Clinical Vignettes Provide an Understanding of Antibiotic Prescribing Practices in Neonatal Intensive Care Units

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Abstract

Objective—To use clinical vignettes to understand antimicrobial prescribing practices in neonatal intensive care units (NICUs).

Design—Vignette-based survey.

Setting—Four tertiary care NICUs.

Participants—Antibiotic prescribers in NICUs.

Methods—Clinicians from 4 tertiary care NICUs completed an anonymous survey containing 12 vignettes that described empiric, targeted, or prophylactic antibiotic use. Responses were compared with Centers for Disease Control and Prevention guidelines for appropriate use.

Results—Overall, 161 (59% of 271 eligible respondents) completed the survey, 37% of whom had worked in NICUs ≥7 years. Respondents were more likely to appropriately identify use of targeted therapy for methicillin-susceptible *Staphylococcus aureus,* i.e., use of oxacillin rather than vancomycin, than for *E. coli*, i.e., use of first generation rather than third generation cephalosporin, (p<0.01). Increased experience significantly predicted appropriate prescribing (p=.02). The proportion of respondents choosing appropriate duration of post-surgical prophylaxis (p<.01) and treatment for necrotizing enterocolitis differed by study site (p=.03).

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

Conclusions—The survey provides insight into antibiotic prescribing practices and informs the development of future antibiotic stewardship interventions for NICUs.

INTRODUCTION

Compared with adult patient populations, fewer evidence-based guidelines for antibiotic prescribing are available for children, and even fewer are available for infants hospitalized in neonatal intensive care units (NICUs). This lack of guidelines may result in substantial variations in practice. Surveys have demonstrated practice variations for common clinical scenarios such as treatment of early-onset sepsis in extremely low birth weight infants[1] and treatment of suspected late onset sepsis.[2]

Clinical practice variation can also be assessed by describing clinical vignettes (brief case histories based on realistic clinical scenarios) and posing questions related to management. Vignettes have been validated to predict physician practices in outpatient settings[3,4] and used to measure adherence to established guidelines or determine the impact of non-clinical factors (e.g., physician age and gender) on practice variation.[5–7]

The objectives of this multicenter study were to employ clinical case vignettes to identify variations in antibiotic prescribing practices among practitioners in the NICU and to compare responses with treatment recommendations from the Centers for Disease Control and Prevention (CDC) to limit antibiotic resistance among hospitalized children.[8]

METHODS

Study Design and Participants

We developed an anonymous, self-administered web-based survey for clinicians who prescribe antibiotics in NICUs. Eligible subjects included attending physicians, NICU fellows, pediatric residents, nurse practioners, and hospitalists in 4 tertiary-care NICUs previously described.[9] All 4 institutions provided infectious diseases consultation upon request. One of the institutions had a formal antimicrobial stewardship program. Medical students were excluded. Participation was voluntary. Recruitment occurred through emails, posters, and staff meetings. Institutional Review Board approval was obtained from each participating site with a waiver of documentation of informed consent.

This survey was a component of an NIH-funded multi-center research study evaluating antibiotic stewardship interventions (R01 NR010821-02), and was administered in April 2009 prior to data collection for the larger study.

Survey

The survey consisted of 12 vignettes derived from previous cases in the study NICUs.[9] Respondents were asked to determine if the described use of antibiotics was 'appropriate', 'inappropriate', or 'cannot determine.' If 'inappropriate', respondents were asked to select one of five reasons why the use was inappropriate: [1] did not narrow coverage, [2] excessive or redundant empiric therapy, [3] prolonged prophylaxis, [4] treatment of contamination or colonization, or [5] duration of treatment too long.

The vignettes were validated by multi-step pilot testing. Initially, 30 potential vignettes were reviewed by 3 members of the research team which described a diversity of antibiotic

indications for infants in the NICU, and 21 were selected for further validation. These 21 vignettes were then independently reviewed by 3 neonatologists and infectious disease physicians who were not members of the study team. These reviewers provided suggestions to delete confusing or ambiguous vignettes and to improve clarity, content, and length. The final 12 selected vignettes represented different principles of antibiotic prescribing. Four described appropriate antibiotic use, 5 described inappropriate use, and 3 were indeterminate.[8]

