

Statement on Acyclovir Therapy in Neonates

Neonates < 4 weeks with fever:

Parenteral acyclovir (20 mg/kg IV q8hours) should be added empirically to antibiotics for neonates admitted with fever in the following situations;

1. Clinical signs of sepsis, toxic (including hypothermia, apneas, hypotension, other signs of shock)
2. Seizure
3. Maternal HSV
4. Physical exam findings consistent with Herpes simplex involvement (skin, eye, mucous membrane)
5. CSF pleocytosis with negative gram stain and consistent with aseptic meningitis.

Anytime acyclovir therapy is started on neonates one should perform a lumbar puncture and send the cerebrospinal fluid for HSV PCR.

In high risk situations where there is concern for disseminated HSV or SEM disease please send whole blood for HSV PCR, obtain swabs for HSV viral culture of at least 3 different mucous membrane (i.e. mouth, conjunctiva, nasopharynx, rectum), and any skin lesions and a panel 18. Obtain an Infectious Disease Consult.

Because of the risk of renal toxicity, patients on intravenous acyclovir should receive maintenance IV fluids and have urine dipped for heme q shift to evaluate for early evidence of nephrotoxicity.

In the absence of the above findings, in the neonates admitted with fever, the following scenarios demand specific attention.

1. Traumatic lumbar puncture: attempts to interpret traumatic CSF may lead to serious misdiagnoses. CSF with RBC > 2000 should be interpreted with caution and should be dealt with on an individual basis.
2. Unsuccessful lumbar puncture: same as above; increased LFTs and low platelets would be suggestive of disseminated HSV. These neonates are addressed above.
3. Strongly consider adding acyclovir in the presence of:
 - a. Decreased platelets
 - b. Increased liver function tests (LFTs), if done
 - c. Pneumonia

In these scenarios when the infant appears more ill than would be expected, the physician's judgment should be used to determine acyclovir use on a case by case basis.

Obtain an Infectious Disease consult if Acyclovir is to be continued more than 48 hours or if index of suspicion for HSV is high.

Afebrile Neonates

Acyclovir should empirically be given to patients admitted with seizure and or physical exam findings consistent with Herpes simplex involvement (skin, eye, mucous membrane) and/or altered mental status.

References:

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2. Long S. In defense of empiric acyclovir therapy in certain neonates. *J Pediatr* 2008;1153:157-8.
3. Caviness AC, Demmier G, Almendarez Y, Selwyn BJ. The prevalence of neonatal herpes simplex virus infection compared with serious bacterial illness in hospitalized neonates. *J Pediatr* 2008;153:164-9.
4. Whitley R, Arvin A, Prober C, Burchett S, Corey L, Powell D, et al. A controlled trial comparing vidarabine with acyclovir in neonatal herpes simplex virus infection. Infectious Diseases Collaborative Antiviral Study Group. *N Engl J Med* 1991;324:444-9.
5. Kimberlin DW, Lin C-Y, Jacobs RF, et al, and the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Safety and efficacy of high-dose acyclovir in the management of neonatal herpes simplex virus infections. *Pediatrics*. 2001;108:230-238
6. Kimberlin DW. When should we initiate acyclovir in a neonate? *J Pediatrics* 2008; 153:155-6.
7. Pinninti SG and Kimberlin DW. Maternal and Neonatal Herpes Simplex Virus Infections. *Am J Perinatol* 2013;30:113-120.
8. Pinninti SG and Kimberlin DW. Neonatal Herpes Simplex Virus Infections. *Pediatr Clin N Am* 2013;60:351-365.

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