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A new perfusion system to reduce the burden of central-venous-line-associated bloodstream infections in neonates

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SUMMARY

Background: Central-venous-line-associated bloodstream infection (CLABSI) is a significant cause of morbidity and mortality in preterm infants. As there is large variation in the reported effect of multi-modal preventive strategies, it could be relevant to propose new additional strategies.

Aim: To assess the impact of a new perfusion system on CLABSI rate.

Methods: A before-and-after study was performed in infants born at <32 weeks of gestation or with birth weight <1500 g who required a multi-perfusion system connected to a central venous line. In the first 12-month period ('before'), the pre-existing perfusion system (multiple stopcocks) was used. An intervention period then occurred with implementation of a new perfusion closed system, without change in 'bundles' related to various aspects of central line care. During the second 12-month period ('after'), the CLABSI rate was assessed and compared with the pre-intervention period.

Findings: In total, 313 infants were included in this study (before: $N=163$; after: $N=150$), and 46% had birth weight <1000 g. The change in perfusion system resulted in a significant decrease in CLABSI rate from 11.3 to 2.2 per 1000 catheter-days ($P<0.001$). The period was independently associated with an 88% reduction in the risk of CLABSI after implementation of the new perfusion system [odds ratio (OR) 0.12, 95% confidence interval (CI) 0.03–0.39; $P<0.001$]. The duration of central line use was also associated with CLABSIs (for each additional day: OR 1.05, 95% CI 1.02–1.07; $P<0.001$).

Conclusions: Implementation of the new perfusion system was feasible in a large neonatal unit, and reduced the CLABSI rate soon after implementation.

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Introduction

Preterm newborns are highly susceptible to late-onset sepsis (LOS; i.e. occurring after the third day of life) due to an immature immune system, poor skin integrity and the need for invasive procedures [1,2]. In very preterm infants, born at <32 weeks of gestation, LOS is associated with increased mortality, short- and long-term morbidity, and healthcare costs [3,4]. In this population, most cases of LOS are related to central-venous-line-associated bloodstream infections (CLABSIs) [5,6]. For instance, Zipursky *et al.* reported that 72% of 3306 very-low-birthweight infants with hospital-acquired infections, hospitalized in 30 Canadian tertiary care units, had CLABSIs [5]; and Sinha *et al.* reported that, in 218 very-low-birthweight infants with LOS, 206 of 311 LOS episodes (66%) were related to CLABSIs [6]. A reduction in the CLABSI rate in preterm infants could therefore help to reduce antibiotic exposure in this population. Data from 25 studies included in two systematic reviews performed to assess the effectiveness of strategies to prevent CLABSIs in neonatal units show that the baseline CLABSI rate in neonates is extremely variable, ranging from 1.33 to 31.6/1000 catheter-days worldwide, with significant geographical differences [7,8]. Indeed, it ranged from 1.33 to 15.6/1000 catheter-days in the 13 studies performed in North America, and from 3.1 to 31.6/1000 catheter-days for the 12 studies performed in other countries (Europe, Australia, Asia, South America) [7,8]; in France, the last national survey reported 12.4/1000 catheter-days [95% confidence interval (CI) 10.8–14.0] [9]. The incidence and severity of CLABSIs underscore the need for innovative and effective prevention strategies.

Major risk factors for LOS are low birth weight, pre-term birth, and presence of a central venous catheter [1,2,10,11]. Catheter hub colonization, exit site colonization and connections/disconnections are major risk factors independently associated with catheter-related bloodstream infections [12,13]. In addition, the type of catheter used affects catheter-related bloodstream infections; in a review of 15 studies comparing single- and (mainly) triple-lumen catheters in adults with perfusion systems available in the 1980s, multi-lumen central venous catheters were associated with a slightly higher risk of infection compared with single-lumen catheters, but there was no significant difference when low-quality studies were excluded [14].

It is of note that CLABSI prevention strategies usually focus on catheter insertion and maintenance, and access to central venous lines [7,8]. However, intravenous administration of drugs and nutrition solutions requires a perfusion system between the catheter and the administration circuit (bags or syringes, and tubes). This perfusion system can be a ramp of stopcocks or perfusion sets with various tubing configurations; more recently, a new closed perfusion system was designed to reduce physical incompatibility during simultaneous administration of drugs in neonates [15–17]. As this is a closed system requiring fewer manipulations (fewer connections/disconnections, purging system, lifetime of 21 days), and is manipulated remotely from the patient, this perfusion system may have a beneficial effect on CLABSIs. As such, the objective of this study was to evaluate the effect of using the new

perfusion system on the incidence of CLABSIs in preterm infants.

Methods

Study design

This was a single-centre, before-and-after study.

