

The use of in-line intravenous filters in sick newborn infants

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Aim: This study assesses the improvement in outcome for newborn infants by decreasing major complications associated with intravenous fluid therapy by using an in-line filter, and evaluates the economical impact this might have in relation to daily changing of i.v. lines. **Methods:** In a prospective controlled study, 88 infants were randomly assigned to receive either filtered (except for lipids, blood and blood products) or non-filtered infusions via a central catheter. Main outcome measures such as bacteraemia, phlebitis, extravasation, thrombosis, septicaemia and necrosis were all scored. The costs attributable to patients during a standard 8-day stay were also recorded. **Results:** Significant reductions were found in major complications such as thrombi and clinical sepsis (control group (21), filter group (8); $p < 0.05$). Bacterial cultures of the filters showed a contamination rate on the upstream surface of 15/109 filters (14%). The mean costs of disposables were less in the filter group, showing a reduction from €31.17 to €23.79.

Conclusions. The use of this in-line filter leads to a significant decrease in major complications and substantial cost savings.

Key words: *i.v. filters, infant, thrombi, sepsis, economic benefit*

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During their stay on a neonatal intensive care unit, many newborn infants are given central venous catheters (CVCs) instead of peripheral intravenous catheters for the administration of parenteral nutrition and medication. CVCs reduce the number of painful i.v. procedures without additional morbidity (1). In the treatment of newborn infants, it has been shown that contamination of intravenous fluids by particles, micro-organisms, endotoxin and air may be the cause of significant complications (2–4). Particulate contaminants have been implicated in the pathogenesis of pulmonary artery granulomata in infants receiving parenteral nutrition (5), and plastic material from a syringe has been the cause of fatal bowel necrosis in a neonate (6). In practice, it is likely that (adult) intensive-care patients receive more than 10^7 particles $>2 \mu\text{m}$ in size per 24 h of infusion therapy (7), and that in these cases the particles tend to be deposited within the lung, damaging the endothelium, causing thrombus and granuloma formation along with foreign-body giant-cell production (8). Newborns with central venous catheters are at great risk of deep venous thrombosis (9). The duration of cannula patency has been shown to be extended in neonates after the removal of particulate debris from infusion fluids by filtration (3).

Microbial contamination has been described in a number of instances, and was often shown to be due to contaminated infusion fluids. Several outbreaks and

isolated cases of sepsis have been reported in neonates and infants (10–13), although infection might be associated with other causes, such as bacterial translocation from the gastrointestinal tract (14). Contamination of the intravenous tubing injection sites or connecting sites with migration of the pathogen up the inside of the catheter into the bloodstream may cause catheter-related sepsis (15). Microbial contamination has been reported to be positively correlated to the frequency with which stopcocks/hubs were manipulated (15, 16).

The Pall ELD 96 filter has been shown to remove micro-organisms, endotoxin, air and particles in adults and older children, which may be a cause of complications in the treatment of newborn infants (2–4).

Therefore, the objectives of this study were twofold: to assess the improvement in outcome for newborn infants by decreasing major complications associated with intravenous fluid therapy, and to evaluate the economic impact this might have in relation to the daily changing of i.v. lines.

Patients and methods

Patients

Infants admitted to the neonatal intensive care unit (NICU) with either an umbilical or a percutaneously

inserted central venous catheter (PCVC) were included in this randomized controlled study.

Premature infants, >26 wk and <37 wk of gestation, with respiratory distress syndrome were considered for entry, as were term infants with asphyxia or pneumonia/septicaemia, and patients on antibiotic therapy. Patients with congenital malformations were excluded as were preterm infants of less than 26 wk, since very few infants of this age are admitted to our unit. The study was approved by the ethical review committee, and informed parental consent was obtained. A computer-generated randomization was carried out by one of the neonatologists who did not participate in the study. Sealed numbered envelopes were opened on admission, and infants were allocated to either the study group or the control group.

