Assessing the impact of a targeted electronic medical record intervention on the use of growth factor in cancer patients

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Background Patients receiving chemotherapy are at risk for febrile neutropenia following treatment. The American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) recommend screening patients for risk of febrile neutropenia and risk stratification based on likelihood of febrile neutropenia events. The impact of the implementation of an electronic medical record (EMR) system on physician compliance with growth factor support guidelines has not been studied.
Objective To investigate whether implementation of automated orders in EMRs can improve adherence to national guidelines in prophylactic G-CSF use in chemotherapy patients.
Methods A retrospective chart review of cancer patients receiving chemotherapy from January 1, 2007 to August 1, 2008 (pre-EMR) and January 1, 2011 to December 31, 2011 (post-EMR) was conducted. Institutional adherence to ASCO and NCCN guidelines for G-CSF after the implementation of automatic electronic orders for pegfilgrastim in patients who received a high-risk chemotherapy regimen were examined. The results were compared with a similar study that had been conducted before the implementation of the EMR system.
Results The number of regimens that included guideline-driven growth factor usage and nonusage was 75.6% in the post-intervention arm, compared with 67.5% in the pre-intervention arm. This is a statistically significant difference between the pre-EMR and post-EMR compliance with national guidelines on growth factor usage ($P = .041$, based on chi-square test). The post-EMR implementation data of 1,042 individual new chemotherapy regimens showed correct use of G-CSF in 89.13% high-risk chemotherapy regimens and 58.74% intermediate-risk regimens, with risk factors and incorrect usage in 26.23% of intermediate-risk regimens without risk factors and 19.34% of low-risk regimens. The appropriateness of use in high- and low-risk regimens was the most compliant, because growth factor was built into chemotherapy plans of high-risk regimens and omitted from low-risk regimens.
Limitations This project was limited by a change in EMR systems at West Virginia University hospitals on January 1, 2009. All pre-EMR data was collected before 2009 and could not be further collected once the project began in 2013.
Conclusions Appropriateness of growth factor usage can be improved when integrated into an EMR. This can improve compliance and adherence to national recommendations. Further development and understanding of EMR is needed to improve usage to meet national guidelines, with particular attention paid to integration of risk factors into EMR to improve growth factor usage compliance.
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Febrile neutropenia (FN) is a complication of chemotherapy that can lead to hospitalization. Inpatient mortality for FN is estimated to be 9.5% in 115 US medical centers between 1995 and 2000, and together with comorbidities, cancer type, and documented infection, is associated with poorer outcomes.[1] In addition, episodes of FN or prolonged afebrile neutropenia often result in chemotherapy dose delay or dose reduction, which compromise the effectiveness of the antineoplastic treatment.[2,3] The use of prophylactic granulocyte colony-stimulating factors (G-CSFs) is a way to mitigate the complications associated with myelosuppressive chemotherapy. The appropriate use of prophylactic G-CSFs has been shown to reduce the duration and severity of neutropenia, decrease the risk of FN, improve the relative dose intensity (RDI) of chemotherapy, decrease hospital length of stay, and reduce the risk of infection-related

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mortality and early death during chemotherapy.[3,8,10] The use of G-CSFs, however, is not without risk. The primary toxicity associated with G-CSF therapy is bone pain in up to 30% of patients.[9] Serious toxicities, including rare cases of splenic rupture, can occur.

Balancing the clinical and cost-effectiveness of a treatment is an essential component in ensuring the delivery of the highest quality patient care. The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have composed guidelines for patient care based on comprehensive review of the evidence and cost-effectiveness models.[6,10] Adherence to those guidelines increases the quality of patient care and reduces costs of care. In oncology practice, adherence to the guidelines for using G-CSFs for prevention of FN is highly variable, ranging from 0%-88% depending on the practice site.[9] The decision to use G-CSFs for prophylaxis of FN is complex, and consideration must be given to a number of factors. Both ASCO and the NCCN recommend a risk-based approach to this decision. Primary prophylaxis is recommended for patients who receive a chemotherapy regimen that is associated with a risk for FN of more than 20%. For patients who receive regimens with a risk for FN of 20% or less than, the decision to use G-CSFs is based on a thorough risk assessment, taking into account patient-specific factors such as cancer type, treatment intent, and comorbid conditions. An electronic medical record (EMR) system with computerized physician order entry (CPOE) and well-designed decision support tools may increase adherence to established guidelines.

In January 2009, an EMR system was established at West Virginia University Hospitals (WVUH). A major advantage of this new system is the ability to establish a standard that automatically includes pegfilgrastim, a long-acting G-CSF, in chemotherapy order sets if the risk of FN for the selected regimen is greater than 20%. In this study, we examined institutional adherence to ASCO and NCCN guidelines for G-CSF after the implementation of automatic electronic orders for pegfilgrastim in patients who received a high-risk chemotherapy regimen. The results were compared with a similar study that had been conducted before the implementation of the EMR system.

