Australian Critical Care 32 (2019) 107–111

Contents lists available at ScienceDirect

Australian Critical Care

journal homepage: www.elsevier.com/locate/aucc

Research paper

Impact of MaxZero™ needle-free connector on the incidence of central venous catheter-related infections in surgical intensive care unit☆

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ARTICLE INFORMATION

Article history:
Received 12 December 2017
Received in revised form
7 March 2018
Accepted 14 March 2018

Keywords:
Catheter-related infection
Infusions
Intravenous
Intensive care unit
Central venous catheters
Vascular access devices
Infection control

ABSTRACT

Background: Central venous catheter-related infections (CRIs) are a complication of central venous catheters in intensive care unit (ICU). Some needle-free connectors have been designed to decrease CRI, but there is a lack of data concerning their impact on infection.
Objectives: The objective was to explore the impact of MaxZero™ connectors (BD; Franklin Lakes, US) on CRI in ICU.
Methods: Observational, pre–post design study (2011–2013 and 2014–2016) conducted in the surgical ICU of a tertiary care hospital (18 beds). Patients with a central venous catheter and a length of stay ≥48 h were included. The connectors replaced all disposable caps used on infusion stopcocks and ramps. The primary parameter was to compare the incidence of CRI between the "before" period and the "after" period.
Results: A total of 1633 patients were included (789 "before" and 844 "after"). There was no difference between groups concerning the global duration of catheterisation (12.5 ± 11.5 days vs. 12.1 ± 10.9 days). There were 61 CRIs before and 28 CRIs after the introduction of connectors; the incidence of CRI in the "before" group was 20.33 CRI/year (6.18 CRI per 1000 catheter-days) vs. 9.33 CRI/year (2.73 CRI per 1000 catheter-days) in the "after" group (incidence rate ratio = 0.44; 95% confidence interval = 0.28–0.68, $p < 0.001$). However, after a global analysis of the 6-year period, when adjusting for seasonal effect and pre-existing linear trend, the effect was no longer significant (adjusted incidence rate ratio = 0.57; 95% confidence interval = 0.24–1.35, $p = 0.20$).
Conclusions: Our results do not allow us to conclude to a potential beneficial effect of MaxZero™ on CRI but are compatible with its prolonged and safe use in ICU. Only future prospective works will be able to confirm the value of these connectors for CRI prevention.

☆ MaxZero™ is a trademark of Becton, Dickinson and Company (BD; Franklin Lakes, US). BD freely provided the connectors throughout the study period. BD did not participate in the collection, analysis or interpretation of the results.

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https://doi.org/10.1016/j.aucc.2018.03.003
1036-7314/

1. Introduction

Central venous catheter-related infections (CRIs) are a severe complication of central venous catheters (CVCs) in intensive care unit (ICU). Several measures have been shown to be effective in preventing these infections: use of a checklist, hand hygiene, chlorhexidine skin preparation, daily consideration of the need for catheters, and avoidance of femoral access.[1–3] Thus, the incidence of CRI in ICU in France gradually decreased from 1.38 per 1000 catheter-days in 2007 to 0.66 per 1000 catheter-days in 2014.[4] However, the decline in CRI remains an ever-present objective, with a final goal of "zero catheter-related infection".[5]

Needle-free connectors were initially designed and promoted to avoid blood exposure for healthcare workers. Connectors with a positive valve mechanism were first described as a cause of CRI outbreak, in particular, in ICU.[6–8] However, a new generation of needle-free connectors with different design (minimal internal complexity; reduction or elimination of interstitial or dead space, visible fluid path to help assess proper flushing technique, flat access surface, etc.) has been designed to lower the risk of infection. These connectors showed *in vitro* low bacterial colonisation, but there is a lack of data concerning their *in vivo* impact on catheter colonisation or infection.[9] Given the high incidence of late CRI in our ICU at the beginning of the study and with regard to the risk of thrombosis which may favour CRI, we need to evaluate a needle-free connector with positive displacement. We chose the MaxZero™ (BD; Franklin Lakes, US) mechanical valve, which is a second generation needle-free connector with positive displacement. With regard to the encouraging *in vitro* data in the literature, our hypothesis was that the MaxZero™ mechanical valve could have a beneficial effect on CRI. The objective of this prospective study was to explore the impact of these connectors on CRI in a surgical ICU over a prolonged period.