Methods

Intravenous fluids and medications were administered from day 1 of life onwards, either with an ELD96 filter (Pall Europe Limited, Portsmouth, UK) (study group) or without a filter (control group). All intravenous fluids (with the exception of lipids, blood or blood products) were given through the filter, and in the study group, filters and sets (i.v. lines, three-way stopcock and stopper) were changed every 4 d. The sets in the control group were changed daily, as is the usual practice in our unit.

In the study group, bacterial cultures were obtained at the time of change from both sides of the discarded filter, according to the method of Geiss (17), and from the lipid solution. For infants in the control group, bacterial cultures were obtained from the intravenous fluids every 4 d. In addition, catheter tips were cultured after removal. In all infants, tracheal aspirate was cultured twice weekly as part of the department's surveillance programme for nosocomial colonization and infection. Blood was cultured only when sepsis was suspected. Bacterial pathogens were identified according to accepted procedures. Additionally, phlebitis, extravasation, thrombosis, secondary septicaemia and necrotizing enterocolitis (NEC) were all recorded. Proven sepsis was defined as characteristic clinical symptoms, plus a positive result on blood culture, and abnormal test results such as leucocytosis, leucopenia or granulocytopenia and CRP levels >10 mg/l. Clinical (unproven) sepsis was defined as characteristic clinical symptoms, abnormal laboratory results and a negative result on blood culture (18). A full differentiated blood-cell count was determined at admission.

Statistical methods

To achieve a reduction in infection rate from 30% to 5% by using an in-line filter with a power of 80% and at 5% significance would require at least 36 infants in each group. Quantitative measurements tended to exhibit positive skewness and hence Mann-Whitney sum of

Table 1. Patient data.

	Study group n = 44	Control group n = 44
Pre-term	39	37
Term	5	7
Gestational age (wk)	30.8	30.5
median (+ range)	(27.3–42.3)	(26.3–41.3)
Birthweight (g)	1395	1402
median (+ range)	(585–4100)	(620–3980)
Number ventilated	34	38
Deceased	0	4

ranks tests have been used. Categorical data were analysed by χ^2 test and Student's *t*-test, or where appropriate by Fisher's exact test. *P* < 0.05 was considered significant. Odds ratios (OR) were also calculated.

Results

Eighty-eight patients (76 preterm and 12 term) were randomly assigned to either the study group or the control group. Gestational age, birthweight, percentage of ventilated infants and mortality rate were comparable between groups (Table 1). Four patients in the control group died from causes unrelated to catheter usage (NEC, pulmonary bleeding, severe intraventricular haemorrhage, circulatory insufficiency).

Phlebitis and extravasation were not seen in either group. Major complications, such as thrombi, sepsis (proven/unproven) or NEC occurred considerably less frequently in the study group than in the control group, although statistical significance was not achieved (Fig. 1). However, these complications did occur in just eight patients of the study group, as compared to 21 of the control group (*p* < 0.05; OR 0.243, 95% CI: 0.09–0.64; relative risk 8 vs 1 = 0.38 (0.19–0.77)); a reduction of 62% (Fig. 1).

There were 65 central venous catheters inserted in the study group and 56 in the control group. The duration of

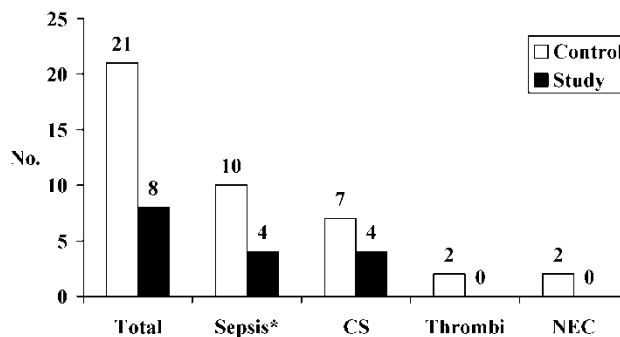


Fig. 1. Major complications. CS: clinical sepsis; NEC: necrotizing enterocolitis; * blood-culture positive.

