Optimizing Use of Antibiotics and Antivirals in Ambulatory Patients with Influenza

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Most antibiotics prescribed in the United States are for acute respiratory tract infections, and roughly half of these prescriptions are intended to treat viral diagnoses for which antibiotics have no benefit.[1] A recent study showed that 17% of all antibiotic prescriptions among outpatients with non-pneumonia acute respiratory illness had influenza.[2] Antibiotics are thought to provide little benefit to the patients with influenza, but expose patients to the risks of adverse drug reactions, Clostridioides difficile infection, drive emergence of antibiotic-resistant bacteria, and increase healthcare costs. Further, antivirals are available for influenza and early, appropriate antiviral use is associated with a reduced risk of infectious complications and antibiotic utilization.[3]

Against this backdrop, Sutton and colleagues reviewed 12,806 Veterans Administration (VA) patients seen in primary care clinics and emergency departments diagnosed with influenza between 2011 and 2019 to look at the impact of antibiotic, antiviral, or combined treatment on hospitalization. Overall, hospitalizations were rare (6%). Patients prescribed antibiotics, antivirals, or both had a lower risk of all-cause hospitalization than patients receiving neither. There were no significant differences in all-cause hospitalizations among patients prescribed antibiotics, antivirals or both. Patients prescribed antibiotics and antivirals had a lower risk of respiratory hospitalization (adjusted relative risk, 0.53; 95% CI, 0.31 to 0.94) compared to patients who only received antivirals.
Given these results, for patients with influenza, should we be reconsidering early antibiotics? For now, no, but additional studies are needed.

Antibiotics only appeared beneficial for a subset of hospitalizations and the absolute differences were very small. Of course, this was an observational study and unmeasured confounding, including confounding by indication, is always a possibility. Patient behavior could also have a role if, for example, patients who received antibiotics and antivirals already thought they received maximal treatment and so did not seek further care).

In addition, the study population was highly selected and markedly different from most other studies.[4-6] This study only included patients with laboratory-confirmed influenza and a variety of diagnosis codes, including fever, chills, cough, hiccough, “abnormality of breathing,” acute bronchitis, Q fever, asthma, and visits for influenza. Few ambulatory adults in other routine clinical practice settings have diagnostics performed for influenza.[6] The study population, from the VA, had high rates of chronic pulmonary disease, drug abuse, and mental health diagnoses in addition to having more frequent use of influenza diagnostics.

Antiviral and antibiotic treatment had to be prescribed on the same day as influenza testing was performed, which does not account for typical delays in prescribing in clinical practice. The rate of antiviral treatment was extremely high (62%) and the rate of antibiotic treatment was much lower (16%) than other studies. In another study with
data from 5 influenza seasons, among high-risk outpatients, only 37% of patients with confirmed with influenza within 2 days of symptom onset were prescribed antivirals.[5] Similar studies have noted that rates of antibiotic prescriptions are typically double the rate of antiviral use.[4, 5]

Lastly, the most commonly utilized antibiotic class in treated patients in this study, macrolides, have been associated with improved outcomes when administered to patients hospitalized with influenza.[7, 8] This is thought to be, in large part, the result of anti-inflammatory effects of this class of antibiotics.[8] Antibiotic class was not included as an adjustment for risk of hospitalization in the authors’ model. Since nearly 40% of patients received this class of drug, it may have contributed to lower rates of hospitalization but was not adjusted for in the models.

To improve care for patients with influenza, future studies should seek to replicate the findings of Sutton and colleagues and to extend them to other patient groups. Such studies should include a more diverse patient population, assessment for both calls and visits for new or refractory symptoms, documented infectious complications, need for new or additional antibiotics, and adverse effects associated with the prescribed therapy. Together, such expanded studies would give a more complete picture of the risks and benefits of the various approaches.

Currently, overuse of antibiotics and underuse of antivirals are common.[2, 5, 9, 10] Approaches that optimize ambulatory triage to identify which patients can safely remain
at home without evaluation and those who require evaluation and management in the clinic or emergency department should clearly be an important focus. Further, approaches to allow patients to access antiviral therapy in a timely fashion should be studied as well.

Clinicians are comfortable prescribing antibiotics but not antivirals for patients likely to have influenza. Approaches that result in the “right” influenza patients getting antivirals should decrease antibiotic use which should improve outcomes and minimize harms, such as antimicrobial resistance and *C. difficile* colitis.[11, 12]
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