Methods

We conducted a retrospective analysis of patients who received chemotherapy during January 1, 2011- December 31, 2011. The study included 736 patients who were older than 18 years and who received chemotherapy at WVUH as an outpatient. Patients who received chemotherapy in preparation for a bone marrow transplant or those participating in a clinical trial were excluded. The period during which the analysis took place allowed for the adaptation and stabilization of processes after the implementation of the EMR system and G-CSF protocols.

Our decisions about the appropriate administration of G-CSFs in the form of pegfilgrastim for primary prophylaxis of FN were based on 2013 NCCN guidelines for the use of myeloid growth factors and 2006 ASCO guidelines for the use of white blood cell colony-stimulating factors. For primary prophylaxis with G-CSFs, patients were classified based on their treatment regimen as being at high risk (>20%), intermediate risk (10%-20%), or low risk (<10%) of developing FN. G-CSF administration is indicated in chemotherapy regimens with a high risk of FN. For chemotherapy regimens with a low risk of FN, the use of primary prophylaxis with G-CSF was not considered as being indicated. Patients who received chemotherapy regimens that presented an intermediate risk for FN were classified into 1 of 2 subgroups: those with at least 1 patient-specific risk factor for FN, or those with no risk factors. Those with at least 1 patient-specific risk factor for FN were considered eligible for primary prophylaxis with G-CSF (Table 1).

After we had determined the guideline adherence rates of G-CSF use, we compared the results with those of a previous study with the same measures but that had been completed before the EMR implementation. Statistical analysis was performed to determine significance between the prescribing methods for the 2 patient populations before and after implementation of the EMR system.

Results

In all, 736 chemotherapy initiations in 736 patients were analyzed after the implementation of the EMR system at WVUH, and 76.2% of the G-CSF use cases were adherent to national guidelines. In the analysis conducted before the EMR implementation, 120 chemotherapy initiations were assessed, showing a 67.5% rate of guideline adherence (Figure 1). That demonstrated a statistically significant improvement in guideline compliance between the pre-EMR and post-EMR periods ($P = .041$, chi-square; Table 2). Of the 736 new

TABLE 1 Risk factors for intermediate risk of febrile neutropenia

1. Older than 65 years
2. Previous chemotherapy or radiation therapy
3. Preexisting neutropenia or documented bone marrow involvement with tumor
4. Preexisting conditions, such as infection/open wounds at chemotherapy initiation
5. Recent surgery (within 6 weeks of chemotherapy)
6. Poor performance status (Eastern Cooperative Oncology Group PS, 2-4)
7. Poor nutrition status
8. Poor renal function (creatinine clearance, <30 ml/min)
9. Liver dysfunction (bilirubin, >2 mg/dL)

TABLE 2 Patients who received chemotherapy initiations in which primary G-CSF prophylaxis is indicated by guidelines (736 chemotherapy initiations).

	Primary prophylaxis indicated		Primary prophylaxis not indicated	
	High-risk regimen (n = 46)	**Intermediate-risk regimen + at least 1 risk factor (n = 143)**	**Intermediate-risk regimen + no risk factors (n = 61)**	**Low-risk regimen (n = 486)**
Received prophylaxis, n (%)	41 (89.1)	84 (58.7)	16 (26.2)	94 (19.3)
No prophylaxis, n (%)	5 (10.8)	59 (41.3)	45 (73.8)	392 (80.7)
Guideline adherence, %				
Each group	66[a]		80[b]	
Total	75.6			

[a]Appropriately received primary prophylaxis. [b]Appropriately did not receive primary prophylaxis.

chemotherapy initiations that were analyzed, 189 (25.7%) were categorized as requiring primary G-CSF prophylaxis according to guidelines. Most of those patients (75.6%) were categorized as receiving an intermediate-risk regimen with at least 1 risk factor for development of FN. Of the 189 new treatment initiations that were recommended by guidelines to receive primary G-CSF prophylaxis, compliance rate was 66% (Table 2). In the 46 patients who received a high-risk chemotherapy regimen, 41 (89.1%) received primary prophylaxis, consistent with guidelines. Of the 143 patients who received intermediate-risk chemotherapy regimens with more than 1 identified risk factor, 84 (58.7%) received primary prophylaxis consistent with guideline recommendations.

Adverse outcomes in the 64 patients who did not receive G-CSF prophylaxis despite guideline recommendations included neutropenia with dose delay in 7 patients (10.9%), neutropenia without dose delay in 5 patients (7.8%), and febrile neutropenia with hospital admission in 5 patients (7.8%; Table 3). In the high-risk chemotherapy regimens, 5 patients did not receive G-CSF despite guideline recommendations, which resulted in 2 episodes (40%) of febrile neutropenia with hospitalization (Table 3). In the intermediate risk chemotherapy regimens, 59 patients did not receive G-CSF

