Changing parenteral nutrition administration sets every 24 h versus every 48 h in newborn infants

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OBJECTIVE: To determine whether changing total parenteral nutrition fluid administration sets (TAS) every 48 h rather than every 24 h results in a greater infusate contamination rate.
PATIENTS AND METHODS: Prospectively, 166 infants were assigned at random to have TAS changed either every 24 h or every 48 h. Samples of the infusate were cultured to determine contamination rates of the infusate in the sets and were tested from 149 of these infants. TAS was replaced every 24 h in the control group, and 445 amino acid plus dextrose solutions (AADS) and 449 lipid emulsions samples were taken for bacterial culture. Fungal cultures were also performed on 449 samples. The study group had TAS replaced every 48 h, and 454 samples of AADS were cultured for bacteria. The numbers of lipid emulsion samples sent for bacterial culture and fungal culture were 449 and 440, respectively. Information on type of intravenous access device, administration of antibiotics and blood cultures was also collected.
RESULTS: There was no difference in bacterial contamination rates for AADS or lipid emulsion from TAS changed every 24 or 48 h (χ^2, P>0.05). Lipid emulsion sampled from the 24 h group showed a statistically significant higher rate of fungal contamination than specimens from the 48 h group (P<0.01).
CONCLUSIONS: Changing TAS every 48 h versus 24 h does not increase the contamination rate of infusate in newborns.

Key Words: *Infection, Neonate, Total parenteral nutrition*

Changer les dispositifs d'administration d'alimentation parentérale chez les nourrissons toutes les 24 heures ou toutes les 48 heures?

OBJECTIF : Déterminer si le changement des dispositifs d'administration d'alimentation parentérale totale toutes les 48 heures plutôt que toutes les 24 heures peut s'accompagner d'un plus fort taux de contamination de la solution perfusée.
PATIENTS ET MÉTHODES : De façon prospective, 166 nourrissons ont été assignés aléatoirement à l'un de deux groupes selon que le dispositif de perfusion était changé toutes les 24 ou toutes les 48 heures. Des échantillons des solutions perfusées ont été mis en culture afin de vérifier les taux de contamination dans les dispositifs d'administration et ils ont été vérifiés pour 149 de ces nourrissons. Le dispositif a été remplacé toutes les 24 heures dans le groupe témoin et 454 échantillons de solutions d'acides aminés plus dextrose (SAAD) et 449 échantillons d'émulsion de lipides ont été prélevés pour cultures. Des cultures fongiques ont en outre été effectuées sur 449 prélèvements. Pour l'autre groupe, on a remplacé le dispositif toutes les 48 heures et 454 échantillons de SAAD ont été mis en culture pour y déceler la présence de bactéries. Les nombres d'échantillons d'émulsion de lipides testés pour culture bactérienne et culture fongique ont été 449 et 440, respectivement. Des renseignements relatifs aux différents types d'accès intraveineux, à l'antibiothérapie et aux hémocultures ont également été recueillis.
RÉSULTATS : On n'a noté aucune différence quant à la contamination bactérienne des SAAD ou des émulsions de lipides dans les dispositifs d'administration changés toutes les 24 ou 48 heures (χ^2, P > 0,05). Pour les échantillons d'émulsion de lipides recueillis chez le groupe 24 heures, on a noté une élévation du taux de contamination fongique statistiquement significative par rapport aux spécimens prélevés dans le groupe 48 heures (P < 0,01).
CONCLUSONS : Le fait de changer les dispositifs d'administration de l'ali-

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Sick neonates, especially those who are premature, are frequently unable to tolerate enteral feedings and have limited nutritional reserves (1). Although total parenteral nutrition (TPN) is critical to growth and recovery, complications are associated with its use, including infection due to the presence of intravenous access devices in immunocompromised patients (2). Potential sources of infection are related to intravenous access device problems such as direct invasion by microorganisms at the site of catheter insertion, hematogenous seeding of the catheter during periods of bacteremia or fungemia, and catheter hub colonization or contamination of infusate (3-6). Both the use of central venous catheters and TPN therapy have been associated with increased risk of sepsis in both adults and neonates (7,8).

