Antiviral Drugs in the Immunocompetent Host: Part II. Treatment of Influenza and Respiratory Syncytial Virus Infections

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Family physicians should be familiar with the various drugs available for treating and preventing viral infections. Part II of this two-part article focuses on agents used to manage influenza and respiratory syncytial virus. Rimantadine and amantadine traditionally have been used to prevent and treat influenza type A infections. The neuraminidase inhibitors zanamivir and oseltamivir have a broadened spectrum of activity in the treatment and prevention of influenza types A and B. Ribavirin has been used in some high-risk infants to treat respiratory syncytial virus infections, and palivizumab can be used for prophylaxis. (Am Fam Physician 2003;67:763-6. Copyright© 2003 American Academy of Family Physicians.)

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NA viruses generally are benign in the early stage of infection, but they have the potential to induce acute respiratory distress syndrome if they spread to the lower respiratory tract or progress to pneumonia. Antiviral drugs can be used to treat and prevent these infections, although they are not a substitute for vaccine. Part II of this article focuses on antiviral agents used in the management of influenza and respiratory syncytial virus (RSV).

Influenza Viruses

Antiviral drugs that prevent and treat influenza should be considered adjuncts to vaccine—not substitutes. Traditionally, amantadine (Symmetrel) and, to a lesser extent, rimantadine (Flumadine) have been used for preventing and treating influenza type A (Table 1). However, in 1999, two drugs that effectively treat and prevent influenza types A and B were introduced. These drugs, zanamivir (Relenza) and oseltamivir (Tamiflu), provide more complete coverage when the type of influenza is unknown (Table 2).

INFLUENZA TYPE A

Amantadine and Rimantadine. Amantadine was the first drug approved for prophylaxis of influenza type A (in 1966), and in 1976, it was approved for treatment and prophylaxis in adults and children older than one year. Rimantadine became available in 1993 for treatment and prophylaxis of influenza type A in adults and for prophylaxis in children. Neither of these drugs is effective against influenza type B.

Treatment usually is continued for three to five days or discontinued 24 to 48 hours following resolution of symptoms. The efficacy of both drugs is similar, and the average duration of illness is shortened by approximately one day.

These drugs can be used for prophylaxis in high-risk patients (Table 3) and for influenza-related complications if an outbreak of influenza occurs within two weeks following vaccination. In a recent review, the average effectiveness of amantadine and rimantadine for the prevention of influenza was 61 and 72 percent, respectively.

Although amantadine is considerably less expensive than rimantadine, it crosses the blood-brain barrier and appears to cause more central nervous system side effects, including dizziness, ataxia, hallucinations, agitation, and confusion. This is especially true in elderly patients and may be associated with higher serum concentrations. A split dosage may help minimize adverse events.

Amantadine is primarily eliminated in the
kidneys as unchanged drug; therefore, the dosage must be modified in elderly patients and patients with reduced renal function (Table 4).8

Rimantadine’s adverse drug-reaction profile is similar to that of amantadine with respect to gastrointestinal side effects such as nausea, vomiting, and dyspepsia, but rimantadine appears to cause fewer central nervous system side effects.9

Oseltamivir and Zanamivir. Oseltamivir, which is taken orally, was approved for prophylaxis of influenza in late 2000, and zanamivir’s approval for prophylaxis is pending. They are equally effective in reducing symptoms and duration of illness when taken within 48 hours of the onset of symptoms.10-14

Zanamivir is inhaled and requires the use of an inhalation device, which may be difficult for elderly patients to use. Because of its potential to induce bronchospasm and reduce lung function, use of zanamivir gener-

