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Evidence-Based Guidelines for Preventing and Managing Side Effects of Multiple Myeloma

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Objective: *To review disease-related symptoms and side effects of treatment in patients with multiple myeloma (MM).*

Data Sources: *Peer-reviewed articles, research studies, and clinical guidelines.*

Conclusion: *New therapies provide patients with extended survival, but in many cases this benefit is counterbalanced by an increased incidence of side effects. Preservation of organ function, while managing side effects, is essential for the care of patients with MM.*

Implications for Nursing Practice: *Disease- and treatment-related adverse events are prevalent in patients with MM. Patient, family, and health care professional education is essential to monitor and manage these side effects.*

Key Words: *side effects, symptom management, multiple myeloma.*

It is well known that a majority of patients with multiple myeloma (MM) will have some evidence of organ damage at the time of diagnosis. Plasma cell–directed, anti-myeloma treatments are aimed at preventing further organ impairment.[1] Common drugs used to treat MM, such as proteasome inhibitors, immunomodulatory drugs, histone deacetylase inhibitors, alkylating agents, and

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monoclonal antibodies, have been shown to prolong survival; however, the benefit has been counterbalanced by an increased risk of disease- and treatment-related side effects. This article reviews disease- and treatment-related side effects and provides an overview of nursing and medical interventions. Drugs to treat MM, their mechanisms of action, and detailed nursing interventions are discussed elsewhere in this issue of *Seminars.*[2,3] This review primarily focuses on the common signs and symptoms of MM at presentation and throughout the disease trajectory (eg, hypercalcemia, bone pain, renal insufficiency, anemia, and infection) and treatment-related adverse events (AEs), which include myelosuppression, venous thromboembolic events (VTE), peripheral neuropathy (PN), gastrointestinal (GI) issues, and cardiotoxicity.

Disease-Related Symptoms

Hypercalcemia and Bone Disease

Hypercalcemia and bone disease are common presenting features of a MM diagnosis. Bone destruction leads to osteolytic lesions, pathological fractures, spinal cord compression, hypercalcemia, and bone pain.[4] Osteolytic bone lesions occur via many mechanisms, but are primarily due to an imbalance between osteoblasts (responsible for bone formation), and osteoclasts (which cause increased bone resorption) and a two-way interaction between the tumor cells and bone marrow microenvironment, leading to release of cytokines, which dissolve bone. As calcium escapes the bone, elevated serum calcium levels will result.[5] Thus, it is recommended to screen all patients with MM for the presence of osteolytic lesions with a whole-body, metastatic skeletal survey magnetic resonance imaging (MRI) or positron emission tomography (PET)/computed tomography (CT) scans as appropriate.[6-8]

Skeletal fractures can lead to increased morbidity and mortality among patients. Consensus guidelines recommend the use of bisphosphonates such as zoledronic acid or pamidronate in all patients with MM to reduce the risk of skeletal-related events (SREs) or fractures[9-12] based on the result of randomized trials.[13,14] Denosumab is not currently indicated for prevention of SREs in patients with MM; however, results of a phase III study were recently released and submission to the US Food and Drug Administration (FDA) is pending.[4,15-17]

Nursing interventions to prevent SREs and optimize bone health in patients with MM include (1) monitoring for hypocalcemia and recommending supplementation with calcium and vitamin D either by diet or external supplementation, (2) educating on the importance of routine exercise, and (3) discussing fall precaution with those at risk for falls.[18] Furthermore, patients should be instructed on types of weight-bearing exercise, such as use of light weights (<5 pounds) and swimming to maintain strength with gentle load on the joints to minimize pain. However, patients should discuss specific recommendations for exercise and mobility with their provider before embarking on an exercise regimen.[18] Other interventions include periodic urinalysis to look for elevated urinary albumin, which can be a sign of renal tubular damage due to bisphosphonates, and skeletal surveys every 1–2 years or when patients develop new or worsening pain.[19,20]

Renal Insufficiency

Renal insufficiency (RI) is one of the most common symptoms on presentation and occurs in approximately 50% of patients during the disease trajectory.[21] The onset of RI can be attributed to multiple factors, which include comorbid conditions, advancing age, dehydration, or cumulative toxicity from the disease, but may also be secondary to cumulative toxic effects of kappa or lambda free light chains, which lead to tubular interstitial damage.[22,23] Large, dense tubular "casts" can precipitate in the distal tubules of the kidney, combining with a Tamm–Horsfall mucoprotein, which leads to cast formation, tubular obstruction, and tubular damage. The degree of RI (acute or chronic) is measured by an increased serum creatinine level, reduced glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2, and serum creatinine clearance <50 mL/min.[22,24] Temporary elevations in serum creatinine or a decline in GFR may be seen in patients experiencing acute dehydration as a result of fluid losses from vomiting, diarrhea, infection, or decreased oral fluid volume intake.[24]

Nurses can help minimize the risk of further renal injury by identifying patients at risk for RI, and by providing education to patients as to the importance of maintaining adequate hydration, and avoidance of nonsteroidal anti-inflammatory drugs and intravenous contrast dyes.[25] The National Kidney Foundation (NKF) identifies persons at increased risk for chronic kidney disease (CKD), including those with diabetes, cardiovascular disease, hypertension, and age >60.[26] It is important