CYTOMEGALOVIRUS INFECTION

Introduction

- This guideline addresses mainly congenital CMV (CCMV) infection, although some information can be used for the management of symptomatic postnatal CMV infection. Some specific guidance for postnatal CMV infection is also provided.
- Overall birth prevalence of congenital CMV infection is 0.64 % (UK). Of them 0.07 % are symptomatic at birth. This equates to 10 – 15 % of the total number of newborns with congenital CMV. > 70 % of these will develop permanent long-term sequelae.
- About 96% of seropositive mother have localised reactivation of CMV in their breast during lactation. Breastfeeding is the biggest source of postnatal cytomegalovirus infection in preterm infants and may be associated with a symptomatic infection (transmission rate 9 – 55 %, 1.5 – 62 % become symptomatic in varying degrees).

General Considerations

- See algorithm below (consider additional tests, e.g. bood viral load)

Diagnostic investigations and treatment with Ganciclovir i.v./Valganciclovir p.o.

- See table below for clinical/diagnostic findings and algorithm for diagnostic decision making
- All newborns qualifying for treatment are started on Ganciclovir i.v. peripherally and continued centrally if i.v. treatment is needed
- Changing to oral treatment can be considered once the viral load starts decreasing and the baby is showing signs of improvement. Change from i.v. to oral treatment, if steady state of concentration achieved.
- Discuss treatment with Dr Fidler or Dr Fernandez or Dr Sudarsan and Dr Hassan Ibrahim. Continue treatment for at least 6 weeks and no more than 6 months unless discussed otherwise with Dr. Fidler.
- Inform Pharmacy at least 1 week in advance about the medication requirement.
- Register baby on CMV registry by contacting Dr Fidler or Dr Fernandez or Dr Sudarsan

Monitoring therapeutic response, drug levels and toxicity

- Check urinary and blood viral load after 48 h, then on day 7 and then weekly
- Check U & E, LFT, conjugated bilirubin, ALT + FBC twice weekly
- Perform Ganciclovir pre-dose level + post-dose level 1 hour after completion of infusion after 48 h, then on day 7 and then weekly. If treatment has been changed to Valganciclovir then the post-dose level needs to be performed 2 hours post-dose.
- Perform additional Ganciclovir/Valganciclovir levels if dose is adjusted

Labelling and sending samples (see table below)

- For choice of specimen collectors see table below.
- Urine, blood and CSF viral load as well as drug level samples are sent to our laboratories to be processed or send away. Ganciclovir levels go to the Bristol Lab. Contact 24 hours in advance on 01179 595653 [Between 09.00 – 15.00 hours].

Prevention of postnatal CMV Infection

- Colostrum has very low infectivity. Most breast milk becomes CMV positive at 2 weeks, peaking at 4-6 weeks.
- Freezing (72 h in -20 ºC) expressed human milk from seropositive women before giving it to ELBW infants is an effective and safe way to reduce rate of CMV transmission (CMV infectivity 1 %).

Follow-up

- Permanent long-term sequelae at follow-up can be cerebral palsy, delayed

psychomotor development, mental retardation, expressive language delay and learning disability, epilepsy, optic atrophy and SNHL.

- Refer early to audiology and check hearing after birth and then at 3, 6, 9, 12, 18, 24, 30, 36 months and then annually to school age
- Refer to ophthalmology and check eyes after birth and then at 12 months, 3 years, and preschool age. Neurological examination and developmental assessment at each paediatric review

Definitions and percentage of occurrence of pathology

Definitions	Occurrence
Microcephaly: head circumference < 2 SD below the mean for age or < 2nd centile.	37%
Symmetric IUGR: birth weight and head circumference < 2SD below mean for age.	43%
Thrombocytopenia: <100,000/microliter.	50%
Conjugated hyperbilirubinaemia: > 66 micromol/l (> 3 mg/dl)	50%
Abnormal CSF with high CSF protein: >120mg/dl	There have been no studies to evaluate the correlation of an abnormal CSF result or CSF viral load with long-term outcome
Abnormal cranial US: moderate to severe ventriculomegaly and intracerebral calcifications - isolated single ventricular dilatation, subependymal pseudocyst or lenticulostriatal vasculopathy are not considered pathognomic	56%
Abnormal cranial CT: cortical atrophy, cortical dysgenesis/dysplasia, moderate to severe ventriculomegaly, cerebellar hypoplasia/asymmetry, migration abnormalities and intracranial calcifications	71% (in asymptomatic newborns), MRI not superior
Abnormal ophthalmology screen: chorioretinitis, retinal detachment, optic atrophy, retinal haemorrhage, retinal scarring or sight threatening infection	14%
Abnormal early hearing assessment:	38%
Abnormal late hearing assessment:	14%

Choice of specimen collectors

Test	Bottle	Amount
Urinary Viral Load	Universal bottle	2 - 3 mls
Blood Viral Load	EDTA bottle	0.5 -1 ml
CSF Viral Load	Universal bottle	0.5 ml
Ganciclovir/ Valganciclovir levels	Li.-Heparin bottle	0.5 -1 ml
FBC	EDTA bottle	0.5 mls
LFT, U & E, ALT, bilirubin	Li.- Heparin bottle	0.5 mls
T-cell immunity, HLA type and IgG avidity	EDTA bottle	2 mls

MANAGEMENT OF CONGENITAL CMV INFECTION IN NEWBORNS > 32 WEEKS GESTATION