CONCISE REPORT

Lipid emulsion increases the risk of central line infection in Japanese adult inpatients: A retrospective study

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ABSTRACT

Background: Several studies have suggested that lipid emulsion (LE) increases the risk of central line infection (CLI) in adult patients. However, there are limited data on the relationship between LE and CLI.

Methods: We retrospectively reviewed all patients who had had a central venous catheter (CVC) inserted during a 13-month period at our institution. CLI was defined as a catheter-related local infection or a central line-associated bloodstream infection.

Results: We observed 25 CLIs in 163 cases (143 patients) of CVC insertion, giving a rate of 4.6 per 1000 catheter days. In multivariate logistic regression analyses, administration of LE was associated with an increased risk of CLI (odds ratio 3.12, 95% confidence interval 1.22–8.58). Parenteral nutrition was also associated with an increased risk of CLI (odds ratio 7.86, 95% confidence interval 1.45–146.10).

Conclusions: Our results suggest that administration of LE is associated with an increased risk of CLI in hospitalized Japanese adults.

KEY WORDS

lipid emulsion, central line infection, parenteral nutrition

INTRODUCTION

Infusion of lipid emulsion (LE) during the early period following injury has been reported to increase susceptibility to infection (1). Further, LE administered more than twice weekly is associated with central line-associated bloodstream infection (CLABSI) in patients receiving home parenteral nutrition (PN) (2). Freeman et al. (3) showed that catheters could be colonized within 24-48 h of insertion, and when a nutrient-rich growth medium such as LE is infused through the colonized catheter, only a few hours of rapid growth are required for numbers of coagulase-negative staphylococci to reach levels sufficient for bloodstream invasion. Moreover, some studies have suggested that infusion of LE is a risk factor for coagulase-negative staphylococcal bacteremia in very low birth weight newborns (4) and *Malassezia furfur* fungaemia in infants (5). Further, in a systematic review and meta-analysis, Austin et al. showed that inclusion of LE in PN is one of several factors that may influence microbial growth (6). These observations suggest that LE may be associated with an increased risk of central line infection (CLI).

However, a database analysis by Pontes-Arruda et al. (7) reported no significant association between LE administered with premixed PN and increased risk of infectious morbidity when compared with PN that did not contain lipids. In contrast, several studies have reported that LE increases the risk of CLI in adult patients receiving critical care (1) and home PN (2), while Austin et al. (6) reported that the evidence base for an association between LE and microbial growth is equivocal. The aim of this study was to examine the relationship between LE and CLI in Japanese adult inpatients.

METHODS

This 13-month retrospective study and its protocol were approved by the Ethics Committee of Kaetsu Hospital. The records of all patients who had undergone insertion of a central venous catheter (CVC) in Kaetsu Hospital, a 261-bed facility

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with 6 wards in Niigata, Japan, between 1 January 2014 and 31 January 2015 were reviewed. The demographic and clinical characteristics of patients who developed CLI were compared with those who did not (Table 1).

The frequency of administration of LE was calculated as the duration of administration of LE divided by the duration of catheter insertion. We excluded patients who received LE for the delivery of pharmaceutical agents (e.g., propofol, flurbiprofen, or alprostadil), had subcutaneous ports, had the catheter removed for ≤ 2 days, did not undergo catheter removal (continued CVC for home PN or transferred to another hospital), or had the catheter removed after February 2015. We excluded episodes of CLI that followed a second CLI during a single hospitalization (several patients experienced multiple CLIs).

The insertion site was selected by the attending physician. Ultrasonography was occasionally used to guide insertion according to the physician's discretion. The skin at the insertion site was disinfected with 1% chlorhexidine in 70% alcohol. After insertion of the CVC, the area surrounding the catheter was cleaned and an occlusive dressing was applied to cover 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 (the standard time interval for dressing changes in Japan) or sooner at the discretion of the nurse caring for the patient if the dressing was contaminated. The insertion area was disinfected with 1% chlorhexidine in 70% alcohol each time the catheter dressing was changed. Connecting lines with an in-line filter were also changed every seven days. The decision to remove the catheter was made by the patient's physician. The catheters were removed when they were no longer required; other reasons for catheter removal included development of complications, accidental removal, or death of the patient. The removed catheter tips were not routinely cultured. No antibiotic creams, antibiotic lotions, or antimicrobial-coated catheters were used. For infusion of LE, 100-250 mL/day of 20% soybean oil-based LE was administered for 3-6 h piggybacked through the CVC line below the in-line filter. The line used for administration of LE was removed after the infusion was complete. The CVC line was not flushed with saline after the LE line was removed.

CLI was defined as catheter-related local infection (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

TABLE 1: Clinical and demographic characteristics

	Non-CLI (n = 138)	CLI (n = 25)
Diagnosis, n (%)		
Gastrointestinal disease	36 (26)	2 (8)
Respiratory disease	35 (25)	13 (52)
Central nervous system disease	33 (24)	7 (28)
Cardiovascular disease	29 (21)	3 (12)
Other disease	5 (4)	0 (0)
Age, years (SD)	81 (12)	81 (6)
Sex, n male (%)	75 (54)	18 (72)
Body weight, kg (SD)	42 (12)	46 (14)
Insertion site, n (%)		
Subclavian	9 (7)	0 (0)
Internal jugular	23 (17)	3 (12)
Femoral	106 (77)	22 (88)
Duration of catheter insertion, days (SD)	33 (35)	37 (27)
Multi-lumen catheter, n yes (%)	12 (9)	2 (8)
Use of maximal sterile barrier precautions, n yes (%)	122 (88)	23 (92)
Use of alcohol-based hand rub, L/1000 patients (SD)	7 (2)	8 (3)
Administration of PN, n yes (%)	93 (67)	24 (96)
Duration of PN administration, days (SD)	19 (33)	27 (22)
Frequency of LE administration 0.2 times or more, n yes (%)	47 (34)	17 (68)

Continuous variables were reported as the mean and standard deviation and categorical variables as the frequency and percentage. Frequency of LE administration was calculated as duration of LE administration divided by duration of catheter insertion.
Abbreviations: CLI, central line infection; LE, lipid emulsion; PN, parenteral nutrition; SD, standard deviation.

apparent source of bacteremia except the catheter (8).

