A Review of Central Venous Catheter Related Infections (CVCRI) in patients receiving home total parenteral nutrition at the Bristol Royal Infirmary: Microbe Epidemiology, Diagnosis of Infections and Management

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Background

Intestinal failure is a group of disorders, with varying aetiology, that results in an inability to absorb protein-energy nutrition from the gut and difficulties maintaining water and electrolyte balance. It can be the consequence of bowel length loss, obstruction, dysfunctional motility and extensive mucosal disease. Long term artificial nutrition and fluids can be provided in the form of total parental nutrition (TPN) through a central venous catheter (CVC). The Bristol Royal Infirmary (BRI) manages over 60 patients requiring home TPN. Home TPN is under-reported, but there are likely 1500-2500 patients accessing home TPN services across the UK (1). However, long term central venous catheters are at risk of microbial colonisation and blood stream infection (central venous catheter related infection, CVCRI). Microbes can originate from the skin microbiome, the catheter hub, or can seed from other infected sites or non-sterile infusions. Bacteria can form biofilm for protection against host immune cells and antibiotics. From this, planktonic (free-swiming) bacteria disperse, causing CVCRI. Disseminated CVCRI can cause endocarditis, osteomyelitis and septic shock (2). Thus CVCRI is a major cause of morbidity and mortality, as well as costly to acute-care providers in healthcare resource use.
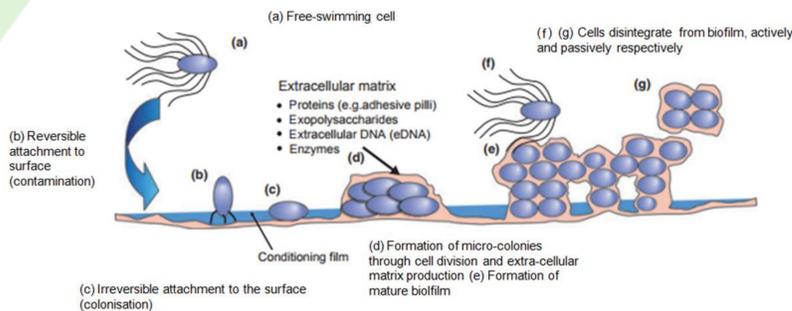

Figure 1: Development process of CVCRI biofilm. Adapted from Römling U, Balsalobre C. Biofilm infections, their resilience to therapy and innovative treatment strategies. J Intern Med. 2012 Dec;272(6):541–61

Aims

Given the relative rarity of home TPN, supporting services must engage in continual audits to ensure high quality, patient centred care is being delivered. Our primary aim was to examine whether we are following University Hospitals Bristol NHS Trust guidelines for diagnosis of CVCRI. Suspected CVCRI should be confirmed through consecutive peripheral and central line cultures with differential delay to positivity and threshold colony counts provided. We examined whether 100% of patients have both a peripheral and central blood culture taken at the time of diagnosis. We also performed an exploratory ecological analysis of; indication for TPN, lines function, microbial epidemiology and treatment pathways. We hope that through a description of baseline infection rates, hypotheses addressing colonisation and infections can be generated.

Methodology

We reviewed the physical and electronic records of patients admitted with CVCRI from a long-term CVC between November 2015 and November 2016. These patients were identified through the GastroHep database on the hospital intranet. Records of admissions with CVCRI are inputted into this database by the community nutrition nurse specialist team.

Results

There were 23 separate infective episodes throughout the year, of which 2 events were from patients with repeated infections. This was out of 64 patients receiving home TPN during the study period.
Mean Age of patients: 51.7yrs
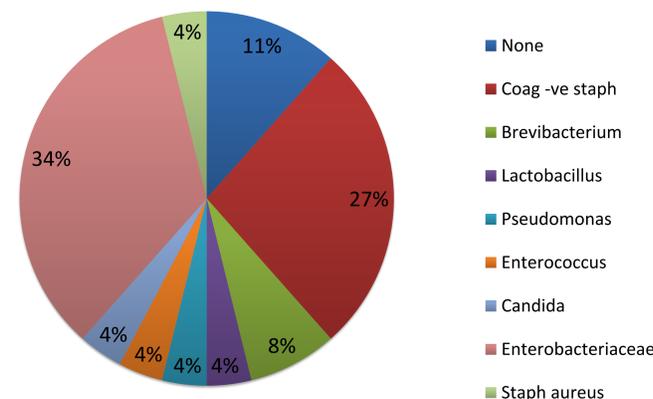Male/Female ratio of patients: 21% M, 79% F

