

Palliative care in patients with hematologic malignancies

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Abstract

Purpose: Patients with haematologic malignancies (HM) present with a significant symptom burden and are more likely to need not only Palliative Care but End-of-Life-care, as these are approaches that improve the quality of life of not only patients but their families facing the burden associated with life threatening illness. This is however not usually incorporated routinely into the management of patients with HM. This literature is to review the role palliative care in the management of patients with HM.

Methods: A search literature was made from Goggle scholar, PubMed Central, Embase search engines from 1990 to 2022 using the following keywords: palliative care, haematological malignancies, leukaemia, lymphoma, multiple myeloma, myelodysplastic syndrome, myeloproliferative neoplasm, polycythemia vera, essential thrombocythemia and primary myelofibrosis. Fifty-six relevant studies focusing on palliative care in the various haematological malignancies were selected.

Results: There are trained palliative care (PC) specialists who receive advanced education in providing individualized specific needs for the patient care. They focus on easing pain and discomfort and helping people get the highest quality of life because majority of patients in less developed countries come in late stage. Clinicians who treat patients with cancer often provide a great deal of PC without PC specialists. Therefore, involving a PC specialist in the care of patients with HM is not expected to replace the primary PC if already being provided by the hematologist-oncologists.

Conclusion: As more patients with HM are seen by palliative care specialists, it will be recognized that collaboration can improve the quality of life in the care of patients with high symptom burden via complementary skill sets; but there is a paucity of PC practitioners who are highly needed because HM patients present late in low-and-middle income countries.

Keywords: Palliative care, burden, hematological malignancies, barriers, quality of life.

Introduction

Hematological malignancies (HM) are a heterogeneous group of primary cancers of the blood and blood-forming organs (bone marrow and lymphoid tissues). They are characterized by way of marked variation in their disease course and capacity for curability that have an effect on their palliative and end-of-life (EoL) care needs when compared to solid tumors [1,2].

The three primary types of HM are:

1. Leukemia: acute leukemia subtypes (acute lymphoblastic leukemia, acute myeloid leukemia); chronic leukemia subtypes (chronic myeloid leukemia, chronic lymphocytic leukemia).

2. Lymphoma: Subtypes include Hodgkin Lymphoma and Non-Hodgkin lymphoma (NHL).
3. Multiple Myeloma: Subtypes include Smouldering (indolent) multiple myeloma (SMM) also called asymptomatic myeloma, without signs and symptoms of the disease; active MM

Other less common types: Myeloproliferative neoplasm (MPN) with subtypes including polycythemia vera, essential thrombocythemia and primary myelofibrosis; myelodysplastic syndromes (MDS).

What is Palliative Care?

The World Health Organisation (WHO) defined palliative care as "An approach that improves the QoL

of patients and their families facing the burden associated with life threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychological and spiritual" [3]. Palliative care (PC) is a specialised medical care for people living with serious illness and involves a multidisciplinary team comprising experts of PC doctors, nurses and social workers, therapists, laboratory scientists; may also work with chaplain, pharmacists, nutritionist, councilors and others; as WHO takes a more broad approach that the principles of PC should be applied as soon as possible.

The three main aims of PC are identifying goals of care, controlling symptoms and caring for the whole person in tandem with curative treatment. Palliative care is used interchangeably with supportive care, comfort care and symptom management and hospice, but minor differences still exist. Patients with HM are known to receive less Palliative care (PC) and it is usually initiated at a later disease stage [1]. Additionally, patients receiving early PC were less likely to use chemotherapy at the EoL, more likely to use hospice services, and actually also lived longer [2]. Hospice-a home providing care for the sick or terminally ill- eligibility requires that two physicians must certify the life expectancy to be less than ≤6 months and that patients forgo further disease-modifying treatments such as chemotherapy. Hospice care focuses on the palliation of a terminally ill person with pain symptoms and attending to their emotional and spiritual needs, prepares for physical changes at the EoL; and help to cope with different thoughts and emotional matter that arise and provide support for the family members. Whereas PC can begin at any point during cancer treatment from when diagnosis was made to the end of life, hospice care begins when curative treatment is no longer the goal of care and it is clear there will be no survival of the illness.

