Influenza Antivirus Use in the Setting of Increased Resistance to Oseltamivir: A National Survey of the IDSA Emerging Infection Network, 2007-2009
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ABSTRACT
Introduction: In December 2008, new interim guidelines on the use of influenza antiviral agents were released in response to a high prevalence of influenza A (H1N1) viruses resistant to adamantane-resistant A(H1N2) virus. Zanamivir, oseltamivir, and rimantadine use in an adenovirus- and oseltamivir-resistant hospitals was recommended, depending on in-vitro type and local surveillance data.

Methods: Two web-based questionnaires were sent in 2007 and 2008 to the IDSA Emerging Infections Network (EIN) members about antiviral prescribing in January and April of the 2007-2008 influenza season and in April of the 2008-2009 season.

Results: In January, 464 (55% of 852 EIN members) responded to the survey in 2007 and 411 (49% of 837 members) in 2008. In January 2008, 66% reported having access to oseltamivir and 9% (p=0.06) reported not having access to oseltamivir. In 2007, 60% reported being able to test for A virus subtype and 9% reported being able to test for B virus subtype. In 2008, 65% reported being able to test for A virus subtype and 11% reported being able to test for B virus subtype. In January, 95% reported being able to test for viral type, but only 5% reported being able to test for viral type. In both seasons, 95% used local surveillance data to make treatment decisions. During both seasons, respondents reported more difficulty providing zanamivir (42% vs. 38%, p=.57) and more difficulty providing oseltamivir (58% vs. 55%, p=.35) during the 2008-2009 season compared with 2007-2008.

Conclusions: The mild influenza season, difficulty obtaining recommended antivirals, and lack of access to in-vitro diagnostic and surveillance data may have contributed to reduced antiviral use during 2008-2009. The emergence of a new adamantane-resistant subtype, 2009 H1N1, could further complicate the use of antivirals. Clinicians obtain new recommendations at www.cdc.gov/flu/for healthcare-professionals.htm.

INTRODUCTION
• Influenza antiviral agents
  - Adenoviruses: adamantane and rimantadine
  - Neuromuscular Inhibitors (NAI): oseltamivir and zanamivir
  - Resistance to antiviral agents
    - 2005-2006: 90% of A(H1N2) viruses resistant to adamantane, 100% to rimantadine
    - Adenoviruses no longer recommended for use
    - 2007-2008: resistance to oseltamivir first detected among 12% of A(H1N1) viruses tested

METHODS
• Emerging Infections Network (EIN)
  - Provider-based sentinel network established in 1995
  - Survey physicians on topics of clinical importance

• Web-based survey distributed two times
  - January 2008: 1,249 members surveyed on antiviral prescribing practices during 2007-2008 influenza season
  - April 2008: 1,316 members surveyed on antiviral prescribing practices during 2007-2008 influenza season

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• April survey not sent due to the 2009 pandemic influenza A(H1N1) outbreak

• Data collected and tabulated by EIN
  - Proportions compared using χ² analyses
  - Fisher’s exact test performed if P ≤0.05
  - P values ≤0.05 considered statistically significant

RESULTS
Table 1: Use of influenza antiviral agents, 2007-2008 and 2008-2009

<table>
<thead>
<tr>
<th>Season</th>
<th>Antiviral Agent</th>
<th>Arotine 2007</th>
<th>Arotine 2008</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oseltamivir</td>
<td>40%</td>
<td>32%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Zanamivir</td>
<td>26%</td>
<td>22%</td>
<td>.0091</td>
</tr>
</tbody>
</table>

During both seasons, respondents reported more difficulty obtaining zanamivir (42% vs. 38%, p=.57) and more difficulty obtaining oseltamivir (58% vs. 55%, p=.35) during the 2008-2009 season compared with 2007-2008.

Factors considered when deciding whether to treat with antiviral agents

Table 2: Reasons for not treating patients with influenza with antiviral agents during the 2007-2008 influenza season

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number of Respondents</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient unable to take PO</td>
<td>131 (35%)</td>
<td>23%</td>
</tr>
<tr>
<td>Patient too young</td>
<td>156 (31%)</td>
<td>24%</td>
</tr>
<tr>
<td>Patient not resistant to NAIV</td>
<td>22 (6%)</td>
<td>4%</td>
</tr>
<tr>
<td>Patient had mild illness</td>
<td>334 (66)</td>
<td>58%</td>
</tr>
<tr>
<td>Patient had severe illness</td>
<td>65 (29)</td>
<td>10%</td>
</tr>
<tr>
<td>Patient presented &gt;2 days after onset of illness</td>
<td>26 (11)</td>
<td>5%</td>
</tr>
<tr>
<td>Underlying medical conditions of patient</td>
<td>23 (10)</td>
<td>5%</td>
</tr>
<tr>
<td>Laboratory confirmation of influenza virus</td>
<td>55 (24)</td>
<td>10%</td>
</tr>
<tr>
<td>National surveillance data</td>
<td>35 (9)</td>
<td>6%</td>
</tr>
<tr>
<td>Time from illness onset to laboratory confirmation</td>
<td>34 (9)</td>
<td>6%</td>
</tr>
</tbody>
</table>

CONCLUSIONS
• Physicians reported prescribing fewer antiviral drugs during the 2008-2009 influenza season
  - 2% vs. 13% for adenovirus
  - 4% vs. 15% for zanamivir
  - 10% vs. 30% for oseltamivir

• Response likely not generalizable to all physicians, especially those in primary care

• Majority with subspecialty training in infectious Diseases

• Most used to within the 2008-2009 influenza season

• Interim guidelines difficult to implement

• Difficulty providing zanamivir and adenoviruses

• Agents less available from pharmaceutical companies

• Laboratory testing results on subtypes not available

• Limited access to local influenza surveillance data

• Pandemic influenza A (H1N1) virus further complicates antiviral use

• <1% pandemic A(H1N1) viruses resistant to oseltamivir

• 90% resistant to zanamidane

• 100% are resistant to adenoviruses

• Antiviral use guidelines can be obtained at: http://www.cdc.gov/flu/flu/treatments.htm

LIMITATIONS
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