Published in final edited form as:
Pediatr Blood Cancer. 2012 February ; 58(2): 303–305. doi:10.1002/pbc.23148.

Time-to-Antibiotic Administration as a Quality of Care Measure in Children with Febrile Neutropenia: A Survey of Pediatric Oncology Centers

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Abstract

Time-to-antibiotic administration (TTA) has been suggested as a quality-of-care (QOC) measure for pediatric oncology patients with febrile neutropenia (FN). Unknown, however, is to what extent pediatric oncology centers utilize TTA. Therefore, we designed and administered an electronic survey (68% response rate) of programs in the Children's Oncology Group to assess TTA utilization. Nearly half of respondents track TTA. Most reported using a benchmark of less than 60 minutes from arrival. TTA is a commonly used QOC measure for pediatric FN despite an absence of studies establishing its validity and a lack of data supporting its impact on outcomes of FN.

Keywords

time-to-antibiotics; febrile neutropenia; quality of care; prevalence

BACKGROUND

Prolonged time-to-antibiotic administration (TTA) has been associated with poor outcomes in adult patients with bacterial meningitis,[1–4] community acquired pneumonia,[5–7] sepsis,[8] and solid-organ transplant patients with bacterial infection.[9] In adult cancer patients with febrile neutropenia and septic shock, a delay in initiating treatment with antibiotics directed against the causative microorganism is associated with increased mortality for patients in the ICU.[10] No published reports have linked prolonged TTA with poor outcomes in pediatric cancer patients with febrile neutropenia (FN). Nevertheless, at the 23rd Annual Meeting of the American Society of Pediatric Hematology-Oncology in April 2010, a symposium on quality-of-care (QOC) included a session on TTA as a QOC measure for pediatric oncology patients with FN. During the symposium, an informal, show-of-hands survey of attendees indicated that many centers are tracking TTA for FN. In this study, we describe the prevalence of TTA usage as a QOC measure in pediatric cancer centers and determine correlates of its usage.

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CONFLICT OF INTEREST STATEMENT The authors have no relevant conflicts of interest to disclose.

METHODS

We conducted a survey of pediatric cancer centers within the Children's Oncology Group. The design and conduct of the survey were performed without the knowledge or consent of the Children's Oncology Group. The survey was up to 28 questions in length (the full survey is available in the Supplemental Appendix.) In the survey introduction, TTA was defined as "as the time required for the administration of the first dose of empiric antibiotics in children with febrile neutropenia." It was implied that the TTA measurement began upon the patient's arrival at the institution, but this was not explicitly stated. Consent for research participation was implied by survey completion. The Institutional Review Board of the University of Texas Southwestern Medical Center approved this study.

Study Procedures

A letter of invitation including a survey link was emailed to the principal investigator (PI) and nursing responsible investigator (NRI) (obtained from the Children's Oncology Group website on May, 4, 2010) at each center from predominantly English-speaking countries represented in the Children's Oncology Group (n = 199). Personalized emails were sent to each PI / NRI pair on week 0 and subsequently resent on weeks 2, 6, and 10 to non-responders. PI / NRI pairs were instructed to have only responder per center. They were also informed that the survey link could be forwarded to the most knowledgeable person (physician, nurse, or other) about TTA at their center. Survey results were collected through the RedCAP system of UT Southwestern. Responses were de-identified when the survey was completed prior to data analysis. The survey instrument was reviewed by several independent providers prior to formal administration to assess for clarity and face validity. No assessment of test/re-test reliability was performed.

Analyses

Responses were included in the analysis if question 5, which asked whether the center follows TTA as a QOC measure, was completed. For the 7 centers in which both the PI and NRI completed the survey, responses were reconciled and consolidated by this study's PI. Discrepancies between respondents were reconciled using the value most consistent with the respondents' other responses. Summary statistics included frequencies and cross-tabulations. The primary outcome was descriptive: the proportion of centers tracking TTA as a QOC measure. Secondary outcomes included the respondents' TTA benchmark / standard, the locations where TTA is collected (inpatient unit, outpatient clinic, or emergency department), and the most recent TTA data from each respondent. In an exploratory analysis, the Jonckheere-Terpstra test was used to test for associations between TTA usage and potential predictors: the number of new cancer cases per year, number of attending oncologists, and the number of nurse practitioners. Additionally, Fisher's exact test was used to test for an association between TTA usage and the elements of an electronic medical record in use at a center. The analyses were completed with SAS 9.2 (SAS Institute, Gary, NC).

RESULTS

One hundred ninety-nine centers were surveyed. Of the 135 respondents (68% reply rate), 42% replied to the first emailing whereas 32%, 14%, and 13% replied to the second, third, and fourth emailing, respectively. Table I describes various attributes of the responding centers. Notably, 75% of responding centers reported caring for less than 100 new cancer patients annually and nearly 50% reported having less than 5 attending oncologists.