Statistical Analysis

Frequencies of responses were calculated for each vignette. Correct responses were scored for each of the 9 vignettes designed to be appropriate or inappropriate and a composite score (range 0–9) of correct responses was calculated. Responses to Likert format questions were dichotomized (e.g., 'agree' and 'strongly agree' were combined). Multiple individual and institutional characteristics (e.g., gender, site, etc.) were coded as categorical predictor variables. Differences in responses to individual questions for predictor variables were analyzed using Fisher's exact tests and Chi square tests. Differences in composite scores by predictor variables were analyzed using t tests and ANOVA. A two-sided level of significance was set at $p<0.05$. All calculations were performed using SAS statistical software version 9.5.2 (SAS Institute Inc, Cary, NC).

RESULTS

Respondent Characteristics

Of 271 eligible respondents, 161 (59%) completed the survey. Respondents included 51 attending physicians, 29 NICU fellows, 48 pediatric residents, 21 nurse practitioners, 7 hospitalists, and 5 persons who preferred not to respond. In all, 92% (47/51) of attending physicians and 95% (20/21) of nurse practitioners had greater than 7 years of experience working in the NICU. Characteristics of the respondents at each site are provided in Table 1. The distribution of eligible participants who responded and the proportion of respondents with ≥7 years of experience in the NICU varied by site (p<0.01), although differences in distribution of attending physicians was not significant (p=0.12).

Vignette Responses

Brief descriptions of the antimicrobial prescribing provided in the vignettes and the percent correct responses are shown in Table 2. Most respondents (82%) considered a short duration (24 hours) of post-surgical prophylaxis for placement of a ventriculoperitoneal shunt to be appropriate and most (75%) considered prolonged antibiotic prophylaxis (10 days) for chest tubes to be inappropriate. The vast majority (97%) thought narrowing vancomycin to oxacillin to treat methicillin-susceptible *S. aureus* infection was appropriate, but fewer (53%) thought continuing use of the broad-spectrum cephalosporin ceftazidime for treatment of cefazolin-susceptible *E. coli* was inappropriate. Fewer than half (46%) felt that treatment of two species of coagulase-negative staphylococci grown from a blood culture obtained from an arterial catheter with a concurrent negative peripheral blood culture was inappropriate. For the five vignettes that described inappropriate antibiotic prescribing, most respondents (range 56–89%) selected the correct reason why the prescribing was inappropriate (Table 3). For the 3 vignettes describing antibiotic use considered by the study team to be indeterminate (Table 4), more respondents considered the use inappropriate (range 42–58%) than appropriate (34–41%) or indeterminate (6%–24%).

Composite scores of correct responses were similar across the 4 sites (5.3–5.9); However, site differences were noted for correct responses to two individual vignettes, i.e., the vignette describing inappropriate antibiotic prophylaxis for 10 days for presence of a chest tube post-

operatively (p<.01) and the vignette describing appropriate duration of treatment for uncomplicated necrotizing enterocolitis for 10 days (p=.03). Attending status (mean composite score 5.5 vs. 5.0 for non-attendings) and ≥ 7 years of NICU experience (mean composite score 5.5 vs. 5.0 for <7 years experience) significantly predicted (p=0.04 and 0.02, respectively) the highest scores.

Perceptions of Local Resources for Antibiotic Prescribing

Sixty-four percent of respondents felt that antibiotic resistance was a problem in their NICU. Sixty-five percent received education on antimicrobial resistance, 55% received education on antimicrobial prescribing, and 33% received feedback on their antimicrobial prescribing. The majority (88%) of respondents reported easy access to the infectious diseases consult service. Few (31%) agreed that computerized physician order entry assisted them in prescribing. Perceptions of available resources were similar at the 4 sites (data not shown). There was no significant association between the perception of resources and correct responses to the antimicrobial prescribing vignettes.

DISCUSSION

To our knowledge, this is the first study to use clinical vignettes to provide insight into patterns and variations in antimicrobial prescribing practices in the NICU. We found that respondents were more likely to identify narrowing antibiotic therapy for methicillin-susceptible *S. aureus* (MSSA) than for gram negative bacilli (GNB) suggesting increased familiarity with the former clinical scenario. In addition, respondents did not identify concurrent use of meropenem and metronidazole as redundant anaerobic coverage for necrotizing enterocolitis suggesting lack of understanding of the spectrum of activity of these agents. These data support the need for antibiotic stewardship and education regarding antibiotic prescribing, particularly spectrum of antibiotic activity, in the NICU setting.