2. Patients and methods

2.1. Patient population

This observational, before–after study was conducted in the surgical ICU of a University Hospital (18 beds). This work and its design had been approved by our local institutional review board ("*Comité d'Ethique de la Recherche Non-Interventionnelle*", n°E2013-26) and therefore was performed in accordance with the ethical standards laid down in the Declaration of Helsinki and its later amendments. Our institutional review board granted a waiver of patient consent given the low and negligible risk to patients as the intervention was already approved and used in current clinical practice.

All patients admitted to surgical ICU with a CVC and a length of stay in ICU superior to 48 h were included. There were no exclusion criteria. With the hypothesis of a 50% decrease in CRI after introduction of MaxZero™ connectors and given the incidence of CRI in our ICU at the time of the study design (approximately 20/year), we estimated that 600 patients would have to be included in each period to obtain a power of 80% and a two-sided α risk of 5%.

2.2. Study design

The "before" period of the study was retrospective and conducted from January 2011 to December 2013. MaxZero™ connectors were introduced in January 2014. The "after" period was prospective and conducted from January 2014 to December 2016. This was preceded by a training course on the use of MaxZero™ connectors for the medical and paramedical teams. The connectors replaced all disposable caps used on infusion stopcocks and ramps (cf. Fig. 1) and were set on catheter at the time of catheter placement. With the exception of the most proximal valves (to avoid the risk of contamination due to a proximal opening of CVC), all the connectors were changed every 7 days as recommended by the manufacturer (except in cases of macroscopic soil—blood, lipid solution—requiring an immediate connector change). There were no changes of protocol in our usual practices for skin preparation procedures before catheter placement, catheter site, number of catheter lines or daily catheter monitoring. All these parameters were left to the discretion of a senior ICU doctor. Data collection of patients included demographic characteristics, Simplified Acute Physiology Score II (SAPS II), admission pattern, length of hospitalisation, and ICU survival.

CRI diagnosis was based on the criteria established by the French national surveillance system for nosocomial infections in ICU (*REA-Raisin* Network) and by the 2010 consensus conference of the French Society of Intensive Care Medicine and the French Society of Anaesthesiology and Critical Care.[4,10] Thus, a diagnosis of CRI was retained in cases of:

1. *Local infection*: exit site or tunnel infection *or* total/partial regression of the infectious signs within 48 h following catheter removal *and* catheter culture $\geq 10^3$ UFC/ml
2. *Bloodstream infection related to CRI*: bacteraemia or fungaemia *and* catheter culture $\geq 10^3$ UFC/ml *or* differential time to positivity > 2 h between catheter and peripheral blood cultures (in both cases for the same germ as bacteraemia/fungemia).

CRI screening was based on data from the continuous prospective weekly surveillance of nosocomial infections carried out by the hospital's hygiene department (incidence of CRI, catheter localisation, and involved germ). A biannual review of CRI was carried out to detect a possible sudden rise in its incidence and, eventually, stop the use of connectors at an early stage.

The main objective of our work was to compare the incidence of CRI between the "before" period and the "after" period. Secondary objectives were to study the global evolution of CRI rates during the whole period (2011–2016) and to confirm the safety of using MaxZero™ connectors during the "after" period (possible rise of CRI incidence due to a potential misuse of connectors).

2.3. Statistical analysis

Values are presented as mean and standard deviations. For analysis of epidemiological characteristics, the two groups were compared using the Student's t-test for quantitative data and Fisher's exact test for qualitative data.

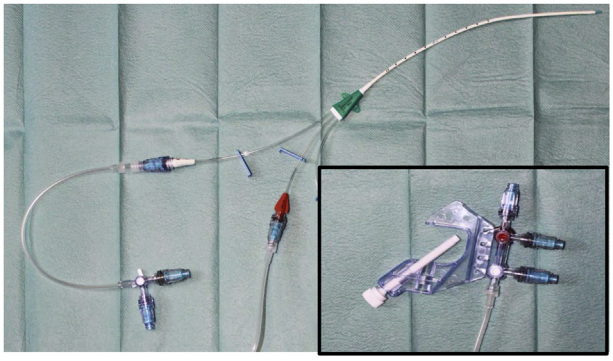

Fig. 1. Illustration of valve positioning on central venous catheter taps, ramps, and extensions.

Missing data concerning the duration of catheterisation (167 missing data) were imputed from the length of stay through a robust linear regression. In view of the biases associated with multiple or recurrent CRI (no independence between episodes), the analysis only concerned the occurrence of a first catheter infection excluding the 2nd, 3rd, or 4th CRI occurring in the same patient. The number of infections was modelled in Poisson regressions. The before–after effect was modelled as binary variable triggered on January 1, 2014. The pre-existing trend was modelled as a linear quantitative effect, and the seasonal effect was modelled as a binary variable with a granularity of 6 months. There were insufficient data to model autoregression.

