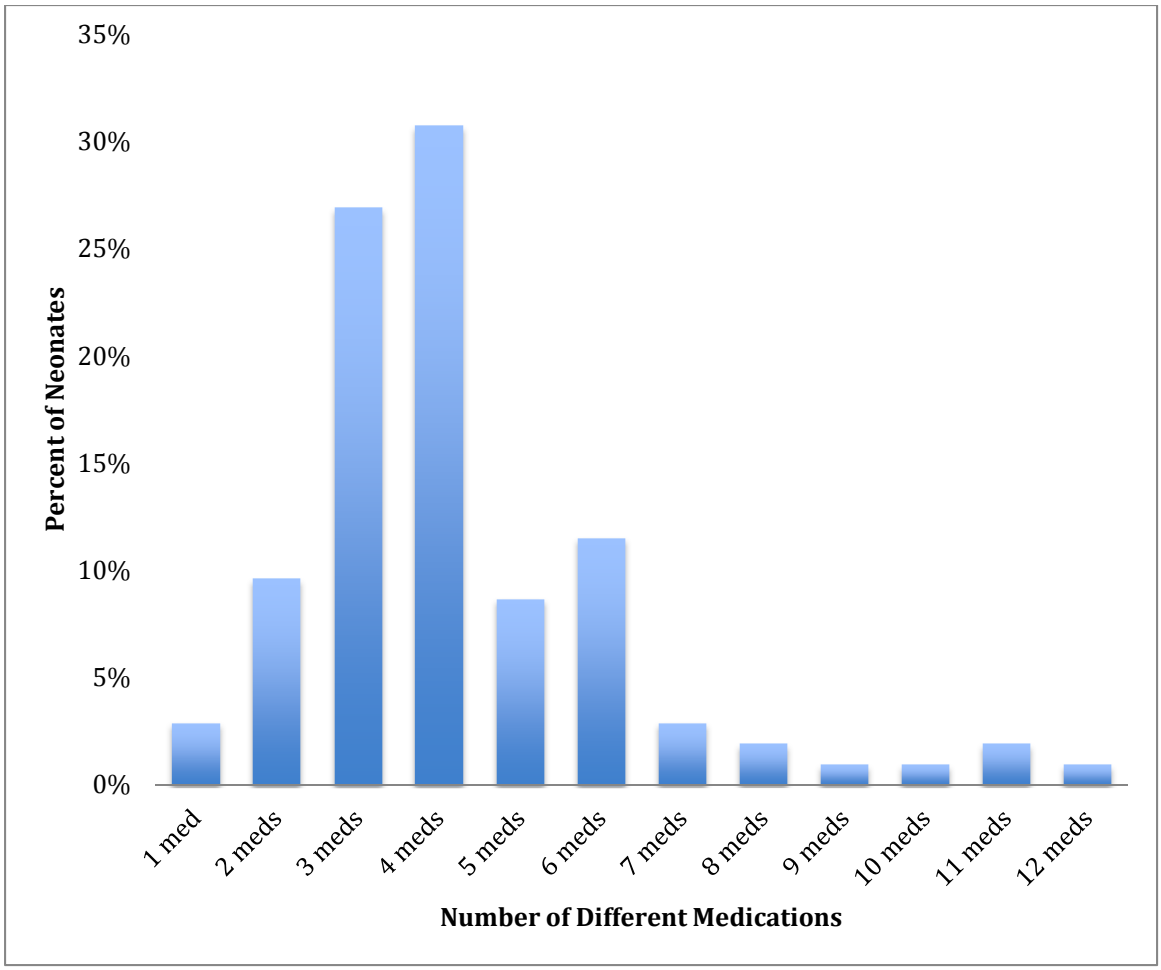

Figure 2. Percentage of Infants Receiving a Various Number of Different Medications Through an Umbilical Arterial Catheter.