Population

This study was conducted in the 50-bed tertiary neonatal intensive care unit (NICU) of Croix-Rousse University Hospital (Lyon, France). Each year, approximately 650 infants are admitted to this unit, including 240–260 infants born at <32 weeks of gestation, and 90–100 infants with birth weight <1000 g. Infants born at <32 weeks of gestation or with birth weight <1500 g who survived for >3 days and required a multi-perfusion system connected to a central venous line (see below) were included in the present study. Infants were admitted either before (1st December 2018 to 30th November 2019) or after (1st January 2020 to 31st December 2020) implementation of the new perfusion system. In December 2019, the new system was implemented in infants who were already hospitalized, and then in newly hospitalized infants, so that, from 1st January 2020, all infants requiring a multi-perfusion system were equipped with the new system. Data collection was performed in infants admitted from 1st January 2020.

Indications for central line

The need for central line placement or continuation was assessed daily during multi-disciplinary rounds. All infants born at <32 weeks of gestation or with birth weight <1200 g, as well as those with severe respiratory distress or haemodynamic failure, received an umbilical central line during the first 3–5 days of life. Next, a peripherally inserted central line was inserted when the duration of intravenous therapy was likely to exceed 6 days. The central catheter was removed as soon as it was no longer needed. Removal was considered when enteral feeding was ≥ 100 mL/kg/day. No blood products were administered through the peripherally inserted central lines.

Perfusion systems used

Simultaneous infusion of several drugs and parenteral nutrition solution requires a central venous catheter and a perfusion system that connects the catheter to the infusion fluid or drug. Before implementation of the new perfusion system, a standard perfusion system based on three-way stopcocks (Cair, Lissieu, France) was used. Stopcocks were changed every 7 days, or earlier if broken. The stopcocks and hubs were disinfected for 30 s using gauze impregnated with 4% chlorhexidine immediately before and after each manipulation, and wrapped in sterile small drape dressing. The intervention was the implementation of the new perfusion system. The Edelwaiss Multiline NEO including an Escape-Line (Doran International, Toussieu, France) was used during the

