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A case series of prevention of Cytomegalovirus by valacyclovir

Goncé A, Castillo KP, Guirado L, Hawkins-Villarreal A, López M, Mª Marcos MA, Salvia S, Sebastiani G, Alarcón A, Figueras F
BCNatal: Fetal Medicine Research Center (Hospital Clínic and Hospital Sant Joan de Déu), Universitat de Barcelona, Barcelona, Spain, Barcelona, Spain

Objective

Cytomegalovirus (CMV) is the most common congenital infection affecting 0.7% of live births. Children born to women who have a primary infection during the first trimester have the greatest risk of sequelae. The rate of vertical transmission after a maternal primary infection (MPI) acquired early in pregnancy is 30–40%. In a recent randomized controlled trial and two case-control studies, high-dosage Valaciclovir (VACV) given following an MPI in the first trimester or in the periconceptional period has been shown to reduce vertical transmission by 65-70%. The objective of this study was to evaluate preliminary results regarding secondary prevention of congenital CMV (cCMV) with high-dosage VACV following MPI in early pregnancy.

Methods

Longitudinal cohort of pregnancies diagnosed with primary infection by first-trimester serology screening or after maternal symptoms at our institution, or referred for decision-making after diagnosis in another centre between January 2021 and February 2023. Time of maternal infection was assessed with maternal serology. In cases with IgG and IgM positive with low IgG avidity, the timing of maternal infection was considered according to the avidity value. Cases with intermediate avidity were considered periconceptional infections. Women were offered oral VACV (8g/24h) up to the time of amniocentesis, and in cases with a negative result, VACV was stopped. Maternal liver and renal function were evaluated before the onset of treatment and every fortnight. cCMV was diagnosed following amniocentesis at 17–21 weeks by polymerase chain reaction and confirmed in newborn urine or fetal tissues in cases with termination of pregnancy (TOP).

Results

Eighteen pregnant women were evaluated during the study period. Among them, 16 accepted the preventive treatment with VACV. Serology was performed at a median gestational age of 11.6 (IQR, 9.4-14.2) weeks. IgG avidity test suggested an infection in the previous 4 weeks in four women (two of them were diagnosed by maternal symptoms), between 4 and 12 weeks in nine, and in the periconceptional period in three cases. VACV was initiated at a median gestational age of 13.3 (IQR, 10.6-16.1) weeks with a time from maternal serology to treatment of 9.5 (IQR, 4.8-15.8) days. All patients underwent amniocentesis at a median gestational age of 19.8 (IQR,17.4-20.6) weeks. The median duration of VACV treatment until amniocentesis was 41.0 (IQR, 27.5–57.5) days. Adherence and tolerance were good in all patients. The rate of vertical transmission was 19% (3/16). The 3 cases with vertical transmission were all MPI in the first trimester, with an estimated time lapsed from infection to VACV initiation of <4 weeks in one, and between 4 and 12 weeks in the remaining two. The time lapsed from maternal serology to VCV initiation was shorter among non-transmitters (10.3 vs 13.3 days), and the duration of VCV was longer (30.7 vs 44.6 days) although the differences were non-significant. All 3 patients with an infected fetus opted for TOP. One on the evidence of ultrasound abnormalities at 22 weeks, another for a concomitant fetal genetic anomaly diagnosed at the time of amniocentesis, and the last due to maternal anxiety. In 10/13 cases with a negative amniocentesis, cCMV was ruled-out in the newborn, and 3 are ongoing pregnancies.

Conclusion

Our results support previous research that VACV is effective in reducing the rate of fetal infection after MPI acquired early in pregnancy. Early treatment after serological confirmation is recommended.