Antivirals for CMV in pregnancy: time to ponder and re-assess screening policies

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Cytomegalovirus (CMV) is one of the most common congenital infections affecting 0·7–1% of all livebirths globally (1). The rate of vertical transmission is 30–40% after maternal primary infection throughout pregnancy (1). Forty to 60% of infants born with signs of congenital CMV (cCMV) disease at birth will have long-term sequelae ((2). Antenatal CMV screening is offered only in few countries; the UK not being one of them (3). We suggest that global and UK policies on CMV screening and treatment in pregnancy should now be reviewed in the context of a recent randomized clinical trial (RCT) (4), indicating antivirals can interrupt transmission and providing a scientific foundation for widening access to protect the unborn baby's legal right to health following similar examples of preventing transmission such as Nevirapine in HIV [5]. Antivirals are currently used in pregnancy mainly for maternal indications rather than to protect the unborn child and it is imperative that both maternal and neonatal outcomes are routinely registered to allow for complementary analysis of real-world data to inform both clinical and economic cost-effectiveness. Current barriers to widening access include the fact that the required valaciclovir dose is high (almost triple the usual dose) and ganciclovir is not licensed for use in pregnancy.

The cases we present, treated in the last 12 months in our tertiary referral unit in central London, illustrate this need estimated to be significant at a population level in the UK given that according to estimates 50% of women booking for antenatal care are CMV seronegative and 1-4% of those will develop primary CMV in pregnancy (6) .

Case 1: A pregnant woman presented, at 7-weeks Gestational Age (GA), with a week-long history of myalgia and fever. In view of a raised ALT, CMV serology was performed, indicating primary CMV infection (IgM and IgG positive of low avidity). Valaciclovir 8g daily was initiated, however transmission was not avoided; amniocentesis, at 21/40 GA, was positive for CMV. The woman opted to continue antiviral therapy for total 20 weeks. Monitoring (maternal bloods, drug levels, fetal ultrasounds) was uneventful. Headaches for a week at initiation and an elevated MCV in the FBC, which resolved at cessation, were observed. The woman reported five non-COVID-19 lower respiratory tract infections in the year following treatment, all requiring antimicrobials and severe mastitis requiring admission. Despite testing urinary-CMV-PCR positive, the baby had a normal MRI brain, required no antiviral treatment and continues to be under neurodevelopmental and hearing follow up displaying no CMV signs.

Case 2: A woman was referred to our service following a CMV PCR-positive amniocentesis at 21-weeks GA and abnormal fetal ultrasound (ascites, cardiomegaly, echogenic bowel, echogenic halo sign around both lateral ventricles and small cerebellum). The family elected to carry the fetus to term with extensive multidisciplinary counselling. Serial serology indicated that, while maternal infection

occurred early in the first trimester, the woman remained highly viraemic (CMVvl 5,600 IU/mL) at 20weeks. Consequently, off-license antiviral treatment with valganciclovir was initiated, for a total of six weeks in the acute phase of presumed fetal myocarditis. No side effects were experienced. CMV vl was undetectable after the first week. Drug levels and biochemistry remained normal. The baby required no admission at birth, hearing/US/MRI results are awaited.

While CMV vaccine clinical trials are underway, they are not expected to change practice for some time. There is thus an urgent need to create a unified and equitable approach to screening, surveillance and treatment especially as some pregnant women are receiving care across countries, following different policies. A similar approach as the American Academy of Pediatrics Registry (5) is imperative if we are to generate evidence to inform future practice.

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Ethical Statement

Both women consented to publication.

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