

Genetic Influence on Chemotherapy-Induced Nausea and Vomiting: A Narrative Review

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Chemotherapy-induced nausea and vomiting (CINV) is a phenomenon common to patients being treated for a solid or hematologic malignancy. This adverse effect to cancer treatment persists in about half of all patients receiving highly emetogenic treatment (He et al., 2014; Zoto et al., 2015), despite prophylaxis with serotonin (5-hydroxytryptamine-3 [5-HT₃]) antagonists, steroids, and additional agents. Two broad categories increase risk for CINV: the emetogenic potential of chemotherapeutic drugs (Hesketh et al., 1997) and patient-specific risk factors, such as younger age (Roscoe et al., 2010), female gender (Hesketh et al., 2006), low or no alcohol intake (Warr, Street, & Carides, 2011), and history of motion sickness or pregnancy-induced nausea (Pirri et al., 2011). Despite these predictors for CINV, guidelines for prophylaxis continue to be based solely on the emetogenicity of agents administered. New strategies for CINV are unlikely until additional data emerge.

Pharmacogenomics may or may not yield such data. New research into serotonin antagonists and how these drugs work differently in individuals with varying genetic makeup is affecting the knowledge of patient-specific CINV risk factors. Single nucleotide polymorphisms (SNPs) are DNA base substitutions that may affect protein function in the serotonin pathway, the neurologic pathway affected

by chemotherapy in the peripheral nervous system in the gut and in the central nervous system (Bayo et al., 2012). This research has generated early knowledge with regard to SNPs that influence serotonin binding, drug metabolism, and drug transport proteins. The purpose of this review is to synthesize the current literature regarding genetic influence on CINV (see Table 1) and to explore the implications this has for nursing practice and research.

Serotonin Receptor Polymorphisms

The neurotransmitter serotonin binds to its associated receptor in the postsynapse of the peripheral and central nervous systems (Bayo et al., 2012). This receptor is made of five protein subunits, 5-HT_{3A-E}. Different combinations of protein subunits bind together to form a pentamer (Niesler et al., 2007). In theory, polymorphisms in any of the genes responsible for receptor proteins could affect that protein's function. In such a case, the pentameric serotonin receptor may become less responsive to serotonin antagonists, placing patients at higher risk for CINV.

From the sole study evaluating 5-HT_{3A} receptor proteins, 21 polymorphisms were identified (Kaiser et al., 2004). However, none of the altered proteins created any statistically significant effect on CINV. Findings from the four studies looking at 5-HT_{3B} were conflicting. One study found 13 polymorphisms