In adults, there has been a trend in practice to change TPN administration sets (TAS) at intervals longer than 24 h. Although cost savings without an increased incidence of contamination or patient bacteremia have been demonstrated, the data are based on adult populations, primarily with clear intravenous solutions; only two studies included amino acid plus dextrose solutions (AADS), and none reported on lipid emulsions (9-14). The current practice in the neonatal intensive care unit (NICU) at the Stollery Children's Health Centre, University of Alberta Hospitals, Edmonton, Alberta, is to change TAS every 24 h using an aseptic technique. We conducted a prospective, randomized study of contamination rates for TAS changed at 24 h versus 48 h intervals. The objective was to examine whether differences in contamination rates would occur.

PATIENTS AND METHODS

Patient enrolment and sample collection: For 12 months, all neonates receiving TPN in the level III NICU at the Children's Health Centre were entered in the study. The study was approved by the Ethics Committee of the University of Alberta Hospitals; the Ethics Committee considered it unnecessary for informed consent to be obtained. After enrolment, a random number table was used to allocate infants in a one to two ratio to either 24 h or 48 h changes of their TAS. Group assignment remained the same for the length of each infant's hospitalization in the NICU. The bag containing AADS was prepared in the hospital pharmacy and was changed daily in both groups. Lipid emulsion bottles were changed with the line sets. For infants in the 48 h group, the AADS bag was removed, and the new one added using the same TAS for 48 h. The TAS was changed by the bedside nurse assigned to care for the patient according to NICU procedure. Samples of solutions were sent for culture at the assigned time intervals regardless of changes in intravenous access devices.

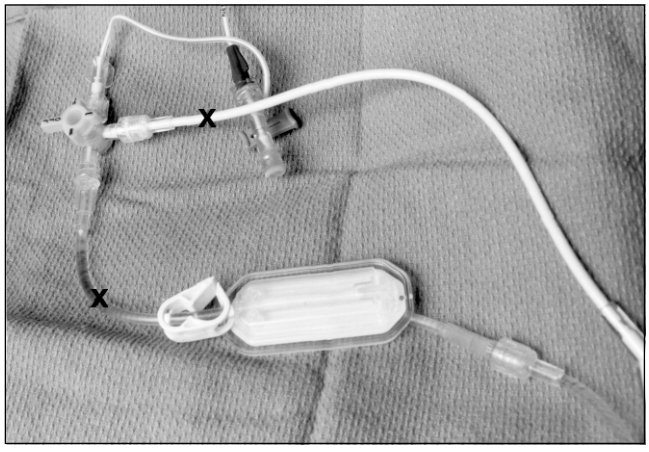

Figure 1) *Sites for sampling fluid for analysis of parenteral nutrition administration set. X Sampling site*

The two types of TAS used during the study period were determined by the type of intravenous pump in use. One preassembled set had an in-line buretrol and a 0.22 μm filter for the AADS Y-connected to an in-line buretrol line for lipid emulsion. The second TAS type required a 0.22 μm filter to be added to an in-line buretrol set for the AADS, which was joined to an in-line buretrol set for lipid emulsion with a connector. This connector was not used for medication administration. After the required tubing was assembled, the connections between tubing sections and intravenous access devices were swabbed with povidone-iodine. The AADS bag and the lipid emulsion bottle were added, and the solutions were run through the tubing. When the TPN was administered by a peripheral intravenous device, the tubing was assembled using an aseptic technique over a sterile field. If the TPN was administered by a central line, the nurse wore sterile gloves while assembling the tubing over a sterile field.

Line care was standardized across both groups and included administering medications through the TAS and adding electrolytes to AADS buretrols when necessary. For peripheral TAS, the injection ports were swabbed with alcohol before punctures, and central TAS injection ports were swabbed with both povidone-iodine and alcohol before punctures. If TAS were disconnected from the intravenous access device for any reason between line changes, the lines were capped with a sterile end. Immediately before a line change, the TAS lines at the sampling sites were disinfected with povidone-iodine and alcohol, and samples were drawn by the nurse caring for the patient. The sampling site in the AADS TAS was the tubing immediately past the bacterial filter, and the sample was taken from the tubing in the lipid emulsion TAS as close to the patient as possible but before the connection with the AADS (Figure 1). With the line clamped at the T-connectors distal to the intravenous access device, a 25-gauge needle attached to a sterile syringe was used to puncture the cleansed tubing at the sampling site, and 3 mL of the infusate was withdrawn to obtain an upstream sample. The fluid was sent in sterile tubes for analysis. Diagnosis, including the need for blood cultures, and treatment of suspected or proven sepsis were determined by the attending clinician. Bacteremia was diagnosed by positive blood cultures.

