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Variation in Management of Fever and Neutropenia Among Pediatric Patients with Cancer: A Survey of Providers in Michigan

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Abstract

Considerable variation in the management of fever and neutropenia (FN) exists, with factors associated with treatment variation not well described. An on-line survey of 90 pediatric cancer providers in Michigan was performed in Spring 2014. The survey frame was pediatric patients with cancer receiving treatment, with a Port-a-cath, who were clinically stable. Criteria for “Decreased” and “Increased” risk groups were defined by respondents. Survey questions addressed FN definitions, risk groups conceptualization, routine clinical practice, and management guidelines, in the context of risk groups and distance to treating institution. Fifty providers responded (56%), the majority defined a febrile event as temperature $>38.3^{\circ}\text{C}$ and/or two events $>38.0^{\circ}\text{C}$ within a 24-hour period. Neutropenia was defined as current or anticipated absolute neutrophil count (ANC) $<500/\mu\text{L}$. Majority of respondents recommended “Decreased” and “Increased” patients present to a local emergency department (ED) if they live >2 hours away. Respondents were significantly more likely to have a “Decreased Risk” patient travel over 2 hours if they rated the local ED as “Poor to Fair” on ability to access Port-a-caths ($p\ 0.048$). Most respondents would discharge patients who are afebrile for 24 hours, blood cultures negative for 48 hours, and neutrophil count of greater than $200/\mu\text{L}$. 40% preferred discharge on oral antibiotics when the ANC $<500/\mu\text{L}$. Triaging for febrile pediatric patients with cancer is significantly influenced by the providers’ perceptions of local EDs. Future investigation of local hospitals’

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ability to provide urgent evaluation, combined with parental perspectives could lead to improvements in timely and effective management.

Keywords

Child; Adolescent; Oncology; Supportive Care; Febrile Neutropenia

Introduction

Fever and neutropenia (FN) is a common complication of chemotherapy for cancer patients [1]. Because FN is a well-recognized risk factor for morbidity and mortality in cancer populations [2], most patients receive emergent broad-spectrum intravenous antibiotics and remain hospitalized until phagocyte count recovery [3,4].

Adult guidelines have incorporated risk stratification systems to decrease hospitalizations or shorten the length of stay for FN among those who are at less risk of serious infections [5,6]. One international panel recommended a series of strategies to apply risk-based concepts to pediatric cancer care [7], but agreement with and adoption of these strategies is unknown. For the population of pediatric patients admitted with FN who are found to have no major infection and are clinically well, these hospitalizations can be burdensome to the patients and their families. As such, clinicians balance the potential for complications while respecting the psychological and financial impacts that the treatment of childhood cancer can impart on a family.

The clinical practices related to the management of FN among pediatric patients with cancer vary across individual institutions [8–10]. Moreover, there is variation in all aspects of FN management; from admission criteria to inpatient clinical practices to discharge standards. It is likely that actual clinical practice is derived from a combination of published guidelines, provider experience and patient preferences, but little is known about the interplay between these factors.

Further complicating clinical practice in certain areas is the influence of distance to tertiary care centers with expertise in pediatric care, which can be a significant factor in states with large rural areas, such as Michigan. When patients live far from a tertiary care center, the local hospital may be more convenient; however, staff at local hospitals that do not routinely care for complex pediatric patients may experience anxiety when faced with a pediatric cancer patient requiring urgent care. In the State of Michigan, there is overlap of pediatric oncology coverage in many regions, compounding the variation in care delivered if providers within those different institutions are practicing a variety management styles.

The objective of this survey was to document the variations in clinical practice for the care of FN among pediatric patients with cancer across Michigan, including the effect of distance to care. This information could provide a framework of common practices that can be utilized to develop a unified guidance for care provided to pediatric patients with cancer when they present to a local ED with a fever.

Materials and Methods

Survey Design

We conducted an online cross sectional survey of Pediatric Hematology-Oncology (PHO) providers in Michigan. The study was approved by the Institutional Review Board of the University of Michigan.

Survey Sample

Our target population was PHO providers who participate in direct care to oncology patients. We utilized the Children's Hematology Alliance of Michigan (CHAMI) provider database. CHAMI is a unique, voluntary alliance of all PHO institutions in the State of Michigan; its goal is to improve the quality of care for children with cancer or hematologic conditions. The CHAMI database is thought to contain all PHO providers in Michigan, including fellows, nurse practitioners, and physicians. Authors of this manuscript were excluded from survey participation. In the State of Michigan, there are 8 institutions that provide care to children with cancer with the number of practitioners ranging from 2 to 35.

