Differences in Bacterial Transfer and Fluid Path Colonization through Needlefree Connector-Catheter Systems In Vitro

MONTANA STATE UNIVERSITY

Center for Biofilm Engineering

M. Ryder[1], G.A. James[2], E. deLancey Pulcini[2], L. Bickle[2], A. E. Parker[2]

(1) Ryder Science, San Marcos, CA, (2) Center for Biofilm Engineering, Montana State University-Bozeman

a National Science Foundation Engineering Research Center in the MSU College of Engineering

INTRODUCTION

Needlefree connectors, injection ports, stopcocks and catheter hubs are immediate entry points to the vascular catheter internal lumen and the bloodstream. The access site surfaces and hubs are exposed to the patients' skin and environmental contamination. Needlefree connectors have been implicated as a source of bloodstream infection. Differences in bacterial transfer rate in the absence of effective disinfection have been evaluated[1]. Equally as important is the disinfection of the connector and catheter hub, and frequency of the device exchange. Disinfection protocols have been vaguely addressed by formal guidelines due to lack of evidence and until recently the availability of effective technology designed specifically for this purpose. In addition, compliance with disinfection protocols by clinicians has been poor.

The CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections[2] advises the exchange of needlefree connectors no more often than 72 hours as a Category II recommendation. Little evidence exists to address this issue.

The assembly of a connector and catheter provides an internal flow path through the connector, catheter hub and catheter internal lumen. Microorganisms entering this system are either flushed directly into the bloodstream (Problem 1) or attach to the intraluminal components during infusion or during the locking period. Biofilm forms (Problem 2) with subsequent release of planktonic bacteria that are then flushed into the bloodstream with infusion (Problem 3). The contribution of biofilm formation in connector vs. the hub, vs. the catheter lumen is unknown.

Numerous risk factors for catheter-related bloodstream infections associated with needlefree connectors have been proposed. Critical factors are attributed to differences in connector device design, aseptic device management, and frequency of connector exchange. The major design components include the access mechanism (split septum, surface septum), the flow path configuration (open path, internal cannula, mechanical valve) and the displacement volume (negative, positive, neutral). A classification model categorizing needlefree connectors based on device design features is seen in Figure 1. The current recommendations are based on particular design features but can these be used to predict infection risk?

PURPOSE

The purpose of this study was to compare six needlefree connectors with regard to the transfer of bacteria through the connector-catheter system and to compare biofilm formation within the connectors, catheter hub and catheter lumen.

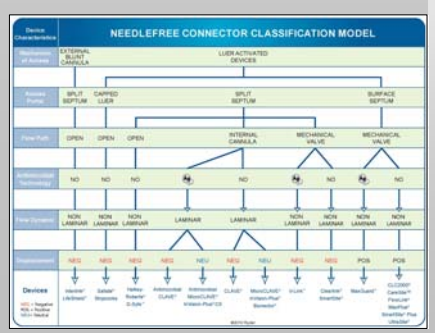

Figure 1. Needlefree connector classification model

METHODS

An in vitro model was designed to simulate clinical use with a 4x daily antibiotic infusion utilizing the SASH method. At the start of each day, the surface of the each connector was inoculated with approximately 10^6 CFU/connector of *Staphylococcus aureus* ATCC # 6538 overnight culture and dried for 30 minutes. A fresh inoculum was prepared at the start of each day. Inoculum density was confirmed by plate count. Connector surface inoculation controls were also plated to confirm inoculation density.

After inoculation of the connectors, each connector was attached to a hub and catheter (5 Fr, single lumen, 60 cm PICC). Each connector-catheter set was placed in a sterile 15 ml conical vial for storage at room temperature (i.e. in between flushes) in order to maintain sterility (Figure 2).

After the 30 minute inoculation dry time, each connector-catheter set was flushed with 3.0 ml of sterile saline. The flush was collected and plated. The catheter-connector sets were flushed two more times with 3.0 ml sterile saline and locked with 2.0 ml sterile Brain Heart Infusion Broth (BHI) for 1 hour. After 1 hour, the catheter connector sets were flushed three more times with 3.0 ml sterile saline. The last flush was collected and plated.