Table 1: Clinical indication for CVC and TPN

Indication	#patients
Short Bowel Syndrome - cancer resection	6
Short Bowel Syndrome - ischaemic bowel	5
Short Bowel Syndrome - IBD resection	4
Short Bowel Syndrome - Adhesions	3
Idiopathic Gastroparesis	2
Ehlers-Danlos Syndrome	2
Bowel Rest - IBD	1

Table 2: Blood Cultures taken on suspicion of CVCRI

Culture taken regardless of site	100%
Central Culture	96%
Peripheral Culture	87%
Both Peripheral and Central Culture	83%

Figure 1: Bacterial growth in admission line cultures

Legend:
- None — 11%
- Coag -ve staph — 27%
- Brevibacterium — 8%
- Lactobacillus — 4%
- Pseudomonas — 4%
- Enterococcus — 4%
- Candida — 4%
- Enterobacteriaceae — 34%
- Staph aureus — 4%

83% of patients had both central and peripheral cultures taken on suspicion of CVCRI (table 1). The most common microbes causing CVCRI were Gram negative bacilli, Coagulase negative *Staphylococci* and then *Brevibacterium*. Interestingly, 11% of cultures did not grow any organisms (figure 1).

18 different combinations of systemic and line lock antibiotics were used in the treatment of CVCRI, with mean course length of 7.36 days (sd of 3.34). 10 patients admitted with CVCRI (43.4%) went on to have line removal and a new line inserted. Line lock was used in 12 cases and statistical analysis showed no significant improvement in treatment of infection (Odds ratio 0.894). Recurrence occurred in two patients, one with Serratia Marcescens, the other Brevibacterium.

75% of infection admissions were using their lines in the community for TPN +/- fluids and IV medications, compared to 25% of admissions who used their lines for fluids alone. Both patients who experienced repeated infections were using their line for TPN, fluids and IV medications.

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Discussion

At the BRI we are not achieving full compliance with guidelines for diagnosis of CVCRI. Only 83% of patients had both central and peripheral cultures taken on suspicion of CVCRI. However this could be due to a number of factors including; poor venous access, needle phobia and electronic mis-coding from which site the culture was taken from.

According to the literature the most common CVCRI causing microbes are, in order of prevalence; coagulase-negative Staphylococci, Staphylococcus aureus, enteric Gram-negative bacilli and Candida spp (2). Our most common pathogens were gram negative bacilli, coagulase-negative Staphylococci and no pathogen cultured. Our findings highlight the challenges of diagnosis through catheter sparing techniques i.e. blood cultures. These methods have 74–84% sensitivity and 98–100% specificity (3). Many of the microbes identified are common skin commensals that might have arisen from suboptimal skin or blood bottle disinfection. In our cohort we see an under-representation of Staphylococcus aureus and Candida compared to the literature, both biofilm forming pathogens that may be strongly held in the biofilm layer and unretrieved.

The volume of antibiotic combinations was unexpected, but not unsurprising. In an era of antimicrobial stewardship guidelines on management encourage discussion with microbiology for tailoring of antibiotics dependent upon blood culture sensitivities and clinical findings. Patient allergies also need to be taken into account. Despite adequate antibiotic therapy, close to half of all patients and 100% of patients with reinfection went on to have their CVC removed. This reflects the challenges of biofilm formation and eradication. There was not enough data to correlate TPN use and increased susceptibility to infections.

In the future we will be working to streamline the GastroHep database. The aim for home TPN patients is to minimise and stop TPN use once oral/enteral intake can be restarted. As a result it can be challenging to track catheter days per patient and this knowledge is essential for calculating the prevalence of CVCRI. Further audit work should also examine central vein thrombosis and occlusion, as well as abnormal liver function tests. Quality improvement projects should also focus on quality of life indicators for these complex patients.

More ambitious work is awaiting funding, but will aim to optimise an *in vitro* model of intra-vascular catheter infection and screen for potential diagnostic biomarkers. Biomarkers have the potential to create rapid and simple tests for the presence of biofilms in CVC and can be developed for identifying and monitoring CVCRI.

Conclusion

Long-term CVC can provide life sustaining nutrition in intestinal failure. However they remain a potential source of difficult to treat infection, with challenging biofilm forming microbes. Our audit highlights the importance of clinical education and dissemination of knowledge to colleagues to remain vigilant for investigating CVCRI in patients with long-term CVC and features of sepsis and to follow guidelines for diagnosis. The descriptive analysis of microbe epidemiology may act to inform future targeted local guidelines. Further work needs to be done on optimising CVCRI treatment, where a delicate balance exists between catheter salvage and managing infection.