Cardiac Toxicity

Using angiotensin-converting enzyme inhibitors to prevent anthracycline-induced left ventricular dysfunction and cardiomyopathy

Catherine Andrea Kobza, MSN, AGACNP-BC, CCRN

BACKGROUND: Anthracycline chemotherapies are effective in many different types of cancer. However, cumulative doses are associated with irreversible cardiac toxicity, most frequently manifested in the development of left ventricular dysfunction, cardiomyopathy, and congestive heart failure. The onset of cardiomyopathy and subsequent heart failure can result in the interruption or discontinuation of therapy. Cardioprotective agents, particularly angiotensin-converting enzyme inhibitors, have been shown to slow the progression of left ventricular dysfunction and prevent heart failure.

OBJECTIVES: This review assesses the efficacy of angiotensin-converting enzyme inhibitors in the prevention of anthracycline-induced left ventricular dysfunction.

METHODS: A literature search was performed using four electronic databases: PubMed®, Scopus, Cochrane Library, and Ovid®. Five relevant articles are included in this review.

FINDINGS: Evidence from this review suggests that angiotensin-converting enzyme inhibitors may be effective in preventing or reducing anthracycline-induced left ventricular dysfunction and subsequent cardiomyopathy and heart failure.

KEYWORDS
anthracycline-induced cardiotoxicity; left ventricular dysfunction; enzyme inhibitors

DIGITAL OBJECT IDENTIFIER
10.1188/21.CJON.259-266

CONTINUED ADVANCES IN CANCER TREATMENTS have resulted in improved patient survival. As a result, long-term treatment-related toxicities have become of greater concern for both providers and cancer survivors (Abdel-Rahman & Alorebi, 2015). One notable long-term toxicity is cardiac toxicity, with cardiovascular disease becoming a leading cause of morbidity and mortality among cancer survivors (Cadeddu et al., 2016). The cardiotoxic side effects of several anticancer agents, including anthracyclines, human epidermal growth factor receptor 2 (HER2)–targeted agents, and tyrosine kinase inhibitors, limit their ability to be safely used (Abdel-Rahman & Alorebi, 2015; Colombo et al., 2013; Tan et al., 2015). Anthracycline cardiac toxicities present in a wide range of clinical conditions, including cardiac ischemia, arrhythmias, pericarditis, and, most commonly, left ventricular dysfunction (LVD) (Abdel-Rahman & Alorebi, 2015).

Anthracyclines, such as daunorubicin, doxorubicin, epirubicin, and idarubicin, are some of the oldest anticancer therapies in use today (Bernstein, 2018) (see Figure 1). They are used in the treatment of a wide range of malignancies, including carcinomas, leukemias, lymphomas, and sarcomas (Henriksen, 2017). They effectively target cancer cells through several mechanisms (Bernstein, 2018; Tan et al., 2015). However, with their widespread use, the occurrence of cardiac toxicities, specifically LVD, has become more common. LVD can be defined as a greater than 10% reduction in left ventricular ejection fraction (LVEF) (Tan et al., 2015). Clinically, this decline in LV function ranges from asymptomatic to symptomatic heart failure (Henriksen, 2017). LVD can be assessed by LVEF (Yancy et al., 2013). Normal LVEF is between 50% and 70%, an LVEF from 41% to 49% is considered borderline, and an LVEF of 40% or lower may be evidence of heart failure (Yancy et al., 2013).

Anthracycline-induced cardiotoxicity (AICT) is a broad term encompassing multiple clinically significant manifestations. Proposed AICT mechanisms include oxidative stress, apoptosis, and toxic effects on cardiac muscle development (Tan et al., 2015). Topoisomerase-2 has been implicated as the main facilitator of AICT (McGowan et al., 2017). In particular, LVD has become a well-recognized specific type of AICT. Several studies have detailed the specific pathologic changes associated with anthracycline-induced LVD (AI-LVD), with cardiac biopsies demonstrating myocardial fibrosis, leading to myocardial remodeling, a reduction in LV mass, and dilation of the left ventricle (Tan et al., 2015).

AI-LVD can be separated into three distinct phases: (a) acute (occurring during fewer than 150 days since starting treatment), (b) early (occurring