Incidence of Febrile Neutropenia in Pediatric Solid Tumor and Lymphoma Patients treated with Chemotherapy

Ah Young Jeon¹, Nayoung Han², Myeong Gyu Kim³, Yoonsook Cho¹, Eun Jeong Cho¹, Min Jung Kim¹, A Jeong Kim¹, Hyoung Jin Kang⁴, Jung Mi Oh², Hee Young Shin⁴

¹Department of Pharmacy, Seoul National University Hospital, Seoul, Republic of Korea

² College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, Republic of Korea

³ Graduate School of Clinical Pharmacy, CHA University, Pocheon, Republic of Korea

⁴ Department of Pediatrics, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea

Introduction

- Febrile neutropenia (FN) is a potentially life-threatening complication of cancer treatments.
- Many guidelines (NCCN, ASCO, EORTC) recommend prophylactic use of granulocyte colony-stimulating factor (G-CSF) if the risk of FN is greater than 20% and are presenting lists of chemotherapy regimens with high risk of FN^{1,2,3}.
- However, information regarding the incidence of FN among different chemotherapy regimens for pediatric patients is scarce.

Objectives

- We aimed to evaluate incidence of FN in pediatric solid tumor and lymphoma patients treated with chemotherapy and assess risk factors in each tumor type and regimen.

Methods

Study design

- Retrospective observational study

Patients

- Pediatric solid tumor and lymphoma patients newly administered chemotherapy from 2011 to 2015 in Seoul National University Children's Hospital

Outcomes

- Primary outcome
 - Time-dependent cumulative incidence (CI) of FN with different tumor types and chemotherapy regimens
- Secondary outcome
 - Risk factors for FN

Statistics

- R function to obtain CI according to chemotherapy regimens
- Cox regression to analyze FN incidence regarding different combinations of chemotherapeutic agents
- Univariate logistic regression for risk factor analysis

Results

- Of the 409 patients, the most common tumor type was central nervous system (CNS) tumor (27%).
- Non-hodgkin's lymphoma (NHL) (16%), retinoblastoma (16%), bone cancer (10%), neuroblastoma (9%), rhabdomyosarcoma (6%), hepato-biliary cancer (4%), wilms tumor (4%), germ cell tumor (GCT) (4%), hodgkin's lymphoma (HL) (3%), soft tissue sarcoma (1%)

Table 1. Patients characteristics

Demographic and clinical characteristics	All patients (N = 409)
Sex	
Male (%)	253 (61.9)
Age, years ^a	6.42 ± 5.28 (0.09-17.97)
0-1	120
2-6	125
7-11	67
12-18	97
BSA (m ²) ^a	0.888 ± 0.457 (0.227-2.082)
Baseline labs ^b	
Hemoglobin (g/dL)	11.46 ± 1.90
Platelet (× 10 ³ /μl)	337.79 ± 137.88
ANC (/μl)	4487.65 ± 5609.99
BUN (mg/dL)	9.9 ± 5.90
Creatinine (mg/dL)	0.45 ± 0.35
Albumin (g/dL)	3.99 ± 0.57
AST (IU/L)	35.54 ± 26.37
ALT (IU/L)	21.91 ± 20.18
CRP (mg/dL)	2.06 ± 4.30
Schwartz eGFR	128.24 ± 47.08

^amean ± SD (range) ^bmean ± SD

Abbreviations:

BSA, body surface area; ANC, absolute neutrophil count; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine aminotransferase; CRP, c-reactive protein; eGFR, estimated glomerular filtration rate

Results (continued)

Figure 1. Time-dependent Cumulative Incidence of Febrile Neutropenia

- Incidence of FN were 45.5% in KSPNO regimen for low risk CNS GCT (CI=0.520), 4.5% in 9952A for low grade glioma (CI=0.048), 6.3% in 5961 modified-COP for NHL (CI=0.063), 80.0% in CarDEC for retinoblastoma (CI=0.906), 87.0% in CCG 7921A for bone cancer (CI=0.870), and 78.8% in CCG 321P2 for neuroblastoma (CI=1.000).

Table 2. Incidence of Febrile Neutropenia treated with Chemotherapy regimen (consisting of more than 10 patients)

Tumor type	Chemotherapy regimen	Combinations of chemotherapeutic agents	All patients	FN(%)	Cumulative incidence (CI)
CNS Tumor	9952A (Induction)	CARB-VCR	22	1 (4.5)	0.048
	KSPNO For Low risk CNS GCT	CARB-CPM-VP	22	10 (45.5)	0.520
	CCRT with TMZ	TMZ	17	1 (5.9)	0.125
	KSPNO-S-1102A	CDDP-CPM-VP-VCR	14	14 (100.0)	1.000
	KSPNO For High risk CNS GCT	BLM-CARB-CPM-VP	13	9 (69.2)	0.892
Non-Hodgkin's Lymphoma	5961 modified-COP	CPM-PD-VCR	32	2 (6.3)	0.063
	106B (Induction)	CPM-DNR-LASP-PD-VCR	16	15 (93.8)	0.938
	(D)-COMP (Induction)	CPM-MTX-PD-VCR	12	1 (8.3)	0.083
Retinoblastoma	CarDEC	CARB-CPM-ADR-VP-VCR	45	36 (80.0)	0.906
Bone Cancer	CCG 7921A (Induction)	CDDP-ADR-MTX	23	20 (87.0)	0.870
	VDC	CPM-ADR-VCR	12	11 (91.7)	1.000
Neuroblastoma	CCG 321P2	CDDP-CPM-ADR-VP	33	26 (78.8)	1.000
Rhabdomyosarcoma	POG-ICE	CARB-VP-IFO	18	12 (66.7)	0.832
Hepato-Biliary Cancer	8881 A	CDDP-VCR-5FU	15	2 (13.3)	0.222
Germ Cell Tumor	CCG 8882 (Induction)	BLM-CDDP-VP	12	7 (58.3)	0.583

CARB, carboplatin; VCR, vincristine; CPM, cyclophosphamide; VP, etoposide; TMZ, temozolomide; CDDP, cisplatin; BLM, bleomycin; PD, prednisolone; DNR, daunorubicin; LASP, l-asparaginase; MTX, methotrexate; ADR, doxorubicin; IFO, ifosfamide; 5FU, 5-fluorouracil

- FN occurred mainly in the first cycle of chemotherapy in most regimens.
- With regard to combinations of chemotherapeutic agents, incidence of FN after treatment with CPM/DNR/LASP/PD/VCR was significantly high compared to CPM/PD/VCR ($HR=6.998$, $p=0.012$) in NHL.
- Low hemoglobin (≤ 12 g/dL) was the risk factor of FN in CNS tumor treated with KSPNO regimen for low risk CNS GCT ($OR=16.5$, $p=0.022$).

Conclusions

- Incidence of FN in pediatric solid tumor and lymphoma patients is largely dependent on tumor type and chemotherapy regimens.