Antimicrobial Stewardship News

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Is Five the New Seven? Updated Treatment Durations for Common Infections

Introduction

By convention, providers treat infections in intervals of 7 days. This mindset, however, results in overuse of antibiotics, which is associated with substantial risks. A recent editorial published in *JAMA Internal Medicine* reviewed the evidence supporting shorter-course antibiotic therapy for common infections and came to the bold conclusion, "Shorter is Better."[1]

This newsletter will review appropriate durations of therapy for common infections and debunk several myths regarding treatment durations.

The Problem: Antibiotics Are Prescribed for Excessive Durations

Duration of antibiotic therapy for hospitalized patients often exceeds recommendations in national guidelines. For example, patients treated for community-acquired pneumonia (CAP) are likely to receive at least 10 days of antibiotics despite the recommended 5 days.[2,3] This common practice is often a result of the misbelief that antibiotics are harmless and that extending antibiotic duration is best for patients. This, in fact, is not often the case. Excessive antibiotic therapy has significant implications on patient outcomes:

1) increased risk for side effects (such as *C. difficile*);
2) increased risk for developing antibiotic resistance;
3) increased burden on healthcare resources (cost).

In order to have an impact on prescribing practices, it is critical to understand several common "myths" that drive our current (and excessive) antibiotic use.

Common Myths Regarding Durations of Antibiotic Therapy

***Myth 1**: Patients must be treated 2-3 days beyond symptom resolution to prevent infection relapse.*

In the early days after penicillin was discovered, physicians customized antibiotic duration for pneumonia based on clinical response. One and a half to 4 days of therapy resulted in high cure rates. Shortly thereafter, a case series suggested increased rates of relapse and ultimately led to a belief that antibiotics should continue beyond symptom resolution.[4] Re-evaluation of that initial case series discovered isolates with different bacterial serotypes, suggesting new infections rather than relapse. Despite this finding, many clinicians continued longer durations which persist in practice today.

Bottom line: Duration of antibiotic therapy should be customized to patients' clinical response.

Trials comparing short- vs. longer-course antibiotic therapy have shown that short-course therapy is just as effective.

***Myth 2**: Antibiotic resistance can be prevented by continuing therapy beyond resolution of symptoms.*

Patients are often instructed to complete their entire prescribed courses of antibiotics in order to prevent resistance, even if they feel better sooner. There is no evidence to support this claim; in fact, it is contrary to everything we know about how antibiotic resistance happens. Studies in pneumonia have actually shown that longer courses of antibiotics result in more emergence of antibiotic resistance.[5,6] In rare cases does antibiotic resistance emerge at the site of infection; instead, resistance emerges among colonizing flora separate from the primary infection.

Bottom line: Continuing antibiotics beyond resolution of symptoms does not prevent resistance; rather, it increases the selective pressure driving antibiotic resistance among colonizing flora.

Table 1. Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent to Longer Therapy[1]

	Duration (days)	
Disease	**Short**	**Long**
Community-acquired pneumonia (CAP) [3,7,8]	3-5	7-10
Nosocomial pneumonia (HAP/VAP)[5,6]	≤ 8	10-15
Pyelonephritis[9]	5-7	10-14
Intraabdominal infection[10]	4	10
Acute exacerbation of chronic bronchitis (AECB) and COPD[11]	≤ 5	≥ 7
Acute bacterial sinusitis[12]	5	10
Cellulitis[13]	5-6	10
Chronic osteomyelitis[14]	42	84

***Myth 3**: Short-course antibiotic therapy is not as effective as traditional (longer) courses in clinical trials.*

Controlled trials comparing short-course with longer course antibiotic therapy show that short-course therapy was just as effective (**Table 1**). Short course therapy limits the selective pressure that drives resistance. In the past, standard treatment for CAP included 7 to 14 days of antibiotics. More recent clinical trials have demonstrated that 3 to 5 days of antibiotics are as efficacious in select CAP patients demonstrating clinical response.[7,8] Similarly, clinical trials for other infections, such as pyelonephritis, intra-abdominal infections, and cellulitis have challenged the standard antibiotic duration of 7 to 14 days and demonstrated similar results. As clinical practice guidelines are updated (such as the 2016 IDSA HAP/VAP guidelines), we see the significant impact of these data on recommendations for treatment duration. Tuberculosis is one important exception which requires long treatment courses because it is a slow growing bacteria.