Survey Instrument

The investigators developed and refined survey items that reflected the primary study aims, drawn from clinical experience and informal conversations with pediatric oncologists.

The survey introduction framed the focus on the survey on patients who were actively receiving therapy for their cancer, have a Port-a-cath central venous line, and are presenting as clinically stable. Respondents were instructed to separate their patient populations into those they perceived as at "Decreased Risk" and those at "Increased Risk" for serious medical complications from FN.

The 19-question survey included fixed-choice and open-ended questions about (refer to Supplemental File 1):

Definitions—Fever and neutropenia definitions for "Decreased Risk" and "Increased Risk" groups.

Conceptualization of Risk Groups—Designated characteristics to be used to universally define "Increased Risk."

Current Routine Clinical Practices—Outpatient triage, initial management of fever in a stable pediatric cancer patient, admission criteria, and inpatient discharge criteria for "Decreased Risk" and "Increased Risk" groups, and for those within 30 minutes versus outside of 2 hours of the PHO's practice site.

Guidelines for the Management of FN—Presence of a clinical practice guideline (CPG) at institution, perceptions of how their CPG/potential CPG should be derived and how it impacts the care they provide.

Individual and hospital characteristics—Age, race/ethnicity, years in practice, proportion of time as clinician, presence of pediatric bone marrow transplant service, open Phase 1 trials, patients who travel greater than 100 miles, and number of new diagnoses per year. Questions were pilot-tested with 3 pediatric oncologists to assess clarity and content; revisions were made on the basis of their feedback.

Survey Administration

Each physician in the study sample received an email with an individually linked online survey. Reminder emails were sent weekly to those who had not yet responded or completed their survey. The online survey was fielded between April 8 and May 5, 2014.

Data Analysis/Key Variables

We calculated response frequencies for all items. Exploratory chi-square analyses were used to assess associations between respondents' recommended location for care when patients exhibit fever (within respondents' institution versus patient's local ED) and their perception of local ED competency (poor/fair versus good/excellent). Chi-square analyses were also used to assess associations between presence of a CPG (yes/no) or preference to always admit (yes/no) and clinical practices including definitions and discharge criteria. *P* values <0.05 were considered statistically significant. No corrections for multiple comparisons were utilized. All analyses were conducted with STATA, version 12.0 (StataCorp LP, College Station, TX).

Results

Of the 90 providers invited to participate, 5 were excluded due to lack of direct patient care. Completed surveys from 48 respondents yielded an overall response rate of 56%. There was at least one respondent from each of the 8 institutions in Michigan that provide pediatric oncology care; the number of respondents per institution ranged from 1 to 24. Respondent characteristics were 63% white and 54% 50 years of age; 15% were fellows, 36% 1–15 years in practice, and 44% >15 years in practice; 67% of respondents spent over half of their time on clinical care. With regard to respondent's practice characteristics, 67% had a pediatric bone marrow transplant service, 58% had open Phase 1 trials, and 75% took care of patients traveling greater than 100 miles. Number of new diagnoses per year was 13% with <25, 34% with 26–100, and 46% with >100.

Routine Clinical Practices

Respondents' definition of fever and neutropenia in a pediatric cancer patient receiving chemotherapy or radiation is presented in Table I. Rather than a single threshold, most respondents considered a fever as greater than 38.3°C or persistence of an elevation in temperature. The majority of respondents chose the threshold for neutropenia as a current or anticipated absolute neutrophil count (ANC) value of less than 500/ μ L.

Table II presents respondents' recommendations for where a pediatric cancer patient with a fever should present when the situation was varied by risk status and distance from the treating hospital. Most respondents recommend that patients living 2 hours away present to

their local ED, however nearly 20% would recommend an “Increased Risk” patient living 2 hours away should present to the treating institution during business hours rather than the local ED. Patterns for during versus after business hours were similar.

For a pediatric cancer patient who presents to the emergency department with a fever, the majority of respondents would recommend that the following be performed: blood cultures from all central line lumens (98%), urine culture (65%), and that antibiotics be given before ANC is determined (77%). Only 40% believe that a peripheral blood culture should be obtained. When asked about decisions related to whether or not to admit a patient who met criteria for FN, fifty four percent of respondents replied that they always admit patients with FN regardless of other factors.