Generally speaking, people who are dying need care in four regions –physical comfort, mental and emotional needs, spiritual issues and realistic duties [4]. The EoL care entails a variety of viable selections including hospice care, PC, patient's right to select, participation in scientific trials ("Home-Clinical Trials.gov) and preference of medical interventions. Increasingly, studies have shown that these PC clinicians are not highly sort after for patients with HM [1,5].

In this review, the types, barriers and benefits of the PC needs of patients with hematologic malignancies including future directions to enhance the QoL and care of patients through collaborative care will be discussed.

The Burden and Course in patients with Hematological Malignancies

The disease course in patients with hematologic malignancy (HM) is unpredictable with the possibility of cure persisting even in relapsed and refractory settings, contrary to most advanced solid tumors [1-5]. Survivors from palliative care needs of HM often deal with quality of life (QoL) impairments, long-term sequel of their illness and associated related therapies [6-9]. Intensive medical therapies are often indicated for older adults and this is usually associated with significant toxicities and risks of mortality [10-12].

The burden of patients with HM extends beyond mortality. People are impacted by the diagnosis experience including physical suffering, distress, and reduced QoL related with disease-related symptoms (state of mind); diagnostic procedures, malignant growth, treatments and long-term antagonistic impact of treatment. Studies have demonstrated that the prevalence of fatigue is high (80% to 90%) especially in those with acute leukemias, MDS, and MM [13-14]. In addition, they experienced a symptom burden that is comparable to or exceeds that of patients with metastatic solid tumors [1-2].

In a review by Bounaix et al on patients with HM, they identified four main groups of symptoms of discomfort: physical, psychological, social and medullary-related [15]. The prevalent burden symptoms that have been seen include lack of energy, difficulty with sleep, pain, and dry mouth The Global Palliative Care Quality Alliance analysis revealed that the rates of pain, fatigue, drowsiness, dyspnea, nausea, and anorexia were similar among those with hematologic and solid malignancies [16]. The finding suggested a need to optimize PC usage in the hematologic cancer population [16].

Many patients with HM are known to receive intensive treatments that require prolonged length of stay in hospital during hematopoietic Stem Cell transplant (SCT) [6, 17-18]. These patients who receive HSCT were shown to have a dramatic decline in their QoL associated with an increase in symptoms such as nausea, vomiting, mucositis, fatigue, and diarrhea during their transplantation course [17, 19-21]. The acute leukemia patients struggled with toxicities from intensive chemotherapy which often requires a prolonged hospitalization and are among the most distressed of all those with cancer [22-23].

In a study of patients with relapsed acute myeloid leukemia (AML) who received intensive chemotherapy, a mean of 14.1 moderate to severe symptoms was reported which brought about considerable impairment across board on the QoL [24-25]. Although the symptoms experienced during in-depth treatments are often temporary in HM

population, they may contribute to long-term psychological distress, anxiety including post-traumatic stress symptoms and depression [15, 17, 26-28].

Another study of 104 patients with HM who received chemotherapy reported 50% with clinically significant distress [29]. Of note, patients with acute leukemia and those who had HCT grappled with acute stress reactions as they endured the shock of a life-threatening diagnosis and the need for prolonged and socially isolating hospitalizations [22, 30,31]. Among the allogeneic HCT recipients, chronic graft-versus-host disease (GVHD) was seen as the major cause of morbidity, physical and functional impairments and poor QoL [32-34]. The GVHD symptoms has been perceived as an important unsatisfied PC need for allogeneic HCT recipients by transplantation physicians in a recent survey [35]. Even among patients with highly curable HM such as Hodgkin's lymphoma, 30% of patients struggle with clinically meaningful distress years after completing their therapy [36]. Similarly, patients with indolent disease like chronic lymphocytic leukemia, who may live with the disease for more than a decade, have been shown to have worse emotional wellbeing than patients with more serious solid tumors [37].