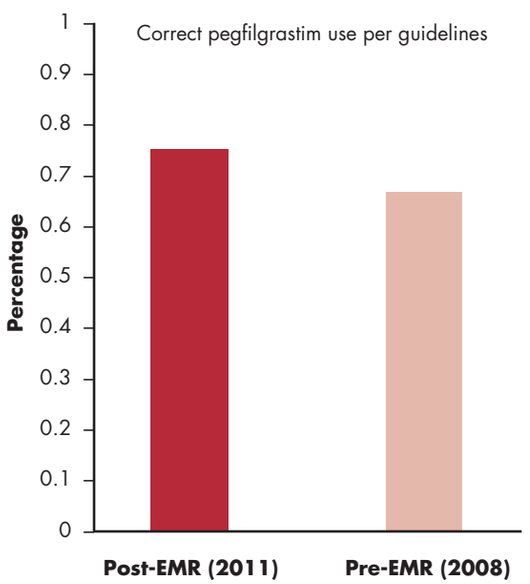

FIGURE 1 Comparison of adherence to national guidelines for prophylactic pegfilgrastim use in chemotherapy patients before and after the implementation of electronic medical record automated orders for G-CSF in high-risk chemotherapy regimens.

TABLE 3 Adverse events due to guideline nonadherence in high- and intermediate-risk chemotherapy initiations in which primary prophylaxis was indicated

Regimen risk	No. of nonadherent regimens	Neutropenic episode with dose delay, n (%)	Neutropenic episode without dose delay, n (%)	Febrile neutropenia with hospital admission, n (%)
High	5	0 (0)	0 (0)	2 (40)
Intermediate + at least 1 risk factor	59	7 (11.9)	5 (8.5)	3 (5.1)
Total	64	7 (10.9)	5 (7.8)	5 (7.8)

despite guideline recommendations, resulting in neutropenia with dose delay in 7 patients (11.9%), neutropenia without dose delay in 5 patients (8.5%), and febrile neutropenia with hospital admission in 3 patients (5.1%; Table 3).

Of the 736 new chemotherapy initiations, 547 (74.3%) were categorized as not requiring primary G-CSF prophylaxis according to guidelines (Table 2). Of the regimens recommended to not receive primary growth factor prophylaxis (low-risk chemotherapy regimen and intermediate-risk regimen without patient-specific risk factors), 20% (110 of 547) received primary prophylaxis with G-CSF outside of guideline recommendations.

Discussion

This study found that primary prophylaxis with G-CSFs was underused in 64 of 736 (8.7%) of new chemotherapy initiations. Moreover, the direct effect of that underuse resulted in adverse outcomes such as therapy dose delays and hospital admissions. These complications are not desirable and are costly because of the hospitalizations, treatment for FN, and increased use of resources with chemotherapy treatment delays. In addition to underuse, the overuse of G-CSFs in the form of unnecessary primary prophylaxis was found in 110 of 736 chemotherapy initiations (14.9%). Overuse of colony- stimulating factors exposes patients to side effects and results in unnecessary costs. The primary form of G-CSF used for primary prophylaxis in practice is the long-acting peglyated form, pegfilgrastim. A single dose of pegfilgrastim has an average sales price of about $3,400, so with 110 new chemotherapy initiations in which primary prophylaxis is deemed unnecessary as per the guidelines, there would be a cost increase to the health system of at least $374,000. In addition, it is likely the patients received pegfilgrastim with each subsequent cycle of chemotherapy, which would have resulted in a much higher actual cost.

The advent of EMR with CPOE for chemotherapy provides an opportunity to increase guideline compliance in the use of prophylactic G-CSF. Our results suggest that the correct use of primary prophylaxis consistent with national guidelines in cancer patients at WVUH has significantly increased since the implementation of the EMR in January 2009 compared with before the implementation. Currently at WVUH, standard chemotherapy order sets are built using EPIC EMR's Beacon oncology system. The order sets include guideline-compliant supportive care orders in addition to chemotherapy. For all regimens that are deemed to have an inherent FN risk of greater than 20%, primary prophylaxis with pegfilgrastim is a standard part of the order set. We believe that set-up contributed to our health system's high guideline compliance (89%) for high-risk regimens. Intermediate-risk regimens do not include automatic orders for pegfilgrastim, because the decision to use primary prophylaxis requires an analysis of patient-specific risk factors. As such, use of pegfilgrastim as primary prophylaxis was much lower in intermediate-risk patients where its use was indicated (58.7%).

The reasons for the intermediate group being far lower is likely because of the absence of a "hard stop whereby the physician is required to make a decision in intermediate patients if risks factors are present or not. Low risk for FN does not have growth factor built in, but high risk does and intermediate requires an extra step. This extra step is likely the reason high-risk patients are given growth factor (89.1% of patients in our study), whereas intermediate risk was notably lower, at 58.7%. The inclusion of an EMR-integrated decision-support tool that would be able to identify patient-specific risk factors and notify the prescriber to consider addition of primary prophylaxis at the time of order placement would represent a welcome advance in the technology of EMR systems, and would likely improve the compliance to national guidelines in the intermediate risk group. In addition to addressing underuse of primary prophylaxis in intermediate risk regimens, such a tool could reduce overuse. Prescribers would expect automated clear identification of risk factors and would thus become less likely to add pegfilgrastim orders without being prompted. However, this tool would not replace accounting for patient variability and the need for physicians to make patient care decisions on an individualized basis.

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