With regard to inpatient discharge criteria, most respondents agreed that patients should be afebrile for at least 24 hours, have negative blood cultures for at least 48 hours, and must have been monitored for at least 48 hours inpatient (Table III). For the neutrophil count threshold for discharge from the inpatient unit, the majority agreed that the ANC must be at least 200/ μ L. Among respondents who reported always admitting FN, there was no significant difference in the variation for discharge criteria. As shown in Table IV, respondents were varied among “Decreased Risk” patients being discharged with an ANC less than 500/ μ L, where 40% believed patients should be discharged on oral antibiotics and 50% would not discharge on any antibiotics.

Opinions of a Clinical Practice Guideline

Among respondents, 69% asserted that their institution follows a clinical practice guideline (CPG) for the management of fever and neutropenia. Respondents agree that a CPG should be derived from evidence-based guidelines (94% with CPG, 100% without CPG). Yet, only 79% of providers at institutions with a CPG believed that all providers should follow the guidelines. A smaller proportion expressed that they agree that a CPG would limit their ability to use clinical judgment (12% with CPG, 17% without CPG). Even among those respondents with a CPG, there was still variation in the definitions of fever and neutropenia.

There were high rates of agreement on which criteria should be included in a universal definition of a pediatric cancer patient at “Increased Risk” for the development of serious medical complications: clinical signs of sepsis (100%), specific cancer diagnoses (98%), patients with organ dysfunction (96%), prolonged neutropenia (93%), and age less than 12 months (84%). Among all respondents, only 71% agreed with all of the above criteria. Criteria with low rates of agreement were: history of positive blood culture in last 6 months (67%), hospital discharge within the past 24 hours (56%), presence of a broviac catheter (51%), and an elevation in CRP or procalcitonin (24%).

Perceptions of Care Provided at Patients’ Local Hospitals

As demonstrated in Tables V and VI, over half of respondents rated the community hospital EDs closest to patients as “Poor” to “Fair” on their ability to access Port-a-Caths and timeliness of ED triage and initiation of evaluation. Respondents also perceived that there was inconsistency with community hospital EDs following their recommendations for which

labs should be drawn (40%), timing of antibiotics (56%), choice of antibiotics (35%), and admission/discharge decision (33%).

Bivariate analyses demonstrated that respondents who perceived that local ED's were poor to fair in ability to access a Port-a-cath were statistically more likely to refer "Decreased Risk" patients who live 2 hours away from the institution to present to their own institution (during business hours 42%, after business hours 33%) rather than to the local ED; this held true both during and after business hours ($p = 0.048$ for both). Among those who rated the time to evaluation at the local ED as poor to fair, there was a trend towards referring "Decreased Risk" patients who live 2 hours away to their own institution after business hours (refer to own institution 36%, $p = 0.067$).

Discussion

Our survey focused on individual providers' preferred clinical practices related to the management of fever and neutropenia in pediatric patients with cancer. There was variation in the recommendations by providers as to where pediatric patients with cancer should be evaluated, with significant impact especially upon those families who do not live near their treating institution. Most importantly, it was found that providers who rated the patients' local EDs as poor to fair on ability to access Port-a-caths were more likely to have their patient drive over 2 hours to be seen at their treating institution. This has implications for safety, patient satisfaction and health care utilization.

Prior work has focused on differences between institutional guidelines and practices [8–10], but has not looked closely at variation associated by provider preferences. The respondents of this survey practice conservative management, with at least half always admitting patients that meet their individual criteria for FN, compared to Canada where several institutions already practice outpatient management of FN for those patients at low risk of complications. This study revealed that respondent perceptions of care provided at local institutions have important consequences for implementation of practices aimed at modifying treatment for low risk patients.

