CONCISE REPORT

Saline flush after administration of lipid emulsion reduces the risk of central line infections: A case-control study

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ABSTRACT

Background: Lipid emulsion (LE) may increase the occurrence of central line infections (CLI). We hypothesized that saline flush after the administration of LE (SFLE) may decrease bacterial contamination of catheters and reduce the risk of CLI.

Methods: To evaluate the effectiveness of SFLE in reducing the risk of CLI, we conducted a retrospective two-year case-control study that included all patients who received LE via a central venous catheter (CVC). Patients who were administered LE without SFLE between 1 February 2014 and 31 January 2015 (non-SFLE group), and patients who were administered SFLE between 1 February 2015 and 31 January 2016 (SFLE group) were studied. CLI was defined to include catheter-related local infection (CRLI) and central line-associated blood stream infections.

Results: The non-SFLE and SFLE groups included 58 cases (52 patients) and 52 cases (45 patients), respectively. CVCs were inserted for a total of 2,757 and 1,715 catheter days in the non-SFLE and SFLE groups, respectively. We observed 17 and 9 cases of CLI in the non-SFLE and SFLE groups, respectively, a rate of 5.8 and 5.2 per 1000 catheter days in each group. In multivariate logistic regression analyses, SFLE was associated with a decreased risk of CLI (odds ratio, 0.33, 95% confidence interval, 0.11–0.89).

Conclusion: Our results suggest that SFLE may decrease the risk of CLI.

KEY WORDS

Saline flush, lipid emulsion, central venous catheter, catheter-related infections

INTRODUCTION

Lipid emulsion (LE) infusion administered more than twice weekly is associated with central line-associated blood stream infections (CLABSI) in patients receiving home parenteral nutrition (1). Additionally, some studies have suggested that LE infusion is a risk factor for coagulase-negative staphylococcal bacteremia in very low birth weight newborns (2) and *Malassezia furfur* fungemia in infants (3). Battistella et al (4) showed that LE infusions during the early post-injury period increased susceptibility to infection, prolonged pulmonary failure, and delayed recovery in critically injured patients. These results suggest that LE may be associated with an increased risk for central line infections (CLI). Freeman et al (5) showed that catheters can be colonized within 24-48 h after insertion, and when nutrient-rich growth mediums, such as lipids,

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are infused through the colonized catheter, only a few hours of rapid growth are required for the numbers of coagulase-negative staphylococci to reach levels sufficient for bloodstream invasion.

We hypothesized that saline flush after the administration of LE (SFLE) may decrease the bacterial contamination of central venous catheters (CVC) and reduce the risk of CLI. However, no studies have examined this method for reducing the risk of infection in CVCs following LE infusion. Therefore, this study aimed to clarify the relationship between SFLE and CLI in inpatients receiving LE infusion.

MATERIALS AND METHODS

This two-year case-control study included all patients who received LE via CVC in Kaetsu Hospital (Niigata, Japan), a 261-bed hospital with six wards, between 1 February 2014 and 31 January 2016. SFLE was started from 1 February 2015. Patients were administered LE without SFLE between 1 February 2014 and 31 January 2015 (non-SFLE group), while patients were administered SFLE between 1 February 2015 and 31 January 2016 (SFLE group) for improved experimental quality. The records of patients from these two groups were reviewed. This study and its protocol were approved by the Ethics Committee of Kaetsu Hospital.

The demographic and clinical characteristics of the patients were reviewed and recorded (Table 1). The frequency of LE administration was calculated as the duration of LE administration divided by the duration of catheter insertion. We excluded patients who were administered LE within three days of CVC