After the last flush, the catheter-connector sets were re-inoculated and dried for 30 minutes and the entire procedure of flushing and locking was repeated so that the connector-catheter sets were flushed for a total of 15 flushes (three flushes x 5 times per day) and were locked with sterile BHI after the first, third, and fourth set of flushes for 1 hour for a final total of 18 flushes per day. The entire inoculation, lock and flush procedure was repeated daily for five days (96 hours). On day 3 (72 hours) and Day 4 (96 hours), two of the connector-catheter sets for each type of connector were removed from the test and destructively sampled.

A total of nine experimental runs were performed. MicroClave was tested in all nine runs.

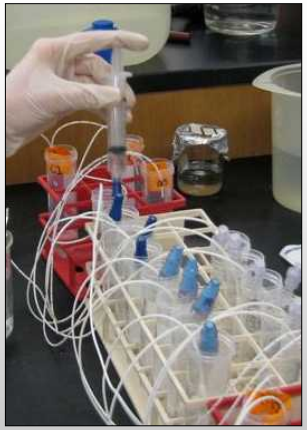

Figure 2. Photo of the connector-catheter sets placed in conical vials between flushes. The technician is flushing one of the connector-catheter sets.

RESULTS

Equivalent Inoculation

Data analysis of the surface inoculation connector controls indicated that there were no significant differences in inoculation density among all six connectors as long as differences as large a 0.86 were assumed to be negligible.

Research Question

Is there a difference between the connectors in the passage rate of bacteria from the connector surface through the catheter and into the bloodstream over time?

The daily mean log density per flush was significantly smaller for MicroClave compared to any of the other connector types tested (Figure 3).

There was a significant increasing trend over the 5 days of the log density per flush for MicroClave, Invision, and Maximus (Figure 3).

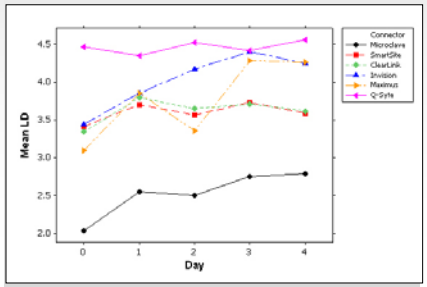

Figure 3. The daily mean log density of the CFU/flush .

The overall mean log density (LD) of the CFUs per flush was significantly smaller for MicroClave than the mean log densities for the other connectors tested (Figure 4).

Q-Syte had the significantly largest mean log density compared to any of the other connector types. SmartSite and ClearLink had significantly smaller mean log densities than Maximus and Q-Syte only (Figure 4).

Connector	Overall Mean Log (CFU/flush)*	p value
MicroClave	2.5	≤ 0.0001
SmartSite	3.6	≥ 0.0677
ClearLink	3.6	≥ 0.0677
Invision	3.8	≥ 0.0677
Maximus	4	≥ 0.0677
Q-Syte	4.8	≤ 0.0001

*calculated as the Least Squares Mean

Figure 4. The overall mean log density of the CFU/flush .

RESULTS

Clinical relevance: These results relate to Problem 1 in intraluminal pathogenesis; the direct transfer of bacteria from the surface of a connector into the bloodstream. The use of a connector with low microbial transfer rate should minimize the risk of bloodstream infection. The Q-Syte split septum design steadily maintained a significantly higher rate of bacterial transfer on each of the five days; even higher than the Maximus positive placement connector while the MicroClave split septum/internal cannula had a significantly lower transfer rate than the other connector designs. These results suggest that the common classification of split septum and mechanical valve is an over-simplification and an unreliable approach for device selection based on infection risk.

Research question

Is there a difference among the connectors in biofilm formation within the connector, catheter hub or catheter lumen?

