

Review

The WHO, HOW and WHEN of Palliative Care in the Hematopoietic Stem Cell Transplant Setting

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Abstract

Palliative care is directed towards symptom control for patients suffering with any terminal illness including cancer. An integral part of this is end of life care. Hematopoietic Cell Transplant (HCT) is associated with a curative intent especially in the allogeneic setting and palliative care discussions are often tricky in these situations. An important aspect is recognizing patient's and appropriate timing to yield the best results. Early palliative care consultation is now considered standard of care in patients with advanced cancer, especially those undergoing a high-risk transplant. This was associated with improved mood, sense of hope, decreased levels of anxiety during HCT which was sustained for a few months post-transplant. Late involvement of the palliative care team during the terminal phase of illness is associated with higher symptom burden on patients and their families. There are certain identifiers that serve as a guide for palliative care intervention in patients with hematological malignancies or those undergoing a HCT. These may be patient or caregiver, disease or treatment related or psychosocial. An important and overlooked side effect that needs to be addressed is depression and

Posttraumatic Stress Disorder (PTSD). To avoid this there should be a shift towards transitioning care to an outpatient setting as soon as safely possible. Advanced care planning is an important aspect of palliative care and the knowledge of its impact in the HCT setting is limited. Lack of completion of such, was associated with a high risk of death and ICU utilization within 14- and 30-days post-transplant, specifically in the case of an allogeneic HCT. There are many barriers identified for the underutilization of this service in the HCT setting with the most important one being the overly optimistic attitude of the HCT physician treating patients undergoing high-risk transplants. To understand this further a HCT physician-based survey revealed that >80% physicians felt that a palliative care consult was associated with a 'giving up' attitude. However, there is now growing awareness of this misconception and efforts are being made to bridge this gap in understanding and knowledge.

Keywords: Comfort care in BMT; HCT; Hospice in BMT; Palliative care; Symptom management

Introduction

The ultimate aim of palliative care in patients with cancer is to decrease the suffering associated with their disease and in return provide them with better Quality of Life (QOL) Hospice is an essential part but not synonymous to palliative care, which is an important difference, and understanding of the same is increasing amongst patients and providers [1]. As the average life expectancy is rising, the proportion of patients with cancer is increasing. Given advancements in detection and treatment of cancer, patients are living longer with symptoms secondary to their disease or side effects from treatment. Addressing these symptoms is of utmost importance in maintaining good QOL and in some cases providing a survival benefits [2].

Palliative care discussions in patients receiving a Hematopoietic Cell Transplant (HCT) are often challenging as this is potentially a curative option for many malignant and non-malignant diseases. The total number of hct is increasing and so is the average age of such candidates. In 2016, >50% of autologous and 30% of allogeneic transplants were in patients >60 years of age [3]. This is possible given improvement in supportive care measures such as better anti emetics and antibiotics to name a few.

Adult HCT, specifically of allogeneic type, is associated with high risk of Graft versus Host Disease (GvHD), reported incidence of chronic GvHD ~40-50%, amongst other complications such as infections, graft failure, late treatment toxicities which can ultimately lead to increased morbidity and mortality [4]. It is in these situations there is a known benefit in addressing the patient's physical symptoms, emotional requirements and psychosocial needs which are essentially the core components of palliative care. Another key role is providing caregiver support, as they always remain underserved. Despite these benefits, their expertise is highly underutilized. In this article we will discuss the importance of an integrated team approach with palliative care and answer a few essential questions.

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WHEN to Consult Palliative Care?

Palliative care has different roles during the disease and treatment trajectory, with the ultimate goal being comfort. Understanding that, consulting palliative care anytime during the disease course is appropriate. Most recently established standard of care is an early consultation especially in the advanced stages of solid malignancies and this was evaluated in the HCT setting as well [5,6].