Forty five percent (n=61) of respondents reported tracking TTA as a QOC measure (Table II). Of those, over 90% reported using a TTA standard/benchmark of < 30 minutes or < 60 minutes and use the same TTA standard/benchmark for the outpatient clinic, the ED, and the inpatient unit. The frequency with which centers review TTA data varied considerably from weekly to annually (Table II). A limited number of centers responded to the survey questions about the mean TTA at the most recent review of their center's data. At the most recent review, over 75% of respondents report a mean TTA less than 60 minutes for their outpatient clinic and inpatient units (Table II). This is contrasted with the ED, in which the most recent review of TTA data revealed over half of centers had a mean TTA over 60 minutes.

Center attributes associated with tracking TTA include a larger number of new cases per year (p=0.014) and a larger number of nurse practitioners (p=0.005). The number of attending oncologists and electronic medical record (EMR) usage were not associated with tracking TTA.

Of centers not tracking TTA (n=74), 34% report not tracking because of inadequate resources, but only 7% report not tracking because of inadequate evidence to support its use. A minority of respondents report not tracking TTA because it is difficult to improve it in the ED (8%), the clinic (7%), or the inpatient unit (4%). Of 69 respondents, 28% plan to start tracking TTA within the next year.

DISCUSSION

No published reports have assessed the validity of TTA as a QOC measure for pediatric FN, and only one previously-published report describes TTA for FN.[11] This report describes an intervention to reduce TTA to < 30 minutes in a single center and does not attempt to associate TTA with outcomes of hospitalization. In reviewing the TTA literature for other conditions in adults, TTA cut points for analysis or benchmarking have ranged from 3–24 hours for bacterial meningitis,[1–4] 4–8 hours for community acquired pneumonia (CAP),[5–7] and 1 hour in sepsis.[8] Given the high risk for bacteremia and sepsis in children with FN, it is not surprising that most centers who are tracking TTA in pediatric FN endorse the use of a benchmark similar to that of adults with sepsis (< 60 minutes.)

In considering TTA for pediatric FN within Donabedian's QOC model of structure-process-outcome for a care episode,[12] TTA would be considered a process measure for FN. The validity of TTA as a process measure for FN is grounded in its focus on the quality domains of efficiency, timeliness, and patient-centeredness.[13] The appeal of TTA as a QOC measure in conditions like sepsis, CAP, and meningitis is its association with outcomes of care including mortality and length-of-stay which reflect the safety and effectiveness domains of quality. To our knowledge, no prior reports have examined a potential association of TTA with outcomes of hospitalization for FN. Any attempt to examine this association will have to account for a variety of known predictors of outcome for FN including age, the underlying malignancy and its treatment, and the degree of neutropenia among others.

In this study, TTA is used as a QOC standard in nearly half of surveyed pediatric oncology centers. An increased number of new cases per year and a larger number of nurse practitioners were associated with tracking TTA. Consistent with this finding, one-third of centers not tracking TTA report inadequate resources as a reason for not tracking although more than one-quarter of those not tracking TTA have plans to do so. Of centers tracking TTA, the vast majority report using a standard or benchmark of less than 60 minutes and do not distinguish between high and low risk patients in analyzing TTA. In a limited number of

responses, centers report longer mean TTA in the ED setting compared to the inpatient unit and outpatient clinic.

The conclusions of this study are limited by factors inherent to the survey methodology. Respondents may not be representative of non-respondents and thereby introduce bias. Similarly we have no means of confirming the accuracy of the responses provided which may have been affected by recall bias and social desirability bias. Additionally, the validity of the survey instrument was not fully established with test / re-test reliability though face validity was evaluated prior to administration of the survey.

In conclusion, many pediatric cancer centers in the US and Canada are tracking TTA as a QOC measure for FN. While TTA for FN would be a welcome addition to other established QOC measures within pediatric oncology such as rates of bloodstream infection and rates of chemotherapy errors, further investigation of its validity as a measure of the process and outcomes of care are warranted before it is accepted as a standard QOC measure in the pediatric oncology community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank Jasmine Tiro, Ph.D. for her help with survey design and Song Zhang, Ph.D. for his help with the analysis of the data.