The mean log density of bacteria in the hub, the catheter segment or connector was always significantly smaller for MicroClave compared to any other connecter except for ClearLink (Figure 5)

There were no significant differences in the mean log densities of bacteria in the catheter segment or connector among ClearLink, Maximus, SmartSite, Q-Syte or Invision connectors (Figure 5).

The mean log density of bacteria in the hub for Invision was significantly larger than any of the other connectors except Q-Syte. The mean log density of bacteria in the hub for Maximus was significantly smaller than Q-Syte and Invision.

Connector	Connector Log Density	Hub Log Density	Catheter Log Density
MicroClave	2.123	1.871	1.011
ClearLink	2.591	2.368	1.101
Maximus	3.432	2.398	1.980
SmartSite	2.878	2.629	1.386
Q-Syte	3.348	3.159	2.223
Invision	3.306	3.046	1.391

Figure 5. The mean log densities of bacteria in the connector, the hub and catheter segments.

Clinical relevance: The attachment of microorganisms transferred through the connector to the internal surfaces of the connector-catheter system is the second problem related to intraluminal pathogenesis. Bacteria entering the flow path can attach during infusion or during the locking period. The colonized bacteria go on to develop biofilm. These results validate the potential for biofilm formation within the hub and the catheter lumen as a result of bacterial transfer through the connector.

REFERENCES

1. Ryder M, Fisher S, Hamilton G, Hamilton M, James G. Bacterial transfer through needlefree connectors: Comparison of nine different devices. The Society for Healthcare Epidemiology of America. Baltimore, MD. April 2007.

2. O'Grady N, et al. Guidelines for the prevention of intravascular catheter-related infections. ICHE. 2002 Dec;23(12):759-69.

RESULTS

Research question

Can biofilm formation within the connector, catheter hub or catheter lumen predict the bacterial transfer rate into the bloodstream?

The log density of bacteria in the connector was the only significant predictor of the log density of bacteria in the flush (p=0.088).

Clinical relevance: Clinical relevance: This question addresses Problem 3 in intraluminal pathogenesis: the release of planktonic bacteria shed from the biofilm is flushed into the bloodstream with infusion. Given that the connector is the predictor of the bacterial burden flushed into the bloodstream, the choice of connector becomes a critical decision point in the prevention of catheter-related bloodstream infection. It also points to the importance of the frequency of exchange of the connector to avoid hub and catheter lumen biofilm formation.

Research question

Is there a difference among the connectors in biofilm bacteria within the connector at 72 compared to 96 hrs?

The differences in the log density in the connecters at 72 and 96 hours was dependent on the connector (Figure 6). Maximus, Q-Syte and Invision maintained the highest counts for both days. Log densities in ClearLink and SmartSite increased between 72 and 96 hours. MicroClave, which also increased in log density from 72 to 96 hours, had the lowest log density of all the connectors tested.

Clinical relevance: The frequency of connector exchange policies varies greatly in clinical practice. Three of the connectors allowed a consistent high number of bacteria transfer on a daily basis while three increased over the 96 hours but still remained below the high levels. The data indicates that the exchange frequency is device dependent which brings into question the 72 hour exchange recommendation.

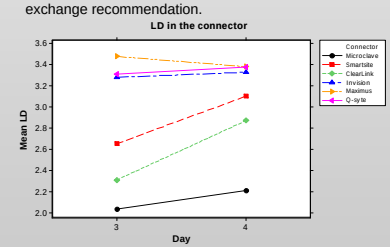

Figure 6. The overall mean log density in the connector.

CONCLUSIONS

- The risk of transfer of bacteria from a contaminated connector surface through the hub and catheter lumen and into the bloodstream is dependent on the type of connector used. The MicroClave had significantly lower bacterial transfer rate than the other connectors.
- Biofilm formation in the catheter hub and internal lumen can result from bacteria transferred through a needlefree connector.
- Biofilm formation within the connector is the best predictor of the number of bacteria flushed into the bloodstream.
- The frequency of connector exchange should be based on the specific connector in use because the use of different connectors results in different levels of biofilm formation within the connector, catheter hub and catheter.

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