The Clinical Problem of Chemotherapy-Induced Nausea and Vomiting

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Beyond the current recommendations for management of chemotherapy-induced nausea and vomiting, recent research has shown significant improvement in emesis control with use of triplet therapy using dexamethasone, an NK1 receptor antagonist, and a 5-HT3 receptor antagonist in patients undergoing non-anthracycline-plus-cyclophosphamide-based moderately emetogenic chemotherapy.

Over the past 2 decades, substantial advances have been made in the management of chemotherapy-induced nausea and vomiting (CINV). This is primarily because of a deeper understanding of the molecular and physiologic pathways critical to CINV. The discovery of the 5-hydroxytryptamine type 3 (5-HT3) receptor and the subsequent development of 5-HT3 receptor antagonists (RAs) in the early 1990s represent significant progress in the treatment of the acute phase of CINV, with early studies showing improved outcomes when standard antiemetic therapy with dexamethasone was combined with the 5-HT3 RAs granisetron[1] or ondansetron.[2] Also, the discovery of the role of neurokinin-1 receptor antagonists (NK1 RAs) in the pathogenesis of the delayed phase of CINV have led to significant developments in the management of the emetogenic complication of anticancer treatment. Building on the benefits demonstrated with dual therapy using a corticosteroid plus a 5-HT3 RA, large phase III studies in the early 2000s showed further benefit from triplet regimens comprising the NK1 RA aprepitant given with dexamethasone plus the 5-HT3 RA ondansetron.[3,4] In their thorough review in this issue of ONCOLOGY, Drs. Nasir and Schwartzberg describe the evolution and optimization of treatment regimens for CINV, highlighting treatment-related, patient-related, and protocol-related factors that influence their effectiveness.[5]

As the authors note, although vomiting is fairly well managed with currently available antiemetic regimens, chemotherapy-induced nausea remains an unmet medical need, with oncology physicians and nurses often underestimating the magnitude of this clinical problem.[6] Despite the proper implementation of pharmacologic and nonpharmacologic methods of prevention, nausea remains a clinically significant side effect both for patients undergoing highly emetogenic chemotherapy (HEC) and those undergoing moderately emetogenic chemotherapy (MEC).[7] For many patients, nausea can have a devastating impact on quality of life and the ability to adhere to their selected chemotherapy treatment regimen.

Olanzapine is a promising agent for the management of chemotherapy-induced nausea. It is an antipsychotic thienobenzodiazepine whose antiemetic properties derive from its ability to target a variety of receptor types involved in CINV pathogenesis. These include dopaminergic receptors (D1, D2, D3, D4); serotonergic receptors (5-HT3 plus 5-HT receptor types 2A, 2C, and 6); and adrenergic (A1), histaminergic (H1), and muscarinic (M1, M2, M3, M4) receptors. Olanzapine has been shown to be beneficial in controlling CINV,[8-10] and may be particularly useful in the management of breakthrough CINV.[11]

Current Practice Guidelines and Recent Developments in the Management of CINV

As Drs. Nasir and Schwartzberg describe in detail, the NK1 RAs aprepitant, fosaprepitant, netupitant, and rolapitant enhance the effectiveness of the antiemetic combination of a corticosteroid and a 5-HT3 RA (ondansetron, granisetron, and palonosetron) in controlling both the acute and delayed phases of CINV. The Multinational Association of Supportive Care in Cancer/European Society for Medical Oncology,[12] the National Comprehensive Cancer Network,[13] and the American Society of Clinical Oncology[14,15] have developed evidence-based guidelines for use of regimens incorporating these agents in the care of patients at risk of CINV. Because of the benefits reported in large randomized controlled trials, current guidelines recommend triplet therapy (an NK1 RA in
combination with a 5-HT3 RA and dexamethasone) as the preferred treatment for preventing CINV associated with anthracycline-plus-cyclophosphamide (AC)-based HEC and MEC.

Beyond the current recommendations for management of CINV, recent research has shown significant improvement in emesis control with use of triplet therapy using dexamethasone, an NK1 RA, and a 5-HT3 RA in patients undergoing non-AC-based MEC (particularly for carboplatin-based treatments).[16,17] Additionally, the use of an NK1 RA was associated with an improvement in CINV control in patients undergoing high-dose chemotherapy with stem cell support,[18-20] as well as patients undergoing multiple-day chemotherapy treatments.[21] These developments will be incorporated into clinical antiemetic guidelines by MASCC/ESMO, and will be available in late 2016 or 2017. As Drs. Nasir and Schwartzberg emphasize, adherence by healthcare providers to the current guidelines for management of CINV, along with consideration of relevant patient-specific and treatment-specific factors, is essential to the “best practice” care of cancer patients in this challenging clinical setting.

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References:


19. Svanberg A, Birgegård G. Addition of aprepitant (Emend®) to standard antiemetic regimen continued for 7 days after chemotherapy for stem cell transplantation provides significant reduction of vomiting.


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