

## Promising Therapies for Fetal Cytomegalovirus Infection

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**Received:** September 30, 2016; **Published:** September 30, 2016

**Keywords:** CMV; Valacyclovir; Antiviral therapy; Hyperimmune globulin

Cytomegalovirus (CMV) is a herpesvirus that is transmitted through infected bodily fluids and is seen in 0.5 to 1.0% of all live births. Congenital CMV infection is mainly due to primary infection of the mother. The risk of vertical transmission in primary infection varies between 40% in first and second trimesters to 80% in third trimester. However, most of infections occurring in the third trimester are asymptomatic [1]. 5-10% of affected infants will be symptomatic at birth, and 10-15% will develop long-term developmental disorders, to include hearing loss, visual loss, and mental retardation [2,3].

CMV is currently diagnosed by the new appearance of virus specific IgM in a pregnant woman previously seronegative, by IgG antibody with low avidity, amniocentesis seven weeks after infection, or CMV polymerase chain reaction (PCR) from percutaneous umbilical cord sampling (PUBS) [4]. Common ultrasound findings of a CMV infected fetus include intrauterine growth restriction, microcephaly, intracranial calcifications, ascites, hyperechogenic bowel, and occipital horn cavity [5]. Once fetal CMV is diagnosed, options are currently limited and all investigational at this point.

Cytomegalovirus hyperimmune globulin has been studied as a way to decrease the transmission of CMV from the mother to the fetus. The IgG is able to bind to virus specific glycoproteins that are crucial for entry into target cells and thus effect the virus's infectivity [6]. It has been shown to be beneficial to the fetus in two clinical trials and two observational studies, however these results were not definitive. A recent phase 2 randomized control trial showed no significant benefit, however with a combination of this most recent study and the original studies, a trend towards efficacy is demonstrated. A large phase 3 double blinded placebo controlled III trial is currently enrolling patients. Hyperimmune globulin has also been evaluated in fetuses already infected with CMV, which has shown a trend towards benefit but no statistical significance [7,8].

The other therapy that has been studied and found effective is valacyclovir. A pilot study demonstrated that adequate drug concentration was seen in the blood stream with a dose of 8 grams/day and that the treatment significantly decreased viral load [9]. A second study showed that valacyclovir was effective in improving the outcome of pregnancies in which a fetus was affected by CMV. After treatment, platelet counts increased significantly and viral load decreased significantly [10].

Though neither of these treatments are FDA approved, the current literature demonstrates their potential benefit in the population of CMV infected mothers without any other future treatments. Though a phase 3 clinical trial is currently undergoing for hyperimmune globulin, further trials need to be done for valacyclovir as this treatment has also shown significant benefit. Both are potential targets to treat an often fatal disease in the fetus that has no current available treatment.

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**Volume 3 Issue 4 September 2016**

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