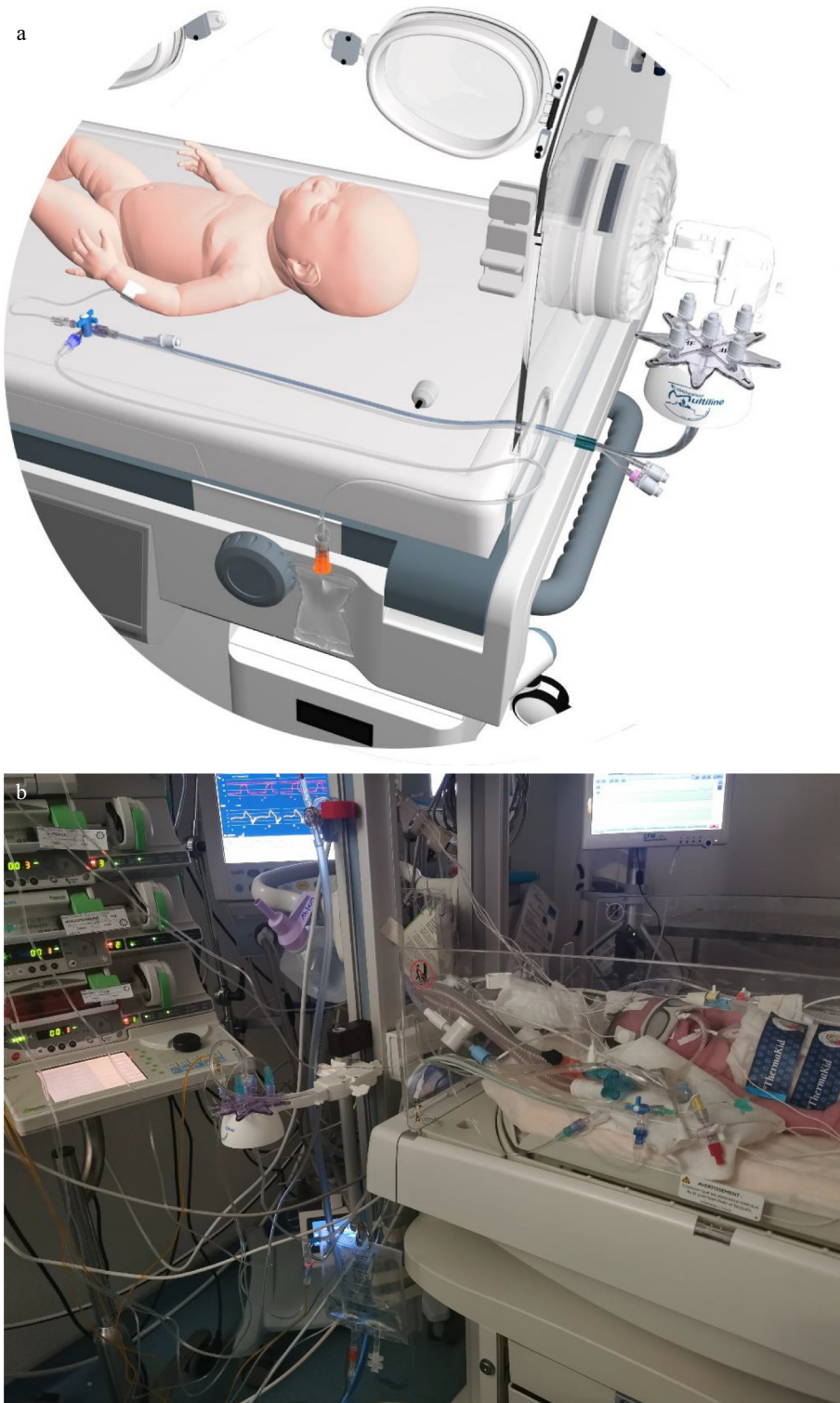


Figure 1. Perfusion systems. (a) Schematic representation of the set-up of the new infusion device Edelwaiss Multiline NEO including an Escape-Line (Doran International, Toussieu, France). (b) Set-up of the new infusion device at bedside. (c) Schematic representation of the standard perfusion system (multiple three-way taps). (d) Schematic representation of the new perfusion system (eight separate lumens enclosed in a single 90-cm-long tube). The solution or drug with the highest flow is connected to the high-flow (HF) lumen to prevent incompatibility between drugs or solutions administered in the four other lumens connected to ports 1–4. It is a closed system, accessed from outside the incubator, except for the short emergency line. The Escape-Line avoids the delay between the application of the product and its administration to the newborn by purging the previous product into a bin bag.

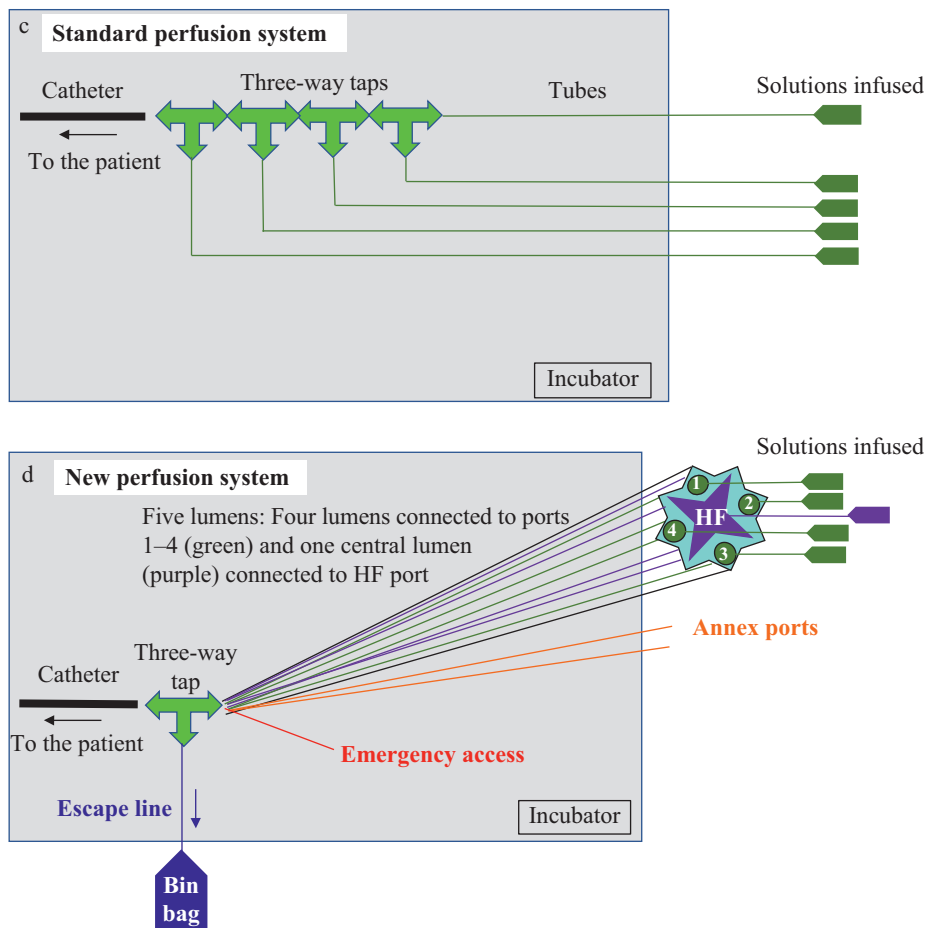


Figure 1. (continued).

