Asparaginase Toxicities

Identification and management in patients with acute lymphoblastic leukemia

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BACKGROUND: Acute lymphoblastic leukemia (ALL) is a common cancer in children, and outcomes have greatly improved because of the refinement of multiagent chemotherapy regimens that include intensified asparaginase therapy. Asparaginase, a cornerstone of modern pediatric chemotherapy regimens for ALL and asparaginase-containing protocols, is increasingly used in adolescent and adult patients historically treated with asparaginase-free regimens.

OBJECTIVES: This article is an overview of commonly encountered asparaginase-associated toxicities and offers recommendations for treatment management.

METHODS: A literature review was conducted, reviewing asparaginase and common toxicities, specifically hypersensitivity, pancreatitis, thrombosis, hyperbilirubinemia, and hyperglycemia.

FINDINGS: The rapid identification and management of common asparaginase-associated adverse events can reduce symptom severity and limit potential interruptions to therapy, possibly improving outcomes.

KEYWORDS
acute lymphoblastic leukemia; toxicities; asparaginase; hypersensitivity

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ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IS THE MOST COMMON CANCER in children aged 1–16 years (Leukemia and Lymphoma Society, 2015). Among all age groups, 5,970 patients were expected to be diagnosed with ALL in 2016 (American Cancer Society, 2017). Although ALL is less prevalent in adulthood, improvements in the survival rates for older patients with ALL have historically lagged behind those of children (Pulte, Gondos, & Brenner, 2009). Outcomes for children diagnosed with ALL have steadily improved, with the current overall survival (OS) greater than 90% (Hunger & Mullighan, 2015). Survival of adult patients is markedly lower, with five-year OS less than 50% (Stock et al., 2011). Clinical evidence suggests that the use of pediatric-like chemotherapy regimens in adolescents and young adults (AYAs) is associated with increased survival compared to traditional adult regimens in the same population (Boissel et al., 2003; Huguet et al., 2009; Stock et al., 2014). Differences exist between adult and pediatric treatment protocols, one of which is the greater cumulative doses of asparaginase used in the pediatric protocols compared to traditional adult regimens, which often omit asparaginase entirely because of its perceived toxicity in older adults.

The inclusion of intense asparaginase therapy is important in improving outcomes in pediatric and adult patients with ALL (Douer, 2008). To ensure optimal antileukemic effect, it is critical that patients receive continuous asparaginase treatment and complete their entire scheduled therapy (Silverman et al., 2001). Adverse events (AEs), such as hypersensitivity, pancreatitis, venous thromboembolic events (VTEs), hyperbilirubinemia, and hyperglycemia, are common reasons for treatment interruption or the discontinuation of asparaginase altogether (Raetz & Salzer, 2010; Shinnick, Browning, & Koontz, 2013; Stock et al., 2011). Rapid identification and management of these common asparaginase-associated AEs are crucial to patient response to therapy (Burke, 2014; Raetz & Salzer, 2010). Asparaginase-associated AEs have been addressed in several other reviews (Hijiya & van der Sluis, 2016; Koprivnikar, McCloskey, & Faderl, 2017; Raetz & Salzer, 2010; Shinnick et al., 2013; Stock et al., 2011; Tripp, 2011).

The goal of this review is to educate oncology nurses on asparaginase therapy and common dose-limiting AEs. An emphasis will be placed on