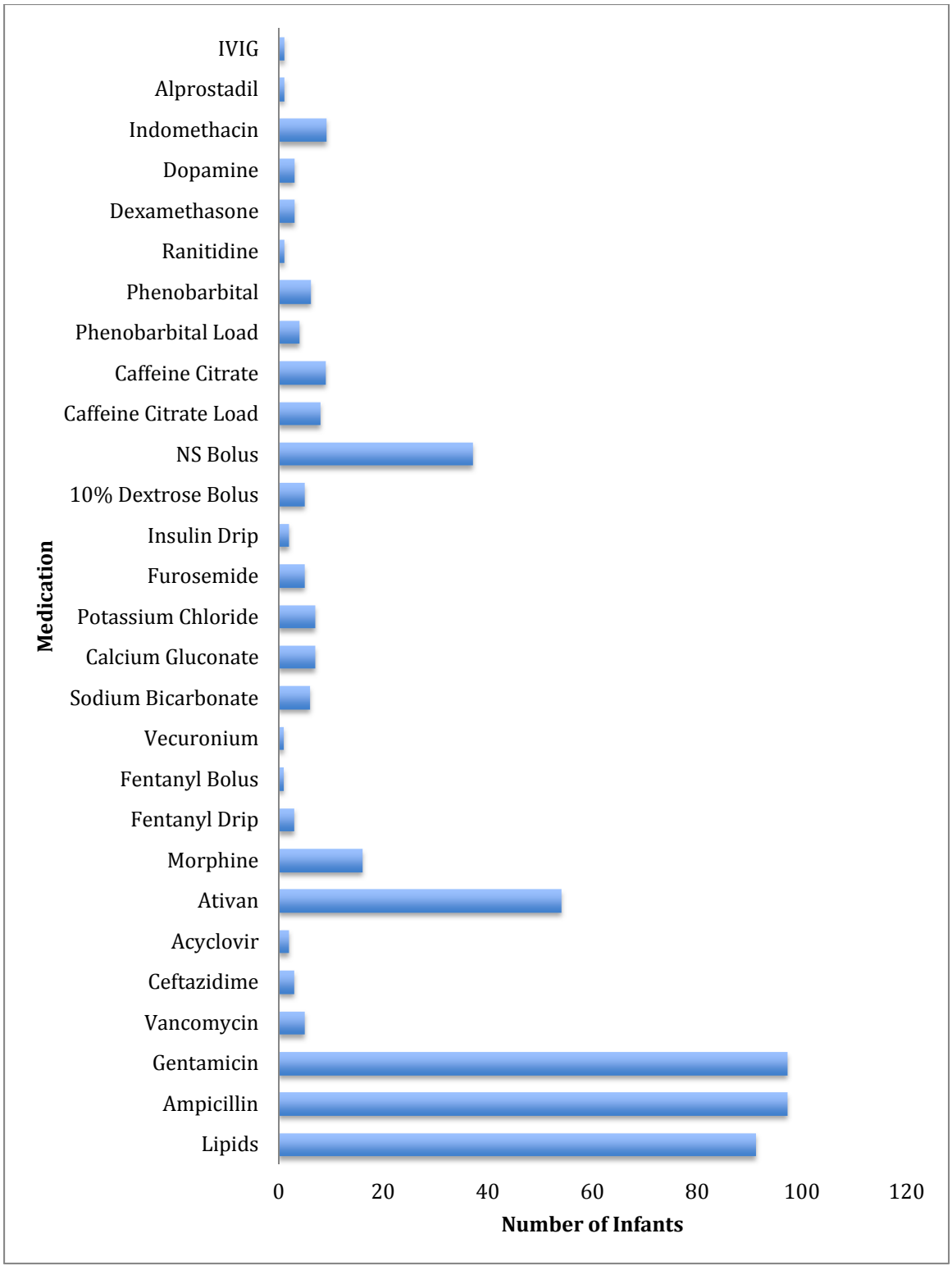

Figure 3. The Number of Infants Receiving Each Medication Through the UAC.

