TRENDS AND EFFECTS OF THE USE OF PROPHYLACTIC G-CSF IN KOREA : analysis of the Korean National Health Insurance database

Soojung Hong [1], Taemi Youk[2], and Soohyeon Lee [3]
[1] Division of Oncology-Hematology, Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Goyang, Korea.
[2] Research Institute, National Health Insurance Service Ilsan Hospital, Goyang; [3] Division of Oncology/Hematology, Department of Internal Medicine, Korea University, Seoul

INTRODUCTION

Bone marrow suppression, particularly affecting neutrophils and their precursors. Febrile neutropenia can worsen the immune response due to infections, leading to prolonged hospitalization and negatively impacting subsequent chemotherapy.

The authors of this study have previously conducted research on the incidence and clinical outcomes of febrile neutropenia in Korean cancer patients, focusing specifically on the therapeutic use of G-CSF. It is important to note that the preventive use of G-CSF was initiated in Korea in January 2014, and the reimbursement conditions have been continuously expanded. However, in comparison to international guidelines, there are still limitations in the reimbursement criteria for preventive G-CSF use in Korea. Therefore, this study aims to investigate the trends and clinical effects of prophylactic G-CSF use in cancer patients who received cytotoxic chemotherapy. The study utilized national claim data to examine the patterns of G-CSF usage and assess its effectiveness as a preventive measure.

METHODS

We analyzed nationwide claim data from the Korean Health Insurance (NHI) database from 2007 to 2021 to select newly diagnosed cancer patients. We analyzed prophylactic and therapeutic G-CSF use and the incidence of febrile neutropenia. Cancer patients were defined as those with Korean Standard Disease and Death Classification (KCD) codes starting with 'C' and having specific V193 or V194 codes. Patients with errors in general information such as gender, age, and residence during the year of cancer diagnosis and those under the age of 19 were excluded. Patients with hematologic malignancy, acquired immune deficiency syndrome (AIDS), or a history of bone marrow transplantation were also excluded.

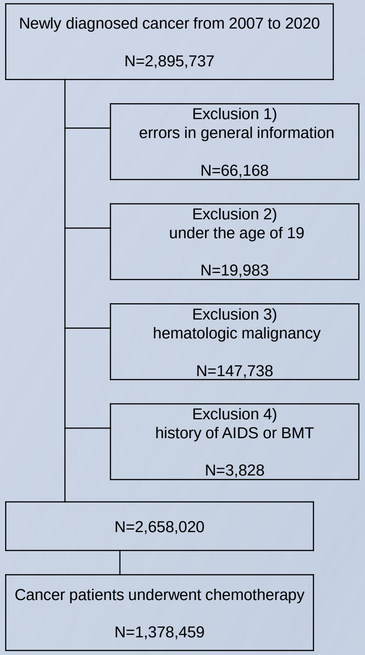

Figure 1. Selection of study population

RESULTS

For overall periods, the total number of claims for G-CSF has continuously increased. However, the number of claims for prophylactic G-CSF has increased, while therapeutic G-CSF has not increased since 2014. Prophylactic G-CSF use was the most common in breast cancer according to reimbursement criteria.

