



The Essentials of Chemotherapy-Induced Infusion Reactions

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Almost all systemic agents used in cancer therapy can cause infusion-related reactions. Hypersensitivity or infusion reactions to platinum compounds are acquired, whereas reactions to taxanes and monoclonal antibodies usually occur during the first few minutes of the first infusion. By understanding the symptoms and treatment of infusion reactions, healthcare team members can provide timely and appropriate treatment and positively impact patient care.

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Reactions related to infusions can occur from almost all of the systemic agents used to treat cancer. An infusion reaction can be defined as any unexpected reaction that is not explained by known drug toxicity. This article discusses the characteristics of reactions experienced with chemotherapy infusions, explains how to assess for risk factors to optimize prevention, and describes how to treat those reactions if they occur.

Mechanism of Infusion-Related Hypersensitivity

The mechanism by which infusion-related hypersensitivity reactions (HSRs) occur varies among agents (Lenz, 2007). Most reactions to chemotherapy agents are consistent with type 1 hypersensitivity, an allergic reaction to re-exposure to an antigen or allergen. These reactions are caused by the immunoglobulin (Ig) E-mediated release of histamines, leukotrienes, and prostaglandins (Ream & Tunison, 2001), which can result in urticaria, rash, angioedema, bronchospasm, and hypotension (Zanotti & Markman, 2001). HSRs to platinum compounds, such as carboplatin and oxaliplatin, generally are associated with type 1 IgE-mediated

hypersensitivity (Gowda, Goel, Berdzik, Leichman, & Javle, 2004). Chemotherapy drugs such as paclitaxel and docetaxel manifest reactions that are clinically similar to type 1 hypersensitivity; however, research indicates these reactions may actually be related to an immune effect or other mechanism (Lenz, 2007). Cremophor® EL (polyoxyethylated castor oil), found in paclitaxel (but not in docetaxel), also has been shown to induce histamine release and hypotension and may play a part in HSRs. The albumin-bound form of paclitaxel does not contain polyoxyethylated castor oil and has been associated with little to no incidence of severe HSRs (Gradishar, 2006). The exact mechanism responsible for infusion reactions to monoclonal antibodies is not known, but like the taxanes, these reactions are unlikely to be solely type 1 IgE-mediated HSRs (Lenz, 2007). Despite the different possible mechanisms underlying hypersensitivity, the associated clinical signs and symptoms overlap. Mild-to-moderate reactions (grades 1 and 2) are characterized by flushing, rash, fever, rigors, chills, dyspnea, and mild hypotension. Severe reactions (grades 3 and 4) are associated with bronchospasms and hypotension requiring treatment, cardiac dysfunction, anaphylaxis, and other symptoms (Lenz,

2007). Although many symptoms overlap, if a patient develops urticaria, repetitive cough, wheezing, and tightness in the throat, one should suspect anaphylaxis (Sampson et al., 2006).

The National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) is widely accepted throughout the oncology community as the standard classification and severity grading scale for adverse events in cancer therapy clinical trials and other clinical oncology settings. The CTCAE distinguishes between infusion-related reactions and acute infusion reactions induced by cytokine release (National Cancer Institute Cancer Therapy Evaluation Program, 2010) (see Table 1).

Depending on the agent, hypersensitivity may be seen almost immediately on exposure, or may occur after repeated exposures. Reactions to platinum drugs (e.g., cisplatin, oxaliplatin) usually occur after multiple treatments (Polyzos et al., 2001). Reactions caused by taxanes (e.g., paclitaxel, docetaxel) usually occur within the first hour of the first or second treatment (Zanotti & Markman, 2001). Although rare with most chemotherapy agents, anaphylaxis can be seen with platinum drugs and taxanes. The most common signs and symptoms of anaphylaxis are

- Cutaneous: flushing, itching, hives, angioedema (usually of face, eyelids, or lips)
- Respiratory: cough, sudden nasal congestion, shortness of breath, wheezing, throat tightening, change in voice quality, hypoxia
- Cardiovascular: faintness, tachycardia or bradycardia, hypotension, loss of consciousness
- Gastrointestinal: nausea, vomiting, abdominal cramping, diarrhea
- Neurologic: sense of doom, tunnel vision, dizziness, seizure.

Reactions to monoclonal antibodies such as rituximab and cetuximab usually