Grant Support: NIH - UL1 RR024982-03

REFERENCES

1. Proulx N, Frechette D, Toye B, et al. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. QJM. 2005; 98(4):291–298. [PubMed: 15760921]
2. Auburtin M, Wolff M, Charpentier J, et al. Detrimental role of delayed antibiotic administration and penicillin-nonsusceptible strains in adult intensive care unit patients with pneumococcal meningitis: the PNEUMOREA prospective multicenter study. Crit Care Med. 2006; 34(11):2758–2765. [PubMed: 16915106]
3. Koster-Rasmussen R, Korshin A, Meyer CN. Antibiotic treatment delay and outcome in acute bacterial meningitis. J Infect. 2008; 57(6):449–454. [PubMed: 19000639]
4. Lepur D, Barsic B. Community-acquired bacterial meningitis in adults: antibiotic timing in disease course and outcome. Infection. 2007; 35(4):225–231. [PubMed: 17646915]
5. Meehan TP, Fine MJ, Krumholz HM, et al. Quality of care, process, and outcomes in elderly patients with pneumonia. JAMA. 1997; 278(23):2080–2084. [PubMed: 9403422]
6. Houck PM, Bratzler DW, Nsa W, et al. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med. 2004; 164(6):637–644. [PubMed: 15037492]
7. Fee C, Weber EJ. Identification of 90% of patients ultimately diagnosed with community-acquired pneumonia within four hours of emergency department arrival may not be feasible. Ann Emerg Med. 2007; 49(5):553–559. [PubMed: 17210202]
8. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006; 34(6):1589–1596. [PubMed: 16625125]
9. Hamandi B, Holbrook AM, Humar A, et al. Delay of adequate empiric antibiotic therapy is associated with increased mortality among solid-organ transplant patients. Am J Transplant. 2009; 9(7):1657–1665. [PubMed: 19459798]

10. Lin MY, Weinstein RA, Hota B. Delay of active antimicrobial therapy and mortality among patients with bacteremia: impact of severe neutropenia. Antimicrob Agents Chemother. 2008; 52(9):3188–3194. [PubMed: 18625778]

11. Corey AL, Snyder S. Antibiotics in 30 minutes or less for febrile neutropenic patients: a quality control measure in a new hospital. J Pediatr Oncol Nurs. 2008; 25(4):208–212. [PubMed: 18539908]

12. Donabedian A. The quality of care. How can it be assessed? JAMA. 1988; 260(12):1743–1748. [PubMed: 3045356]

13. Institute of Medicine (U.S.). Crossing the quality chasm : a new health system for the 21st century. National Academy Press; Washington, D.C.: 2001. Committee on Quality of Health Care in America.

Table I

Attributes of responding centers

Center Attribute	All Centers Percentage (N = 135)	Centers Tracking TTA Percentage (N=61)	Centers Not Tracking TTA Percentage (N=74)
Number of new diagnoses per year			
< 50	40	29.5	48.6
50 – 99	35.6	42.6	29.7
100 – 149	12.6	9.8	14.9
150 – 199	6.7	8.2	5.4
>200	5.2	9.8	1.4
Number of attending oncologists			
< 5	48.9	49.2	48.6
5 – 9	32.6	26.3	37.8
10 – 14	14.1	16.4	12.1
> 15	4.4	8.2	1.4
Number of nurse practitioners			
< 5	78.5	68.9	86.5
5 – 9	14.1	19.7	9.5
10 – 14	3.7	3.3	4.1
> 15	3.7	8.2	0
Elements of an electronic medical record			
Only result reporting, CPOE, or provider documentation	21.5	14.8	26.3
Result reporting and CPOE	12.6	13.1	12.2
Result reporting and provider documentation	20.7	18	23
Result reporting, CPOE, and provider documentation	45.2	54.1	37.8

TTA – time to antibiotics; N – number; CPOE – computerized provider order entry

Table II

Features of centers tracking TTA as a QOC measure

Center Attribute	Percentage
Where is TTA tracked in your center? (N = 61)	
Clinic	6.6
ED	19.7
Inpatient unit	13.1
Clinic & ED	4.9
Clinic & Inpatient Unit	19.7
ED & Inpatient Unit	8.2
Clinic, ED, & Inpatient unit	24.6
What is the TTA standard for your center? (N = 51)	
30 minutes	31.4
60 minutes	58.8
90 minutes	5.9
120 minutes	0
180 minutes	2.0
>180 minutes	0
Different TTA standard for high risk patients? (N=58)	
No	98.3
Yes	1.7
Frequency of review of TTA data (N=53)	
Weekly	3.8
Biweekly	0
Monthly	20.8
Bimonthly	0
Quarterly	37.7
Semi-annually	9.4
Annually	11.3
Other	17
Mean TTA - outpatient clinic – most recent review (N=24)	
< 30 minutes	33.3
30 – 59 minutes	50.0
60 – 89 minutes	0
90 – 119 minutes	16.6
120 – 179 minutes	0
> 179 minutes	0
Mean TTA – ED – most recent review (N=20)	
< 30 minutes	0

Center Attribute	Percentage
30 – 59 minutes	45
60 – 89 minutes	30
90 – 119 minutes	10
120 – 179 minutes	15
> 179 minutes	0
Mean TTA - inpatient unit – most recent review (N=24)	
< 30 minutes	20.8
30 – 59 minutes	54.2
60 – 89 minutes	20.8
90 – 119 minutes	4.2
120 – 179 minutes	0
> 179 minutes	0

TTA – time-to-antibiotics; QOC – quality of care; N – number; ED – emergency department