Hypersensitivity Reactions

Priming practice change to reduce incidence in first-dose rituximab treatment

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BACKGROUND: Strategies to reduce hypersensitivity reaction (HSR) incidence with rituximab include premedications and slow titration. Literature is lacking on the priming method used when preparing rituximab IV lines and the potential impact on HSR incidence.

OBJECTIVES: The primary objective is to evaluate HSR incidence in titrated first-dose rituximab infusions when priming IV lines with rituximab, as compared to priming with diluent.

METHODS: A retrospective, comparative, descriptive study with two arms (rituximab- versus diluent-primed) was conducted. Variables were HSR incidence in relation to priming method, age, sex, diagnosis, and premedications. For patients with HSR, severity, time to onset, and infusion rate were examined.

FINDINGS: HSR incidence was significantly higher in the diluent- versus the drug-primed arm. Other significant findings included higher HSR incidence in women and lower HSR incidence in patients premedicated with dexamethasone.

KEYWORDS
rituximab; cytokine release syndrome; priming; hypersensitivity reaction; IV lines

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RITUXIMAB (RITUXAN®) IS A WIDELY USED chimeric murine/human monoclonal antibody (MAB) and is the cornerstone of recommended treatment for B-cell lymphoid malignancies, including chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), and primary central nervous system lymphoma (PCNSL) (National Comprehensive Cancer Network [NCCN], 2014, 2018a, 2018b; Plosker & Figgitt, 2003). Rituximab is administered weekly or intermittently in combination with chemotherapy regimens, or as part of a single-agent maintenance schedule, depending on indication. Rituximab kills cancer cells through direct signaling against CD20 antigens, complement-dependent cellular cytotoxicity, and antibody-dependent cellular cytotoxicity (Weiner, 2010). Similar to other MABs, rituximab has a high potential for hypersensitivity reactions (HSRs); symptoms vary from mild to life threatening (Chung, 2008).

HSRs with MAB treatment are attributed to cytokine release syndrome because of their mechanism of targeting immune system antigens such as CD20 (Chung, 2008; Gobel, 2007). As tumor antigen-expressing cells are destroyed, cytokines, such as tumor necrosis factor, interleukin, and interferon, are released into the blood (Breslin, 2007; Chung, 2008; Gobel, 2007). Rising blood levels of cytokines can trigger symptoms similar to those observed with a natural inflammatory response and can include fever, chills, rigors, rash, headache, hypotension, shortness of breath, bronchospasm, nausea, vomiting, and abdominal pain (Breslin, 2007; Chung, 2008; Gobel, 2007).

Genentech (2016), the manufacturer of rituximab, reported a 77% incidence of HSR with the initial dose based on data from 2,783 patients treated with rituximab in its original studies. The highest percentage of targeted cells are destroyed with this first dose, resulting in a decreased tumor burden and less cytokine release with subsequent infusions and, therefore, a reduced incidence of HSR (Breslin, 2007).

Colwell et al. (2007) studied the impact of infusion reactions on patients, their caregivers, and the healthcare providers treating the patients. In a survey of 202 oncology nurses, Colwell et al. (2007) reported that infusion reactions were most common in patients receiving rituximab and were extremely or very disruptive to patients, caregivers, and nurses. Other findings were that HSRs