When asked about recommendations for where a pediatric cancer patient with a fever should be evaluated, up to a quarter of respondents recommend that patients present to their treating institution, even if they lived over 2 hours away. The location of initial evaluation of fever in a pediatric oncology patient should be related to the ability to quickly assess and provide emergent care if warranted [11,12]. The ability to provide rapid evaluation and treatment is dependent on many logistic factors including quick access to a provider, availability of rapid antibiotic administration, and resuscitative capabilities/direct nursing care, which can vary greatly among institutions and settings of care (outpatient clinic versus ED). Patients may prefer to go to their treating institution ED or outpatient clinic since it has familiar providers and setting, but this may not be the safest option depending on traveling distance, institutional resources, and allocation of providers. Additionally, the providers perceptions of the patients' local emergency departments appear to impact decision making significantly, especially for patients who live far away from their treating institution. It will be imperative to understand the parental and patient preferences as well as investigate if the

providers' perception of local EDs is actually true. Qualitative and quantitative measures should be utilized to characterize the appropriateness of care provided to children with cancer at the patient's local ED. One specific aspect highlighted in this survey would be to further analyze the difficulties experienced in Port-a-cath accessing in the local ED.

For the initial laboratory evaluation, the majority of respondents agreed that there should be blood cultures drawn from all central lines, but only 40% recommended having a peripheral blood culture obtained. This remains an area of intense debate with some evidence that peripheral cultures contribute to the identification of bacteremia versus a central line infection [3], but this is balanced against the patient preferences and possibility of contaminants associated with peripheral cultures [7]. Further investigation of the implications of a peripheral culture on alteration in management should be evaluated including changes to antibiotic type, duration of antibiotics or hospital length of stay. Also, more detailed provider and patient/family perspectives on the necessity of peripheral blood cultures could be explored to further understand barriers or facilitators to implementing peripheral cultures as a standard of practice.

Even after evaluation, over half of the respondents indicated that they would always admit a pediatric cancer patient that met their criteria for fever and neutropenia. This is not surprising given that the adult low risk strategies have not yet been widely adopted in pediatric cancer patient population [13,14]. One could imagine that the providers who always admit might be more likely to have "safer" rules and therefore might lean towards higher thresholds for discharge, but this was not the case among our respondents. After an inpatient admission for FN, respondents were nearly equally divided in regards to recommending discharge home on oral antibiotics. This speaks to issues underlying this decision from evidence-based studies to practical concerns, including insurance coverage/prior authorization and patient/parent preferences for the addition of an oral medication to be given at home.

The presence of an individual institution CPG for the management of FN can lead to uniformity and potentially improved patient outcomes [15]. Yet, simply having a CPG does not mean that there are widely used standard definitions and practices between institutions. Moreover, it is not clear is whether the presence of a CPG at a single institution necessarily equates with all providers following the same algorithms. A CPG is intended to provide a framework for decision making and increasing uniformity, which can serve to limit the confusion caused by significant variation among providers and patients [16]. As well, it could function as a useful template for monitoring outcomes.

Limitations

The small sample size of our respondent population limited our ability to test associations between perceptions and practices. The intent of this study was to investigate a single state's variation in management of fever and neutropenia with a focus on future areas for collaboration among CHAMI providers. Understanding the association between these variables would require a larger, national study. The conceptualization of the risk groups was different among respondents, which may have contributed to some of the variability observed in the responses. We chose a priori to not evaluate variation between individual

institutions given that some Michigan institutions had too few providers to allow statistical analysis (3 or fewer providers). Also, there was overrepresentation of a single institution, which is related to the differences in institution sizes in Michigan.

However, our report has several strengths. Our findings from the State of Michigan could be generalized to other states with large rural areas, but more than one major center for pediatric cancer treatment. Several key areas have been highlighted for future investigation including the quality of life implications and logistical factors related to pediatric patients with cancer being evaluated in EDs closer to where they live.

Conclusion

Our study highlights the importance of variation among providers on the management of febrile oncology patients. Importantly, we found that provider recommendations for location of evaluation for febrile pediatric patients with cancer are significantly influenced by the providers' perceptions of the patient's local EDs. The variability in clinical practice observed in this study reconfirms the need for a better understanding of the practical implications of managing febrile neutropenia in pediatric patients with cancer. Investigations of the local hospital's ability to provide urgent evaluation and studies of parental perspectives of the initial triage for febrile oncology patients could provide insight for interventions for the management of FN. This could eventually lead to reductions in hospitalizations, decreases in length of stay, and improvements in the quality of life of pediatric patients with cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Respondents' Preferred Definition of "Fever" and "Neutropenia" for a Pediatric Cancer Patient Undergoing Chemotherapy or Radiation Therapy, by Patient Risk Category

