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Pain Syndromes and Management in Adult Hematopoietic Stem Cell Transplantation

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KEYWORDS

Pain • Hematopoietic stem cell transplant • Opioids • Neuropathy

KEY POINTS

- Pain is a significant physical symptom in hematopoietic stem cell transplant (HSCT) patients that can be present across the HSCT spectrum of care.
- Common pain syndromes in HSCT patients include oral mucositis, bone pain, and chemotherapy-induced peripheral neuropathy.
- Unique considerations in HSCT patients require that pain management approaches be individualized.
- Utilization of early palliative care for pain and symptom management is recommended for HSCT patients.

INTRODUCTION

Hematopoietic stem cell transplant (HSCT) is a high-risk procedure focused on the possibility of cure in patients with otherwise incurable benign or malignant disorders. The indications for HSCT, as well as eligibility, vary, often due to patient factors, such as age, performance status, response to prior therapy, and disease status. Disease-specific prognostic factors, such as availability of a suitable graft source and time

Disclosures: J.D. Ma, A.R. El-Jawahri, and E.J. Roeland declare no relevant disclosures. T.W. LeB-lanc has received honoraria from Celgene, Pfizer, Helsinn Therapeutics, Medtronic, and Otsuka as well as research funding from Seattle Genetics.

Hematol Oncol Clin N Am ■ (2018) ■-■ https://doi.org/10.1016/j.hoc.2018.01.012 0889-8588/18/© 2018 Elsevier Inc. All rights reserved.

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to transplant are additional factors for consideration. Autologous HSCT is indicated to treat conditions, including, but not limited to, multiple myeloma, germ cell tumors, and some autoimmune disorders (eg, systemic lupus erythematosus). Allogeneic HSCT is used for patients with acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, myeloproliferative disorders, myelodysplastic syndromes, and other related diseases. Those with non-Hodgkin lymphoma, Hodgkin disease, and acute myeloid leukemia might receive either an autologous or allogeneic HSCT. According to the Worldwide Network for Blood and Marrow Transplantation, there has been a steady increase from 2006 to 2012 in the number of allogeneic and autologous transplants performed annually. Data from 2012 from 77 countries reported 68,146 HSCTs, with 36,220 autologous and 31,926 allogeneic transplants performed.

Despite the advances made in HSCT and improvements in overall survival, many patients experience physical symptoms and emotional distress that result in significant morbidity and decreased quality of life. In autologous HSCT patients, the incidence of physical symptoms of fatigue, pain, and insomnia can range from 8% to 55%. In allogeneic HSCT patients, 1 study reported an incidence of fatigue, pain, and insomnia ranging from 60% to 80%. Emotional distress is present in approximately 15% to 50% of HSCT patients and peaks prior to and immediately after transplant. In a pilot study of 61 patients who received HSCT, one-third of patients reported pain, impaired daily functioning associated with pain, and emotional distress. Although anxiety and depression were associated with functional impairment due to pain (r = 0.33–0.44, P<0.05), no such associations were observed with pain intensity (r = 0.21–0.27; P>0.05).

This review summarizes specific pain syndromes and management approaches in adult HSCT patients. General pain assessment in hematology and oncology patients is reviewed in Regina M. Fink and Jeannine M. Brant's article, "Complex Cancer Pain Assessment," in this issue. The HSCT-related pain syndromes that are discussed in this article include procedural pain, growth factor–induced bone pain, oral mucositis, chemotherapy-induced peripheral neuropathy (CIPN), and postherpetic neuralgia. Clinical approaches to the management of pain syndromes are discussed, highlighting relevant issues in adult HSCT patients. Pain management in the pediatric HSCT population is described elsewhere.^{8–10}

UNIQUE CONSIDERATIONS IN HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

In HSCT patients, the oral route may be limited due to oral mucositis and/or delirium. Commonly used neuropathic pain medications, such as pregabalin, gabapentin, and antidepressants, are exclusively formulated for oral administration. Furthermore, the rectal route of administration is frequently avoided due to concerns about bacterial translocation with rectal manipulation in the setting of neutropenia. Additionally, intestinal GVHD with severe diarrhea may limit drug absorption. Nonopioid adjuvant medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), may be contraindicated for HSCT patients, due to thrombocytopenia and renal compromise. Drug-drug interactions must be also be assessed, especially when considering methadone for patients receiving concomitant immunomodulatory or anti-infective agents (Table 1).

PERITRANSPLANTATION PAIN SYNDROMES Pain from Bone Marrow Biopsy and Aspiration

Bone marrow biopsy is a required procedure for diagnosis and staging of most hematologic malignancies. Patients typically lay prone or in the lateral decubitus position,

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