A prospective evaluation of the clinical impact of Unyvero Multiplex PCR in blood stream infections

Ms Gosia Poznalska, Dr Thomas Smith, Dr Aiden Plant, Dr S Murdoch, Dr Cressida Auckland,
Department of Microbiology, Royal Devon and Exeter Foundation Trust, UK.

Introduction:

- Blood culture (BC) remains the gold standard for guiding antimicrobial treatment in blood stream infections (BSI).
- Although BC has a reported high specificity, results are limited by a considerable time delay and often slow-growing or fastidious organisms are not identified.
- PCR has been proposed to offer early identification of pathogens (most studies report results available within 4-6 hours) and detection of certain antimicrobial resistance genes.
- To help assess the clinical benefit of this at our institution we conducted a small, prospective, laboratory verification trial, comparing routine practice with the added diagnostic step of Unyvero multiplex PCR.

Blood culture bottles

Methods:

A single centre, prospective, verification trial, comparing routine practice with an added initial diagnostic step (Unyvero multiplex PCR) was conducted at the Royal Devon and Exeter Hospital.

Inclusion criteria

- 'Positive' BC samples will be submitted for Unyvero multiplex PCR, if, as determined by attending clinical microbiology consultant:
- Initial gram stain suggests GNR or yeast and there is a high index of suspicion of a resistant organism, or
- Initial gram stain is suggestive of Streptococci and there is a high index of clinical suspicion of a pathogenic organism

Exclusion criteria

- Patient death before completion of PCR analysis or laboratory errors that leads to disruption of standard methods.

Primary outcome was the concordance of Unyvero multiplex PCR with standard methods. Further **secondary outcomes** included: antimicrobial stewardship, infection control precautions (initiated or stopped), and effect on length of hospital stay, retrospectively collected and interpreted by a medical microbiologist.
The study protocol was followed for the first 22 blood cultures received that meet the inclusion criteria, commencing February 2018.