Microbiology: According to standard laboratory practice,

TABLE 1
Patient data (mean ± SD) for groups randomized to have parenteral nutrition administration sets changed every 24 or 48 h

	Randomization group	
	24 h (n=51)	48 h (n=97)
Birth weight (g)	2004±1057	2053±1062
Gestational age (weeks)	32.7±5.4	32.9±5.2
Postnatal age (days)	10.9±9.4	14.0±20.5
Antibiotic score*	0.48±0.40	0.48±0.39
Line score†	0.32±0.40	0.36±0.43

**Proportion of samples while infants on antibiotics; †Proportion of samples while infants had central line. All values were not significant*

TABLE 2
Contamination rates of total parenteral nutrition solutions

	Randomization group		
Parenteral solution	24 h	48 h	P value
AADS			
Bacterial	14/445 (3.1 %)	13/454 (2.9%)	NS
Lipid emulsion			
Bacterial	27/449 (6.0%)	23/449 (5.1%)	NS
Fungal	14/449 (3.1 %)	2/440 (0.5%)	<0.01

AADS Amino acid plus dextrose solution; NS Not significant

TABLE 3
Organisms in positive cultures of total parenteral nutrition solution samples

	Randomization group	
Organism	24 h (n=1343)	48 h (n=1343)
Coagulase-negative staphylococci	38	34
Candida species	13	0
Fungi	1	2
Enterobacter species	1	0
Enterococcus species	0	1
Streptococcus viridans	2	0
Gram-negative bacilli (glucose nonfermenting)	0	1

AADS and lipid emulsion samples were each plated on chocolate agar, and a sample of lipid emulsion was incubated on a phytone biplate. The chocolate agar plates were read, and growth identified as required after 24 and 48 h. The phytone biplates were read three times weekly for two weeks. Cultures were reported in three groups: no growth; 1 to 9 colony forming units (cfu)/mL, which was defined as questionable contamination; and 10 cfu/mL or more, which was defined as positive contamination. Blood was cultured if indicated clinically.

Statistical analysis: The unit of measurement was the infusate sample not the patient. Patient data for birth weight, gestational age, postnatal age, antibiotics and type of line were expressed as mean ± SD and analyzed by unpaired *t* test.

Contamination rates of the TAS sets, and the proportion of samples from infants with central lines or receiving antibiotics were analyzed by using χ^2 analysis, and Yates correction was applied. Previous studies in adult intensive care units have demonstrated a 4% contamination rate of AADS (5). Assuming an alpha of 0.05 and a power of 0.8, demonstration of a difference in contamination rate of 5% required a sample size of 440 cultures in each group. Infants were enrolled in the 48 h group in a two to one ratio in order to have a similar number of line changes in each arm of the study.

RESULTS

A total of 2686 infusate samples was taken from the lines of infants entered into the study. One hundred and sixty-six infants were randomly assigned to have TAS changed every 24 or 48 h. As per the study design, 53 infants were allocated to the 24 h group, and 113 to the 48 h group. Due to discontinuation of TPN, samples from two infants in the 24 h group and 12 in the 48 h group were not sent. Three patients in the 48 h group died before samples were taken. Samples of infusate from one infant randomly assigned to the 48 h group were incorrectly sent every 24 h. In the final analysis, TAS samples were taken from 51 infants in the 24 h group and from 97 infants in the 48 h group.

There was no difference between the infants in the 24 and 48 h groups for birth weight, and gestational and postnatal age (Table 1). The range of weight was 530 to 4525 g; gestational age and postnatal age at study enrolment varied from 23 weeks to 42 weeks and one day to 64 days, respectively. About half of the cultures were taken while the patients were receiving antibiotics, a proportion similar for both groups (Table 1). For both groups, approximately one-third of the samples were taken from patients with a central line (Table 1).

Bacterial contamination rates for AADS and lipid emulsion varied from 2.9% to 6.0% with an overall rate of 4.3% (Table 2). The overall bacterial contamination rate for the lipid emulsion was higher at 5.6% than that for AADS at 3.0%. Fungal contamination rates of the two interval groups were quite different at 3.1% for the 24 h group and 0.5% for the 48 h group.

There was no significant difference between the 24 and 48 h groups for bacterial contamination of AADS or lipid emulsion (Table 2). Comparison of fungal contamination rates of lipid emulsion showed significantly higher contamination rates in the 24 h group than the 48 h group ($P<0.01$; Table 2). This difference in fungal contamination of lipid emulsion was influenced by one patient in the 24 h group; the patient had candida septicaemia and meningitis with subsequent contaminated TAS fluid cultures. When this infant was excluded from the analysis, fungal

contamination rates between the 24 and 48 h groups were similar at 0.2% and 0.5%, respectively.