Other burden symptoms are neuropathy, infertility, cardiomyopathy, neurocognitive deficits, fear of recurrence, all resulting in diminished QoL compared with the normal population. [19-21, 38-41]. Thus, interventions are critically needed to address the immense emotional and psychological burden that patients with HM experience during their illness course.

Integration of a medical specialty known as Palliative Care (PC) including hospice care need has been shown to improve a wide range of the burden and outcomes but are initiated at terminal end, and so are more likely to die from escalating interventions [15, 42-45].

Modern PC is provided alongside curative cancer-directed therapy. In a recent study, Loggers et al [46] reported that early PC consultation before transplantation is feasible and acceptable for patients with high-risk HM who undergo allogeneic HCT; as PC is not a curative therapy but rather a highly useful adjunct to the targeted therapy already being provided by the hematologist-oncologist. This will help in making swift decision between chemotherapy and PC, or receive them simultaneously. A successful PC in hematological oncology patients requires physicians handling particular issues encountered in care: difficulty in individual prognostication; ongoing therapeutic goals of curability or long-term survival; the technical nature and complications of the treatment; speed of change to terminal event; need for pathology testing and transfusion of blood products as death approaches.

What do Palliative Care Providers do?

Palliative care can be provided in hospitals, nursing homes, outpatient palliative care clinics and certain other specialized clinics, or at home by different categories of health care workers. Specialists with core competencies are trained in QoL assessment, complex symptom management, communication skills, spiritual assessment, family-centered care, and high-quality EoL care (including but not limited to "hospice care"). The PC is usually individualized into specific needs of the patient care. The concerns addressed in PC are usually the physical and emotional effects of the cancer. This include:

- i) Physical symptoms-severe pain, fatigue, nausea and vomiting, difficulty in sleeping etc. they can provide expertise to facilitate management.
- ii) Providing resources to help cope with emotional issues that arises when diagnosis of cancer is made; not only for the index person but also for the families as the burden for cancer is high-depression, anxiety and fear etc.
- iii) Spiritual help as they look on to their maker with disbelief and asking the question "Why me" looking for deeper meaning of the whole situation in their lives. Some are saved through their faith in Jesus Christ hoping for a miracle or other spiritual beliefs; an expert can assist in helping to explore the various belief systems and values in order to find peace or acceptance.
- iv) Caregiver needs including families and friends are very important in the cancer care. They may be overwhelmed by the extra responsibilities while still trying to handle other obligations such as work and house chores. These challenges can compromise caregivers own health.
- v) Practical needs by the specialists can assist with financial and legal worries, insurance questions and employment concerns; and planning for patients in dealing with a lot of prognostic uncertainty.
- vi) Serve as effective communication bridge between the hematologist-oncologist and the patient, especially in situations when the patient does not fully discuss their fears and concerns with the oncology team.

In a randomized trial of patients receiving early PC intervention the study revealed that early PC improves patients' QoL, mood (higher satisfaction with care), lower symptom burden at four months, and other key aspects of cancer care including prognostic awareness, and quality of EoL care [47]. Also, a recent randomized controlled trial of early versus delayed PC (ENABLE III) for family caregivers of patients with advanced cancer, family caregivers receiving the early

PC intervention reported less depression and stress burden, highlighting the importance of PC in addressing the needs of families struggling with cancer [48]. The efficacy of diverse PC delivery models, which include telephone-based interventions, may permit for easier dissemination of services.

Who are the Recipients' of Palliative Care in Hematology?

- The American Society of Clinical Oncology (ASCO) recommends that anyone with terminally or advanced cancer with unmet PC needs should receive or be offered PC as soon as diagnosis of the cancer is made or 8 weeks of diagnosis; as this improves the QoL and also benefits the family health and well-being [49].
- However, many hematology-oncologists who treat HM do not have experience partnering with PC clinicians in the care of their patients, or may harbor mistrust or misconceptions as they already provide a great deal of "primary palliative care" to their patients.

