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The Search for More Meaningful Metrics: A look at Antibiotic Spectrum Scores

Introduction

One important goal of antimicrobial stewardship is to increase quality and safety of patient care through the optimization of antimicrobial therapy. However, the data typically collected to guide our interventions may not always be helpful in telling the full story of the work of Antimicrobial Stewardship Programs (ASP). In order to evaluate new stewardship interventions and remain agile we require readily accessible data about local antimicrobial use. As a result, much of the work we do as antimicrobial stewards is dependent on being able to act upon antibiotic use metrics such as Days of Therapy (DOT) and Length of Therapy (LOT).

To that end, there has recently been a great deal of interest in the development of novel metrics with a particular focus on the integration of antimicrobial spectrum of the agents being used. This newsletter seeks to briefly review current metrics and introduce some potential new tools for the future.

Where we are now

Days of Therapy (DOT) is currently the preferred antibiotic use metric in the ASP guidelines published by the IDSA and SHEA.[1] DOT is defined as any calendar day in which at least a single dose of antibiotics is received. Days are counted separately for each agent. For example, a patient who receives both ceftriaxone and azithromycin would count as 2 DOT per calendar day.[2]

While DOT are helpful there are a few notable limitations, particularly when using it as a benchmark to compare hospitals.[3] Notably, DOT, alone or standardized by the days of inpatient stay, do not account for the case mix and complexity differences across different types of hospitals and units, nor does it account for the spectrum or types of microorganisms targeted. And lastly, DOT does not always accurately reflect the work of the ASP during a de-escalation or an optimization event.

To address these limitations several other metrics have been introduced and are widely used. The Standardized Antimicrobial Administration Ratio (SAAR) used as part of the National Healthcare Safety Network (NHSN) antimicrobial Use and Resistance (AUR) module is a way to adjust for facility-level and unit-level case mix differences. For a more detailed discussion on this topic we would refer you to the May 2019 DASON Newsletter dedicated to this topic.

Finding metrics to represent antibiotic spectra and then better reflect de-escalation or optimization events is a burgeoning area of study for AU metrics. De-escalation and use of narrower spectrum therapies is associated with decreased rates of *C difficile* infection, days of hospitalization, and decreased rates of antimicrobial resistance.[4,5] Many of our stewardship interventions are targeted at these clinical endpoints and better metrics to reflect those efforts will be essential to continued program success.

Spectrum Scores: A new frontier?

A variety of different attempts have been made to try and capture antimicrobial spectra of activity. On one end, a 5 point scale was proposed by Stenehjem et al based on expert opinion, emphasizing simplicity and pragmatism but offering less discrete or actionable information.[6] On the other end, Madaras-Kelly et al proposed a highly complex computer-generated spectrum score which accounted for organisms, drug classes and local susceptibility patterns which provides a wealth of information but is less intuitive and more challenging to implement.[7] Another described by DASON's, Dr. Moehring, et al, focused in on stewardship

applications, in particular, by weighting agents by spectrum and program priorities such as agents with high toxicity or high cost.[8] Several hospitals in DASON will remember playing a role in evaluating this metric.

While each of these individual metrics has its individual pros and cons, the methodology which has been referenced most often and become the basis for a number of new metrics is the Antibiotic Spectrum Index (ASI) proposed by Gerber et al in 2017.[9] The ASI is based around creating a list of relevant organisms or categories (MSSA, Enterococci, anaerobes, atypicals, ESBLs, etc.) and assigning one point for each relevant category or organism it covers. For example, ceftriaxone has an ASI of 5 (MSSA, oral anaerobes, *H. influenzae*, *E. coli*/Klebsiella, penicillin resistant *S. pnemoniae*), while piperacillin-tazobactam has a score of 8 for the additional coverage of Enterococci, *B. fragilis* and Enterobacter. The score ranges from 0-14 and accumulates with each day of therapy. More recently Kakiuchi et al proposed the novel metric Days of Antibiotic Spectrum Coverage (DASC) which builds off the ASI to include a more robust list of antimicrobials and adds further categories of interest for 16 possible points per day of therapy.[3]

While an exact standard has yet to be established, due to the amount of interest in this topic, developing a familiarity with the underlying concepts will be important as the field move towards using these scores as a tool for benchmarking

Potential Applications

A number of studies have looked at practical applications of these scores and their utility in demonstrating the work of antimicrobial stewardship programs.