second period (Figure 1). This is a closed system allowing the administration of eight medications or nutrition solution simultaneously without mixing to prevent physical incompatibility and precipitate formation [17]. Eight ports are connected to eight separate lumens enclosed in a single 90-cm-long tube. Seven ports are accessible outside the incubator, which reduces the need for intervention on the central line close to the insertion site inside the incubator and therefore in a warm and humid atmosphere [18]. One port – the high-flow port – is central, connected to the central lumen, and is used to administer the solution with the highest flow, which is often parenteral nutrition solution. Four other ports, numbered 1–4, are connected to four lumens. There are also two annex ports that are connected to two tubes close to the multi-lumen tube upstream of the three-way stopcock. The last port is the emergency port, allowing administration as close as possible to the patient. The Edelwaiss Multiline NEO is connected directly to the single lumen of the venous catheter through a Luer-lock connection. The Escape-Line is connected to a bin bag to purge products, and therefore avoids opening the system and also avoids delay between the application of a product and its administration to the patient. According to the manufacturer, the perfusion system is validated for a 21-day period (European Community marking), which may reduce the number of perfusion system changes, and therefore the number of manipulations of the central venous line [12,13]. A first version of this multi-lumen perfusion system was planned to be evaluated in a

prospective study registered in 2015 (ClinicalTrials.gov, NCT02633124) [19], but the study was stopped in 2020 for technical reasons related to product availability. Since then, a modified version has been manufactured, including the addition of an Escape-line and two supplementary ports, allowing the administration of eight medications simultaneously, to better correspond to the needs of drug administration in the most severely ill neonates (Figure 1).

The same central line insertion and maintenance procedures were used before and after implementation of the new perfusion system (Table S1, see online supplementary material). These concerned hand hygiene, barrier precautions, skin antisepsis, dressing assessment and change, replacement of administration sets, and catheter hub disinfection.

Training sessions are mandatory before using the new perfusion system, according to the manufacturer's recommendations. These sessions were organized for all members of the team likely to use the new perfusion system (nurses and neonatologists).

Data collected

Characteristics of infants at birth and at discharge, neonatal morbidities and treatment (insulin, vancomycin and systemic postnatal steroids) during hospitalization were collected from electronic medical files (ICCA; Philips, Suresnes, France). Infants were considered to be inborn when they were born at a

tertiary care centre. Data were collected about moderate or severe bronchopulmonary dysplasia (BPD; ventilatory support or oxygen therapy at 36 weeks), patent ductus arteriosus (PDA), grade ≥ 3 intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL), stage ≥ 2 retinopathy of prematurity (ROP) and grade ≥ 2 necrotizing enterocolitis (NEC). Severe morbidity was defined as the presence of at least one of the following: surgical PDA, stage ≥ 2 ROP, grade ≥ 2 NEC, moderate or severe BPD, grade ≥ 3 IVH or PVL. Anthropometric data were collected at birth and at 36 weeks or discharge, whichever came first. Z-scores were calculated, with infants considered to be small for gestational age when the z-score for body weight was ≤ -1.28 (10th percentile equivalent) [20].

The number of LOS cases was noted, with LOS defined as infection occurring after the third day of life. The main outcome measure was the CLABSI rate, expressed as the number of infections/1000 catheter-days. CLABSI was defined as a laboratory-confirmed bloodstream infection (see below), not related to an infection from another site, which developed 48 h after placement of a central line or within 48 h of its removal [21]. When a skin commensal was identified, infection was confirmed when the micro-organism grew in two blood cultures; and when only one blood culture was positive, infection was confirmed only when at least one of the following criteria were present: C-reactive protein >10 mg/L, bacterial growth <15 h, another sterile site with identical antimicrobial susceptibility pattern of each isolate, and clinical signs suggestive of infection together with positive laboratory results not related to an infection at another site [22,23]. CLABSI was diagnosed by two senior neonatologists based on these criteria. There was no change in antibiotic treatment guidelines between the two periods.

For each central venous catheter insertion, the type of catheter (umbilical or peripherally inserted) used and duration of use were noted to calculate the number of catheter-days (i.e. number of days with a central line). The catheter utilization ratio was calculated by dividing the number of catheter-days by the number of patient-days for the total study population.

Diagnosis of bloodstream infection

In infants with suspected infection, two blood cultures were obtained. The minimum volume for a blood culture inoculated in each (aerobic and anaerobic) bottle was 1 mL (Bac/Alert; bioMérieux, Marcy l'Etoile, France). Blood cultures were incubated in a continuous detection automaton (Bactalert Virtu; bioMérieux) for 5 days. When it revealed bacterial or fungal growth, subculture was performed on adapted plates followed by identification by matrix-assisted laser-desorption and ionization time-of-flight mass spectrometry (Vitek MS; bioMérieux), and antibiotic susceptibility testing was performed using a Vitek 2 instrument or disc diffusion method, according to the recommendations of the Committee on Antibiogram of the French Society of Microbiology/European Committee on Antimicrobial Susceptibility Testing.