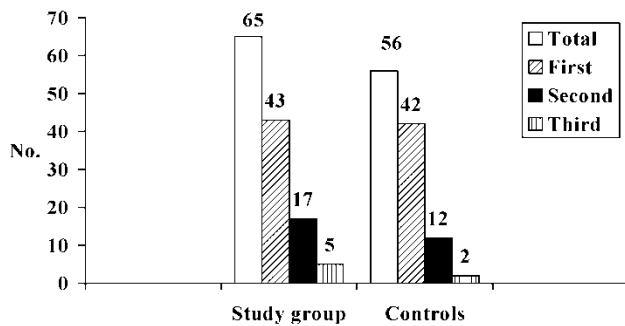


Fig. 2. Number of catheters. Umbilical (1st) or percutaneously inserted central venous catheter.

the catheters remaining in place was 525 (mean 8.1) patient days in the study group and 493 (mean 8.8) patient days in the control group. The distribution is shown in Fig. 2. Due to malposition, one umbilical catheter in the study group and two umbilical catheters in the control group were replaced by a PCVC within 1 h; these three PCVCs were counted as "first" catheters. Thus, in the study group, 42 umbilical catheters and 23 PCVCs were inserted; in the control group these numbers were 40 and 16, respectively. Bacterial cultures from intravenous catheters were found to be positive in 14% (study group 2.5%, controls 11.5%); *Staphylococcus epidermidis* being the organism most commonly isolated. Bacterial cultures of the filters proved to be positive in 20 of 109 cases; 15 on the upstream side of the filter (Fig. 3). The major organisms isolated were *Staphylococcus* and *Enterococcus*, representing 85% of cases. In three cases, the downstream sides of the filter were positive. Only in one infant with a *Staphylococcus epidermidis* on the downstream side of the filter was a positive culture from the arterial and venous umbilical catheter found. The infant showed no signs of clinical sepsis and the blood cultures were negative. In the other two cases and in two cases with

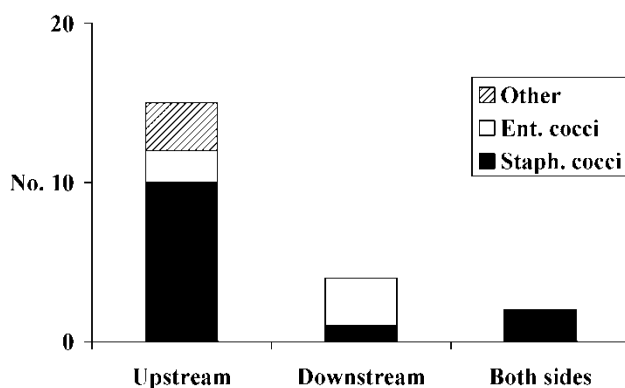


Fig. 3. Bacterial cultures of ELD filters, results from 20 positive cultures.

positive cultures from both sides, none of the infants had (clinical) sepsis or positive cultures from the catheter tip. Strains from the downstream side were different from the strains of bacteria on the upstream side.

The costs attributable to patients in both control and study groups were calculated on a "cost of disposables" basis during a standard 8-d stay. Additionally, the time taken for line change was calculated by direct assessment, and an estimate of the relative nursing costs was built into the cost analysis. Results are shown in Table 2.

Discussion

Nosocomial infection is a major problem in neonatal intensive care. It is responsible for significant morbidity and mortality. Preterm and term neonates that require intensive care are immuno-compromised and susceptible to opportunistic infections. For any intravascular line infection, the potential sources of bacteraemia are related to the cannula, to contamination of the infusate (2), to duration of intravenous fluid administration (19) and to prolonged catheter placement (20). A study in term newborn infants showed a significant increase in catheter-site life by using a 96-h in-line filter (3). The ubiquitous intravenous line provides a potential for direct intravenous inoculation, as was proposed for an *Acinetobacter* septicaemia outbreak due to contaminated intravenous nutrition fluids (11).