2.4. Role of the funding source

The Department of Anaesthesiology and Critical Care of the authors' University Hospital designed the study. Becton–Dickinson (BD; Franklin Lakes, US) Corporation, the manufacturer of the MaxZero™ needle-free connectors used in this study, provided the connectors. BD had no role in the trial initiation, study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit. The corresponding author had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

3. Results

3.1. Epidemiological characteristics

During the study period, 2263 patients were hospitalised in our surgical ICU for more than 48 h (1019 in the "before" period and 1244 in the "after" period; cf. Fig. 2). After a first screening, 1633 catheterised patients were included, 789 in the "before" period (77.4% of the "before" population) and 844 in the "after" period (67.8% of the "after" population; $p < 0.0001$). During this 6-year period, the mean length of stay was 16.2 ± 15.9 days, the mean SAPS II was 44.6 ± 18, and the survival rate was 82.4%. Significant differences were found between the "before" and "after" groups concerning length of ICU stay (respectively 17.8 ± 18.5 vs. 14.7 ± 12.9, $p < 0.0001$) and reasons for ICU admission with fewer admissions for a medical cause but more admissions for a surgical cause in the "after" period in comparison with the "before" period. There was no significant difference concerning age, gender ratio, SAPS II, and survival rate between the two groups. Data concerning the population are summarised in Table 1.

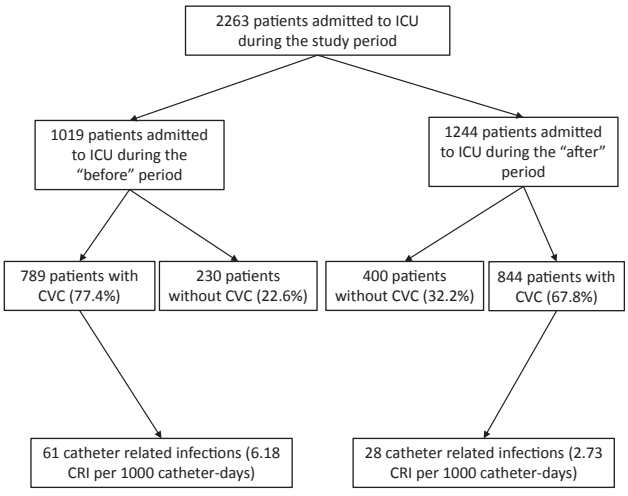

Fig. 2. Flow chart of the study. CRI = catheter-related infection; CVC = central venous catheter; ICU = intensive care unit.

3.2. Incidence of catheter-related infections

There were 61 CRI before and 28 CRI after the introduction of connectors; the incidence of CRI in the "before" group was 20.33 CRI/year (6.18 CRI per 1000 catheter-days) vs. 9.33 CRI/year (2.73 CRI per 1000 catheter-days) in the "after" group (incidence rate ratio = 0.44, 95% confidence interval = 0.28–0.68, $p < 0.001$; cf. Figs. 2 and 3). There was no significant decreasing linear trend of CRI during the "before" period (3-year period), but a global analysis of the 6-year period adjusted for biannual and seasonal effects showed a progressive decrease in the incidence of CRI over 6 years without a sudden discontinuity effect in January 2014 (cf. Fig. 3). Thus, in the Poisson model taking into account these data, the drop in CRI in the "after" period was no longer significant (adjusted incidence rate ratio = 0.57, 95% confidence interval = 0.24–1.35, $p = 0.20$). Concerning patients with CRI, there was no significant difference between the "before" and "after" groups for the duration of central venous catheterisation before diagnosis of CRI. There was no significant difference concerning the bacteria species involved in CRI between the two groups.

3.3. Catheterisation modality

There was a significant difference concerning the insertion site with more jugular and fewer femoral catheters in the "after" group than in the "before" group (57.7% vs. 43.9% and 21.3% vs. 29.8%, respectively; $p < 0.0001$; cf. Table 2). There was no difference between the "before" and "after" groups concerning the global duration of central venous catheterisation (12.5 ± 11.5 days vs. 12.1 ± 10.9 days, respectively).

4. Discussion

Our work shows a significant decrease in the incidence of CRI during the 6-year period introducing the use of MaxZero™ connectors. The pre-existing linear trend could mask an effect at the introduction of the MaxZero™ connectors, but there was no visible discontinuity or any inflection on the trend. To our knowledge, this is the first study that has prospectively analysed the use of these devices over such a long period of time. We did not find any increase in the number of CRI after the introduction of connectors.