JMP9 statistical software (SAS Institute Inc., Cary, NC) was used for all statistical analyses. Continuous variables are reported as the mean and standard deviation and categorical variables as the frequency and percentage. Multivariate modelling was performed using logistic regression with a stepwise backward-forward selection ($P < 0.25$) procedure to identify independent factors associated with CLI. Patient age, sex, and 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 hand rub during the month of CVC insertion in the ward, administration of PN, and frequency of LE administration were included in the multivariate analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. $P < 0.05$ was considered to be statistically significant.

RESULTS

The study included 143 patients (55% male) with a median age of 83 (range 26-97) years and a median body weight of 41 (range 21-97) kg. One hundred and sixty-three cases (143 patients) of CVC insertion were included. Fifty cases were excluded, including 18 episodes for which LE was used for administration of another pharmaceutical agent (13 and 5 cases received flurbiprofen and alprostadil, respectively), one case of repeat CLI after a second CLI during a single hospitalization, eight cases where the catheter was not removed (four instances each where the CVC was continued for home PN or the patient was transferred to another hospital), and 23 cases where the catheter was removed after February 2015. No patient underwent insertion of a tunneled catheter, subcutaneous port, or a peripherally inserted central catheter.

The case profiles are shown in Table 1. The non-CLI and CLI groups included 138 and 25 cases and had 4565 and 916 catheter days, respectively. We identified 25 cases of CLI, giving a rate of 4.6 per 1000 catheter days. Twelve microorganisms were isolated from blood culture, including five methicillin-resistant *Staphylococcus epidermidis,* four *Staphylococcus aureus* (three of which were methicillin-resistant), and three methicillin-resistant coagulase-negative staphylococci.

The results of multivariate logistic regression analyses of factors potentially associated with CLI are shown in Table 2. Administration of LE 0.2 times or more was associated with an increased risk of CLI (OR 3.12, 95% CI 1.22–8.58). Administration of PN was also associated with an increased risk of CLI (OR 7.86, 95% CI 1.45–146.10).

DISCUSSION

Administration of LE was associated with an increased risk of CLI in multivariate analyses. Our findings in Japanese adult inpatients are similar to those of other studies suggesting that LE increases the risk of CLI in adults being treated in critical care units (1) and in those on home PN (2). It has been reported that administration of LE supports growth of bacteria in a CVC. Freeman et al. (3) showed that only a few hours of rapid growth are required for the numbers of bacteria to reach levels sufficient for bloodstream invasion when LE is infused through a colonized catheter. This report is consistent with our observations. However, it is difficult to stop infusions of LE when they are being administered for nutrition. We have reported that a saline flush after administration of LE might decrease the risk of CLI (9) and now recommend routine use of saline flushes for this purpose.

In our study, multivariate analyses showed administration of PN to be associated with an increased risk of CLI (the OR for PN was higher than that for LE). Austin et al. (6) showed that microbial growth could be influenced more by vitamins, trace elements, and amino acids than by LE and in this regard their findings are consistent with those of our study. Accordingly, administration of PN might increase the risk of CLI more than LE.

Femoral access tended to be associated with an increased risk of CLI in multivariate analyses, and was the site of CVC insertion in 80-90% of cases in this study to prevent accidental catheter removal by patients who were elderly and/or had dementia. In contrast, only 5-10% of CVCs were inserted via the femoral route in a study by Youn et al. (10). Femoral access has been reported to be associated with a greater risk of infectious and thrombotic complications than subclavian access (12) in patients admitted to intensive care units. Our findings regarding the risk of infectious complications are similar.

TABLE 2: Multivariate logistic regression analyses of factors associated with CLI

	OR	95% CI	*P*-value
Frequency of LE administration less than 0.2 times	1.00		
Frequency of LE administration 0.2 times or more	3.12	1.22–8.58	0.02
No administration of PN	1.00		
Administration of PN	7.86	1.45–146.10	0.01
Insertion site was not via femoral access	1.00		
Insertion site was via femoral access	2.85	0.87–13.06	0.09
Increase in BW by 1 kg	0.98	0.94–1.01	0.16

Abbreviations: BW, body weight; CI, confidence interval; CLI, central line infection; LE, lipid emulsion; OR, odds ratio;

In some studies, CLI (including CRLI and CLABSI) occurred at a rate of 8–9 per 1000 catheter days for CVCs (10,11). In our study population, the rate of CLI was lower and infection with *Staphylococcus epidermidis* strains was the most common. These findings are again similar to those of previous studies (10,11).

Our study has some limitations, in particular its retrospective design and small sample size. Other shortcomings include a lack of randomly assigned CVC insertion sites, with femoral access being the most common, unlike in the previous reports.

Overall, our results suggest that administration of LE is associated with an increased risk of CLI in Japanese adult inpatients. However, further prospective studies are needed to confirm our findings.

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