Background: *Clostridium difficile* infection (CDI) is common among hospitalized patients and is particularly serious in patients with cancer. Acid suppression therapy, particularly that which uses proton pump inhibitors (PPIs), has been shown to place hospitalized adult patients at greater risk for CDI, but this relationship has not been proven among patients with cancer.

Objectives: This review assesses risk factors for CDI among patients with cancer, with a specific focus on acid suppression therapy using PPIs and histamine-2 receptor antagonists (H2RAs).

Methods: A literature search was performed using four electronic databases: CINAHL®, Embase®, MEDLINE®, and PubMed®. Six articles were deemed relevant and included in this review.

Findings: CDI increases morbidity and mortality in patients with cancer and interferes with their active treatment plans. PPIs and H2RAs increase the risk of developing CDI among patients with cancer, but PPIs carry a higher risk. Other risk factors include antibiotics, transplantation, and chemotherapy.

Keywords: *Clostridium difficile* infection; acid suppression therapy; PPIs; H2RAs; prevention

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