Loop-mediated isothermal AMPlification PCR (LAMP) for the rapid identification of invasive meningococcal disease in the Emergency Department

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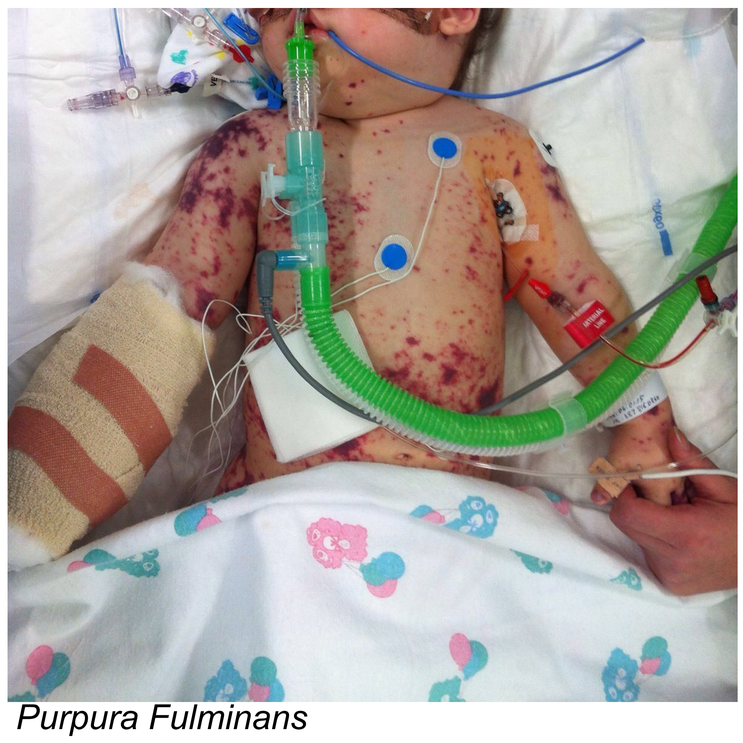
Background

Despite successful vaccination programmes meningococcal disease (MD) remains the leading infectious cause of septicaemia and death in children in the UK and Ireland (1,2). The early diagnosis of MD significantly improves outcomes with reduced morbidity and mortality (1,2). The early stages of MD are often indistinguishable from a simple viral illness making an early positive diagnosis of MD difficult (1). Hibergene diagnostics have developed a commercially available bedside Loop-mediated isothermal AMPlification PCR (LAMP-MD) test that is a highly sensitive 0.89 (95%CI 0.72-0.96) and specific 1.0 (95%CI 0.97-1.0) for identifying children with invasive MD (4,5).



Purpura Fulminans

LAMP-MD test being performed

Loop Mediated Isothermal Amplification for Meningococcal DNA – LAMP MD

- Loop Mediated Isothermal Amplification meningococcal assay developed by BHSCT / QUB team
- Amplification performed at a single temperature (63^{o}C)
- Targets the conserved *ctrA* gene, specific to capsular meningococcus
- More rapid than traditional PCR techniques
- Provides positive results within 20 minutes
- Requires relatively "low tech" and suggested as suitable for point of care testing

Aims

The aims of this Royal College Emergency Medicine funded study were:

- Assess the ease of use and suitability for the ED
- Determine the time taken to perform the test
- Independently verify LAMP-MD performance against TaqMan® quantitative PCR (qPCR)

Dry nasopharyngeal swabs

LAMP MD analyser

Method

The LAMP-MD was assessed for practicality and ease of use within the ED including an assessment of training needs, footprint and a consideration of health and safety requirements.

For verification of the Hibergene LAMP-MD analyser and assay we used dry nasopharyngeal swabs sent for viral screening. Additional verification was undertaken using *N. meningitidis* genomic DNA spiked into swabs over a range of concentrations. This included serogroups A, B, C, W, X, and Y and a dilution series to determine the limit of detection. All samples were then analysed using real time TaqMan® qPCR.

Results

The LAMP-MD analyser was easy to use and could be accommodated in the ED.

- The mean time for detection of Meningococcal DNA was 14.01 minutes.
- Detection of meningococcal serogroups A, B, C, W, X and Y was confirmed
- The detection limit for dry nasopharyngeal swabs was below 2 genomic copies per µl.
- No non-specific amplification was observed in 17 randomly selected negative clinical swabs.
- The LAMP-MD assay was 100% sensitive and specific relative to TaqMan® qPCR.

Conclusions

LAMP-MD is a practical, rapid point of care test that can reliably detect all Meningococcal serotypes in less than 15 minutes.

Funding has been secured to perform a PERUKI supported pilot study to investigate the potential for LAMP-MD in the diagnosis of meningococcal disease in children.

References

1. Meningitis Research Foundation – Meningococcal Meningitis and Septicaemia Guidance Notes 2014

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3. NICE; Management of petechial rash

4. Bourke TW et al. Diagnostic accuracy of loop-mediated isothermal amplification as a near-patient test for meningococcal disease in children: PMID: 25728843

5. http://www.hibergene.com/products/hg-meningococcus

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