In our study, 14% of the intravenous lines were found to be positive for microbial contamination, and *Staphylococcus epidermidis* was the most commonly isolated organism from the bacterial cultures of the filters. Recent studies have shown contamination rates of 28.8% and 52% without the use of antibiotics (19, 21) and of 13.3% with antibiotic prophylaxis (21). Antibiotic prophylaxis, although effective, may lead to resistance among coagulase-negative staphylococci (22). In a meta-analysis on the use of antimicrobial impregnated catheters in adults, a decrease in catheter-related bacteraemia of 2.2% was found; however, again the risk of antimicrobial resistance was emphasized (22). Our results correlate with the trend for an increase in *Staphylococcus* as an infectious agent for septicaemia

Table 2. Costs/infant with or without filter (in €).

	Study group with filter	Control group without filter
i.v. line	$8 \times 0.54 = 4.32$	$32 \times 0.54 = 17.28$
Filter	$2 \times = 16.00$	
3-way stopcock	$6 \times 0.54 = 3.24$	$24 \times 0.54 = 12.96$
Stopper	$2 \times 0.13 = 0.26$	$8 \times 0.13 = 1.04$
Disposables costs	€23.82	€31.28
Including nursing time	€13.62	€54.47
Total costs	€37.44	€85.75

(23), and in causing 75% of septicaemia in one unit (11). Although a recent study shows that the presence of a PCVC had no independent effect on sepsis (19), we found that the use of a filter does make a difference in the rate of sepsis.

The fact that the downstream side of the filter was positive in three cases (with a positive culture from both umbilical catheters in one infant) may be due to contamination from the skin or from the insertion side. Since strains were different in the infants with positive cultures from both sides of the filter, we speculate that there was a retrograde contamination from the skin or the insertion site.

An air embolism is a rare, but potentially devastating, complication of intravenous therapy. Several neonatal case studies illustrate the problem—the results of an air embolism during the insertion of a peripheral intravenous line may vary from resolution of symptoms within a few minutes (20) to paraplegia due to a “run-dry” during peripheral venous administration of fluid and antibiotics (24). These authors suggest that the use of a filter should be standard practice.

The use of intravenous fluid filters to remove microbial contamination for protracted periods of 96 h will potentially lead to the accumulation of Gram-negative bacteria on the membrane. In this situation, and especially with the infusion of antibiotics via this line, breakthrough of released endotoxin poses a severe clinical threat. Therefore, any filtration device used for extended periods must be capable of removing endotoxin.

The in-line filters used in our study have been shown to remove endotoxin over a period of >96 h in simulated extended infusions (25), amino acid-based parenteral nutrition solutions (26), and with paediatric total parenteral nutrition solutions (27). This is not the case with other filters (25, 26, 28).

Intravenous filters retain such contaminants and can potentially reduce the incidence of infection, which is especially important for the immuno-compromised neonatal/paediatric patient (29). This proved to be the case in our study, with a significant (62%) reduction in the total complication rate. Reductions occurred for thrombi, NEC and sepsis, even though the infants in the study group were ventilated longer than those in the control group, and longer ventilation is associated with a higher risk of sepsis (20).

Incorporating the filter into the intravenous administration system enables various cost reductions. Bennion and Martin in 1991 showed a saving of £8.44 (£17.28 without filter compared to £8.84 with filter) per day (30) derived from reducing disposable costs. We have shown that the use of the 96-h filter reduced our cost whilst giving the patients significant clinical benefit. If the nursing time reduction is also brought into play, the cost benefits shown are even more substantial.

In conclusion, the use of a 96-h filter has been shown to reduce significantly the complication rate encoun-

tered in our patients, and allows for considerable cost savings as a result of reduced use of disposable items and increased available nursing time for other duties. As a result it has become an integral part of our unit policy.

For neonates, the flow through any filter and administration set is low, and the hold-up volume of the ELD96 filter is 1.6 ml. Since this study was completed, we are aware that a neonatal version of this filter is now commercially available, with a priming volume of only 0.4 ml.

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