Influenza Prophylaxis in Children: Could a Single Dose of One Drug Be an Option?

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During annual influenza epidemics, the highest illness rates occur among children, who are also known to play substantial roles in influenza transmission among households and communities. The Centers for Disease Control and Prevention recommend postexposure chemoprophylaxis with neuraminidase inhibitors for close contacts at elevated risk for influenza complications who have not been vaccinated or are unlikely to be protected through vaccination or other contact precautions at the time of exposure.[1] The effectiveness of postexposure prophylaxis with neuraminidase inhibitors is estimated to be 68% to 90%. The American Academy of Pediatrics recommends oral oseltamivir prophylaxis in infants starting at 3 months of age and in high-risk children, and inhaled zanamivir prophylaxis is recommended only in children ≥5 years old.[1,2] Intravenous peramivir is not approved for children or for prophylaxis in the United States. The recommended duration of prophylaxis currently is 7 to 10 days from last exposure or ≤1 weeks after vaccination. Similar to treatment, antiviral prophylaxis is recommended preferably within 48 hours of exposure. Its use is limited by concerns for antiviral availability, development of resistance, and potential side effects.

Nakano et al[3] report the results of a randomized, double-blind, placebo-controlled, multicenter clinical trial evaluating the efficacy of 1 dose of an investigational long-acting neuraminidase inhibitor, laninamivir octanoate, in preventing influenza in children 2 through 9 years of age who were exposed to a household member with laboratory-confirmed influenza during the 2014 to 2015 influenza season in Japan. The single 20-mg dose of intranasally inhaled laninamivir was administered within 48 hours of onset of influenza illness in a household index case, reducing the risk of laboratory-confirmed, symptomatic influenza illness by 45.8% (95% confidence interval, 7.5%–68.2%) in children who received prophylaxis (n = 171) compared with placebo recipients (n = 170). Interestingly, the risk reduction was notably higher, at 64.5% (95 confidence interval, 26.7–82.8), in children who were negative for influenza virus at the time of receiving drug (baseline). This result mirrors the ∼63% efficacy reported for children ≥10 years old and adults[4,5] and supports the efficacy of prophylaxis in both noninfected and infected, but not yet symptomatic, household contacts of influenza cases. However, the results of Nakano et al[3] were significant only for children 2 through 6 years old but not for those 7 through 9 years old. The authors attribute this finding in the older age group to smaller numbers of participants and more influenza test–positive children at the initiation of prophylaxis. This drug was well tolerated, without significant adverse events reported, including no neurologic symptoms or abnormal behavior, which has occurred with influenza illness and with other neuraminidase inhibitors in Japan.[6]

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Although vaccination remains the preferred approach for influenza prevention, additional options for influenza prophylaxis in children are important, given concerns for the emergence of resistance, the known antiviral adverse side effect profiles, possible limited supplies, and the potential for spotty patient compliance. Inhaled laninamivir octanoate is approved for treatment and prophylaxis of influenza in Japan but not in the United States.[7] It is converted into its active form in the lungs, where a high concentration persists for a long period of time.[8] Laninamivir has displayed clinical efficacy comparable to that of oseltamivir and zanamivir against pandemic H1N1, seasonal H3N2, and the B influenza viruses.[8]

The single-dose administration and good safety profile of laninamivir octanoate make it an appealing option for influenza prophylaxis in children. This drug appears practical in ensuring timely intervention and improved compliance with prophylaxis. The intranasal inhalation route of administration might limit its use in young children, who are unable to use the dry powder inhaler device properly. However, Nakano et al[3] confirmed that their pediatric-aged subjects had sufficient inhalation capability to use the inhaler with a whistle device test. Prompt initiation of influenza prophylaxis is necessary to ensure efficacy, which hinges on proper and prompt identification of index cases. Therefore, efforts to educate parents and families on the early signs and symptoms of influenza and the importance of seeking medical attention to confirm the diagnosis in the index case are crucial for timely initiation of prophylaxis in household contacts.

More investigation of the safety and efficacy of laninamivir octanoate prophylaxis in specific pediatric populations at high risk for influenza and its complications, such as children with chronic cardiac or pulmonary disease and the immune suppressed, is needed. The efficacy of the prophylaxis regimen on specific influenza virus strains and the risk for developing antiviral resistance should be explored. There also is a need for influenza antiviral agents with different mechanisms of action than the neuraminidase inhibitors because of the potential for development of antiviral resistance in seasonal and pandemic influenza virus strains. Perhaps we can reasonably anticipate a single-dose, long-term drug as a future option for influenza prophylaxis.

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