Vignettes have been used to evaluate antibiotic use among other providers and patient populations. Vignettes administered to medical students demonstrated potential inappropriate use of antibiotics for upper respiratory tract infections.[10] They have revealed knowledge deficits regarding appropriate vancomycin use for the treatment of *Clostridium. difficile* colitis and for perioperative prophylaxis.[11] Vignettes about antibiotic use have been shown to have high interrater reliability when stringently validated. For example, discussion amongst reviewers of common appropriate and inappropriate examples of antibiotic use led to more refined treatment guidelines with higher interrater reliability. [12]

Nevertheless, we postulate that responses to clinical vignettes probably *underestimate* prescribing variation. Respondents may have provided desirable answers even if their own practices diverged from their responses. Second, respondents may not be aware of their own prescribing practices as we found that some responses were incongruous with actual antibiotic prescribing at these 4 study sites.[9] While 97% thought narrowing vancomycin to oxacillin to treat MSSA was appropriate, we previously reported that failure to 'target the pathogen' was the most common reason for inappropriate use. Similarly, while 75% of respondents found antibiotic prophylaxis for the duration of a chest tube placement to be inappropriate, we previously reported this practice was the most common reason for prolonged antibiotic prophylaxis. Prescriber feedback on antimicrobial use may narrow the gap between perceived and actual practices and may improve future use as has been shown in other pediatric populations.[13,14] For example, individual and practice-level feedback to pediatricians on antibiotic prescribing for upper respiratory infections led to decreased prescribing rates.

Site differences occurred for two vignettes--identification of inappropriate prolonged perioperative prophylaxis for chest tubes and appropriate duration of treatment for medically managed necrotizing enterocolitis. These differences in response to the clinical vignettes may represent NICU-specific differences, individual knowledge deficits, and/or a lack of evidence-based treatment guidelines for these conditions. In the absence of national guidelines, potential interventions include examining local practices and developing institution-specific guidelines to limit intra-site variability. While attending status and clinical experience predicted correct responses in this study, another survey evaluating antibiotic management of early onset sepsis in extremely low birth weight infants did not describe variation in practice attributable to clinician experience. Differences were seen, however, between non-academic and academic institutions; neonatologists from non-academic hospitals were more likely to start antibiotics for extremely low birth weight infants with suspected sepsis.[1]

There are several limitations to our study. The distribution of types of providers was not the same across the 4 study sites. The sample size was not large enough to perform analysis of the interaction of respondents' years of experience and site with attending status. Because we asked about hypothetical case scenarios, responses may represent socially desirable answers and not represent actual antibiotic prescribing practice. As mentioned above, vignettes may underestimate prescribing variation and the need for additional educational interventions. We did not evaluate incorrect dosage, a common medication error when treating neonates.[15] Vignettes include considerably fewer data when compared to the full spectrum of information available during patient rounds and in medical records, although our vignettes contained the recommended amount of data intended to strike a balance between clinical detail and survey fatigue.[16] Furthermore, all of our vignettes were derived from actual patient examples, and were pilot tested for content validity with neonatologists and infectious disease physicians.

Our data highlight important areas for improvement in antibiotic prescribing, education and antimicrobial stewardship in NICUs. Our research also provides a potentially important performance improvement tool for NICUs. When appropriate management is clear, vignettes can measure quality or be used for training. When guidelines or clinical consensus are lacking, vignettes can assess variation in practice and be used to craft guidelines to address specific clinical indications. Specific thresholds for initiating antibiotics and factors affecting duration of therapy can be measured. Further studies are required to validate whether clinical vignettes fully predict actual antibiotic prescribing in the NICU and what components of antibiotic prescribing decisions can best be measured using clinical vignettes.

