Febrile neutropenia in paediatric oncology and haematopoietic stem cell transplant patients: Utilising microbiology data to inform ongoing antimicrobial stewardship

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BACKGROUND

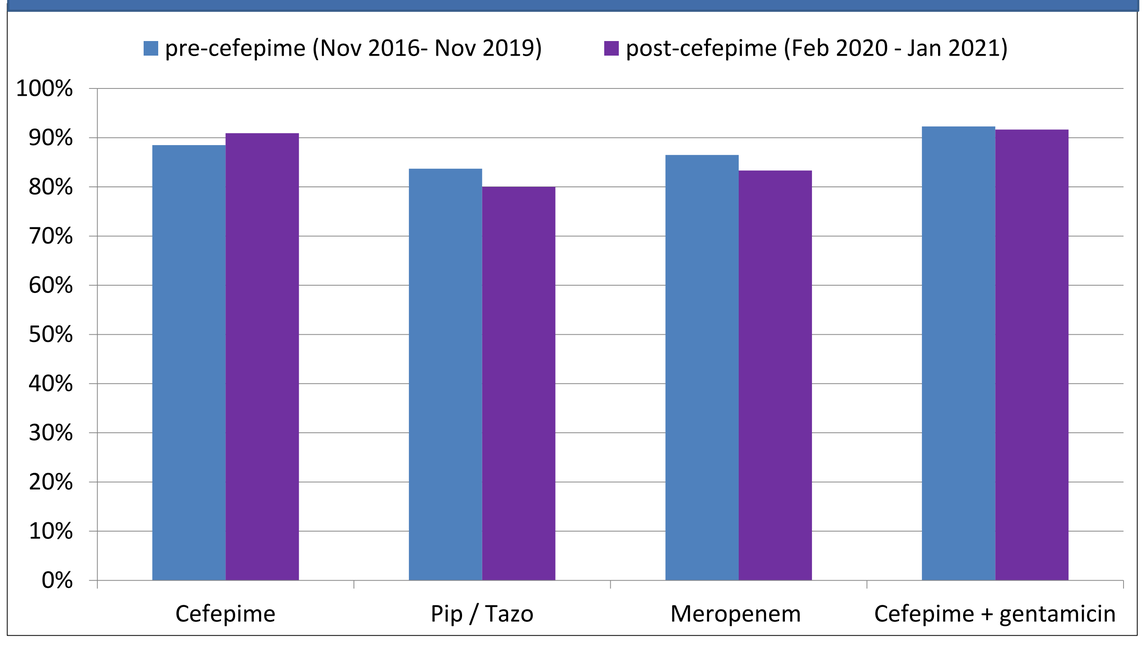
In an era of emerging antibiotic resistance, optimising antibiotic use in febrile neutropenia (FN) is an important challenge. Balancing the desire to minimise antibiotic selection pressure and related toxicities with the need to deliver timely, appropriate and potentially lifesaving antibiotic therapy necessitates an understanding of local pathogen and resistance patterns. In children with FN, gram negative enteric bacteria represent a significant proportion of initial blood culture isolates[1]. Viridans group streptococci, (VGS) which are often penicillin resistant, are also an important cause of bacteraemia in this group[2]. To inform a review of our institutional guideline for FN, we reviewed local microbiological data and implemented prospective microbiological surveillance to guide ongoing stewardship.

METHODS

From November 2016 to October 2019 all positive blood cultures from children with haematological malignancy and or undergoing haematopoietic stem cell transplantation (HSCT) in our oncology unit were reviewed. For all gram-negative isolates, susceptibility to piperacillin-tazobactam, meropenem and cefepime with or without concomitant gentamicin was compared. For significant gram-positive isolates (Viridans group streptococci, methicillin-resistant *Staphylococcus aureus* (MRSA), or Bacillus cereus) antibiotic susceptibility and time to blood culture positivity were determined.

A change from piperacillin tazobactam to cefepime as first-line therapy for febrile neutropenia was implemented in January 2020. Prospective surveillance of gram-negative resistance and *Clostridioides difficile* infections was implemented following this change. Addition of vancomycin in patients at high-risk of VGS continued to be recommended.

