

Neonatal Herpes Simplex Virus (HSV) Infection

- Abstract** Surveillance of neonatal herpes simplex virus (HSV) infection over a three-year period (37 months) is proposed, to ascertain the birth incidence of HSV disease in the British Isles, its clinical presentation and subsequent outcome. A similar study was previously undertaken through the BPSU in 1986-1991, and provided a prevalence estimate of 1.65/100,000. Neonatal infection was attributed to HSV-1 and HSV-2 in equal proportions, but the virus could not be typed in one third of cases. It was considered at that time that antenatal screening of women with a history of genital herpes was not justified. The increasing prevalence of sexually transmitted diseases, as well as demographic and social changes within the population may have contributed to a change in the incidence and serotype of neonatal HSV. Improvements in diagnostic techniques mean that virus type should now be ascertainable in a higher proportion of cases.
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- Coverage** United Kingdom and Republic of Ireland
- Duration** January 2004- January 2005 (13 months)
- Background** Neonatal herpes simplex virus (HSV) infection is a rare but potentially devastating condition. It can follow primary or recurrent maternal infection, or be acquired postnatally through direct contact with infected secretions. Transplacental transmission is unusual, and perinatal infection is usually acquired during vaginal delivery through an infected birth canal.
- The relative contribution of primary and recurrent maternal infection to neonatal disease, the prevalence of neonatal infection and the proportion of neonatal disease associated with HSV-1 and HSV-2 varies between countries. Primary maternal infection close to term is estimated to lead to neonatal infection in about one third of cases, and to be about 10 times more likely to result in neonatal infection than a recurrence of maternal infection. Although oral infection is predominantly associated with HSV-1, and genital infection with HSV-2, there is considerable crossover, and genital HSV-1 is common, and becoming more so. The natural history of genital HSV-1 and HSV-2 are different, and reactivation is more frequent following HSV-2. There is some evidence that prior infection with HSV-1 is partially protective against the acquisition of HSV-2, and it usually prevents the severe clinical manifestations associated with primary infection. Overall, the majority of women who have had genital HSV are probably not aware of the fact, as both primary infection and reactivation can be asymptomatic.
- Infants who present with disease *localised* to the skin, eye and/or mouth (SEM) have the best prognosis and death is unusual, although impairment can occur, possibly associated with sub-clinical CNS infection. Those who present with acute *disseminated* HSV infection have multiple organ involvement, including the liver, lungs, gastrointestinal tract and CNS; the likelihood of death is high, and most survivors have severe handicap. Infants with *encephalitis* alone often present late; mortality is over 50%, and the long-term prognosis poor for survivors. Disseminated disease and encephalitis can present with or without SEM infection; early diagnosis is vital in all cases since antiviral therapy can significantly affect outcome.
- Surveillance of neonatal HSV was undertaken through the BPSU in 1986-1991. The estimated prevalence of infection was then 1.65/100,000 (CI 1.3-2.0/100,000). HSV-1 and HSV-2 were reported in equal proportions, but in one third of cases the virus was not typed.

Approximately equal numbers of infants presented with localised, disseminated and CNS infection. Given the rarity of the condition, and the observation that most infants were born to women with no prior history of infection, it was considered at that time that antenatal screening of women with a past history of genital herpes, as was then practised in the US, was not justified.

There have been changes in the prevalence of HSV infection in the British population, as well as changes in the demographic profile in the last 15 years, and there is concern about the increasing prevalence of sexually transmitted diseases; these factors could also influence the incidence of neonatal HSV in the British Isles.

Case Definition

Surveillance

1. Any infant under one month
 - (a) with a diagnosis of HSV infection, based on virus detection by culture, PCR or IF, or serology – IgM and/or seroconversion, **or**
 - (b) treated with antiviral drugs for suspected HSV infection
2. Any stillborn infant in whom HSV infection is suspected

Analytic

Confirmed case of neonatal HSV:

1. Virus detection by culture, PCR or IF, or serology – IgM and/or seroconversion, confirming HSV infection on a specimen taken within four weeks of birth, or
2. Typical clinical manifestations with maternal infection confirmed by either seroconversion during pregnancy or virus isolation around the time of delivery

Suspected case of neonatal HSV:

3. Typical clinical manifestations and treated with antiviral drugs for suspected HSV infection.

Research Questions

- 1) To estimate the current birth incidence of neonatal herpes infection in the British Isles, and to distinguish the proportion attributable to HSV-1 and HSV-2.
- 2) To explore the presentation of neonatal infection, and management of diagnosed cases.
- 3) To assess subsequent morbidity and mortality through the notifying paediatrician.
- 4) To compare findings with the 1986-91 BPSU cohort, and with INOPSU studies currently being undertaken in Australia, Canada and Switzerland, in order to clarify changes in epidemiology of HSV and outcome of neonatal infection over time, and in different situations.
- 5) To inform the current debate on antenatal screening.

Methods

Paediatricians reporting a case will be sent a questionnaire seeking demographic details, and information on presenting symptoms, diagnosis of infection, and immediate clinical management and outcome. Full date of birth is required to exclude duplication, and to establish age at diagnosis and subsequent events. The child will be classified as having confirmed or suspected neonatal HSV. Further brief questionnaires will be sent to the notifying paediatrician to establish the outcome of neonatal infection in survivors at the age of one and three years. Families will not be approached.

To minimise under-ascertainment, laboratory reports to HPA will be monitored in order to identify any without a corresponding paediatric report. In those cases, if the source laboratory is able to identify the clinician responsible for the case, we will ask them to remind the clinician to notify the case through the BPSU or direct to the study investigator.

Reporting Instructions

Any liveborn or stillborn infant born since the beginning of 2004 in the UK or Ireland with confirmed or suspected neonatal HSV infection, seen by you for the first time in the last month.

Funding

National Screening Committee

Ethics Approval

This study has been approved by the London MREC

Patient Support Group

The Herpes Viruses Association, 41 North Rd, London N7 9DP.
Telephone helpline 0207 609 9061

References

Available from the BPSU office or <http://bpsu.inopsu.com/Current#HSV>