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Prevention and treatment of fetal cytomegalovirus infection with cmv-hyperimmune globulin: a multicenter study in madrid

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Objective

To investigate the use of cytomegalovirus (CMV) hyperimmune globulin (HIG) in prevention and treatment of CMV fetal infection in Madrid (Spain).

Methods

A retrospective observational study comprising all pregnancies treated with CMV-HIG (2009-2015) in three tertiary hospitals in Madrid was conducted. Investigators offered HIG treatment (200 UI/kg) in pregnancies with a CMV primary infection (prevention group; HIG before amniocentesis) or with fetal infection (treatment group: positive PCR in amniocentesis/cordocentesis). Symptomatic congenital CMV infection at birth was defined as the presence of at least one: abnormal physical exam (petechiae, jaundice, hepatosplenomegaly, neurologic abnormalities), hearing loss, laboratory abnormalities, or abnormal ultrasound or MRI.

Results

During the study period, 36 mothers received at least one dose of HIG. Main reasons for consultation were seroconversion (39%), positive IgM and IgG with low avidity test (28%), CMV related findings in fetal ultrasounds (14%), CMV related symptoms in pregnancy (8. 3%) and known contact with a CMV infected person (8. 3%). Infection was symptomatic in 54. 5% of pregnancies. Median gestational age (g. a) at diagnosis was 20w [IQR=10-25], and at amniocentesis was 21 weeks [20-26]. No severe adverse events of HIG were observed, and median g. a at birth was 38. 3 weeks [38-40]. Three children from treatment group were lost to follow up after birth. Prevention group included 17 pregnancies, all with a primary CMV infection. One pregnancy of this group was interrupted due to abnormal cordocentesis and fetal symptoms on follow-up (the necropsy also showed congenital CMV findings). Fetal infection was confirmed in 7/17 (38. 5%) patients, and 1/16 (5. 9%) was symptomatic at birth (abnormal ultrasound; mild unilateral hearing loss (50 dB), but with good neurodevelopmental outcome at 12 months of age). No other children presented long term sequelae at 12 month of age in the prevention group. Treatment group included 19 pregnancies with positive PCR either in amniotic fluid or fetal blood. One child was born uninfected and asymptomatic after a positive amniotic fluid PCR and 1 dose of HIG. Hearing loss at birth was present in 4/19 (21%), motor impairment in 3/19 (16%) and 9/19 (47%) were symptomatic at birth. At 12 months of age, three children (3/16; 18. 8%) in the treatment group presented motor impairment and 4 children (4/16 ; 25%) presented hearing loss. Fetuses with abnormalities in central nervous system (CNS) in fetal ultrasound (US) before HIG treatment, presented a high risk of long term sequelae (3/3; 100%) compared with those without CNS abnormalities (2/29; 6. 7%; p=0. 009; OR=77; 95%CI: 3-1954).

Conclusion

In our population CMV-HIG treatment was not associated to relevant adverse events. A high rate of infected fetuses were found in the prevention group. Almost half of children in the treatment group had symptoms at birth. Fetuses without CNS abnormalities in US before HIG treatment presented low risk of long term sequelae. HIG seems not to be useful in fetuses with previous brain abnormalities in US. Randomized controlled trials are needed to close the evidence gap in the HIG treatment of CMV infected fetuses.