A previous prospective multicentre study showed a decrease in CRI after changing from either negative or positive intravenous connectors to a zero fluid displacement connector. However, owing to some methods and data presented in this work and after interdisciplinary scientific investigation, this article was retracted.[11] A recent meta-analysis reported a significant decrease in CRI after implementation of second generation needle-free connectors.[12] However, the data included in this study only concerned "grey literature" (poster or oral presentation reports) were set in medical, paediatric, or cardiac ICU and were mainly retrospective over short time periods. MaxZero™ devices allow the maintenance of the catheter as a "closed system" without the need to open the catheter lines for infusion which could explain the beneficial trends observed. Therefore, our prospectively obtained results in a surgical ICU are not discordant with this previous meta-analysis.

The use of second generation positive valve connectors is still relatively new and not generalised in ICU. Their impact on the management and complications of central venous catheterisation is still poorly understood. There was a potential risk that, after a first period of rigorous valve use following the initial training course (with a decrease in CRI), we might have found an increase in CRI

Table 1
Epidemiologic characteristics of the studied population.

Patient's characteristics	Global population	"Before" period (January 2011–December 2013)	"After" period (January 2014–December 2016)	p Value
Number of patients	1633	789	844	
Age (years)	59.7 ± 16.9	59.8 ± 17	59.7 ± 16.7	0.88
Sex ratio (M/F)	2.3	2.52	2.11	0.11
Length of stay (days)	16.2 ± 15.9	17.8 ± 18.5	14.7 ± 12.2	**<0.0001**
SAPS II score	44.6 ± 18	45.2 ± 17.8	44 ± 18.2	0.19
Reason for ICU admission				**<0.05**
Medical	281 (18.7%)	163 (21.5%)	118 (15.9%)	
Surgery	981 (65.3%)	475 (62.7%)	506 (68%)	
Trauma	240 (16%)	120 (15.8%)	120 (16.1%)	
Missing data	131 (8%)	31 (3.9%)	100 (11.8%)	
Survival	1336 (82.4%)	639 (81.3%)	697 (83.4%)	0.3

SAPS II = Simplified Acute Physiology Score II; ICU = intensive care unit.
Results are expressed as mean ± standard deviation for quantitative data or absolute value with percentage for qualitative data. p value < 0.05 are in bold.

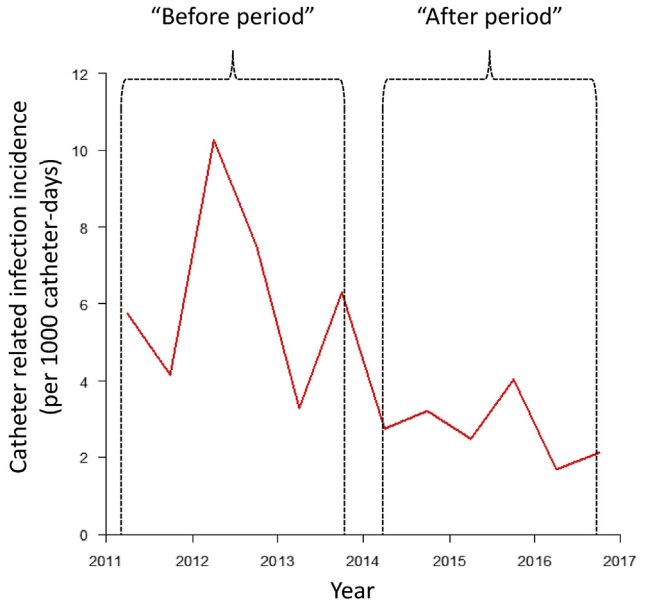

Fig. 3. Evolution of the incidence of catheter-related infections during the study period.

due to misuse. Over the 3 years of the "after" period, we did not see any new rise in CRI rates. However, it has been shown that improper use of connectors could lead to an increase in infection; therefore, it appears important to continue CRI monitoring to detect misuse of needle-free connectors.[8] Our work only focused on the consequences of connectors on CRI, but some studies have reported that positive-displacement connectors may decrease thrombotic catheter occlusions through prevention of blood reflux in the intravascular catheter.[13] It might be interesting to prospectively study the impact of their use on the thrombotic complications related to CVCs in ICU. A recent study has shown that some needle-free connectors may lower the infusion rate of rapid fluid administration.[14] However, this work did not include the MaxZero™ connector and was not interested in the CVC. During our 3-year experience using the MaxZero™ connector, we encountered no problems with rapid fluid administration. A new work focussing on this concern with MaxZero™ connectors could also be considered.