Bottom line: Shorter courses of antibiotic therapy are preferred over longer courses of therapy for most infections.

Is Shorter, in Fact, Better?

As discussed above, excessive antibiotic use does not reduce the risk for relapse, prevent resistance, or improve patient outcomes. Rather, it increases the selective pressure driving antibiotic resistance and the risk of adverse effects in patients. Therefore, use of shorter courses of antibiotics and avoidance of excess antibiotic days is a primary goal for ASPs.

How to Identify Excessive Antimicrobial Use

There are numerous stewardship interventions targeting excessive antibiotic treatment durations; however, none are useful unless appropriate targets (i.e., antibiotics and/or disease states) for intervention are identified. Antibiotic stewardship champions can use the DASON Antimicrobial Stewardship Assessment Portal (ASAP) to quickly and easily identify agents with longer than desired lengths of therapy (LOT).

In ASAP, the "drill down" feature may be used to populate local statistics for an individual agent. To interpret these data, the metrics "% admissions receiving selected antimicrobial(s)" and "length of therapy/ targeted antimicrobial use admissions" are useful for comparison. For example, if many patients receive a short duration of a broad-spectrum agent, this may reflect appropriate empiric use and subsequent de-escalation. In contrast, longer durations may reflect appropriate or inappropriate use. For example, longer durations may be appropriate for certain drugs (i.e., daptomycin if treating several inpatients with MRSA endocarditis) and inappropriate for others (i.e., daily azithromycin for COPD exacerbation prophylaxis).

Table 2. Using ASAP to Identify Potentially Excessive Durations of Therapy

	Ex. 1- Appropriate empiric vancomycin use (de-escalation)		Ex. 2- Excessive azithromycin durations of therapy	
	Hospital	DASON Mean	Hospital	DASON Mean
% Patient Admissions Receiving Select Antimicrobial	16.4%	12.8%	5.4%	4.58%
LOT/Targeted Antimicrobial Use Admissions	2.5 days	3.4 days	7.1 days	3.1 days

For more information on how to interpret antimicrobial use metrics, please see our March 2016 newsletter, "You Cannot Manage What You Cannot Measure: Understanding Nuances in Antimicrobial Use Metrics."

What Are ASPs Doing to Target Excessive Durations of Antibiotic Therapy?

Many DASON community hospitals have developed and implemented specific interventions targeting excessive antibiotic durations identified through ASAP or medication use evaluations. Examples include implementing facility-specific treatment algorithms that restrict antibiotic duration during order entry, removing default durations appearing on discharge orders for oral antibiotics, communicating with outpatient pharmacists to tailor durations, and implementing antibiotic time out procedures. We encourage you to work with your liaison clinical pharmacist to develop and implement interventions at your hospital.

Take Home Message:

1. Excessive durations of antibiotics increase the risk for developing unwanted side effects, such as *C. difficile*.
2. Antibiotic duration should be customized based on clinical response in accordance with local and national guidelines.
3. Trials comparing short- versus longer-course antibiotic therapy show that short-course therapy has been just as effective.
4. ASAP helps identify areas to target interventions focused on shorter durations. A number of interventions targeting shorter durations have been deployed at DASON hospitals with success.

Stewardship News

- MARK YOUR CALENDARS! The DASON/DICON Fall 2016 Symposium will be held on Friday, November 18 at the Sheraton Greensboro Hotel at Four Seasons from 8:30AM-3:30PM – We look forward to seeing you there!
- Please join us in congratulating the teams from Nash, Southeastern, and Piedmont for presenting projects at IDWeek 2016 in New Orleans, LA!

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