Safety

Since 2012, care-related adverse events have been collected prospectively through an online system (ENNOV Software, Ennov, Paris, France) at the study centre. Each file completed by any health professional is reviewed and analysed

by the risk management team (senior attending and senior nurses) who propose corrective action if needed, and provide half-yearly reports to the team. Adverse events specifically related to the perfusion system during the study period were extracted from these reports from the following two categories: mild events (i.e. procedure not followed, broken device without any effect for the patient, etc.); and severe events (i.e. events requiring immediate medical intervention, such as involuntary drug bolus with clinical effect). The number of central line losses due to obstruction was also noted.

Statistical analysis

Categorical variables have been described in terms of number and percentage, and continuous variables in terms of median and interquartile range (IQR). For categorical variables, comparisons between groups were performed using Chi-squared test or Fisher's exact test, as appropriate. For continuous variables, comparisons between groups were performed using Student's *t*-test for normally distributed data and a sample size >30 in each group, or the non-parametric Mann–Whitney *U*-test otherwise. Normality was tested using the Shapiro–Wilk test.

Univariate and multi-variable logistic regression analyses were carried out in order to identify factors potentially associated with CLABSIs. Variables with $P < 0.05$ on univariate analysis or known or suspected to be associated with the endpoint were included in the multi-variable analysis. Results of this analysis are expressed as odds ratios (OR) and 95% CI. Multi-collinearity was assessed by calculating the variance inflation factor (VIF). $P < 0.05$ was considered to indicate significance. All analyses were performed using R Version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

Ethical approval

The study was approved by the Hospices Civils de Lyon Ethics Committee (n°21_658) and registered on [ClinicalTrials.gov](https://www.clinicaltrials.gov) (NCT05058534).

Results

Among 1294 infants admitted between 1st December 2018 and 31st December 2020, 313 were eligible and all were included; 163 received the standard perfusion system (before) and 150 received the new perfusion system (after; [Figure 2](#)).

Characteristics of infants were not significantly different before and after implementation of the new perfusion system, except a significantly higher number of infants were treated by vancomycin before implementation compared with after implementation ([Table I](#)). Nearly half (45.4%) of the infants had birth weight <1000 g, and this did not differ significantly between the two periods (48.5% vs 42.1%; $P=0.33$); the vast majority of infants were exposed to antenatal steroids [92.6% (before: 91.4%; after: 94.0%); $P=0.53$] and were inborn [81.5% (before: 79.8%; after: 83.3%); $P=0.42$]. No infants were transferred from another hospital with a central line already *in situ*.

There was no significant difference in central venous line use between the two periods ([Table II](#)). Twenty-six adverse events were observed: 10 before and 16 after implementation of the new perfusion system. All 16 cases after implementation of the new perfusion system were mild events, while two of 10

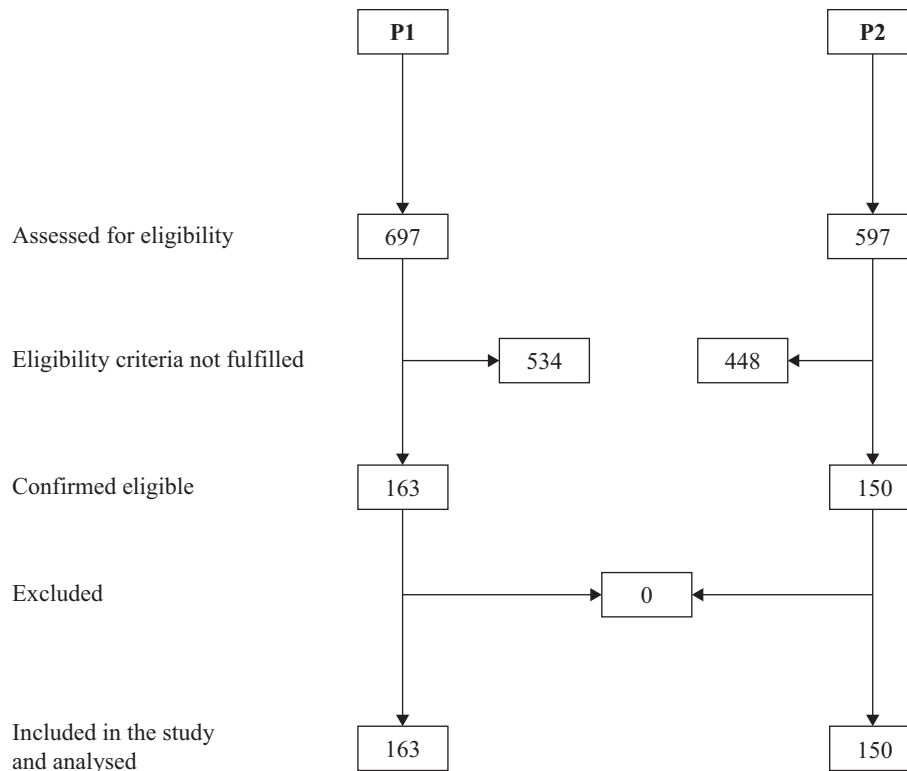


Figure 2. Flow diagram of 322 neonates included in the study and the number of infants with different insertion sites for central venous lines. P1, before implementation of new perfusion system; P2, after implementation of new perfusion system.