BACTEC blood culture system

Unyvero blood culture cartridge


Unyvero Multiplex PCR system

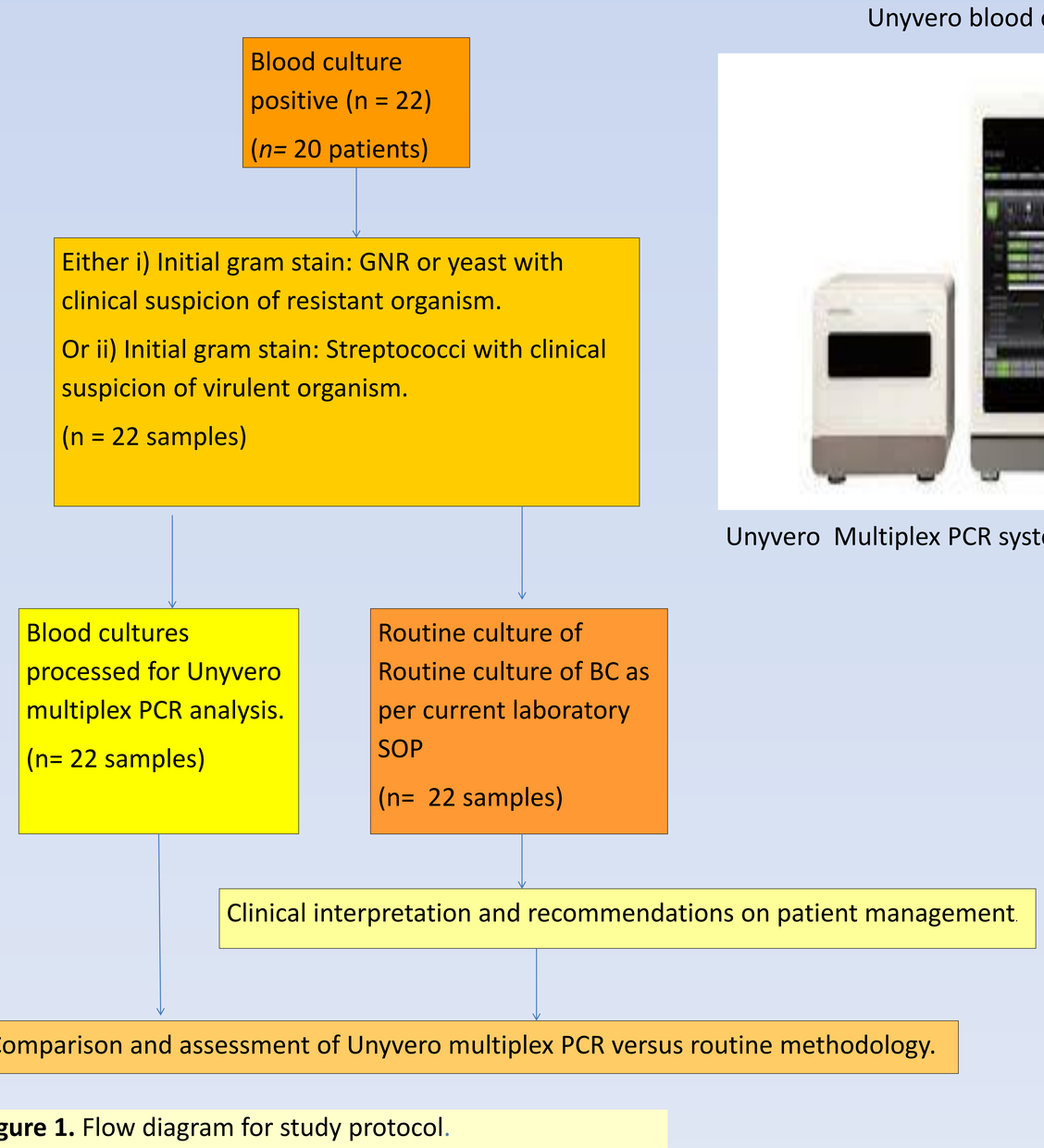

Figure 1. Flow diagram for study protocol.

Results:

- The 20 tests included (2 tests excluded as per criteria) yielded 33 PCR results.
- There were 22 true positive results- 16 where Unyvero matched routine methods and provided both the genus and species and 4 where Unyvero matched genus but there was no identification of species. For 2 results 'Universal bacterium' was detected; in these cases the Unyvero P50 PCR panel did not include the bacteria identified by culture.
- There were 4 false negative results. There were 6 false positive results.
- Average time to Unyvero result was 5 hours. Standard methods produced organism identification in a mean of 18 hours 17 minutes and sensitivities within 48 hours.
- In 2 cases the resistance marker was detected: aac(6')/alph(2"). In neither case did it impact upon secondary outcomes.
- Interpretation of PCR result did not affect measured clinical outcome with regard to: infection control measures or time to discharge in any case. In 5 cases antibiotic stewardship would have been affected- a net sum of 1 dose of restricted antibiotic would have been saved.

Table 1. True positive results lacking genus and/or species

Standard method ID	PCR ID
Streptococcus *parasanguinis*	Streptococcus spp.
Enterococcus *faecium*	*Enterococcus spp.
Streptococcus *mitis/oralis*	Streptococcus spp.
Streptococcus *constellatus*	Streptococcus spp.
Pantoea *agglomerans*	Universal bacterium
Cedecea davisae	Universal bacterium
Streptococcus sanguinis	Universal bacterium

Table 2. False negatives

Standard method ID	PCR ID
Bacteroides *fragilis*	Nil
Staphylococcus *capitis*	Nil
Staphylococcus *hominis*	Nil
Lactobacillus *plantarum*	Nil

Table 3. False positives

Proteus spp.
Escherichia *coli*
Enterobacter *cloacae complex*
Klebsiella *oxytoca*
Citrobacter *freundii/koseri*
Propionibacterium *acnes*

Table 4. Concordance of PCR with standard methods

True positive	False positive	
23	6	**SENSITIVITY = 85%**
False negative	**True negative**	
4	0	
PPV = 79%		

Discussion:

- Use of PCR result would have had no effect on the clinical outcome, with regard to time to discharge or infection control procedures.
- There was small effect on antimicrobial stewardship due to saving a dose of restricted antibiotic.
- A substantial reduction in time to positive result was noted, as expected.
- Overall, the information gleaned from the initial gram stain and clinical history was usually sufficient to formulate an initial plan, including antibiotic choice, and PCR results did little to change this.
- Whilst PCR offers the potential for early identification of organism and resistance markers, this small study shows this does not necessarily significantly impact clinical outcome. Further evaluation, with greater number of samples, and broader inclusion criteria is required to further elucidate its true value.

Currently, the RDE is a low prevalence area for carbapenemase-producing enterobactericeae (CPE) and no CPE were included in this study. Further evaluation in high prevalence CPE areas is required.

Declaration of interests:
CA, TS, GP, SM, AJP: none to declare

The testing platform and consumables provided by Curetis. Curetis GmbH,Max-Eyth-Str. 42,71088 Holzgerlingen , Germany.Tel.: +49 (0)7031 / 49195-10 email: contact@curetis.com
Data collection, management, analysis, interpretation and write up are conducted equally between CA, TS and GP.