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The effects of ganciclovir and valganciclovir antiviral treatments in children with congenital Cytomegalovirus Infection

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Introduction

Congenital Cytomegalovirus Infection (CMV) is a herpes virus that is passed from mother-to-child from bodily fluids. CMV can be identified at birth through a urine culture or blood test. There are two types of CMV: symptomatic and asymptomatic. Children that have symptomatic CMV will present indicators of the infection at birth, while on the other hand, children with asymptomatic CMV will not present any signs of the virus at birth. Indicators of CMV include a blueish rash, thrombocytopenia (reduce platelet count in the blood), microcephaly, and jaundice. The most prominent symptom of CMV is sensorineural hearing loss (SNHL). SNHL due to CMV is one of the leading causes of nonhereditary SNHL in children. The SNHL can be bilateral or unilateral; ranging from mild to profound; and, in some cases, can be fluctuating. "...CMV is estimated to account for 20% or more of SNHL in young children... More children may be affected by CMV than by other, better known childhood conditions, such as Down Syndrome, fetal alcohol syndrome, and spina bifida," (Duval & Park, 2014). Recently, new advances in medicine have shown that the antiviral drugs, ganciclovir and valganciclovir, can help eliminate the viral load of CMV in the child's blood. "The presence of viraemia was first reported to be associated with a poor hearing outcome in neonates with CMV disease in 2005," (Sharland et al., 2011). The antiviral drugs help decrease the viral load and simultaneously improve hearing. Some studies use the drugs separately, while others use them consecutively, respectively.

Two types of antiviral treatments

Ganciclovir (GCV)

- Intravenous form of the drug
- Acts as an alternative substrate in the blood and helps lead to the viral DNA chain to be terminated

Valganciclovir (VGCV)

- Oral form of the drug
- Considered a prodrug to GCV
- Works in a similar manner as GCV, but has enhanced bioavailability

Common side effects

- Neutropenia (low count of a specific white blood cell)
- Anemia (reduced amount of red blood cells)

A comparison of hearing outcomes from different studies of children who have CMV

Study	Sample size (mean age)	Pre Treatment	Dose GCV and/or VGCV	Duration	Post treatment	Side effects
Rosal et al. (2012)	13 (5.3 months)	30% had normal hearing	32 mg/kg/day of VGCV	VGCV was given for 6 months	50% had normal hearing	6 patients reported Neutropenia
Kimberlin et al. (2015)	96 (22 days)	53% had normal hearing	16 mg/kg/ 12 hours of VGCV	VGCV was given for 6 weeks	67% had normal hearing	Neutropenia reported in patients
Kimberlin et al. (2015)	43 (11 days)	65% had normal hearing	16 mg/kg/ 12 hours of VGCV	VGCV was given for 6 months	77% had normal hearing	Neutropenia reported in patients
Amir, Wolf, and Levy (2010)	23 (2.3 years)	54% had normal hearing	5 mg/kg/12 hours of GCV followed by 2 doses of 17mg/kg/day of VGCV followed by 1 dose of 17mg/kg/day	GCV given for 6 weeks. First dosage of VGCV for 6 weeks and second dosage for 1 year	76% had normal hearing	12 patients reported Neutropenia

Interpreting the studies

- All studies indicate an improvement in hearing when administered the drug(s) with at least a 12% hearing improvement.
- Even if a child had normal hearing at baseline, s/he was still given the drug(s).
- Since the drug(s) dosage is administered by body weight (kg), as the patient's weight increases, so does the dosage.
- Neutropenia is the most common side effect of using antiviral drug(s).
- When neutropenia occurs, the individual's dosage is lowered until his/her white blood cell count is back to normal.
- Longer duration of the drug does not necessarily mean a better outcome of hearing.
- The earlier a drug is started does not always lead to a better outcome of hearing.
- When GCV and VGCV are used consecutively, GCV is always used first.

Conclusion

Antiviral treatments seem to be a hopeful alternative to improving hearing in children with CMV. When ganciclovir and/or valganciclovir are used, hearing improvements are seen in some subjects; however, ganciclovir and valganciclovir are not shown to work for every individual. In recent studies, it has been shown that antiviral treatments are most effective on hearing losses that are less severe (i.e. mild or moderate hearing losses). It is important that, if these antiviral treatments do not work, that the child is fitted with appropriate amplification as soon as possible. Due to the potential fluctuating nature of the hearing loss, if a child does receive amplification, proper amplification should be maintained during hearing level changes (Fowler).

Future research

- Is there a vaccine that is being made for children who are born with CMV?
- Is there a vaccine to prevent mother-to-child transmission?
- Is it possible to use GCV and/or VGCV while the baby is in-utero?
- Is there a drug that could minimize neutropenia?
- Would it be effective and cost efficient to have universal newborn screening for CMV?

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