cases were severe (hypoglycaemia, hypertension) before implementation of the new perfusion system. Obstruction of the central venous line occurred in 2.5% (4/163) infants before implementation of the new perfusion system and 1.3% (2/150) infants after implementation of the new perfusion system ($P=0.69$).

The number of infants with CLABSIs decreased between the two periods (before: $N=23$; after: $N=5$). There was a significant reduction in the CLABSI rate between the two periods (before: 11.3/1000 catheter-days, 95% CI 7.3–16.5; after: 2.2/1000 catheter-days, 95% CI 0.8–4.7; $P<0.001$; Figure 3). Most CLABSIs were related to coagulase-negative staphylococci, and there was no significant difference between the two periods (Table III). The number of infants treated by vancomycin was significantly higher before than after implementation of the new perfusion system (Table I). The factors independently associated with CLABSIs were the period, associated with an 88% reduction in the risk of CLABSIs after implementation of the new perfusion system (OR 0.12, 95% CI 0.03–0.39; $P<0.001$), and the duration of central line use (for each additional day: OR 1.05, 95% CI 1.02–1.07; $P<0.001$; Table IV). Since the duration of parenteral nutrition and duration of central line use are highly correlated ($r>0.9$ in study dataset), both variables cannot be entered into the multi-variate model simultaneously, so the authors decided to enter duration of central line use alone. All VIF scores were close to 1 (1.21 for period, 1.14 for gestational age, 1.02 for small for gestational age, 1.36 for duration of central line use), suggesting the absence of multi-collinearity.

Discussion

In a population of very preterm infants, the implementation of a new multi-perfusion system was found to be associated with a significant reduction in CLABSI rate.

The baseline CLABSI rate was in line with the previously reported rate in France (12.4/1000 catheter-days; 95% CI 10.8–14.0) [9], and also rates in other European countries, such as Belgium (8.4/1000 catheter-days) [24], Greece (12.0/1000 catheter-days) [25], the Netherlands (12.9/1000 catheter-days, 95% CI 5.1–27.0) [26], Portugal (14.1/1000 catheter-days) [27] and Austria (13.9/1000 catheter-days) [28], as well as certain centres in North America where the incidence is generally lower than elsewhere (15.6/1000 catheter-days [29]; 11.6/1000 catheter-days [30]). The pooled rate of CLABSI rates in neonatal intensive care units reported by the International Nosocomial Infection Control Consortium is 16.4 (95% CI 15.2–17.6) in a population of 14171 neonates, including 32% with a birth weight <1000 g (45.4% in the study population) [31]. The beneficial effect on CLABSI rates observed herein is therefore likely reproducible in other neonatal units. This may be of great importance as, after multi-line implementation, the CLABSI rate was low [2.2 (95% CI 0.8–4.7) per 1000 catheter-days], and it is of note that only 10 of 25 studies included in the two large systematic reviews reported a post-intervention CLABSI rate <2.2 per 1000 catheter-days [7,8]. In addition, the reduction in CLABSI rate after implementation of the new perfusion system represented an 88% decrease, and it is of note that only three of 25 studies included in the

Table I

Characteristics at birth and during hospitalization of infants admitted before or after implementation of the Edelwaiss Multiline NEO perfusion system