Figure 1 – Gram negative isolate susceptibility prior to and following change to cefepime as first-line therapy for febrile neutropenia

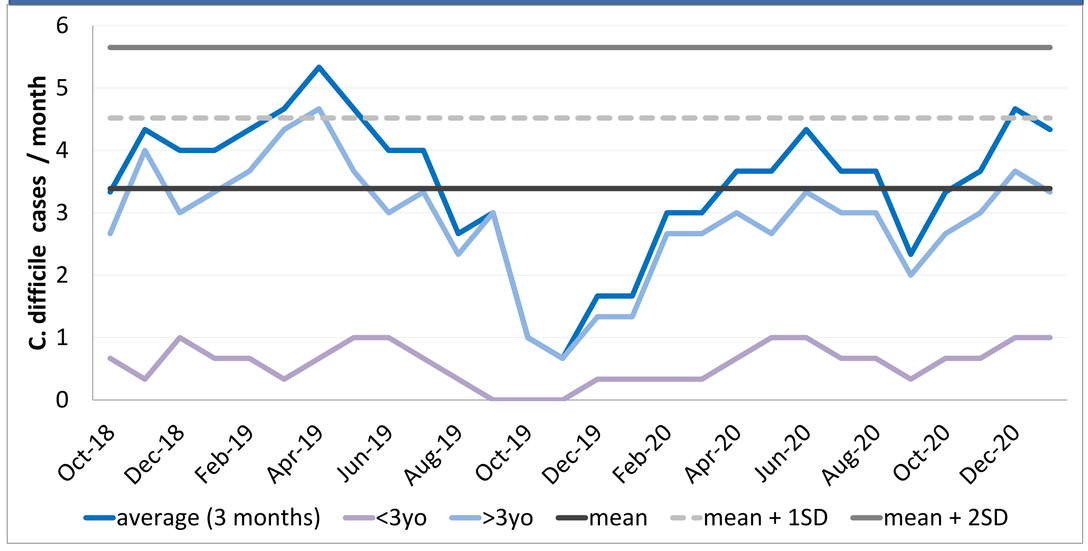


RESULTS

Amongst 49 gram-negative isolates prior to change in FN guideline, susceptibility to cefepime was 88% (43/49), piperacillin-tazobactam 83% (38/46) and meropenem 86% (42/49) (Figure 1). Excluding *Stenotrophomonas* spp. 100% (45/45) of isolates would be susceptible to cefepime and gentamicin combination. Following change to cefepime as first-line FN therapy, there were 10 gram-negative isolates from children with haematological malignancy or undergoing HSCT from February to October 2020. Susceptibility to cefepime remained high (88.9% - 8 of 9 isolates with reported cefepime susceptibility) (Figure 1).

The incidence of *C. difficile* on the haematology oncology ward remained stable compared to previous years (Figure 2)

Figure 2 – *Clostridioides difficile* surveillance (3 month rolling average)



For the 20 significant gram-positive isolates from November 2016 to October 2019 (18 viridans streptococci, 1 B. cereus, 1 MRSA) median time to positivity was 10.5 hours and all isolates flagged positive by 18 hours after sample collection. Of viridans streptococci: 22% (4/18) were penicillin resistant; 89% (16/18) were positive on the first blood culture drawn during the febrile episode.

There were no infection related deaths.

CONCLUSIONS

We utilised local antimicrobial resistance profiles to inform an update to our institutional guideline for management of FN using cefepime as first line therapy. In the 12 months following implementation, ongoing microbiological surveillance did not detect an increase in cefepime resistance or incidence of *C. difficile.* Feedback of time-to-positivity data from gram positive isolates has been used to highlight that empiric vancomycin can be ceased in clinically stable patients with negative blood culture at 24 hours.

Continuation of microbiological surveillance is planned to inform future updates to our FN treatment guideline and to increase prescriber engagement with antibiotic stewardship.

References

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