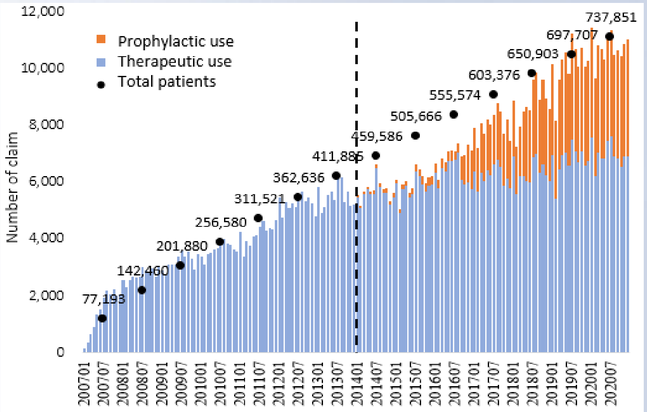

Figure 2. The number of G-CSF claim

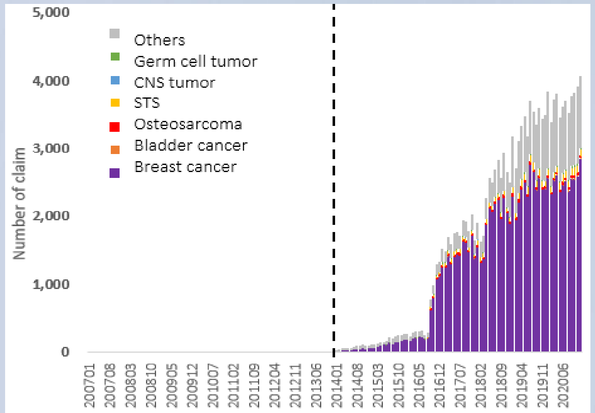

Figure 3. Prophylactic use of G-CSF by cancer type

RESULTS

We examined the compliance rate with clinical guidelines for prophylactic G-CSF use and investigated clinical outcomes in four cancer treatments eligible for reimbursement. We observed a high adherence to guidelines in breast cancer and sarcoma treatment. Notably, in the neoadjuvant TCHP regimen in breast cancer, a remarkable compliance rate of 92% was observed. The effectiveness of prophylactic G-CSF was evaluated by analyzing the incidence of febrile neutropenia with each treatment regimen. In patients with early breast cancer, the incidence of febrile neutropenia was reduced by 92% with the neoadjuvant TCHP regimen and by 98% with the adjuvant TC regimen. Additionally, in the ICE regimen for bone and soft tissue sarcoma, prophylactic G-CSF can lead to an 88% reduction in the incidence of febrile neutropenia. Furthermore, we investigated ER visits after chemotherapy, and the results confirmed that prophylactic G-CSF significantly reduced adverse events.

Caner type	N	Chemotherapy	# of chemo	Prophylactic G-CSF #	(%)
Breast	15,981	Neoadjuvant TCHP	15,339	14,043	(**91.6%**)
		Adjuvant TC	45,555	34,776	(76.3%)
Bladder	661	(Neo)adjuvant dose dense MVAC	1,058	307	(29.0%)
Bone and Soft tissue sarcoma	451	ICE	1,811	1,541	(85.1%)
	17,093		63,763		

N, number of patients; T, Docetaxel; C, Carboplatin; H, Trastuzumab; P, Pertuzumab; M, Methotrexate; V, vinblastine; A, Doxorubicin; C, Cisplatin; I, Ifosfamide; E, Etoposide

Table 1. Utilization of prophylactic G-CSF and Adherence rate to clinical guideline

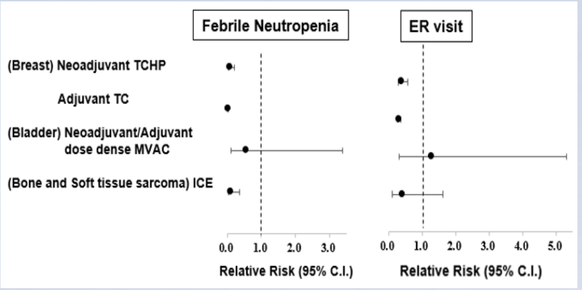

Figure 4. Risk of febrile neutropenia occurrence

We conducted the following analysis to explore possibilities for expanding insurance coverage of prophylactic G-CSF usage. We compared (neo)adjuvant AC therapy, where prophylactic G-CSF is reimbursed, with palliative AC therapy, which is not. Prophylactic G-CSF use in (Neo)adjuvant AC therapy reduced the incidence of febrile neutropenia by 96%, and G-CSF could be more effective with younger age. The incidence of febrile neutropenia in the palliative AC regimen without prophylactic G-CSF was 5.4%, similar to that in the (Neo)adjuvant AC regimen without prophylactic G-CSF. If G-CSF coverage is expanded to palliative AC, the same effect of reducing the occurrence of febrile neutropenia can be expected.

Chemotherapy	# of chemo	prophylactic G-CSF		Febrile Neutropenia		RR	
			n	(%)	n	(%)	Est.	95% C.I.
(Neo)adjuvant AC	101,629	Yes	30,685	(30.2%)	806	(2.6%)	0.038	(0.032-0.044)
		No	70,944		3,797	(5.4%)		
65+	9,805	Yes	5,498	(56.1%)	331	(6.0%)	0.116	(0.074-0.183)
		No	4,307		168	(3.9%)		
45-65	68,659	Yes	18,586	(27.1%)	500	(2.7%)	0.038	(0.031-0.046)
		No	50,073		2,682	(5.4%)		
-45	23,165	Yes	6,601	(28.5%)	138	(2.1%)	0.020	(0.014-0.033)
		No	16,564		784	(4.7%)		
Palliative AC	**6,105**	No			330	(5.4%)		

Table 2. Risk of febrile neutropenia in both AC chemotherapy.

CONCLUSIONS

Since the reimbursement of prophylactic G-CSF began in 2014, its usage has increased, especially in patients with early breast cancer. We identified the clinical benefits of prophylactic G-CSF in patients undergoing cytotoxic chemotherapy. Considering these benefits, it is necessary to expand the reimbursement criteria.

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