Acknowledgments

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Table 1

Participation rate and experience of respondents by site

Site	Eligible Respondents	Respondents n, (% of eligible)	NICU Experience ≥ 7 years n (%)	Number of Respondents by Position n, (% of respondents per institution)					
				A	**F**	**R**	**NP**	**H**	**U**
1	66	34 (52%)	16 (47 %)	13 (38)	10 (29)	0 (0)	4 (13)	5 (15)	2 (6)
2	73	64 (88%)	31 (48%)	23 (38)	5 (8)	19 (30)	12 (19)	2 (3)	3 (5)
3	68	26 (38%)	16 (62%)	9 (35)	6 (23)	11 (42)	0 (0)	0 (0)	0 (0)
4	64	37 (58%)	8 (22%)	6 (16)	8 (22)	18 (49)	5 (14)	0(0)	0 (0)
Total	271	161 (59%)	63 (39)%	51 (32)	29 (18)	48 (30)	21 (13)	7 (4)	5 (3)

NICU, neonatal intensive care unit; A, attending physicians; F, fellows; R, residents; NP, nurse practitioners; H, hospitalists; U, unknown

Table 2

Vignettes use category by Centers for Disease Control and Prevention recommendations, antibiotic prescribing described, and correct responses

CDC Recommendations (Correct Rating)	Antibiotic Prescribing Described in Clinical Vignette	# Correct/# Total Responses (% Correct)
Narrow coverage (appropriate)	Change from vancomycin to oxacillin for treatment of blood stream infection caused by methicillin-susceptible *S. aureus*.	143/147 (97%)
Duration of perioperative prophylaxis (appropriate)	Perioperative prophylaxis with cefazolin for 24 hours for placement of ventriculoperitoneal shunt.	117/142 (82%)
Duration of perioperative prophylaxis (inappropriate)	Perioperative prophylaxis for 10 days for chest tube following resection of cystic adenomatoid malformation.	104/138 (75%)
Duration of therapy (inappropriate)	Treatment of *P. aeruginosa* blood stream infection for 21 days.	101/136 (74%)
Judicious use of broad spectrum agent (appropriate)	Empiric use of meropenem to treat sepsis with severe hypotension caused by gram negative bacilli.	96/145 (66%)
Duration of therapy (appropriate)	Treatment of uncomplicated necrotizing enterocolitis for 10 days.	89/137 (65%)
Judicious use of broad spectrum agent (inappropriate)	Use of metronidazole and meropenem for suspected necrotizing enterocolitis.	85/136 (63%)
Narrow coverage (inappropriate)	Treatment of urinary tract infection caused by *E. coli* with ceftazidime when organism is susceptible to cefazolin.	77/145 (53%)
Avoid treatment of contamination or colonization (inappropriate)	Treatment of 2 species of coagulase-negative staphylococci grown from blood culture obtained from arterial catheter with concurrent negative peripheral blood culture.	64/138 (46%)

Table 3

Respondents' identification of reasons for inappropriate antibiotic use

Antibiotic Prescribing Described in Vignette Clinical	Correct Reason Inappropriate/# Considered Inappropriate (%)	
Perioperative prophylaxis for 10 days for chest tube	Prolonged prophylaxis	66/104 (87%)
Treatment of *P. aeruginosa* blood stream infection for 21 days.	Duration of therapy too long	90/101 (89%)
Use of metronidazole and meropenem for suspected necrotizing enterocolitis.	Excess or redundant empiric therapy	48/85 (56%)
Treatment of urinary tract infection caused by *E. coli* with ceftazidime when organism is susceptible to cefazolin.	Did not narrow coverage	52/77 (67%)
Treatment of 2 species of coagulase-negative staphylococci grown from blood culture obtained from arterial catheter with concurrent negative peripheral blood culture.	Treatment of contamination or colonization	61/64 (80%)

Table 4

Indeterminate Vignettes by Centers for Disease Control and Prevention recommendations with antibiotic prescribing described, and distribution of respondents ratings

CDC Recommendations	Antibiotic Prescribing Described in Clinical Vignette	Distribution of Respondents Ratings
Judicious Use of broad spectrum agent	Use of meropenem for increased apneas, blood pressure instability, and renal insufficiency.	Appropriate 34% Inappropriate 42% Indeterminate 24%
Duration of perioperative prophylaxis	Perioperative prophylaxis with ampicillin, gentamicin, and clindamycin for 48 hours after uncomplicated colostomy revision.	Appropriate 37% Inappropriate 59% Indeterminate 4%
Avoid treatment of contamination or colonization	Treatment for 10 days with vancomycin for coagulase-negative staphylococci isolated from peripherally inserted central line, with negative peripheral cultures and normal complete blood count	Appropriate 41 % Inappropriate 52% Indeterminate 7%