Despite these encouraging results, our study has several limitations. First, it is a pre–post design study that can only test association and not cause–effect relation. Currently, it does not seem reasonable to consider a prospective randomised controlled trial to explore the impact of these connectors on CRI: low incidence of CRI in ICU (with a need for several thousand patients in each group) and difficulty in isolating a specific action or device with a beneficial effect in a bundle of care combining several simultaneous actions. We retrospectively analysed the "before" period, and the effect of valve introduction was indistinguishable from the pre-existing linear trend. There was a slow and continuous decline from 2011 to 2016 (with some oscillations), but we did not identify any discontinuity, and therefore, the assumption of a pre-existing trend cannot be rejected (nor affirmed because, by restricting to the first 3 years, the downward trend was not significant). However, data from the medical literature concerning these kinds of connectors are in favour of the benefits of the MaxZero™ valve.[15] Second, recommendations and practices related to the placement of CVCs have greatly evolved between 2011 and 2016 (especially with the recommended use of alcoholic chlorhexidine and ultrasound guidance). These aspects of catheter insertion were not controlled and left to the discretion of the senior intensivist. However, it is likely that individual changes in our practice could have had an impact on the decrease in CRI. Thus, there were fewer femoral catheters in the "after" group, whereas the literature suggests that femoral catheters show more CRI than jugular or subclavian catheters.[16] Moreover, maintenance practices by the nurses caring for the lines (frequency of dressing changes, cleaning practices of needle-free connectors, etc.) could also impact CRI rates. Therefore, it is possible that all these changes in practices could have contributed to the downward trend in CRI observed in our study. However, as shown by the average time between insertion and infection diagnosis, the overwhelming majority of our CRI occurred late and were therefore more related to catheter maintenance problems than with initial placement procedure (impacted by echography or chlorhexidine disinfection). Finally, although nosocomial infection rates were found to be higher in surgical ICU and in trauma patients compared to medical ICU, our incidence of CRI at the beginning of the study was above the average incidence in France (6.18 CRI per 1000 catheter-days in the "before" period vs.

Table 2
Sites of insertion of central venous catheters during the "before" and the "after" periods.

Insertion site	"Before" period (January 2011–December 2013)	"After" period (January 2014–December 2016)
Jugular	336 (43.9%)	470 (57.7%)
Subclavian	202 (26.4%)	171 (21%)
Femoral	228 (29.8%)	174 (21.3%)
Missing data	23 (2.9%)	29 (3.4%)
Total	789 (100%)	844 (100%)

Data are expressed as absolute value and percentage.

0.84 CRI per 1000 catheter-days in 2011 in France).[4,17] The MaxZero™ valve was the first device used for CRI prevention by our team. However, as we were already sensitised to our high level of CRI and to the changes in practices for venous catheterisation, it could also be considered that the use of the connectors could fit into a gradually introduced care bundle. Therefore, we can assume that it might be more difficult to demonstrate a potential benefit of MaxZero™ needle-free connectors in ICUs with a lower incidence of CRI and/or in ICUs that have already set up bundles to prevent these infections.

5. Conclusion

In conclusion, our results, which are not in contradiction with previous works designed over shorter durations, are compatible with the prolonged and safe use of MaxZero™ needle-free connectors in ICU. Thus, the use of these connectors could be a part of care bundles to lower CRI in ICU. Only future prospective works will be able to confirm the value of these connectors for CRI prevention.

Authors' contributions

TC was involved in the study conception and design, in patient recruitment, in acquisition of data, in analysis, and interpretation of data and in manuscript draft. MF was involved in analysis and interpretation of data. PG was involved in the study conception and design, in patient recruitment, and in acquisition of data. AG was involved in analysis and interpretation of data and in statistical analysis. MD was involved in analysis and interpretation of data and in statistical analysis. VM was involved in the study conception and design, in acquisition of data, and in manuscript revision. BV was involved in the study conception and design, in study coordination, in interpretation of data, and in manuscript revision. All authors read and approved the final manuscript.

Acknowledgements

The authors are grateful to Nikki Sabourin-Gibbs, Rouen University Hospital, for her help in editing the manuscript.

Supplementary information

Supplementary data related to this article can be found at https://doi.org/10.1016/j.aucc.2018.03.003.

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