

A new diagnostic tool for rapid detection of bloodstream infections using droplet digital polymerase chain reaction in patients on home parenteral nutrition

A rapid diagnostic test for bloodstream infections

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Introduction: Patients on home parenteral nutrition (HPN) support have an increased risk for catheter-related bloodstream infections. Currently, diagnosing bloodstream infections relies on blood cultures in order to identify the causative pathogen(s). Although blood cultures are considered the gold standard, it takes time for blood cultures to become positive (fungi 2-5 days, bacteria 1-2 days), resulting in a significant window before a correct diagnosis is made. A more rapid pathogen detection is critical for patient and catheter care, as well as guidance of early antibiotic treatment.

The droplet digital polymerase chain reaction (ddPCR) is a novel culture-independent sensitive molecular technique that allows rapid identification of microbial pathogen DNA in whole blood. The aim of this study was to determine the feasibility and the diagnostic accuracy of the ddPCR to detect bloodstream infections in the HPN-setting.

Methods: We analyzed a set of historically collected frozen blood samples from adult HPN patients with a suspected bloodstream infection, and compared these with blood cultures drawn on the same day. Whole blood samples with possible DNA from microorganisms were isolated and analyzed with ddPCR. The analyses were independently performed by two research analysts, without knowledge of the blood culture results. Study outcomes included the time-to-diagnosis, the detection limit of bacteria and fungi, and the sensitivity and specificity of the ddPCR.

Results: In total, 45 blood samples were collected, of which 15 (33%) had positive blood cultures. Five (33%) blood cultures showed Gram-positive bacteria, three (20%) Gram-negative bacteria, three (20%) contained fungi, and four (27%) blood cultures were polymicrobial. In a short procedure of 4 hours, blood samples were isolated and analyzed. The ddPCR detection limit was approximately 1 to 5 bacteria and 1 to 2 fungi per PCR reaction (approximately one copy of DNA per 40,000 human cells). The sensitivity of the ddPCR was 80% (95%CI 52–96) and the specificity 87% (95%CI 69–96).

Conclusions: This study shows that the ddPCR technique has great potential and that it is able to detect pathogen DNA in whole blood within a short time span of four hours. Currently, the ddPCR has an acceptable sensitivity and specificity for identifying pathogens from whole blood. The ddPCR seems to work especially well in predicting true negative results. A larger prospective study will be conducted to confirm these results.