Nursing Management of Epidermal Growth Factor Receptor Inhibitor–Induced Toxicities

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New drug technologies can pose a challenge for nurses, whether it is by educating patients about potential side effects or by helping them deal with sequelae for which there has been little research. Epidermal growth factor receptor (EGFR) inhibitors are new, targeted cancer therapies that are being prescribed with more frequency. Common side effects of EGFR inhibitors include skin rash and diarrhea. An outline of the typical manifestations of EGFR-inhibitor side effects and how nurses can participate in their management to maximize quality of life and treatment adherence follows. Managing side effects is critical to improving tolerance, and failure to manage side effects can lead to treatment cessation. Patient education prior to treatment initiation, as well as ongoing support, is essential to maintaining adequate control of side effects.

EGFR over-expression has been linked to the conversion of normal cells to malignant cells (Toffoli et al., 2007). The identification of epidermal growth factor (EGF) as important in the growth, angiogenesis, anti-apoptosis, and metastasis of some tumor types has resulted in the development of cancer therapies that target EGF receptors. A number of EGFR inhibitors currently are being used, including erlotinib, cetuximab, panitumumab, and gefitinib.

EGFR inhibitors work by interrupting the pathway that uses EGF to promote tumor growth and metastasis. One mechanism is tyrosine kinase inhibition, in which the drug binds to the EGFR's intracellular tyrosine kinase and blocks adenosine triphosphate from using the same receptors for malignant cell processes (Dick & Crawford, 2005). Monoclonal antibodies, another approach to EGFR inhibition, block the extracellular component of the receptor, interrupting downstream signaling (Lynch et al., 2007). Malignant cells, which rely on EGF for survival, are particularly vulnerable; growth is arrested and apoptosis occurs when EGFR is inhibited (Lacouture, 2006).

EGFR inhibitors target receptors specifically found in cancer cells and normal epidermal cells. The target specificity of the drugs also is the reason that there tend to be fewer systemic side effects than in common chemotherapy drugs (Lacouture, 2006). The side effects that do occur are a result of the interruption in EGFR in normal cells, which rely on it for development and function, such as stratified squamous epithelium. EGFR is expressed in the undifferentiated keratinocytes of the basal layer of the epidermis and is lost as cells in the layer progress outward and differentiate into cells that ultimately form the stratum corneum, or outermost skin layer (Lacouture). EGFR inhibitors bind to the receptors on the surface of the normal cells in the skin and lining of the digestive tract. When the normal pathway is interrupted by an EGFR inhibitor, several different mechanisms occur to interfere with keratinocyte growth and survival, cell differentiation, attachment, and migration of cells from basal to stratum corneum. This interruption results in inflammation and xerosis, or dryness of the skin. In time, this hyperkeratosis causes a folliculitis, which progresses to a papulopustular rash (Wyatt, Leonard, & Sachs, 2006) that usually occurs on the sebhorreic areas, such as the face, arms, and upper trunk (Segaert & Van Cutsem, 2005). Inflammatory reactions and sensitivity to ultraviolet radiation exposure increase in the presence of EGFR inhibitors. Skin reactions often are worse on sun-exposed areas, such as the face, upper chest and back, and dorsal arms. Inflammation in the gastrointestinal tract results in diarrhea.

Complex Management

The pathophysiology and management of EGFR inhibitor–induced skin reactions is complex, and a number of different treatment approaches have been suggested. A recent consensus has been developed on what currently is termed "best practice" to treat these rashes because no randomized studies have been conducted to date (Eaby, Culkin, & Lacouture, 2008). Suggested treatments include antiinflammatory therapy for lower-grade reactions, clindamycin gel and tetracycline for moderate to severe cases (Eaby et al.; Segaert & Van Cutsem, 2005), topical vitamin K (Perez-Soler, Zou, Li, Tornos, & Ling, 2006) and topical corticosteroids, antibiotics, and oral corticosteroids (Eaby et al.; Perez-Soler, 2004). Of note, it has been shown in two large trials that the severity of side effects (particularly rash) experienced with EGFR-inhibitor therapy positively correlates with the effectiveness of the

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