The Need for Palliative Care Specialist and Benefits

With the growing evidence of the numerous benefits of PC for patients with cancer, the American Society of Clinical Oncology (ASCO) released its provisional clinical opinion recommending concurrent PC from the time of diagnosis for all patients with metastatic cancer and/or high symptom burden [50]. Analysis of other data's confirmed that PC visits have distinct features from oncology clinic visits, and that the roles of each clinician are complementary in the care of patients with advanced cancer [51]. With evidence demonstrating benefits of integrated PC for patients with serious illness, demand for PC services has increased dramatically.

The Palliative care team members are engaged in the following conditions:

- Presence of high symptom burden or refractory symptoms of-life in order to improve symptom control.
- To improve QoL while receiving active treatment and it may allow them to better tolerate effective therapies, mood and prognostic understanding; although the mechanism by which PC improves survival is not fully known.
- Hospitalized for SCT so as to improve symptom control, provides excellent supportive care and alleviate psychological distress significantly.

- When there is difficulty coping with their illness; bring out measures to enhance patients' coping attitude.
- When there are complex family caregivers and patients' social needs to be addressed.
- When patient does not understand the overall prognosis and/or persistent misperceptions about their illness.
- To help facilitates EoL care planning, prepares patients emotionally and psychologically.

Other benefits of the Palliative Care include:

- Provide guidance, support, and evidenced-based strategies for individuals and populations to reduce cancer risk advances, save and celebrate lives, and lead the fight for a world without cancer- mission of the American Cancer Society (ACS).
- Improved survival in the early integration of PC with standard oncology care may facilitate optimal and appropriate care at the EoL, leading to overall clinical stability and prolonged survival.

Barriers to Palliative Care

Bouneax et al found a number of barriers hindering early integration of PC in hematology: the difficulty establishing diagnosis, clinical course features and the clinicians [15]. Other studies revealed that barriers can also be grouped under illness-specific, cultural, and system-based barriers that contribute to low rates of PC use seen in cancer treatment. [52] These are:

1. Illness-specific barrier

- Hematological malignancies often require intensive treatments with significant morbidity and mortality.
- There is no clear transition between curative and palliative phase of treatment.
- Prognosis is uncertain because many patients with relapsed and refractory HM can still achieve a cure.
- The uncertain prognosis in treatment of patients with HM leads to lack of early PC use.

2. Cultural barriers

- Misperceptions that equate PC with just EoL care.
- Oncologists' reluctance to involve other providers in their patients' care.
- Lack of knowledge with regard to the potential role of PC.

3. System-Based barrier

- Paucity of data that support the role of PC for patients with HM, rather than evidence to the contrary, has served as an important barrier;

- Increasing demand for integrated PC may exacerbate the shortage of PC clinicians;
- Limitations on the ability to provide blood product support to alleviate symptoms, and intravenous antibiotics at the EoL with hospice services.
- Exclusion of patients with HM from prior PC intervention trials in oncology.
- EoL care delivery models are inadequate for addressing the needs of patients with HM.
- Transfusion support is not allowed by many agencies because of the logistics and costs involved [53-55].

4. Staff Barrier

- There are not enough palliative specialists to care for all patients including HM patients'.
- Evidence suggests that oncology trainees lack competence at core specialty PC tasks, like doing basic opioid conversions.

Five stages known to be involved in palliative care include:

- **Stage 1:** The palliative team work together to devise a plan for EoL care that improves QoL.
- **Stage 2:** Hospice interdisciplinary team come into play which include chaplains to provide the spiritual and emotional care.
- **Stage 3:** The physicians work to make sure independence to a certain level is attained. This may include home health aides, certified nursing assistance, and volunteers to help with household duties.
- **Stage 4:** In patient care arrangements at a hospital or hospice center if wanted/needed.
- **Stage 5:** Bereavement support for the family once the patient passes on. This is very critical and families can be supported with any form of services as deem fit to cope and heal with the challenging time.

Is there a difference between effective Palliative care and Supportive care?

- The Multinational Association of Supportive care in Cancer defines **supportive care** as "the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms, social and spiritual problems related to a disease or its treatment; and side effects across continuum of the cancer experience from diagnosis through treatment to post-treatment care. Enhancing rehabilitation, secondary cancer prevention, survivorship and end of life care are integral to supportive care." [<https://dailynews.ascopubs.org>]
- The aim of the supportive measures is to achieve therapeutic goals; and focus on

relieving pain, stress and other symptoms to help alleviate suffering and optimize QoL. It is usually an adjunct form of care to the definitive form of treatment that is being used for the cancers.