Traditionally, palliative care is consulted during the terminal phase of disease or treatment, to discuss grave prognosis and end of life care. This is changing. Pre-transplant consultation, in an outpatient setting, for those undergoing a high risk HCT (Hematologic Cell Transplantation-Comorbidity Index (HCT-CI) of 3 or higher, relapse risk >25%, or mismatched donor transplant) was evaluated. This was associated with improved patient outcomes such as mood and sense of hope along with better coping skills during the whole transplant process and 3 months post-transplant [7]. In one of the first ever reported randomized trial involving 160 HCT patients, 81 received early post-transplant intervention with twice weekly palliative care visits, whereas the other group of 79 received palliative care only if consulted. The intervention group had a smaller QOL loss from baseline at 2 weeks ($p=0.045$) and improved control of symptoms and mood with lesser anxiety. This benefit was also seen 3 months post-transplant with higher QOL and lesser depressive symptoms [8].

A decrease in QOL and increased symptoms of depression while admitted for HCT are important predictors of 6-month QOL, hence these need to be managed appropriately [9]. Another study assessing early palliative care starting with the first interaction of the HCT team and any subsequent admissions was associated with a feeling of better preparedness for transplant. This helped alleviate anxiety with improved symptoms [10].

Based on recent CIBMTR data (Center of International Bone and Marrow Transplant Research) the most common cause of death in a patient after an autologous transplant is disease relapse (69%). The 3 year mortality after a matched related and matched unrelated donor transplant is 58% and 47% respectively [3]. It is at these times patients and their families require additional support. A study looked at this exact scenario and reported that a delay in integration of palliative care and end of life discussions towards the terminal phase of illness leads to a higher symptom burden on both the patient and their families. This is an important gap that needs to be filled [11].

WHO is the Right Candidate?

There are certain identifiers that may serve as a guide for palliative care intervention in patients with hematological malignancies or those undergoing a HCT. These may be patient or caregiver, disease or treatment related or psychosocial. Such triggers were reported by Leblanc et al., and are: HCT patients at the time of hospitalization or at the time of development of GvHD, high symptom burden either chronically or acutely related to treatment (iatrogenic symptoms), patients or families having difficulty coping financially or emotionally with illness or at end of life [12,13]. In a small pilot study, high levels of pre transplant distress (anxiety and depression) was highly predictive of post-transplant distress ($p<0.0001$) [14]. There are many scales that can help providers understand patient's symptom burden such as the Edmonton symptom assessment scale, NCCN distress thermometer, FACT-BMT [15,16]. These can be utilized with the understanding

that not all were validated in HCT patients. NCCN has also set forth guidelines which are patient and caregiver focused [16].

HOW Can Palliative Care Help?

Symptom management with a team approach

Majority of the symptoms that require management arise from toxicity secondary to chemotherapy or complications from HCT. Given that these are iatrogenic, there is a need to reverse these symptoms aggressively. Guidelines to manage these have been put forth by multiple organizations such as NCCN, ASH, ASCO though they are not specific to HCT patients. In this section we will discuss the often-overlooked symptoms in HCT and their non-pharmacological management.

One such important and often overlooked side effect that plagues this population is depression and Posttraumatic Stress Disorder (PTSD). Increase in depression and decline in QOL during hospitalization are important predictors for developing PTSD at 6 months [9]. To avoid this there should be a shift towards transitioning care to an outpatient setting as soon as safely possible. To make this successful a team approach is prudent, which requires assistance from physical and occupational therapy, home health services, dietary services, spiritual care and palliative care [17,18]. There is also decreased hospitalizations, ICU transfers and better caregiver bereavement with such an integrated approach [19,20].

There are multiple non pharmacological ways to allow for symptom control such as yoga, music therapy, cancer rehabilitation program, meditation and spiritual care [18,21-25]. Management of symptoms may require only short term interventions but may transition into long term based on their disease course. In one of its kind studies that looked at benefit of physical therapy and exercise done before, during and after high dose chemotherapy and HCT, reported an improved sense of physical and psychological well-being as well as quicker rehabilitation [26]. Again to make this successful a team approach is prudent [17].