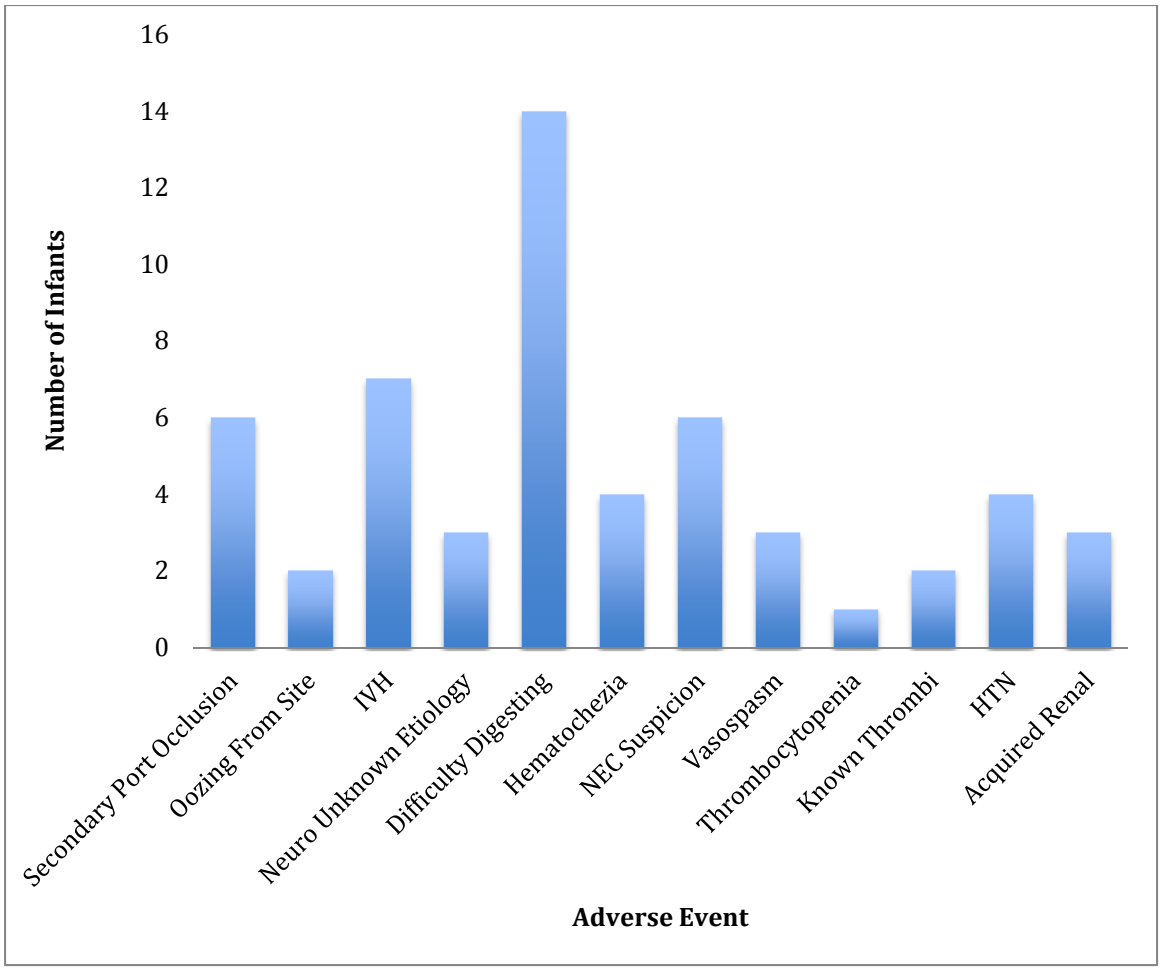

Figure 4. Incidence of Adverse Events.

