Antiviral Drugs in Newborn and Children

Claudette L. Poole, MD*, David W. Kimberlin, MD

KEYWORDS

• Influenza • Herpes simplex virus • Cytomegalovus • Hepatitis

KEY POINTS

- Recommendations for the use of antivirals to treat herpetic diseases in neonates and children, including herpes simplex virus, varicella zoster virus, and cytomegalovirus, are based on randomized controlled trials.
- Guidelines for the treatment of influenza, including prophylaxis in neonates and children, also are evidence based.
- Food and Drug Administration– approved antivirals for the treatment of hepatitis B virus and hepatitis C virus in children are limited, but there are multiple agents in current phase III trials in the pediatric population.
- Antiretroviral agents for the treatment of HIV are beyond the scope of this article.

INTRODUCTION

The availability of safe and effective antiviral medications is a recent addition to the antimicrobial armamentarium. Knowledge of viral pathogenesis and development of enhanced diagnostics coalesce with the development and application of novel antiviral agents to make this an exciting time for advancements in the treatment of viral infections in children.

ANTIVIRAL CATEGORIES

Antiviral agents can be classified into a few broad categories based on their mechanism of action. These include the following.

Nucleotide/Nucleoside Analogues

The nucleotide/nucleoside analogue agents are similar in structure to naturally occurring nucleotides/nucleosides. Once these are incorporated in the growing nucleic acid chain during transcription, they either result in chain termination, because their

Department of Pediatrics, University of Alabama at Birmingham, 1600 6th Avenue South, CHB 308, Birmingham, AL 35233, USA
* Corresponding author.
E-mail address: cpoole@peds.uab.edu

Pediatr Clin N Am 64 (2017) 1403–1415
http://dx.doi.org/10.1016/j.pcl.2017.08.014 **pediatric.theclinics.com**

structure does not allow for another nucleotide to be added, or in impaired function of the polymerase, which is the enzyme involved in translation.

These are by far the largest group of antiviral agents in clinical use. Their toxicity relates to their specificity to being incorporated into the growing viral nucleic acid chain versus the host cell DNA.[1,2]

Neuraminidase Inhibitors

The neuraminidase inhibitor agents are directed to a viral specific enzyme that is involved in the process of release of the newly formed viral particles from the host cell. This enzyme is present in influenza viruses.[3]

Interferons

Interferons are naturally occurring products of the cellular immune response targeting viruses. Interferons currently are used with other agents to treat hepatitis B virus (HBV) and hepatitis C virus (HCV) in children. They have many side effects and are used less frequently as safer and highly effective small molecules active against hepatitis viruses come to market.[4]

ANTIVIRAL RESISTANCE

The viral replication process in general has low fidelity, resulting in a high mutation rate. In any given host there are many different mutant viral populations. In the presence of an antiviral agent, viruses that have developed a mutation conferring resistance to the present antiviral then replicate more efficiently and become the predominant virus present in the host, resulting in treatment failure. These resistant viruses usually are less virulent than wild-type virus but can still cause significant disease. Resistant viruses require an alternate agent that targets a different mechanism. Antiviral resistance testing often identifies these genetic mutations.[5]

Patient categories

In presenting antiviral therapies in pediatrics, 4 specific scenarios are focused on:

1. Treatment and prophylaxis of influenza
2. Neonatal herpes simplex virus (HSV) infection and congenital cytomegalovirus (CMV) disease
3. Treatment of herpes viral diseases beyond the neonatal period, including in immunocompromised hosts, together with other viral infections specific to an immunocompromised child
4. Approved antiviral treatments for HBV and HCC chronic infections in children

INFLUENZA

- Oseltamivir, administered orally, is the only drug currently Food and Drug Administration (FDA) approved for both the treatment and the prophylaxis of influenza in children less than 5 years of age.
- Inhaled zanamivir is FDA approved for prophylaxis for children 5 years and older and for treatment of children 7 years and older. (Intravenous [IV] zanamivir is currently undergoing clinical trials and data on pediatric dosing have recently been published.)
- IV peramivir is only licensed for use in those 18 years and older.