	Before N=163	After N=150	P-value
At birth			
Male sex, N (%)	76 (46.6)	73 (48.7)	0.72
Gestational age, weeks	28 [26–29]	28 [27–29]	0.65
Birth weight, g	1000 [805–1220]	1050 [810–1260]	0.51
Birth weight <-1 SD, N (%)	28 (17.2)	26 (17.3)	0.97
Birth weight <1000 g, N (%)	79 (48.5)	63 (42.1)	0.33
Length, cm	35 [33–38]	36 [34–38]	0.44
Head circumference, cm	25 [24–27]	25 [24–27]	0.99
During hospitalization			
PDA	61 (38.3)	54 (36.2)	0.11
Parenteral nutrition, days	11 [6–16.5]	11 [8–18]	0.45
Assisted ventilation, h	86 [14–481]	110 [15–438]	0.57
Insulin treatment, days	7 [4–10]	8 [6–10.8]	0.11
Non-invasive ventilation, days	36.4 [19.7–50.1]	38.4 [21.8–59.0]	0.25
Brain lesions (IVH \geq grade 3, PVL), N (%)	12 (7.5)	13 (8.7)	0.71
Late-onset sepsis, N (%)	48 (29.9)	26 (17.5)	0.03
Vancomycin treatment, N (%)	43 (26.4)	17 (11.3)	<0.001
NEC \geq grade 2, N (%)	5 (3.2)	4 (2.7)	0.99
Moderate or severe BPD, N (%)	52 (44.4)	60 (53.1)	0.19
Systemic postnatal steroids, N (%)	23 (14.1)	32 (21.3)	0.09
ROP grade \geq 2, N (%)	11 (6.9)	7 (4.7)	0.40
Severe morbidity, N (%)	69 (42.9)	68 (45.3)	0.66
Hospital stay, days	52 [36–74]	62.5 [6.5–80]	0.15

PDA, persistent ductus arteriosus; NEC, necrotizing enterocolitis; BPD, bronchopulmonary dysplasia; ROP, retinopathy of prematurity; IVH, intraventricular haemorrhage; PVL, periventricular leukomalacia; SD, standard deviation.

Continuous variables presented as median [interquartile range]. Categorical variables were compared using Chi-squared test or Fisher's exact test, and continuous variables were compared using Student's *t*-test or Mann–Whitney test, as appropriate.

Severe morbidity was defined as at least one of the following complications: surgical PDA, stage \geq 2 ROP, grade \geq 2 NEC, moderate or severe BPD, grade \geq 3 IVH or PVL.

Table II

Central venous line and type of catheter in preterm infants born before or after implementation of the new perfusion system

	Before N=163	After N=150	P-value
Duration of central venous line use			
Total, days	10 [5–14]	10 [6–17]	0.36
Peripherally inserted catheter, days	9 [6–15]	9 [7–17]	0.48
Umbilical venous catheter, days	4 [3–5]	3 [2–5]	0.60
Catheter utilization ratio ^a	0.19 [0.12–0.33]	0.19 [0.12–0.38]	0.90
Insertion site			
UVC then PIC, N (%)	115 (70.5)	111 (74.0)	
UVC alone, N (%)	48 (29.5)	39 (26.0)	0.50

UVC, umbilical venous catheter; PIC, peripherally inserted catheter.

Continuous variables presented as median [interquartile range].

^a Number of catheter-days divided by the number of patient-days.

systematic reviews reported a reduction in CLABSI rate >88% [29,32–34]. However, further multi-centre trials are needed to confirm that these beneficial effects can be achieved in other settings with different baseline practices. Another point of note is that the decrease in CLABSI rate occurred quickly after implementation of the new perfusion system, but it is not comparable to care bundle interventions with multiple interacting components that include behaviour changes and last for a few months to a few years [6,28–30]. In addition, there was also a significant reduction in exposure to vancomycin related

to the significant reduction in the number of CLABSI cases, as there was no change in antibiotic treatment guidelines between the two periods. This reduction is potentially beneficial for the health of preterm infants as it is well known that antibiotic exposure favours dysbiosis, and this has been associated with increased risk of NEC, BPD and ROP [35,36]. However, this study was not designed to evaluate these potential benefits.

During the study period, no severe adverse events related to the perfusion system were observed. There were more mild