### TABLE 1

Comparison of Amantadine and Rimantadine

<table>
<thead>
<tr>
<th>Drug factors</th>
<th>Amantadine (Symmetrel)</th>
<th>Rimantadine (Flumadine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic availability</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dosage forms</td>
<td>Liquid and tablet</td>
<td>Liquid and tablet</td>
</tr>
<tr>
<td>Treatment and prevention of influenza type A in adults</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Treatment of influenza type A in children</td>
<td>Yes</td>
<td>Not approved</td>
</tr>
<tr>
<td>Prevention of influenza type A in children</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dosages for treatment of influenza type A</td>
<td>Adults* and children ≥12 years of age: 200 mg daily until 24 to 48 hours after symptoms have disappeared or 100 mg twice daily until 24 to 48 hours after symptoms have disappeared Children one to nine years of age: 5 mg per kg daily (up to 150 mg daily) until 24 to 48 hours after symptoms have disappeared Children 10 to 11 years of age: 100 mg twice daily until 24 to 48 hours after symptoms have disappeared</td>
<td>Adults* and children ≥10 years of age: 100 mg twice daily for seven days Not approved for children &lt;10 years of age</td>
</tr>
<tr>
<td>Dosages for prevention of influenza A†</td>
<td>Adults* and children ≥12 years of age: 200 mg daily for at least seven days or 100 mg twice daily for at least seven days Children one to nine years of age: 5 mg per kg daily (up to 150 mg daily) for at least seven days Children 10 to 11 years of age: 100 mg twice daily for at least seven days</td>
<td>Adults* and children ≥10 years of age: 100 mg twice daily for at least seven days Children &lt;10 years of age: 5 mg per kg daily (up to 150 mg daily) for at least seven days</td>
</tr>
<tr>
<td>Prevention and treatment of influenza B</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Dosage reduction in renal impairment</td>
<td>Yes (creatinine clearance ≤50 mL per minute [0.83 mL per second])</td>
<td>Yes (creatinine clearance ≤10 mL per min [0.17 mL per second])</td>
</tr>
<tr>
<td>Side effects</td>
<td>CNS and GI</td>
<td>Primarily GI</td>
</tr>
<tr>
<td>Cost (generic)§</td>
<td>Five-day treatment (adult dosage) $18 ($4 to $5) $106 ($28 to $31)</td>
<td>$29 ($26) $171 ($154)</td>
</tr>
<tr>
<td>42-day treatment (adult dosage in community outbreaks)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CNS = central nervous system; GI = gastrointestinal.

*—Dosage for adults up to age 64. Dosage for adults age 65 and older is 100 mg daily.
†—If CNS effects develop with the once-a-day dosage, the split dosage might reduce side effects.
‡—All dosages may be used for up to 42 days during community outbreaks.
§—Estimated cost to the pharmacist based on average wholesale prices in Red book. Montvale, N.J.: Medical Economics Data, 2002. Cost to the patient will be higher, depending on prescription filling fee.

Information from references 1 through 4.
ally should be avoided in patients with asthma and chronic obstructive pulmonary disease.

**INFLUENZA TYPE B**

Oseltamivir and zanamivir are first-line choices for prevention and treatment of infection during outbreaks of influenza type B.

**Respiratory Syncytial Virus (RSV)**

RSV is a frequent cause of bronchiolitis in children. Treatment consists primarily of supportive care with fluids, oxygen, and aerosolized bronchodilators.

**Ribavirin.** In a select group of high-risk infants (premature infants younger than 36 weeks and infants with bronchopulmonary dysplasia, congenital heart disease, or immunodeficiency) with severe infections, aerosolized ribavirin (Virazole) has been used. The use of this drug requires special equipment and expert respiratory monitoring. It is expensive, with a cost exceeding $1,000 per day.

**RSV Immune Globulin and Palivizumab.** In
high-risk patients, prophylaxis against RSV should be considered. During the winter months, monthly administration of intravenous RSV immune globulin (RespiGam) or intramuscular palivizumab (Synagis) may decrease the number of RSV episodes. Because of increased morbidity, RSV immune globulin should not be given to patients with congenital heart disease.

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REFERENCES