	“Decreased Risk” Patients	“Increased Risk” Patients
	Total respondents = 48	
	n (%)	
Fever ¹		
Greater than 38.0°C	9 (19)	18 (38)
Greater than 38.3°C	6 (13)	4 (8)
Any temp greater than 38.3°C and/or 2 temps between 38–38.2°C 1 hr apart in a 24 hour period	32 (67)	26 (54)
Neutropenia ²		
<1500/μL	6 (13)	4 (8)
<1000/μL	6 (13)	12 (25)
<500/μL	12 (25)	5 (10)
Less than 500/μL OR 500–1000/μL but anticipated to decline	24 (50)	27 (56)

¹ For evaluation of patient at initial presentation,

² as relates to admission criteria for a patient with fever

Table II

Preferred Location of Evaluation for Febrile Pediatric Cancer Patient: Recommendation When Patients Call for Guidance

	Respondent's PHO Clinic	Respondent's ED	Respondent's Inpatient Unit	Patient's Local ED
	n (%)			
DURING BUSINESS HOURS				
“Decreased Risk” patient living:				
30 minutes away	24 (50)	22 (46)	2 (4)	0
2 hours away	8 (17)	5 (10)	3 (6)	32 (66)
“Increased Risk” patient living:				
30 minutes away	12 (25)	28 (58)	7 (16)	1 (2)
2 hours away	3 (6)	2 (4)	4 (8)	39 (81)
AFTER BUSINESS HOURS				
“Decreased Risk” patient living:				
30 minutes away	N/A	41 (85)	5 (10)	2 (4)
2 hours away	N/A	9 (19)	3 (6)	36 (75)
“Increased Risk” patient living:				
30 minutes away	N/A	36 (75)	11 (23)	1 (2)
2 hours away	N/A	1 (2)	4 (8)	43 (90)

ED = Emergency Department, PHO = Pediatric Hematology Oncology

Table III

Preferred Inpatient Discharge Criteria For Pediatric Cancer Patient Admitted with Fever and Neutropenia

	“Decreased Risk” Patient	“Increased Risk” Patient
	n (%)	
Duration of afebrile:		
24 hours	41 (85)	34 (71)
48 hours	6 (13)	10 (21)
72 hours	0	3 (6)
Other	0	0
Blood cultures negative for:		
24 hours	2 (4)	1 (2)
48 hours	43 (90)	38 (79)
72 hours	1 (2)	7 (15)
Other	1 (2)	0
Duration inpatient monitoring		
24 hours	5 (10)	2 (4)
48 hours	38 (79)	32 (67)
72 hours	1 (2)	10 (21)
Other	3 (6)	3 (6)
Neutrophil count:		
>200	7 (15)	3 (6)
>200–300 and rising over 2 measures	27 (56)	29 (60)
>500 and rising over 2 measures	6 (13)	10 (21)
Other	7 (15)	5 (10)

Totals may not sum to 100% due to item non-response.

Table IV

Discharge Antibiotic Preference for Pediatric Cancer Patients Admitted with Fever and Neutropenia

	“Decreased Risk” Patients	“Increased Risk” Patients
	n (%)	
ANC Less Than 500/μL		
Oral antibiotics	19 (40)	23 (48)
Intravenous antibiotics	1 (2)	3 (6)
No antibiotics	24 (50)	18 (38)
ANC Less Than 1000/μL		
Oral antibiotics	3 (6)	6 (13)
Intravenous antibiotics	2 (4)	1 (2)
No antibiotics	38 (79)	37 (77)

Table V

Respondent's Ratings of Their Patient's Community Hospital Emergency Departments

	Poor/Fair	Good/Excellent
	n (%)	
Ability to access Port-a-Caths	33 (69)	15 (31)
Timeliness of ED triage and initiation of ED evaluation/treatment	25 (52)	23 (48)
ED provider communication with PHO service after ED discharge	15 (31)	33 (69)
ED provider decision-making around when to consult PHO service	13 (27)	35 (73)
Availability of appropriate antibiotics	11 (23)	37 (77)

Table VI

Perceptions of How Consistently the Patients' Community Hospital ED Provider Follow The Respondents' Recommended Guidance

	Consistently	Inconsistently	Never
	n (%)		
Timing of antibiotics	20 (42)	26 (54)	1 (2)
Which labs to be drawn	29 (60)	19 (40)	0
Choice of antibiotics	31 (65)	17 (35)	0
Admission/Discharge decision	32 (67)	16 (33)	0