Consultative Council on Obstetric and Paediatric Mortality and Morbidity

Herpes Simplex Virus (HSV) in the newborn

Good practice point

OFFICIAL

Aim

The aim of this good practice point is to remind clinicians that a negative cerebrospinal fluid (CSF) HSV DNA polymerase chain reaction (PCR) or “BioFire®” have false negatives, especially if collected early in the illness.

Background

Herpes Simplex Virus (HSV) can be acquired perinatally and can be lethal if not treated early with anti-viral therapy such as intravenous acyclovir. Consideration of this potential pathogen in the newborn who presents with sepsis is imperative. Infants may be tested for the presence of HSV by sending CSF or other specimens for detection of HSV1 or 2 related nucleic acid. The most commonly available HSV nucleic acid test is the BioFire®.

Recommendations

Biofire® testing can be falsely negative for a number of reasons i.e. there may be insufficient nucleic acid in the specimen to be detected, there may be strain variation making the nucleic acid sequences unrecognisable, or there can be contamination of the specimen.

All tests have false positives and negatives but being falsely reassured by a negative HSV meningitis/encephalitis test can have devastating consequences if treatment is not started and continued.

HSV has long been identified as occurring in infants whose mothers have no history of clinical HSV, making diagnosis impossible to rule out on clinical history alone (Pinninti and Kimberlin, 2014). Whilst HSV DNA PCR has greatly improved the speed of diagnosis, its sensitivity is reported as low as 75%.

BioFire® has reported sensitivities as low as 51% for HSV-1 (Trujillo-Gómez *et al*., 2022)

In cases where HSV needs to be ruled out, relying solely on a negative CSF result is insufficient and further tests need to be employed- specifically swabs from mouth, conjunctiva, nasopharynx, rectum, any vesicles (if present) and blood for HSV DNA PCR and LFT (Especially ALT). Repeating CSF two to three days later may also be helpful.

References:

Pinninti, S.G. and Kimberlin, D.W., 2014. Management of neonatal herpes simplex virus infection and exposure. *Archives of Disease in Childhood-Fetal and Neonatal Edition*, *99*(3), pp.F240-F244.

Trujillo-Gómez, J., Tsokani, S., Arango-Ferreira, C., Atehortúa-Muñoz, S., Jimenez-Villegas, M.J., Serrano-Tabares, C., Veroniki, A.A. and Florez, I.D., 2022. Biofire FilmArray Meningitis/Encephalitis panel for the aetiological diagnosis of central nervous system infections: a systematic review and diagnostic test accuracy meta-analysis. *EClinicalMedicine*, *44*.