De-escalation as defined by a reduction in antibiotic spectrum score has been shown to correlate moderately well with de-escalation by more traditional metrics.[7,8,10] In a study looking at de-escalation of antibiotics for pneumonia the ASI was used to quickly define de-escalation as an ASI score reduction on day 3 vs day 1. The authors found ASI based de-escalation was associated with fewer episodes of *C. difficile* infection and fewer days of hospitalization.[5] In a further analysis of this data they demonstrated that a reduction in ASI was more predictive of a reduction in *C. difficile* infection risk than their "traditional" definition of de-escalation, based upon cessation of an anti-staphylococcal or anti-pseudomonal agents.[10]

Yarrington et al included the ASI as part of their analysis of antimicrobial use across different locations at their institution and at different times of day.[11] This demonstrates the potential utility of ASI to aid in targeting interventions to particular units of interest or staff on specific shifts with high utilization of broad-spectrum agents.

The power of spectrum scores to aid in antimicrobial stewardship efforts is best demonstrated by an example case. Consider a patient admitted for sepsis who is started on empiric coverage with vancomycin and piperacillin-tazobactam. After three days of therapy, discussion with the stewardship teams results in de-escalation of therapy to ceftriaxone and metronidazole to complete a total 7-day course of therapy. Using the DOT metric this patient received 14 days of therapy regardless of the intervention and there's no reflection of the AS team's efforts in this metric. However, using the DASC metric there is a sizeable reduction in days of antibiotic spectrum coverage from 112 if no intervention was taken to 80 as a result of the de-escalation (**Table 1**). Here, the efforts of the stewardship team are clearly captured.

Table 1

	DOT	DASC
Day 1 vanc +pip-taz	**2**	**16**
Day 2 vanc +pip-taz	**2**	**16**
Day 3 vanc +pip-taz	**2**	**16**
Day 4 ceftriax + metro	**2**	**8**
Day 5 ceftriax + metro	**2**	**8**
Day 6 ceftriax + metro	**2**	**8**
Day 7 ceftriax + metro	**2**	**8**
Total (Total without de-escalation)	**14 (14)**	**80 (112)**

De-Escalation

This measure could have significant implications in discussions with hospital leadership in demonstrating the efficacy and cost effectiveness of stewardship programs.

Perhaps the most impactful potential application of a spectrum score is in hospital benchmarking which Kakiuchi et al explored in detail with their proposal of the DASC metric.[3] Kakiuchi compared DOT vs DASC for benchmarking 124 VA hospitals in a manner similar to our ranking across the DASON network. Under the DASC ranking schema 27 hospitals (21.8%) had their ranking change by greater than 10%. Interestingly when DOT and DASC for hospitals were directly compared there was little correlation between the two scores, suggesting a marked change in the information being captured. Further study will be needed to understand this difference in new ranking.

Limitations

While these spectrum scores do have a number of significant benefits, it is also important to take note of the limitations inherent in these metrics. Given these data are based on medication administrations taken from the electronic medical record they retain some of the limitations seen with DOT. These include duplicated counts for same-day administrations of a medication switch, and missed counts for patients on extended interval dosing in the setting of hepatic or renal dysfunction.[3] Spectrum scores still do not capture the patient level case mix or local resistance patterns which may justify the use of broader spectrum agents. Additionally, while there is reasonable concordance between expert opinion and spectrum score-based definitions for de-escalation there is still a moderate amount of disagreement in both human-human and human-computer definitions of de-escalation.[3,8] Since many of these scores weigh each category of bacteria equally they can be imperfect representations of stewardship program priorities. While there is some data connecting spectrum scores to relevant clinical outcomes such as antimicrobial resistance, C difficile infection or disruption of host microbiome, further studies are needed to establish impact of reducing these spectrum scores on a patient and facility-wife level.

Conclusions

Antibiotic spectrum scores are exciting new metrics which have the potential to better represent the important work our antimicrobial stewardship programs are doing every day. Familiarity with the core concepts, strengths, and weaknesses of these metrics aid programs in the qualitative assessment of their interventions.

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