Comparison of broad-range 16S rDNA PCR with blood culture in diagnosis of bloodstream infections

Jan Tkadlec[1], Milan Kvapil[2], Lucie Šrámková[3], Pavel Dřevínek[1]

[1]*Department of Medical Microbiology;* [2]*Dept. of Internal Medicine and* [3]*Dept. of Paediatric Haematology and Oncology, 2nd Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czechia*

Poster no. #P1938
jan.tkadlec@lfmotol.cuni.cz

Introduction: Rapid identification of causative agents of bloodstream infection (BSI) is one of crucial needs of today's microbiology. A delay in the start of targeted antimicrobial therapy is associated with a decrease in survival of 7.6% with each hour after the start of BSI-associated hypotension[1]. As blood cultures are found to be positive in only 30-40% of patients with serious BSI[2], alternative tests with a higher sensitivity are required to ensure timely targeted treatment and/or de-escalation of empiric antibiotic therapy. For nucleic acid amplification techniques (NAAT), the gratest obstacles in BSI diagnostics seem to be low starting volume of blood and an excess of interfering human DNA.

Objectives of the study: To compare the performance of conventional blood culture (BC) and commercially available broad-range 16S rDNA PCR followed by sequencing (16S PCR).

Material and Methods:

482 blood samples (330 pts) with suspected BSI hospitalized at:

- Department of Internal Medicine (**IM**) – 257 samples (207 pts)
- Department of Paediatric Haematology and Oncology (**HOD**) – 225 samples (123 pts)

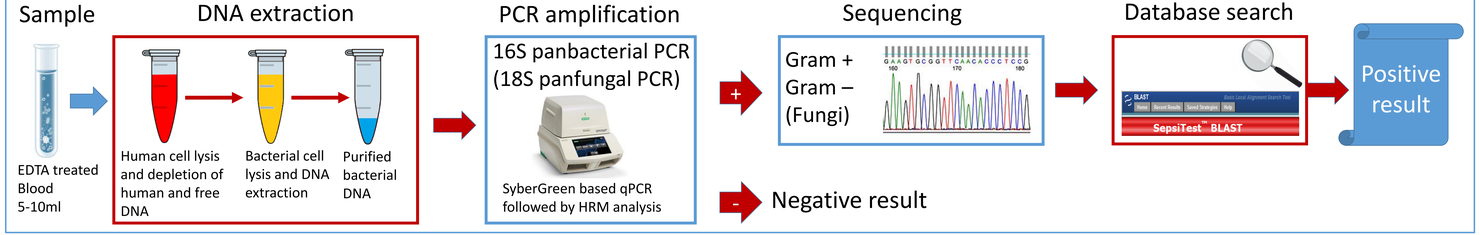
BC (BACTEC™ FX, Beckton Dickinson, USA)
at least one pair aerobic/anaerobic BC bottles per episode

16S PCR (UMD SelectNA, Molzym, Germany)

Clinical significance of positive broad-range PCR findings results was evaluated based on:

- Agreement with blood culture result
- Patient's medical history
- Additional patient's microbiological findings (pre- and post-study testing, when available)
- Opinion of clinician taking care of the patient

16S PCR sample processing



Results:

Table 1: Comparison of 16S PCR and Blood culture results

	16S PCR/Culture					Total
	Concordant results		Discordant results			
	PCR-/BC-	PCR+/BC+	PCR+/BC-	PCR+/BC+	PCR-/BC+	
HOD children	153	11	37	9	15	225
IM	148	35	44	20	10	257
Total	301	46	81	29	25	482

Table 2: Analytical parameters of 16S PCR

Sensitivity	Specificity
0.781	0.835
PPV*	**NPV***
0.558	0.934

*Positive and negative predictive values

Table 3: Analysis of discordant results

	Discordant	Added value of 16S PCR+ result[a] (%)	16S PCR failure[b] (%)
HOD Children	61	15 (6.7)	6 (2.7)
IM	74	21 (8.2)	17 (6.6)
Total	135	36 (7.5)	23[c] (4.8)

[a] Aetiological agens of BSI detected only by 16S PCR
[b] False negative 16S PCR results
[c] in 16 of 23 samples presence of multiple organisms

Conclusions: The NAAT-based approach was applied to 5-10 ml of blood samples after depletion of human DNA which was expected to improve the diagnostic value of the method. The 16S PCR and the culture provided concordant results in 347 of 482 samples. In addition, the 16S PCR detected a new or additional relevant organism in 36 (7.5%) samples, while in 23 (4.8%) more samples it failed and was regarded to be false negative. Therefore, the NAAT-based method seems to be worth considering to complete the BSI diagnostics, but negative PCR results are requested to be carefully checked by blood culturing.

Acknowledgements: Supported by Ministry of Health of the Czech Republic, grant no. AZV15-28157A.

References:
[1]Kumar, A. *et al*. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006 Vol. 34, No. 6
[2]Cohen, J. *et al*. Sepsis: a roadmap for future research. The Lancet Infectious Diseases, 2015 Vol. 15, Issue 5.

28th ECCMID Madrid, Spain 21 – 24 April 2018
ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES