The association between infections and chemotherapy interruptions among cancer patients: Prospective cohort study

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Summary   *Objectives:* Adherence to scheduled chemotherapy is important for optimal outcomes of cancer patients. We examined causes for delay or cancellation of planned chemotherapy, focusing on mild respiratory infections during the winter.
Methods: Prospective cohort study. We included all adults with solid or hematologic cancer receiving active chemotherapy treatment during the winter of 2010—2011 in a cancer center. We compared baseline characteristics and outcomes between patients with and without chemotherapy delays, cancellations, or dose-reductions ("chemotherapy delay").
Results: We included 547 patients receiving chemotherapy during the winter of 2011. Of these, 213 (38.9%) patients experienced 306 episodes of chemotherapy delays. The main documented reasons for the chemotherapy delay were neutropenia (84/306, 27.4%), fever or infection (73/306, 23.9%) and thrombocytopenia (26/306, 8.5%). Independent risk factors for chemotherapy delays were upper respiratory infections (OR 1.87, 95% CI 1.27—2.76), lymphopenia, prior hospitalization, peripheral vascular disease and colon cancer relative to hematologic cancer. In the adjusted analysis focusing on chemotherapy delays due to infection alone, upper respiratory infections (OR 5.25, 95% I 2.81—9.84) and age were significant independent risk factors.

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Discussion: Mild respiratory infections were associated with chemotherapy delays. Our results should encourage modalities to prevent influenza and other upper respiratory infections among cancer patients.

Background

Cancellation or delays of chemotherapy protocols are common in cancer patients and might adversely affect prognosis. Associations between non-adherence to chemotherapy protocols or reduction in dose intensity in the adjuvant setting were shown to impact disease control or decrease survival for colorectal cancer,[1–4] breast cancer[5,6] and small-cell lung cancer.[7]

Infections constitute an important reason for non-adherence to chemotherapy protocols. Of all infections, influenza and other viral respiratory infections are the most preventable through vaccination or other prevention measures. Previous studies have focused mainly on cytopenias and mucositis as causes of chemotherapy rejections.[1–7] The association between viral respiratory infections and chemotherapy delays has not been previously assessed to our knowledge. Quantification of this association might help direct prevention efforts. In the current study we aimed to examine the reasons and risk factors for interruption (delay or cancellation) of planned chemotherapy in a cohort of cancer patients, focusing on the relative contribution of influenza and influenza-like illness.

Methods

Study design and setting

The study methods have been previously described.[8] This was a prospective cohort study conducted during the 2010–2011 influenza season at Davidoff Center, Rabin Medical Center aimed primarily at examining the effects of influenza vaccine in cancer patients. Patients were followed until May 2011 or death. The study was approved by the local ethics committee and oral informed consent was obtained for telephone/personal interviews.

Participants

The study included patients aged 18 years and older, with hematologic or solid cancer receiving active chemotherapy during the 2010–2011 influenza season (October 2010–February 2011). We included only patients insured through Clalit Health Services, since the hospital belongs to this health maintenance organization (HMO) and its electronic records capture outpatient visits of this HMO and only a small proportion of patients treated in Davidoff's Center belong to other HMOs.

Dependent variable

Any cancellation or delay of planned chemotherapy during the 2010–2011 influenza season, coded as a dichotomous variable.

Main exposure variable

Influenza-like illness (ILI), defined as fever (temperature of 100 °F [37.8 °C] or greater) and a cough and/or a sore throat without a known cause other than influenza.

Confounders and other variables

We collected data on other variables that may affect adherence to the planned chemotherapy protocol, including socio-demographic factors, background conditions including the Charlson Comorbidity Index (CCI),[9] data on the primary malignancy and its stage, cytopenias, other infections, influenza and pneumococcal vaccination and technical factors. We categorized immune-suppression as primarily cellular (post-engraftment allogeneic hematopoietic stem cell transplantation (HSCT), chronic lymphocytic leukemia (CLL), multiple myeloma (MM) treated with novel agents) or related to neutropenia post chemotherapy (solid malignancies, lymphoma and acute leukemia). Patients were assigned to a socio-economic cluster according to their address.[10] Performance status was classified using the ECOG classification.

Data sources

Data were collected from the electronic and hard copy medical records of inpatient and outpatient visits and from patient-unique dispensation records of the hospital's pharmacy. Data regarding ILIs were supplanted by a telephone/personal questionnaire conducted once at the end of the influenza season. The planned chemotherapy protocol and any deviations from the planned protocol are recorded in the outpatient records with their reasons. The drugs actually administered to patients are recorded in patients' charts.

Sample size

A sample size calculation was performed for the study's primary aim. The sample gave us a power of >90% to find a link between ILI and delay/cancellation of chemotherapy with odds ratio >2 in a single variable model, assuming a chemotherapy delay/cancellation rate of 20% among patients without ILI ($\alpha = 0.05$).

Statistical methods

We evaluated the association between ILI and other risk factors and delay/cancellation of the planned chemotherapy, in univariate analysis. In a secondary analysis, we considered only infection-related delays/cancellations. Dichotomous data were compared using a Chi-square test