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THE PATHCARE NEWS

NEW GUIDELINE: ORAL VALACICLOVIR FOR THE PREVENTION OF CONGENITAL CMV

Introduction

Congenital cytomegalovirus (cCMV) infection carries a significant burden with a 0.64% global prevalence[1], while in resource-limited settings the prevalence may be in excess of 5%. Historically, the rate of vertical transmission is 30–40% after a maternal primary infection (MPI) acquired early in pregnancy[3]. The risk of serious congenital morbidity is greatest after MPI occurring periconceptionally or during the first trimester[3]. Due to the potential for severe sequelae with cCMV infection, antenatal prevention of vertical transmission is warranted.

Antiviral options for the prevention of foetal infection with CMV

Until recently, there were no proven antenatal treatments for the prevention of cCMV following MPI. Valaciclovir, the prodrug of acyclovir, has recently been shown to be effective at preventing cCMV after MPI[1, 3, 4, 5]. A randomised, double-blind, placebo-controlled trial from 2020 showed that valaciclovir is effective in reducing the rate of fetal cytomegalovirus infection after MPI acquired early in pregnancy by 71%[3]. Subsequently, an observational study from Italy confirmed that valaciclovir significantly reduced the rate of cCMV diagnosis at the time of amniocentesis, with a good tolerability profile and showed that the treatment is associated with a reduction of termination of pregnancy and symptomatic congenital cytomegalovirus infection at birth[4]. In 2024, a consensus recommendation for prenatal, neonatal and postnatal management of cCMV infection was published by the European congenital cytomegalovirus initiative (ECCI). Highlights of this consensus recommendation are tabled below.

Table. Excerpt from Table 1 and Table 2 of the ECCI guidelines for primary prevention of cCMV and the use of valaciclovir in pregnancy for the secondary prevention of cCMV[1]

Recommendation	Evidence level
We recommend advising women on hygienic measures prior to pregnancy (or as soon as possible once pregnant) especially those known CMV seronegative.	Grade B
We recommend to perform CMV serology in the first trimester of pregnancy as early as possible, followed in seronegative women by a retest every 4 weeks until 14–16 weeks. CMV serology is not recommended in pregnant women beyond 16 weeks except in cases with ultrasound CMV compatible symptoms	**Grade A**
We recommend using IgG avidity testing to exclude a recent (less than 90 days) maternal primary infection in cases with positive IgM and positive IgG.	Grade B
We do not recommend testing for CMV PCR in blood or in urine since it is not helpful for dating maternal primary infection in women with positive IgG and IgM.	Grade B
We do not recommend testing CMV serology or CMV PCR in blood or urine in women known to be seropositive before pregnancy.	Grade B
We recommend the administration of oral valacyclovir at a dose of 8 g/day in cases with maternal primary infection in the periconceptional period or the first trimester of pregnancy, as early as possible after the diagnosis and until the result of the CMV PCR in amniocentesis.	**Grade A**
We recommend against the administration of hyperimmune globulin, at doses of 100 IU/kg every 4 weeks, in pregnant women with primary CMV infection.	**Grade A**
Fetal ultrasound assessment and MRI assessment in the third trimester is recommended in infected fetuses, as it can provide information regarding the presence of CMV associated findings which will provide prognostic information.	Grade A

CMV MPI and laboratory testing

Laboratory testing for maternal primary infection is challenging as up to 90% of adult patients may be asymptomatic. CMV serology will diagnose an MPI if IgG seroconversion is demonstrated on two samples taken 4 weeks apart, or if both IgM and IgG tests are positive with low avidity IgG being demonstrated. If CMV IgG avidity is high in the latter scenario, a recent maternal primary infection (defined as during the past three months) is excluded. IgM positivity in isolation is not diagnostic of an MPI.

Summary – What's new?

- Baseline CMV IgG testing is now advised in pregnant women in the first trimester
- Pre-pregnancy CMV IgG testing for individuals at high risk of infection may also be considered
- If a periconceptual or first trimester MPI is diagnosed, valaciclovir therapy is indicated for the prevention of vertical transmission of CMV infection

References

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