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Microbial molecular detection

Rapid and accurate detection of Neisseria meningitidis DNA in clinical specimens using the Hibergene “HG Meningococcus” LAMP assay

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Background: Molecular detection of meningococcal DNA in sterile site (blood or CSF) specimens using real-time PCR is accepted as a gold standard method for confirming a diagnosis of meningococcal disease. Due to resource limitations in hospital laboratories, PCR testing for this important pathogen is generally available only as a reference laboratory test. The Hibergene “HG Meningococcus” assay is a new rapid molecular diagnostic test based on loop-mediated isothermal amplification (LAMP). We evaluated the diagnostic accuracy of this test for detection of meningococcal DNA in blood, cerebrospinal fluid (CSF) and respiratory swabs.

Material/methods: Analytical and clinical sensitivity and specificity were investigated using three manufactured batches of the HG Meningococcus assay, compared to reference laboratory testing using real-time PCR. Analytical sensitivity was evaluated using *N. meningitidis* genomic DNA spiked over a range of concentrations into whole blood, CSF and respiratory swabs. Analytical specificity was evaluated using a panel of DNA samples from potentially cross-reacting bacterial species, and serogroup inclusivity was evaluated using a panel of meningococcal type strains. Clinical sensitivity and specificity were evaluated using residual clinical specimens with ethical approval from the Northern Ireland Infectious Disease BioArchive (Belfast Health & Social Care Trust). An additional panel of artificial whole blood specimens, prepared by resuspending cells from negative donor blood with PCR-positive plasma, was also evaluated.

Results: After testing 30 replicate spiked samples at each test concentration, the lower limits of detection (with 95% CI) for whole blood, CSF and swabs respectively were found to be 1.4 (1.0-2.5), 1.0 (0.7-1.7) and 1.9 (1.6-2.5) genome copies per µl. No non-specific amplification from non-target bacterial species was observed, and detection of meningococcal serogroups A, B, C, W135, X, Y, Z and 29E was confirmed. Whole blood specimens (n=30), CSF specimens (n=51) and swab specimens (n=57) from patients being investigated for possible meningococcal infection were also tested. In total, 47 of the tested specimens were PCR positive for meningococcal DNA, and 90 were PCR negative. The HG Meningococcus test had a sensitivity of 100% (47/47 positive) and a specificity of 100% (90/90 negative) relative to real-time PCR. The HG Meningococcus test was more sensitive than the reference PCR method when testing artificial whole blood specimens, with 27/28 (96%) positive using the LAMP assay, compared to 20/28 (71%) positive by PCR.

Conclusions: The HG Meningococcus test performed better than a reference laboratory real-time PCR assay for detection of meningococcal DNA in clinical specimens. The assay was simple to use, fast (<30 minutes) and accurate, and the stable freeze-dried format is practical for use in any hospital laboratory.