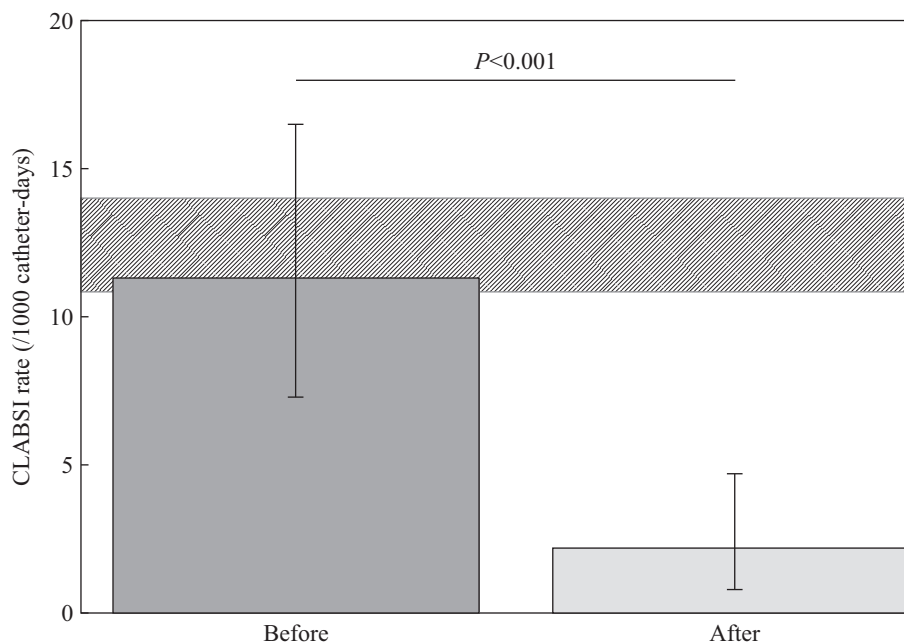


Figure 3. Incidence of central-line-associated bloodstream infections (CLABSIs). Hatched area represents national CLABSI rates (12.4 per 1000 days, 95% confidence interval 10.8–14.0) before and after implementation of the new perfusion system in 313 very preterm infants.

Table III

Pathogens identified in 28 infants with central-venous-line-associated bloodstream infections (CLABSIs) observed in 313 preterm infants born before (P1) or after (P2) implementation of the new perfusion system

	P1	P2
<i>N</i>	23	5
Coagulase-negative staphylococci, <i>N</i> (%)	19 (83)	4 (80)
<i>Staphylococcus aureus</i> , <i>N</i> (%)	2 (9)	0
Gram-negative bacilli, <i>N</i> (%)	1 (4)	1 (20)
Bacillus, <i>N</i> (%)	1 (4)	0

adverse events after implementation of the new perfusion system than before, which is related to the learning curve [37].

The main limitation of this study is the before-and-after design. Firstly, this implied that the staff were not blinded; however, although a double-blind randomized controlled trial is not feasible to evaluate such a new perfusion system, a stepped wedge design could be used in future studies seeking to further investigate the efficacy of a new perfusion system.

Secondly, practice changes could explain the CLABSI rate reduction. This is, however, unlikely because the only change that occurred between the two periods was the use of the new perfusion system. Specific training sessions on the new perfusion system started at the end of 2018, but it did not influence practices as the standard perfusion system was the only system used until December 2019. Routine monthly hygiene education sessions were performed similarly during the two periods. Therefore, practices did not differ between the two periods, notably hygiene practices during aseptic procedures, but also the use of central lines and catheter use rates. As the study was conducted over the course of the coronavirus disease 2019 pandemic, infection control measures were heightened after March 2020, and this could have enhanced adherence to these measures. The authors cannot, however, confirm this as the design of the study did not allow the assessment of adherence to infection control measures and no audit was performed, but infection control measures could have contributed to the decrease in CLABSI rates which started from January 2020. Another limitation could have been related to the number of subjects, because this study only analysed a 2-year period.

Table IV

Univariate and multi-variate analysis for the risk of central-venous-line-associated bloodstream infection in 322 preterm infants

	Univariate analysis		Multi-variable analysis	
	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
Period (after implementation vs before)	0.21 (0.08–0.57)	0.002	0.12 (0.04–0.41)	<0.001
Sex (female vs male)	0.90 (0.41–1.96)	0.790	-	-
Gestational age (for each additional week)	0.69 (0.56–0.84)	<0.001	0.84 (0.66–1.07)	0.163
Antenatal steroids	0.98 (0.52–1.83)	0.944	-	-
Small for gestational age at birth	2.52 (1.07–5.94)	0.033	1.55 (0.58–4.14)	0.378
Duration of central line use (for each additional day)	1.04 (1.02–1.07)	<0.001	1.05 (1.01–1.07)	0.004
Severe morbidity	1.09 (0.51–2.36)	0.820	-	-

CI, confidence interval.

However, this did not prevent the observation of a significant difference between the two periods. Further analyses of 2021 and 2022 are planned to obtain a longer follow-up period.

In conclusion, the present study showed that implementation of a new perfusion system in a large tertiary care unit was associated with a significant reduction in CLABSI rate. This can help to design future randomized trials in populations large enough to confirm the effect on CLABSI rates in other settings, and to assess the impact on short- and long-term health of very premature infants.

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Conflict of interest statement

None declared.

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Author contributions

Jean-Charles Picaud conceptualized and designed the study, designed the data collection instruments, drafted the initial manuscript, and critically revised the manuscript. Sarah Faton collected data, contributed to the analysis of data, and critically revised the manuscript. Pierre Pradat designed the data collection instruments, supervised data collection, carried out analyses, and critically reviewed and revised the manuscript. Blandine Pastor-Diez designed the data collection instruments, contributed to data collection, and critically revised the manuscript. Anthony Martelin contributed to the design of the study, collected data, and critically reviewed and revised the manuscript. Xavier Armoiry contributed to the design of the study and critically revised the manuscript. Dr Stephane Hays designed the study, carried out the initial analyses, and critically revised the manuscript. All authors approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2023.10.004>.

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