Assessment and Management of Gastrointestinal Toxicities and Lab Abnormalities Related to Targeted Therapy

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Objectives: *To identify the most common gastrointestinal toxicities and laboratory abnormalities associated with targeted therapies, as well as the assessment and management necessary to minimize adverse events related to these side effects.*

Data Sources: *Peer-reviewed articles and national guidelines for oncology practice.*

Conclusion: *Common toxicities of diarrhea, mucositis, and laboratory abnormalities are often associated with the use of targeted agents and require skilled assessment and early management interventions to prevent severe complications or treatment interruption.*

Implications for Nursing Practice: *Emerging trends focused on targeted therapy increase the importance of the oncology nurse's role in assessment, education, and evidenced-based recommendations to meet patient needs.*

Key Words: *Targeted therapy, toxicity, gastrointestinal, management, laboratory abnormalities*

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THE definition of targeted therapies, as well as the associated toxicity profile, has expanded significantly in the almost 40 years since tamoxifen was approved. Targeted agents are often marketed to both patients and health care providers as having a milder side effect profile than traditional chemotherapeutic agents.[1] However, monoclonal antibodies (MoAbs) and small-molecule drugs can lead to higher incidences of toxicities in the gastrointestinal (GI) tract, liver, and kidneys such as diarrhea, mucositis, and hepatotoxicity, which can lead to lab abnormalities (Table 1).[1-4]

The severity and incidence of these toxicities vary based on the mechanism of action of the agent in question,[2] and have the potential to not only be dose-limiting but severe enough to cause altered nutritional status, fluid-electrolyte imbalances, dehydration, and infection.[5] Early intervention and appropriate management is essential to minimize dose interruption, life-threatening adverse events, and to maintain patient compliance with targeted therapies.[6,7]

PATHOPHYSIOLOGY

GI Toxicities

Targeted therapies in cancer treatment impact numerous cellular pathways, including two main growth proteins responsible for cell proliferation and angiogenesis, epidermal growth factor receptor (EGFR) and vascular epidermal growth factor (VEGF). Another difference is that MoAbs may be more specific in selecting for their targets and, as a result, can have less severe side effects then small-molecule drugs, like the tyrosine kinase inhibitors (TKIs).[1,2,8] Many commonly used US Food and Drug Administration-approved drugs fall into one of these two categories and are directly linked to toxicities of the GI tract.[1,2]

TABLE 1.
Common Toxicities From Targeted Therapy[1-8]

Toxicity	Commonly Associated Agent	
Diarrhea*	Erlotinib	Gefitinib
	Lapatinib	Imatinib
	Dasatinib	Sorafenib
	Bortezomib	Cetuximab
Mucositis	Everolimus	Sunitinib
	Cetuximab	Gefitinib
	Erlotinib	
Hepatotoxicity	Imatinib	Sunitinib
	Lapatinib	Sorafenib
	Nilotinib	Erlotinib
Pancreatic enzyme elevations (hyperlipasemia and hyperamylasemia)	Sunitinib	Sorafenib
	Lapatinib	
Hypomagnesemia	Cetuximab	Panitumumab

*Incidence of toxicity for the listed agents is >30%.

There is no single pathophysiology of the GI toxicities associated with targeted agents.[6] Instead there are varying hypotheses extrapolated from known mechanisms of the targeted receptors in normal tissue. Three primary hypotheses are the most understood and supported by the literature. The first being that GI toxicity is a result of altering EGF, which is responsible for maintaining mucosal integrity, repair of the epithelium, and mucin production in the GI tract.[1,2] Diarrhea in particular is thought to be associated with a localized effect of the oral agents on the GI tract because toxicity severity is directly proportional to dose but not serum concentration.[2,8] Additionally, EGF is known to decrease chloride secretion in the bowel, resulting in increased secretory diarrhea when the regulating mechanism is altered by EGF inhibition.[6,8] Finally, some data has been shown to link mTOR inhibition with atrophy of the mucosal villi and changes in the normal microflora of the intestines, thereby altering absorption and resulting in diarrhea. Small-molecule drugs in the mTOR inhibitor category are known to have immunosuppressive properties as well, which could be linked to the changes of microflora in the intestines and mucositis development.[6,9]

Additionally the incidence and severity of these toxicities can be greatly increased when given in combination with other targeted agents or with chemotherapy. This is thought to be caused by a dual impact of the above described mechanisms in combination with the direct effects of tissue damage from chemotherapy on the rapidly dividing cells of the GI epithelium.[1,3]

Laboratory Abnormalities

Multiple laboratory abnormalities may occur as a result of targeted therapies. Hepatotoxicity, pancreatic enzyme elevations (potentially leading to pancreatitis), and hypomagnesemia are among the most common. The pathophysiology of these toxicities varies, and like GI toxicities, is not conclusively known but extrapolated from knowledge of the drug