The organisms isolated from the TPN samples are listed in Table 3. Coagulase-negative staphylococci and candida accounted for 91% of all positive cultures. Results of blood cultures drawn for clinical indications were examined with respect to infusate cultures. Positive blood cultures were observed in 13 patients in the 24 h group, and the organism isolated was similar to that in the TPN sample in nine infants. In the 48 h group, 20 infants had positive blood cultures, and 10 infants had an organism isolated from a blood culture similar to that in the infusate samples. None of these values was statistically different between the two groups.

DISCUSSION

Infusate may be contaminated during attachment and/or manipulation of TAS. In adult populations, infusate contamination levels are low. Rates of 0.3% to 3.6% have been reported in studies examining infusate contamination rates for intravenous fluid administration sets replaced at 24 to 72 h (9-14). Only one of the studies showed a correlation between contaminated infusate and patient bacteremia; however, contamination of the infusate did not precede patient bacteremia (14). Two studies included AADS with other infusates, and none included lipid emulsions. Our study is the first to examine AADS and lipid emulsion exclusively, while AADS formed a small subset of the lines examined in previous adult studies.

In adults, the greatest contamination rate reported of AADS infused through a central line was 3.6% (9). lnfusate contamination rates were higher in an intensive care unit setting, which was attributed to greater manipulation of the intravenous lines (9,11,12). In our study, the measured infusate contamination rate of TPN infused through peripheral and central intravenous access devices was 4.3%, which was higher than that reported for the adult population. The contamination rate measured for AADS was 3.0% in our study, which is similar to that reported in the adult literature. There are no published lipid emulsion contamination rates, so we cannot comment on the significance of the rate measured in this study. There also are no reports of infusate contamination rates for neonatal populations with which to compare rates. It is possible that TAS were manipulated to a greater extent in this population because of intravenous access problems. We did not find a higher contamination rate in neonates when TAS were changed less frequently, even when the infusate was AADS and lipid emulsion.

Many of our specimens grew coagulase-negative staphylococci. This has also been reported in adult studies (9-14). These organisms may have been an outside contaminant of the TAS tubing rather than the infusate, but 10 cfu or more were required before the infusate was classified as contaminated. Because this organism is a frequent pathogen in the NICU, these results could not be ignored.

Contamination of the infusate with the same organism found in a positive blood culture occurred 75% of the time, but the timing of infusate contamination varied. Infusate samples were positive before, at the same time or after positive blood cultures were obtained. Therefore, it is not possible to conclude that contaminated infusate caused blood infection in all cases. In one study, bacteremia was associated with positive infusate samples in five patients (14). Infusate contamination did not precede the onset of bacteremia. More information regarding infusate contamination compared with blood contamination would have been possible if more frequent blood culture samples had been obtained. This was not done because it would have been unethical to draw blood culture samples from stable babies. Therefore, the physician caring for the infant determined whether the clinical status of the patient warranted blood cultures.

It has been speculated that a significant factor in the contamination of infusates is the number of times that intravenous administration lines are manipulated. There was no control exercised or information collected about the number of TAS manipulations (disconnection of TAS from the intravenous device or injection into the TAS). This information may have been helpful in determining why the infusate contamination rate was elevated compared with published results of other infusates, but the number of TAS manipulations proved too difficult to determine accurately. However, the current practice of multiple entries extended an additional 24 h does not lead to a significant increase in TAS infusate contamination.

There are significant cost savings to the NICU if TAS are changed every 48 h rather than every 24 h. The cost of administration sets for TPN varies with the type of TAS and the type of intravenous pump used within an NICU. Currently, a complete administration set for TPN costs $8.57, and a bottle of lipid emulsion is $7.08. Therefore, a total of $15.65 can be saved for every line change eliminated. Total savings would vary with the number of patient days of TPN. During the past year, changing TAS every 48 h would have realized a savings of $15,509.15 (1982 patient days of TPN divided by two and multiplied by $15.65).

These findings indicated that changing TAS every 48 h rather than every 24 h seems safe and does not increase bacterial or fungal contamination rates of AADS or lipid emulsion infusates. In addition, change to this practice would result in cost savings.

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