Table 1

Probability of a Non-Chance Relationship Between Secondary Port Occlusions and Infusates

Secondary Port Occlusion:	p-value
Lipids	.5607
TPN	1
NaCl Only	.0629
NaAcetate Only	.3488
Dextrose Only	.277
Dextrose, NaCl, CaGlu	.0577
Dextrose, CaGlu	1
Dextrose, CaGlu, KCl	.1126
Dextrose, NaCl, CaGlu, KCl	.3063
Ampicillin	.3488
Gentamicin	.3488
Vancomycin	.2615
Ceftazidime	.1648
Ativan	.6796
Morphine	.2298
Sodium Bicarbonate	.0378*
Calcium Gluconate	.3488
Insulin Drip	.0028**
Caffeine Load	.389
Caffeine Maintenance	.4272
Dexamethasone	.1648
Indomethacin	.0836
PRBCs	.0259*
IVIG	.0577

Table 2

Probability of a Non-Chance Relationship Between Oozing at Insertion Site and Infusates

Oozing at Insertion Site:	p-value
Lipids	1
TPN	1
Dextrose, CaGlu	.5491
Ampicillin	1
Gentamicin	1
Ativan	1
Morphine	.2853
Calcium Gluconate	.1307
NS Bolus	1

Table 3

Probability of a Non-Chance Relationship Between Delayed Digestion and Infusates

Difficulty Digesting:	p-value
Lipids	1
TPN	.3528
NaCl Only	.2577
NaAcetate Only	1
Dextrose Only	1
Dextrose, NaCl	1
Dextrose, NaCl, KCl	1
Dextrose, NaAcetate, CaGlu	.1346
Dextrose, NaCl, CaGlu	.1346
Dextrose, NaAcetate, CaGlu, KCl	.1346
Dextrose, CaGlu	.1327
Ampicillin	.238
Gentamicin	.238
Vancomycin	.1331
Ceftazidime	.047*
Ativan	.5696
Sodium Bicarbonate	.1842
Potassium Chloride	1
Furosemide	.5221
Insulin Drip	.2522
10% Dextrose Bolus	.5221
NS Bolus	.5596
Caffeine Load	.293
Caffeine Maintenance	.348
Phenobarbital Load	.4443

Table 3. Probability of a Non-Chance Relationship Between Delayed Digestion and Infusates (continued)

Difficulty Digesting:	p-value
Phenobarbital Maintenance	.5897
Dexamethasone	.3549
Indomethacin	.348
PRBCs	.1331

Table 4

Probability of a Non-Chance Relationship Between Hematochezia and Infusates

Hematochezia:	p-value
Lipids	1
TPN	1
NaCl Only	.5382
NaAcetate Only	.2465
Dextrose Only	.1375
Dextrose, CaGlu	.6012
Ampicillin	.2465
Gentamicin	.2465
Vancomycin	.1813
Ativan	1
Morphine	.4929
Fentanyl Drip	.112
Calcium Gluconate	.2465
Furosemide	.1813
10% Dextrose Bolus	.1813
NS Bolus	.6145
Caffeine Load	.2775
Caffeine Maintenance	.3076
Ranitidine	.0385*
Indomethacin	.3076
PRBCs	.1813
Fresh Frozen Plasma	.112
Cryoprecipitate	.112
Platelets	.0385*

Table 5

Probability of a Non-Chance Relationship Between Suspicion of Necrotizing Enterocolitis and Infusates

NEC Suspicion:	p-value
Lipids	1
TPN	1
Dextrose Only	.277
Dextrose, NaCl, KCl	.3488
Dextrose, CaGlu	.661
Ampicillin	.0515
Gentamicin	.0515
Vancomycin	.2615
Ceftazidime	.1648
Ativan	1
Furosemide	.2615
10% Dextrose Bolus	.2615
NS Bolus	1
Caffeine Load	.389
Caffeine Maintenance	.4272
Ranitidine	.0577
PRBCs	.2615
Platelets	.0577

