**Case Report: Application of Acyclovir Serum Concentrations and Herpes Simplex Virus Inhibitory Concentrations in the Treatment of Neonatal Disseminated Herpes Simplex Virus with Concomitant Extracorporeal Membrane Oxygenation and Continuous Venovenous Hemodiafiltration**

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### Abstract

**Background:** Disseminated neonatal herpes simplex virus (HSV) is associated with significant morbidity and mortality; therefore prompt adequate treatment with antiviral therapy is of great importance. There is little pharmacokinetic/pharmacodynamic data available to guide acyclovir dosing recommendations for neonates maintained on concomitant extracorporeal membrane oxygenation (ECMO) and extracorporeal membrane perfusion (CVVHDF) and with extracorporeal membrane oxygenation and venovenous hemodiafiltration (CVVHDF) and ECMO in vivo. This report follows the course of two full-term, previously healthy male neonates who were treated with acyclovir for disseminated HSV infection at about 1 week of age. Both were placed on CVVHDF and ECMO due to respiratory failure. During the course of the treatment, serum trough and HSV inhibitory concentrations were used to adjust acyclovir dosage according to need.

**Methods:** Intravenous acyclovir was given to both neonates at the recommended dose of 20 mg/kg/dose at intervals of every 8 and every 12 hours for the treatment disseminated HSV infection. HSV inhibitory concentrations (IC) were measured to assess resistance to acyclovir.

**Results:** Intravenous acyclovir was given to both neonates at the recommended dose of 20 mg/kg/dose. The dosing frequency in the neonate receiving ECMO and CVVHDF was every 8 hours and in the neonate receiving only CVVHDF alone was every 12 hours. Acyclovir serum peak and trough concentrations were drawn to assess the efficacy and safety during CVVHDF and ECMO treatments. HSV inhibitory concentrations (IC) were measured to assess resistance to acyclovir.

**Conclusions:** Optimal acyclovir serum concentrations can be achieved in the presence of CVVHDF and ECMO despite early initiation of acyclovir and adequate serum concentrations. HSV inhibitory concentrations (IC) were 3 mcg/mL with serum peak concentrations of 23 mcg/mL and trough concentrations of 17 mcg/mL. The HSV1 IC for the neonate receiving ECMO and CVVHDF was every 8 hours and in the neonate receiving CVVHDF alone was every 12 hours. Acyclovir serum peak and trough concentrations were drawn to assess the efficacy and safety during CVVHDF and ECMO treatments. HSV inhibitory concentrations (IC) were measured to assess resistance to acyclovir.

**Limitations:** Generalizability limited by the CVVHDF and ECMO prescriptions utilized in the two cases.

### Summary and Conclusion

**Methods**

- A literature search was performed to identify recommended acyclovir dosage adjustments. Despite patients receiving CVVHDF and/or ECMO the acyclovir dose was not changed from 20 mg/kg/dose due to inconsistencies in the literature, however the dosing interval selected was based on the presence of HSV1 IC for the neonate receiving ECMO and CVVHDF.

**Results**

An efficacy pharmacodynamic target was established based on comparison of serum acyclovir concentrations in relationship to in vitro IC for the HSV1 IC 30% ID concentration. Acyclovir IC in the neonate receiving ECMO and CVVHDF was every 8 hours and in the neonate receiving CVVHDF alone was every 12 hours. Acyclovir serum peak and trough concentrations were drawn to assess the efficacy and safety during CVVHDF and ECMO treatments. HSV inhibitory concentrations (IC) were measured to assess resistance to acyclovir.

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### References

1. Sample Reference 1
2. Sample Reference 2
3. Sample Reference 3
4. Sample Reference 4
5. Sample Reference 5
6. Sample Reference 6
7. Sample Reference 7
8. Sample Reference 8
9. Sample Reference 9
10. Sample Reference 10
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17. Sample Reference 17
18. Sample Reference 18
19. Sample Reference 19
20. Sample Reference 20

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**Figure 1. Continuous Renal Replacement Therapy (CRRT) Flow Rates and Acyclovir Levels**

**Table 1. Patient Demographics and Case Information**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Birth History</th>
<th>Acyclovir-Dosing</th>
<th>HSV Diagnostics</th>
<th>CVVHDF Closity</th>
<th>ECMO Closity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>Full term, Normal delivery &amp; no known maternal history</td>
<td>20 mg/kg/dose, every 12 hours</td>
<td>(+) HSV1 IC (serum)</td>
<td>&lt;3 mcg/mL for oral dosing</td>
<td>&lt;3 mcg/mL</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>Full term, Normal delivery &amp; no known maternal history</td>
<td>20 mg/kg/dose, every 12 hours</td>
<td>(+) HSV1 IC (serum)</td>
<td>&lt;3 mcg/mL for oral dosing</td>
<td>&lt;3 mcg/mL</td>
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