Histamine Type 2 Receptor Antagonists as Adjuvant Treatment for Resected Colorectal Cancer

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Objective

To assess whether histamine type 2 receptor antagonists (H₂RAs) improve overall survival when used as pre-, peri-, or postoperative therapy in patients with colorectal cancer who had surgical resection with curative intent.

Type of Review

A review of six randomized, controlled trials (RCTs) to assess the outcome of an intervention on overall survival.

Relevance for Nursing

Colorectal cancer is the third most commonly diagnosed cancer in the world. Surgical resection is the main treatment strategy for colorectal cancer; however, chances of postsurgical relapse exist because of the undetected spread of cancer cells from the primary tumor to other tissues. In general, metastatic colorectal cancer is not curable. Therefore, adjuvant therapies that target remaining cancer cells are administered around the time of surgery to improve patient outcomes.

H₂RAs, including ranitidine and cimetidine, bind to cognate H₂ receptors and block the action of histamine. H₂RAs block H₂ receptors that also are present on other cells types, mediating processes that have been investigated for their anticancer effects. Histamine acts as a growth factor for some gastrointestinal cancer cell lines, and inhibition of histamine activity through H₂RAs has been shown to reduce colon cancer cell proliferation. H₂RAs also have immunologic effects that collectively act to increase immune function. In addition, cimetidine has been shown to inhibit adhesion of metastatic cancer cells to healthy endothelial cells in a dose-dependent manner. Therefore, H₂RAs, particularly cimetidine, may be suitable for use as adjuvant therapies delivered around the time of surgery to simultaneously stimulate patients’ immune function, reduce cancer cell proliferation and spread, and potentially improve patients’ outcomes. A systematic review of the effect of H₂RA use as an adjuvant therapy for the treatment of colorectal cancer was warranted.

Summary of Key Evidence

The results of the meta-analysis showed an overall trend of improved patient survival with H₂RA use around the time of surgery; however, the effect was not statistically significant when all six studies were combined. The largest trial (N = 560) included in the meta-analysis used ranitidine and showed the least effect on overall survival. The other five studies (N = 421) investigated the effect of cimetidine and demonstrated a statistically significant increase in overall survival with the use of cimetidine as an adjuvant therapy for the treatment of nonmetastatic colorectal cancer (hazard ratio = 0.53; 95% confidence intervals [0.32, 0.87]).