Table 6

Probability of a Non-Chance Relationship Between Acquired Renal Problems and Infusates

Acquired Renal Problems:	p-value
Lipids	1
TPN	1
NaCl Only	.0767
Dextrose Only	.438
Dextrose, NaCl, CaGlu	.0288*
Dextrose, CaGlu	1
Ampicillin	1
Gentamicin	1
Vancomycin	.1387
Ceftazidime	.0849
Ativan	1
Sodium Bicarbonate	.1648
Calcium Gluconate	.1904
Potassium Chloride	.1904
Insulin Drip	.0571
Dexamethasone	.0849
Indomethacin	.2399
PRBCs	.1387

Table 7

Probability of a Non-Chance Relationship Between Hypertension and Infusates

Hypertension:	p-value
Lipids	1
TPN	1
NaCl Only	.1375
NaAcetate Only	.2465
Dextrose, CaGlu	.5894
Ampicillin	1
Gentamicin	.2465
Ativan	.6188
Morphine	.111
Furosemide	.0108*
Caffeine Load	.2775
Caffeine Maintenance	.0367*
Phenobarbital	.2144
Indomethacin	.3076
PRBCs	.1813

Table 8

Probability of a Non-Chance Relationship Between Thrombus Formation and Infusates

Thrombus:	p-value
Lipids	1
TPN	1
NaCl Only	.3176
Dextrose, NaCl, KCl	.1307
Dextrose, CaGlu	1
Ampicillin	1
Gentamicin	1
Vancomycin	.0943
Ceftazidime	.0571
Ativan	1
Morphine	.2853
10% Dextrose Bolus	.0943
NS Bolus	1
Dopamine	.0571

Table 9

Probability of a Non-Chance Relationship Between Thrombocytopenia and Infusates

Thrombocytopenia:	p-value
Lipids	1
TPN	1
Dextrose Only	.1731
Ampicillin	1
Gentamicin	1
10% Dextrose Bolus	.0481*
Ranitidine	.0096**
Platelets	.0096**

Table 10

Probability of a Non-Chance Relationship Between Vasospasm and Infusates

Vasospasm:	p-value
Lipids	.3329
TPN	1
NaCl Only	.438
Dextrose Only	.438
Dextrose, CaGlu	1
Ampicillin	1
Gentamicin	1
10% Dextrose Bolus	.1387
NS Bolus	1
Ranitidine	.0288*
Platelets	.0288*

Table 11

Probability of a Non-Chance Relationship Between Intraventricular Hemorrhage and Infusates

IVH:	p-value
Lipids	.5921
TPN	.1593
NaCl Only	.3487
NaAcetate Only	.0697
Dextrose Only	.3487
Dextrose, NaCl, KCl	.3953
Dextrose, CaGlu	.6852
Ampicillin	1
Gentamicin	1
Ativan	.7082
Morphine	1
Sodium Bicarbonate	.3488
Calcium Gluconate	.3953
Furosemide	.2992
NS Bolus	1
Caffeine Load	.0092**
Caffeine Maintenance	.0134*
Phenobarbital	.3488
Dexamethasone	.1904
Indomethacin	.1116
PRBCs	.2992
Fresh Frozen Plasma	.1904
Cryoprecipitate	.1904

Table 12

Probability of a Non-Chance Relationship Between Neurological Problems of Unknown Etiology and Infusates

Neurological Problems of Unknown Etiology:	p-value
Lipids	1
TPN	1
Dextrose Only	.0767
Dextrose, CaGlu	.2614
Dextrose, CaGlu, KCl	.0571
Dextrose, NaCl, CaGlu, KCl	.1648
Ampicillin	1
Gentamicin	1
Ativan	.6071
Calcium Gluconate	.1904
NS Bolus	1

Note. p-values obtained using Fisher's two-tailed exact probability test.

*p < .05. **p < .01

Appendix A
Conceptual Framework