- It is not a signal that treatment is not working, does not mean you will not get better or that you are dying neither can it be used as a replacement for the definitive treatment. It also does not signal that you are weak when you ask for these adjunct supportive care.
- They are necessary when cytotoxic or other forms of therapy fails to induce or maintain lasting complete remission and improve the QoL.
- Every patient who has been diagnosed to have cancer or HM needs a supportive care.

Survival non-conventional medical methods for persons' living with cancer

It's of note here that there are still ongoing debate on whether conventional or standard medicine such as the PC is better than alternative medicine. A main benefit of the standard medical care is that it has undergone clinical trials with evidence to support. In contrast, though not much, the alternative medicine has been researched to some extent; and it focuses on natural substances believed to be safer, gentler and more suitable for the human body; though they can also cause side effects like the conventional treatment. Alternative medicine, Complementary medicine and Integrative medicine are used interchangeably. These include:

1. Biological cancer medicine: Cancer immunotherapy (biological therapy) consists only of certified biological treatment method that supports the healing process through the activated will of the patient. The will to live and positive thinking can improve the healing process dramatically.
2. They act as a replacement for conventional medicine by using energy healing for the condition rather than mainstream treatments. This alternative therapies involves the use of natural, nontoxic substances including phytonutrients, vitamins, minerals, enzymes, lipids, botanicals, peptides and other compounds that help in fighting cancers. They have synergistic effects of causing cancer cells to die (apoptosis), reinforce the immune system, assist the body in its detoxification process and revert cancerous cells back to normal cells.
3. Integrative approach with an open minded oncologist tries to combine both conventional and less conventional methods in a coordinated, evidence based way- Consortium of Academic Health Centers.
4. Complementary and Alternative Medicine (CAM) are grouped into 5 types: [56]
 - a) Mind-body therapies focus on the relationship between the mind and body to

help manage a condition following manual manipulation with the body fully focused on the part of illness. Examples include chiropractic and osteopathic medicine, body movement therapies, hypnosis, massage, meditation, yoga-mind body exercise that originates in spiritual practices.

- b) Traditional alternative medicine is the more accepted form of therapy eg Acupuncture (American College of Physicians recommends acupuncture as the first line to relieve discomfort or lower back pain associated with a variety of disease), Homeopathy, Naturopathy, Chinese/Oriental medicine.
- c) Biological therapies use substances such as plants and foods to improve health eg dietary supplements like vitamins, minerals, and botanical plant compounds like cannabis, curcumin from turmeric, garlic.
- d) Bio field therapies involves restoring invisible flow of external energy fields around the body which acts by relieving disturbances or blockages in the body.
- e) Senses of touch, sight, healing smell, and taste are believed can affect overall health.

Conclusion

Though PC is recommended as a standard part of comprehensive cancer care, most patients with a HM do not have access to PC specialists or services. Targeted PC interventions based on the specialized needs of the diverse populations of patients with HM must be developed. PC is not EoL care or hospice, but it is rather a multidisciplinary approach to the management of symptom, psychosocial support, and assistance in treatment decision-making for patients with serious illness, along with their families. It emphasizes well-being at any point along the disease trajectory, irrespective of the prognosis. At present, many patients with HM often have significant need for PC. However, there are many unanswered questions on how to effectively integrate specialist PC into the care of HM patients to meet those needs.

List of abbreviations

ACS – American Cancer Society
AML – Acute myeloid leukemia
ASCO – American Society of Clinical Oncology
CAM – Complementary and Alternative Medicine
EoL – End-of-life
GVHD – Graft-versus-host disease
HM – Hematological malignancies
MPN – Myeloproliferative neoplasm
NHL – Non-Hodgkin lymphoma
PC – Palliative care
QoL – Quality of life

SCT – Stem Cell transplant

WHO – World Health Organisation

Declarations

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflict of interest associated with this work.

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Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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