Original Article

Evaluation of Risk Factors Predicting Chemotherapy-Related Nausea and Vomiting: Results From a European Prospective Observational Study

Alexander Molassiotis, RN, PhD, Matti Aapro, MD, Mario Dicato, MD, FRCP, Pere Gascon, MD, PhD, Sylvia A. Novoa, MD, Nicolas Isambert, MD, Thomas A. Burke, PhD, Anna Gu, MD, PhD, and Fausto Roila, MD

School of Nursing (A.M.), The Hong Kong Polytechnic University, Hong Kong; Medical Oncology and Radiation (M.A.), IMO Clinique de Genolier, Genolier, Switzerland; Hematology-Oncology (M.D.), Luxembourg Medical Center, Luxembourg, Luxembourg; Hospital Clinic (P.G.), IDIBAPS, University of Barcelona, Barcelona, Spain; Hospital Teresa Herrera—Complejo Hospitalario Universitario A Coruña-CHUAC (S.A.N.), A Coruña, Spain; Centre G-F Leclerc (N.I.), Dijon, France; Global Health Outcomes (T.A.B.), Merck Sharp & Dohme Corp., Whitehouse Station, New Jersey, USA; St. John's University (A.G.), New York, New York, USA; and Medical Oncology (F.R.), Santa Maria Hospital, Terni, Italy

Abstract

Context. Demographic, personal, clinical, and behavioral factors predicting chemotherapy-induced nausea and vomiting (CINV) have been assessed in the past, but inconsistencies exist in the literature, studies have methodological shortcomings, and many risk factors have been examined in cross-sectional studies and univariate analyses.

Objectives. To evaluate the predictive power of personal and treatment-related characteristics in the development of CINV, using a large and prospectively evaluated sample of a heterogeneous group of cancer patients receiving routine chemotherapy.

Methods. This was a multicountry, multisite prospective study over three cycles of chemotherapy. Adult patients from eight European countries about to receive highly and moderately emetogenic chemotherapy were recruited. Clinicians completed a case report form at or before the initial chemotherapy treatment, recording patient demographic and baseline clinical characteristics. Participants completed a daily patient diary for six days per chemotherapy cycle describing their CINV experience. Baseline patient data also included a history of nausea/vomiting (yes/no), patient expectation of nausea (0−100 mm visual analogue scale [VAS]), prechemotherapy anxiety (0−100 mm VAS), and prechemotherapy nausea (0−100 mm VAS) measured during the 24-hour period before chemotherapy initiation.

Address correspondence to: Alexander Molassiotis, RN, PhD, School of Nursing, The Hong Kong Polytechnic University, Hong Kong. E-mail: alex.molasiotis@polyu.edu.hk

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Results. There were 991 evaluable patients with complete Cycle 1 data, 888 for Cycle 2 data, and 769 for Cycle 3 data. A complex picture of predictor variables was shown, with different contribution of variables to the acute, delayed, and overall phases of CINV. Key predictor variables included the use of antiemetics inconsistent with international guidelines, younger age, prechemotherapy nausea, and no CINV complete response in an earlier cycle (all at $P < 0.05$). Anxiety, history of nausea/vomiting, and expectations of nausea were important predictors for some phases and cycles but not consistently across the CINV pathway.

Conclusion. The results of this study provide clarity for the relative contribution of a set of characteristics in the development of CINV. Following evidence-based clinical antiemetic guidelines is of paramount importance, alongside treating patients with increased risk for CINV more aggressively, which both could lead to more optimal CINV management. These data can assist clinicians in making decisions about the antiemetic management of their patients. J Pain Symptom Manage 2014;47:839–848.

Key Words
Chemotherapy, nausea, vomiting, emesis, risk factor, prediction

Introduction

Interest in personal and treatment-related predictive factors for chemotherapy-induced nausea and vomiting (CINV) was significant in the 1980s, and a number of such factors were identified, summarized in the work by Morrow[1] and more recently by Roscoe et al.[2] With the advent of 5-HT3 receptor antagonists, this work was less visible, but in the past decade, with the development of more aggressive chemotherapy protocols, it surfaced again as an important clinical consideration. A number of variables have been implicated in the development of CINV, including female gender,[3–8] younger age,[5–7,9,10] history of nausea/vomiting,[4,5] the emetogenicity of the chemotherapy,[6,8] or anxiety.[5,11] Expectation of nausea/vomiting has consistently been shown to predict actual CINV.[5,12–14] Three studies have pooled data from several trials: Roscoe et al.[14] used data from three behavioral interventional studies and showed that gender was an important factor for the development of nausea when doxorubicin was used (but there was no evidence of gender effects for gender-neutral cancers) alongside age, expectation, and susceptibility to nausea (for average nausea only but not severity). Warr et al.[10] pooled data from three aprepitant trials in patients receiving Adriamycin-cyclophosphamide and showed that aprepitant use, age, low alcohol use, and a history of motion sickness were predictive of CINV. Finally, Hesketh et al.[7] pooled data from two trials of aprepitant in Cisplatin-treated patients and showed that aprepitant use, gender, chemotherapy dose, age, and low alcohol use were implicated in the development of CINV.

Besides the secondary analyses of pooled data that focus on trial patients often with good performance status, which impacts on the generalizability of the results, most studies have typically small sample sizes (N = 29–143,[4,5,9,11,12] $N = 200$,[8] and $N = 335$[6]), primarily focused on patients with breast cancer,[4,5,9,11–13] included a limited number of potential predictor variables, used nonparametric tests for data analysis or univariate methods, and were mostly cross-sectional in nature. There is inconsistency related to some factors, particularly among the smaller scale studies (i.e., role of gender per se), and although it is clear that acute and delayed CINV may be linked with different predictor variables,[5] the tendency in the literature has been to use CINV as a single variable. There also is limited evidence to date from large prospective studies using many of the implicated risk factors that would allow for more advanced multivariate methods to be used. Furthermore, with the exception of the study by Pirri et al.,[8] there is no clear evidence about