TABLE 1: Case characteristics: administration of lipid emulsion via CVC

	Non-SFLE (n = 58)	SFLE (n = 52)
Diagnosis, n (%)		
Respiratory disease	18 (31)	15 (22)
Gastrointestinal disease	13 (22)	16 (24)
Central nervous system disease	13 (22)	13 (19)
Cardiovascular disease	14 (24)	5 (7)
Other disease	0 (0)	3 (4)
Age, y (SD)	82 (8)	79 (15)
Body weight, kg (SD)	42 (12)	41 (12)
Insertion site, n (%)		
Subclavian	3 (5)	0 (0)
Internal jugular	11 (19)	21 (40)
Femoral	44 (76)	31 (60)
Duration of catheter insertion, day (SD)	48 (46)	33 (32)
Multi-lumen catheter, n yes (%)	3 (5)	4 (8)
Use of maximal sterile barrier precautions, n yes (%)	55 (95)	48 (92)
Use of alcohol-based hand rub, L/1000 patients (SD)	8 (2)	9 (3)
Administration of PN, n yes (%)	52 (90)	51 (98)
Duration of PN administration, day (SD)	35 (43)	24 (30)
Duration of LE administration, day (SD)	30 (24)	24 (30)
Frequency of LE administration, times (SD)	0.8 (0.4)	0.7 (0.3)
Development of CLI, n (%)	16 (28)	9 (17)
Number of CLI per 1000 catheter days	5.8	5.2

Continuous variables were reported as means and standard deviation; and categorical variables, as frequency and percentage.

Frequency of LE administration was calculated as duration of LE administration divided by the duration of catheter insertion.

In 2 patients, the body weight measurements were not available (1 patient from the non-SFLE group and SFLE group each).

CLI, central line infections; LE, lipid emulsion; PN, parenteral nutrition; SD, standard deviation SFLE, saline flush after the administration of lipid emulsion.

insertion or received another LE preparation (e.g., propofol, flurbiprofen, or alprostadil), had subcutaneous ports, had the catheter removed for at least two days, or did not undergo catheter removal (continued CVC for home parenteral nutrition or transfer to another hospital). In addition, we excluded the episodes of CLI after the second CLI during a single hospitalization, since there were several patients who experienced repeated CLI. Moreover, in the non-SFLE group, we excluded patients who had the catheter removed after starting SFLE.

The insertion site was decided by the physician. Ultrasonography was occasionally used to guide the insertion, based on the physicians' discretion. The skin at the insertion site was disinfected with 1% chlorhexidine in 70% alcohol. After CVC insertion, the area surrounding the catheter was cleaned, and an occlusive dressing was applied covering the site. The insertion area was examined daily for the presence of any abnormality by the nurse assigned to the patient. Catheter dressings were changed every seven days or sooner at the discretion of the nurse caring for the patient if the dressing was contaminated (this is the standard duration in Japan). The insertion area was disinfected with 1% chlorhexidine in 70% alcohol every time the catheter dressing was changed. The connecting lines using an in-line filter were changed every seven days. The decision to remove the catheter was made by the patient's physician. Catheters were removed when they were no longer needed; other reasons for catheter removal included occurrence of complications, accidental removal, or death. No antibiotic cream or lotion was applied around the insertion area. The catheters were not antimicrobial-coated. Removed catheter tips were not routinely cultured. For LE infusion, 100–250 mL/day of 20% LE was administered for 3–6 h piggybacked through the CVC line below the in-line filter. The line for LE was removed after administration was completed. The SFLE protocol was started on 1 February 2015. After the LE line was removed, the CVC line was flushed using 10 mL of saline.

CLI was defined as CRLI or CLABSI. CRLI was defined as the presence of any sign of local infection (induration, erythema, heat, pain, or purulent drainage). CLABSI was defined as a positive blood culture obtained from a peripheral vein and presence of signs of a systemic infection (fever, chills, and/or hypotension), with no apparent source of bacteremia except the catheter (6).

TABLE 2: Microorganisms isolated from blood culture

	Non-SFLE	SFLE
Staphylococcus epidermidis	3	2
Staphylococcus aureus	1	2
Serratia marcescens	0	1

In the non-SFLE group, all strains of Staphylococcus epidermidis and Staphylococcus aureus showed methicillin resistance.

In the SFLE group, 1 strain of Staphylococcus epidermidis and Staphylococcus aureus each showed methicillin resistance.

SFLE, saline flush after the administration of lipid emulsion.

The statistical software JMP9 (SAS Institute Inc., Cary, NC) was used for all statistical analyses. Continuous variables were reported as means and standard deviation, and categorical variables were recorded as frequency and percentage. Multivariate modeling was performed using logistic regression with a stepwise backward-forward selection ($p < 0.25$) procedure to identify the independent factors associated with CLI. For multivariate analysis, SFLE, age, sex, body weight, duration of catheter insertion, femoral CVC insertion, use of maximal sterile barrier precautions, use of a multi-lumen catheter, use of alcohol-based handrub during the month of CVC insertion in the ward, administration of PN, and frequency of LE administration were included as variables. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. $P < 0.05$ was considered statistically significant.