Advance care planning for HCT

Dying with dignity and as per the patient's wish is the sole purpose of Advance Care Planning (ACP). These wishes address end of life care such as, extent of aggressive measures like ICU admission, mechanical ventilation, artificial nutrition etc. ACP has shown to have a positive impact with decreasing hospitalizations and use of life-sustaining treatment and increasing the use of hospice and palliative care services. Patients that utilized ACP were more likely to die outside the hospital and with hospice services, on their own terms [27,28].

There is limited data regarding the use of ACP and its outcomes in the HCT setting. Studies report only about 50% of patients undergoing HCT had advance directives either discussed with the clinician, family member or documented in the chart. Lack of completion of such, was associated with a high overall risk of death and higher ICU utilization within 14 and 30 days post-transplant, specifically in the setting of allogeneic transplant [29,30]. Some of the barriers identified in the utilization of ACP were age (high intensity end of life care for pediatric and young adults whereas higher use of ACP with older age), race/ethnicity (higher ACP in whites and less common in Asians and Hispanics), lack of communication between physician and patient/family regarding outcomes during illness and lack of time to address these during clinic visits [31].

Models for delivering palliative care

There are multiple models suggested for the integration of palliative care in the 'HCT' team. These are usually utilized differently at different centers based on availability of resources. One such model is discussed here as suggested by Levine et al. The Traditional model refers to consulting palliative care based on the primary team decision. This is the most conservative approach and is shown to be associated with a worse prognosis on survival. Palliative care is involved late in the treatment course. The Trigger based model is common and identifies patients that will benefit the most based on certain triggers (1st or 2nd transplant, relapsed disease, high symptom burden etc). This allows for best utilization of resources. Universal Tiered model is when patients have a first consult before HCT and then subsequently based on a 'need basis'. Identification of such patients is via screening consults. Finally, the universal model which is more liberal and all HCT patients receive a palliative consult before transplant with regular follow up. This is most resource intensive, but all patients were shown to benefit [32].

Ability to deliver palliative care services varies based on centers. There is a growing shortage of palliative care specialists worldwide, though this gap is shrinking [33,34]. Hence, frequently the onus for symptom management falls on the patient's primary team. This would constitute as Primary palliative care. Secondary palliative care is when the primary team is provided with input from the palliative care specialists for symptom management. Final decisions are made by the primary team. This can be utilized in the inpatient or outpatient setting and is the most commonly used mode of delivery. Tertiary palliative care is when the palliative care team manages complex symptoms such as pain, palliative sedation etc requiring high skill [35]. Quaternary palliative care is when the palliative care team assumes all care for the patient, usually seen in the end of life/ terminal phase of disease [36]. HCT patients are usually managed with a mix-match of these services during their treatment course providing them with additional support when needed.

Barriers

HCT is a complex and long process starting from donor identification and disease control and may take months, especially in the allogeneic setting. During this period patients' physical symptoms, spiritual and emotional requirements, psychosocial and financial needs as well as caregiver support are usually overlooked. This could be due to time constraints during a clinic visit, lack of understanding of the treating provider of these symptoms.

Despite the growing awareness of benefits of palliative care this service is underutilized. One of the important reasons identified is the overly optimistic attitude of the HCT physician treating patients with high risk transplant. The reasons for this are multi factorial. A HCT physician based survey identified a few barriers and an important one was the perception of palliative care as being end of life or associated with the feeling of 'giving up' by the patient and their families (>80%). Others were, lack of understanding the role of palliative care by HCT physicians and cultural factors (women HCT physicians and <10 years into practice were more likely to make palliative care referrals) [37]. There is now growing awareness and efforts are being made to bridge this gap between the HCT physicians and palliative care with increased educational activities, seminars and lectures [38].

Conclusion

Palliative care is not synonymous with hospice and aims at symptom management and patient's comfort in different phases of HCT. There is a noted benefit for early palliative care involvement and assistance with advance care planning which will eventually lead to decreased ICU admissions and health care utilizations. There are many models for delivery for these services either directly by the HCT team and physicians or directly from the palliative care team. Despite this there is a limited utilization of these services by the HCT team and this gap is to be bridged. Efforts for the same are currently underway. More research needs to be undertaken to identify high risk HCT patients that will benefit the most from palliative care.

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