Febrile neutropenia rates with adjuvant docetaxel and cyclophosphamide chemotherapy in early breast cancer: discrepancy between published reports and community practice—a retrospective analysis

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KEY WORDS

Febrile neutropenia, breast cancer, adjuvant chemotherapy

1. INTRODUCTION

Adjuvant therapies, including chemotherapy, are a major reason for the improved survival in early breast cancer in North America and Europe. As treatments have become more successful, the indications have expanded to include cancers in node-negative and in older women [1,2]. Recent clinical trials have largely supported the additional benefit of taxane therapy, including benefit in older patients [3].

The increase in the proportion of women treated and the improved survival mean that toxicities become increasingly important. One of the most serious acute toxicities is febrile neutropenia (FN). A newer report has demonstrated the benefit for disease-free and overall survival of 4 cycles of docetaxel–cyclophosphamide (TC) chemotherapy over doxorubicin–cyclophosphamide chemotherapy and has also reported acceptable toxicity with a FN rate of 5% [4]. The TC regimen has become very popular in Ontario, particularly in older age groups who are at increased risk of cardiotoxicity with anthracyclines, or in those eligible for trastuzumab [5].

Here, we share our preliminary experience at the London Regional Cancer Program with FN incidence related to the use of TC chemotherapy in the adjuvant setting.

2. METHODS

This short report is based on a consecutive series of 39 patients treated with 4 cycles of TC from January 2008 to May 2009 and assessed by retrospective chart review as a quality assurance tool. The final review was done June 17, 2009.

These women all had early-stage (high-risk node-negative, node-positive, or T1, 2, or 3, but not locally advanced or inflammatory) breast cancer and were treated with docetaxel 75 mg/m^2 plus cyclophosphamide 600 mg/m^2 every 3 weeks for 4 cycles. All patients were evaluable for review and analysis after completion of the prescribed treatment (admissions may have been at our host hospital or at a community hospital) and include those who stopped treatment early. Medical records for all hospitals in the region but one are available via electronic health record, and all discharge summaries were available for patients admitted with FN. Our institution defines FN as a temperature of 38.0°C, for which patients are instructed to seek emergency medical assessment, including clinical assessment and complete blood count, by a physician. The standard definition of neutropenia is a cell count below 0.5×10^9/L (or below 1.0×10^9/L and expected to worsen).

3. RESULTS

In this group of patients, median age was 65 years (range: 39–84 ywears). Comorbidities were present in 12 patients (4 diabetes mellitus, 2 pulmonary embolism, 3 prior chemotherapy, and 1 each Crohn disease, sleep apnea, and delayed wound healing), and 11 patients had received primary prophylaxis with filgrastim or pegylated filgrastim. Three patients were unable to complete treatment, and none were lost to follow up. Table I summarizes the FN rate in these patients by subgroup.

The FN rate was 33% (13/39) across all patients. Patients 65 years of age and older had a documented FN rate of 40% (8/20). One of the 3 patients that stopped treatment early had FN. Of the 11 patients that received primary prophylaxis, none experienced FN, despite risk factors of older age and comorbid conditions in 2, older age in another 3, and comorbidity in another 2. For patients not receiving primary prophylaxis, the FN rate was 46% (13/28); in patients older than 65 years with comorbidities not receiving primary prophylaxis, it was 100% (5/5).

TABLE I Age group, comorbidities, use of granulocyte colony–stimulating factor (G-CSF) and incidence of febrile neutropenia (FN)

Group	*Pts (n)*	*FN rate*		
		(%)	*Given G-CSF (n)*	*(%)*
Age<65, no comorbidities	14	21	3	0
Age≥65	20	40	5	0
Comorbidities	12	58	4	0
Age≥65, comorbidities	7	71	2	0

Pts = patients.

4. DISCUSSION AND CONCLUSIONS

Based on these limited observations, it appears that TC chemotherapy is associated with a higher FN rate than has been published or reported. No patients died or required intensive care as a result of FN complications. Our rate may be a result of treatment of a population older or with more comorbidities than is usually entered into a clinical trial, which is consistent with risk factors from the National Comprehensive Cancer Network and the American Society of Clinical Oncology guidelines [6,7].

We used age 65 as a benchmark because our provincial government health insurance does not cover supportive care drug costs for outpatients younger than 65 years of age and also because age 65 is considered a risk factor for FN. Interestingly, the risk of FN also seems high in the younger group. The average age on the U.S. oncology trial was 52 years as compared with 67 years in our cohort. We also suspect that primary prophylaxis is underreported. The initial report of TC [8] did not mention whether primary prophylaxis was used; the subsequent report indicated that prophylactic quinolones were recommended (but not required) and did not mention how many patients were given prophylactic antibiotics.

We feel that age, comorbidities such as diabetes [9], and less-routine use of prophylaxis are significant factors increasing the risk of FN. Although primary prophylaxis with granulocyte colony–stimulating factor has little effect on mortality from FN [10], our experience should serve to encourage more consistent and complete reporting of supportive care drugs and comorbidities when assessing the toxicities of adjuvant chemotherapy. Our rate of FN, if confirmed by studies in larger patient cohorts, would argue for a greater role for primary prophylaxis.

5. REFERENCES

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