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Health Care Use and Primary Prophylaxis with Colony-Stimulating Factors

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A B S T R A C T

Objectives: We examined health care use in conjunction with primary prophylaxis use of colony stimulating factors (CSF) during patients' initial course of chemotherapy.
Methods: This retrospective cohort study identified adults aged 25 years and older with a diagnosis of breast, colorectal, or nonsmall cell lung cancer between 2002 and 2005 from the Western Washington Surveillance Epidemiology and End Results Puget Sound registry. We linked these records to health insurance claims from four payers representing 75% of those insured in the state. Claims records were used to determine chemotherapy regimen type, CSF use, febrile neutropenia occurrences, and supportive care. Chemotherapy regimens were categorized as conferring high, intermediate, or low risk of myelosuppression according to the National Comprehensive Cancer Network guidelines. CSF use was described as primary prophylaxis, other, or none. Antibiotics and antifungal and antiviral agents per National Comprehensive Cancer Network guidelines for supportive care for cancer infection were categorized using Healthcare Common Procedure Coding System and National Drug Code assignments.
Results: Use of CSF as primary prophylaxis is not significantly associated with a reduction in antibiotic use or inpatient or outpatient visits. Primary prophylactic CSF use was associated with less use of antiviral drugs.
Conclusions: CSF use is not associated with a reduction in health care use, with the exception of antiviral drug use. Given the expense associated with CSF use, pragmatic trials and additional research are needed to further assess the affects of CSF on health care use.

Introduction

Cancer patients who receive cytotoxic chemotherapy are at risk of developing febrile neutropenia (FN), a lack of white blood cells that puts patients at high risk of hospitalization [1–3] and death due to infection [4]. In clinical trials, prophylactic treatment with granulocyte colony stimulating factors (CSF) at the start of chemotherapy can reduce the incidence of FN by as much as 50% for chemotherapy regimens with a high or intermediate risk of FN [5–11]. The American Society for Clinical Oncology, the National Comprehensive

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Cancer Network (NCCN), and the European Organization for Research and Treatment of Cancer have published guidelines recommending the use of CSF agents as primary prophylaxis when the patient's chemotherapy regimen possesses a substantial risk of FN or other neutropenic event(s) [12–14].

CSFs have been shown in clinical trials and two retrospective studies to reduce the risk for FN-related hospitalization [11,15–17]. There are little data, however, concerning the influence of CSF on hospitalizations and other FN-related health care use in usual practice settings. To address these questions, we evaluated the association of CSF use, presence of FN, and health care use for patients with breast, colorectal, or nonsmall cell lung cancer who received myelosuppressive chemotherapy after linking Surveillance, Epidemiology, and End Results (SEER) cancer registry information to medical and pharmacy claims data from four large health insurers in western Washington State.

Methods

Data sources

For this study, patient-level data obtained from the SEER Puget Sound cancer registry were merged with health care claims data from four regional payers: Medicare Region X, Washington State Medicaid, Premera Blue Cross, and Regence Blue Shield of Washington. SEER records provided information regarding cancer tumor characteristics, stage at diagnosis, and survival. Health insurance status, cancer treatment information, and medical care use data were extracted from the enrollment files and health care claims databases from the four payers. The SEER Puget Sound registry provides data on the incidence, treatment, and follow-up of all newly diagnosed cancers, with the exception of nonmelanoma skin cancers, occurring in residents of 13 counties in northwest Washington State [18]. Certified abstractors obtain data through visits to and reports from hospitals, outpatient surgical centers, pathology laboratories, clinician offices, and death certificates.

Premera Blue Cross and Regence Blue Shield, both nonprofit regional health plans, are two of the largest private health insurers in Washington State. Premera Blue Cross serves more than 1.4 million members in Washington State [19] whereas Regence Blue Shield provides coverage for more than one million Washington State residents [20]. Premera and Regence data was pooled as commercial data for the purpose of analysis.

Medicaid is managed under the auspices of the Washington State Department of Social and Health Services and the Health Recovery Services Administration and serves approximately 330,000 clients in the Medicaid fee-for-service program, which covers the full spectrum of care [21].

The Medicare program is administered by the Centers for Medicare and Medicaid Services. Medicare is composed of part A (inpatient hospital care) and part B (outpatient care, doctors' services) [22]. Medicare outpatient prescription drug records for Medicare patients are not available for the years of this analysis because part D did not start until January 2006.

Study population

Approval was obtained from the appropriate institutional review boards, and Health Insurance Portability and Accountability Act authorization waivers were approved before database linkage was conducted. To identify subjects with incident cases of the relevant cancers, we cross-linked person-level identifiers (full name, sex, date of birth, and zip code if available) from each payer's enrollment files with the SEER Puget Sound registry. Linkage was limited to newly diagnosed cancers for each enrollee living within the SEER Puget Sound Registry's 13-county coverage area. Detailed inclusion and exclusion criteria for our study population have been previously described [23].

Identification of CSF exposure, antibiotic use, and FN events

The focus of this study was to investigate the relationship between guideline-determined prophylactic CSF use, subsequent development of FN, and specific measures of health care and prescription drug use. Following NCCN guidelines, CSF should be administered 24 to 72 hours after initial chemotherapy administration if used as primary prophylaxis [12].

First, patients were grouped into categories based on the myelosuppressive risk posed by the chemotherapy regimen they received. We used our previously described algorithm [23] to identify the chemotherapy regimens commonly used for breast, colorectal, and nonsmall cell lung cancers. The algorithm considers the agents delivered and their timing in relation to each other. The myelosuppressive risk of each regimen (i.e., the risk for developing FN in the absence of CSF administration) was based on the high, intermediate, and low-risk chemotherapy regimen categories published by the NCCN [12]. If a chemotherapy regimen was not categorized by NCCN, a board-certified oncology pharmacist (JSM) categorized remaining regimens based on descriptions of their FN incidence from the literature.

Then, using medical and pharmacy claims, we identified the dates and type of initial chemotherapy agents used, the initial date of CSF use, and FN events in relation to the initial chemotherapy regimen. We defined CSF primary prophylaxis as any use of CSF products within 3 days of the initiation of chemotherapy.

Claims records also were used to determine the use of antibiotics and other supportive care associated with FN. Records were searched for Healthcare Common Procedure Coding System and National Drug Code assignments for agents appearing in the NCCN guidelines for supportive care for cancer infection (online Appendices A and B, available at doi:10.1016/j.jval.2010.09.005.) [24] from the initial date of the first chemotherapy agent delivered to 14 days past the last date when a chemotherapy agent code from the initial regimen appeared in the patient's claims records.