RESULTS

The study included 96 patients (58% men), aged 22-98 years (median, 83 years) and with body weight ranging from 25 to 97 kg (median, 39 kg). A total of 110 cases (96 patients) who received LE via CVC were included in this study. Subsequently, 53 cases were excluded from the study, including 20 cases that received LE within 3 days of CVC insertion, 18 cases that received another LE preparation (15 and 3 cases who were administered flurbiprofen and alprostadil, respectively), five cases that experienced repeat CLI after the occurrence of a second CLI during a single hospitalization, one case wherein the catheter was not removed due to transfer to another hospital, and nine cases in the non-SFLE group that had the catheter removed after starting SFLE. No patients received the insertion of a tunneled catheter, subcutaneous port, or a peripherally inserted central catheter.

Case profiles are shown in Table 1. The non-SFLE and SFLE groups included 58 cases (52 patients) and 52 cases (45 patients), respectively. One patient was included in both the non-SFLE and the SFLE groups, and happened to be present in both periods of the study. CVSs were inserted for a total of 2,757 and 1,715 catheter days in the non-SFLE and SFLE groups, respectively. We observed 16 and nine cases of CLI in the non-SFLE and SFLE groups, respectively, and a rate of 5.8 and 5.2 per 1000 catheter days in each group.

TABLE 3: Multivariate logistic regression analyses of factors associated with CLI

	Odds ratio	OR (95% CI)	P
Non-SFLE	1.00		
SFLE	0.33	0.11–0.89	0.03
Sex: female	1.00		
Sex: male	5.21	1.73–19.15	< 0.01

CI, confidence interval; OR, odds ratio; SFLE, saline flush after the administration of lipid emulsion.

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The microorganisms isolated from blood cultures are shown in Table 2. In the non-SFLE group, we observed four microorganisms, including three methicillin-resistant Staphylococcus epidermidis and one methicillin-resistant Staphylococcus aureus. In the SFLE group, we observed five microorganisms, including two strains of *Staphylococcus epidermidis* and *Staphylococcus aureus* each (of which one strain each showed methicillin resistance) and one strain of Serratia marcescens.

The results of multivariate logistic regression analyses of the factors associated with CLI are shown in Table 3. SFLE was associated with a decreased risk of CLI (OR, 0.33, 95% CI, 0.11-0.89). Additionally, male sex was associated with an increased risk of CLI (OR, 5.21, 95% CI, 1.73-19.15).

DISCUSSION

In this study, the rate of CLI decreased from 5.8 to 5.2 per 1000 catheter days after starting SFLE, and the use of SFLE was associated with a decreased risk of CLI in multivariate analyses. No study has previously reported the usefulness of SFLE in preventing CLI. Freeman et al (5) showed that catheters can be colonized within a few hours following LE administration. We considered that SFLE may clean the catheter following LE infusion and prevent bacterial colonization.

In some studies, CLI (including CRLI and CLABSI) occurred at a rate of 8-9 per 1000 catheter days for CVCs (6,7). The rate of CLI in our study was lower. We observed four and five strains of microorganisms isolated from blood cultures in the non-SFLE and SFLE groups, respectively. *Staphylococcus epidermidis* strains were the most common in both groups. These findings are similar to those of previous studies (7,8).

Femoral access was the most common site for CVC insertion in our study (60-70%). Because many patients were elderly and/or had dementia, femoral access was used to prevent accidental removal. Youn et al[7] showed that 5-10% of CVCs were inserted through femoral access; among patients admitted to intensive care units, femoral access has been associated with a greater risk of infectious and thrombotic complications than subclavian catheterization (8).

Male sex was associated with an increased risk of CLI in multivariate analyses. Moro et al (9) showed that the risk of skin colonization was higher among males, probably due to the presence of facial hair, which facilitates the multiplication of microorganisms. However, since femoral access was the most common site of CVC insertion in our study, the presence of facial hair may not be related to the increased risk of CLI observed in males.

Our study has some limitations. First, it used a retrospective design and had a small sample size. Second, the insertion sites were not randomly assigned. Third, femoral access for CVC insertion was the most common, in contrast to previous reports.

CONCLUSIONS

Overall, our results suggest that the administration of SFLE instead of LE infusion alone may decrease the risk of CLI. However, further prospective studies are needed to confirm these findings.

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