

# Palliative Therapy in Cancer Patients: An Overview

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## Introduction

There is an ever-growing number of cancer patients in the world today. Of the estimated nine million new cancer cases diagnosed in 1997 worldwide, 52% occurred in developing countries (1). Cancer rates could increase by 50 % to 15 million new cases in the year 2020 (2). The mortality from cancer too is expected to rise around the globe. About 7 million deaths per year occur in the world due to cancer, of which, approximately 0.8 million occur in India (1). In India one in 10 deaths is related to cancer and a sizeable section of this huge population die in unrelieved pain and suffering (3). More than 70% of all cancer patients in India require palliative care for relief of pain, other symptoms and psychosocial distress (1-3). There is no cure to date for this disease but definitely a lot can be done to make the lives of these people meaningful and productive. With this idea the concept of palliative care was initiated.

## What is Palliative Care?

Palliative care is the active total care of patients whose disease is not or no more responsive to curative treatment. Palliative medicine includes clinical palliative care, education, and research that focus on the quality of life of patients with advanced disease and their families (4). In palliative medicine, symptom control, and no longer prolongation of survival, takes a preponderant place to finally become the only goal to reach.

Palliative care is not restricted to end-stage disease. It should be envisaged and organised as soon as it is known that the disease is incurable. Thus, palliative and curative care are often complementary and are intricate over months or years to improve the quality of life of the patient (3,4). Palliative Medicine must be present from the diagnosis through the different evolutive stages of cancer patients, and is not just the care programs for terminally ill cancer patients. Surgery, radiotherapy and chemotherapy are used as specific palliation

in some situations in order to improve quality of life, survival time or symptomatic control.

## Components and Principles of Palliative Care

Key components of palliative care of cancer patients include compassionate communication; exploration of patient and family values and goals of care; expert attention to relief of suffering; management of pain, depression, delirium, and other symptoms; awareness of the manifestations of grief; and sensitivity to the concerns of bereaved survivors (4). The general principles of palliating most distressing symptoms in terminal cancer are:

1. To define and treat the underlying cause of symptom wherever possible and reasonable for the patient.
2. To relieve the symptom without adding new problems by way of side effects, interactive effects, social or financial burdens.
3. To consider whether a treatment will be worthwhile for the patient and his family bearing in mind his prognosis and adverse effects of invasive procedures.
4. To discuss all reasonable treatment options (including the decision of "no intervention") with the patient and his family, allowing them to make the final decision as far as possible by themselves.

## Concept of Home Care

Caring for a patient with terminal illness at home is the preferred option for most people with a terminal illness (5). The benefits of palliative care at home include a sense of normality, choice, and comfort; and it is more cost-effective than hospital care. The responsibilities of a family caregiver may encompass some or all of the following: personal care (hygiene, feeding); domestic care (cleaning, meal preparation); auxiliary care (shopping, transportation); social care (informal counselling, emotional support, conversing); nursing care (administering medication, changing catheters); and planning care

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(establishing and coordinating support for the patient). Good palliative care can be delivered to patients at home by general physicians (supported by specialist palliative care teams) and community nurses, with access to an inpatient facility when required. Home care involves a considerable commitment on the part of family caregivers, and attention must be given to the caregiver's needs as well as those of the patient.

#### Main Symptoms in a Terminal Cancer Patient

In cancer patients, the symptoms may be caused by primary malignancy, as well as by treatment (surgery, radiotherapy or chemotherapy), debility conditions (anemia, COPD etc) and concurrent second disorders. A patient with advanced cancer may suffer from a plethora of symptoms involving multiple function systems (6). The ten most prevalent symptoms are pain, easy fatigue, weakness, anorexia, lack of energy, dry mouth, constipation, early satiety, dyspnea, and greater than 10% weight loss (6,7). Main symptoms in a terminal cancer patient have been tabulated in Table-1 (6,7).

Table. 1 Main Symptoms in a Terminal Cancer Patient (6,7)

1.	General: Pain, cachexia, hiccups, lymphedema etc.
2.	Oral Cavity: Stomatitis/ mucositis, dry mouth
3.	GIT: Anorexia, vomiting, dysphagia, peptic ulcers, hematemesis, malaena, intestinal obstruction, ascites, constipation, diarrhoea
4.	Respiratory symptoms: Dyspnoea, cough, hemoptysis, pleural effusion
5.	Hematological: Anemia, leucopenia, thrombocytopenia, neutropenia
6.	CNS: Headache, papilloedema, altered sensorium, sensory-motor deficit, diplopia, seizures

#### A) General Symptoms

i) Pain: The sources of pain in terminal cancer patients may be classified as: (1) Directly related to tumor: bony metastases, soft-tissue infiltration, nerve infiltration; (2) Indirectly related to malignancy: infection, intestinal obstruction, massive edema, ascites, nerve-compression; (3) Due to therapeutic interventions: post-surgical pain, radiotherapy-induced, painful peripheral neuropathy due to chemotherapy (e.g. vinca alkaloids), peptic ulceration, opiate induced constipation (7,8,9).

The patient may suffer from acute or chronic pain; which may be mild, moderate or severe. The prevalence of chronic pain is about 30-50% among patients with cancer who are undergoing active treatment for a solid tumour and 70-90% among those with advanced

disease (7,8). The pain may be somatic, visceral or neuropathic in origin. In the cancer population, neuropathic pain is often related to compression, direct neoplastic invasion of the peripheral nerves or spinal cord, or to a neuropathy caused by chemotherapy (10). Various assessment tools to evaluate the severity of cancer pain include a 10-point visual analogue scale (VAS), Brief Pain Inventory (BPI), the satisfaction questionnaire and visual analogue scale quality of life (VASQOL) (11).

The treatment options for pain-relief in cancer are outlined in Table-2 (9,10,12,13). WHO provides a treatment algorithm using a step-ladder approach: Non-opioids like NSAIDs, paracetamol etc in the first step; weak opioids like codeine, dextropropoxyphene in the second step; and strong opioids like morphine, methadone, levorphanol, buprenorphine etc in the third step. Each ladder may be associated with adjuvant treatment with antiemetics, antidepressants and anticonvulsants as needed (9).

Table. 2 Treatment Options for Cancer Pain (9,10,12,13)

i)	Surgical intervention: For abscess, pathological fracture, intestinal obstruction etc.
ii)	Radiation therapy: a) External beam radiotherapy: for painful metastases; superior venacava & spinal cord compression b) Brachytherapy: Strontium-89 for painful bony metastases in carcinoma prostate, breast etc.
iii)	Pharmacological agents: (a) Analgesics like NSAIDs, opiates etc. alone or combined. (b) Bisphosphonates: Pamidronate, clodronate etc to decrease osteoclastic bone destruction to relieve bony pain of breast cancer and multiple myeloma.
iv)	Anesthesiologic techniques: Sympathetic blocks and neurolytic agents like ethyl alcohol, phenol etc.
v)	Neurosurgical procedures: Neuronal decompression.
vi)	Palliative chemotherapy for the underlying aetiology of the pain, depending upon patient's tolerability.

ii) Hiccup: The causes of hiccup in a cancer patient are gastric distension, diaphragmatic irritation, phrenic nerve irritation, brain tumor, infection and rarely iatrogenic ie chemotherapy-induced. The treatment includes reducing gastric distension by antifatulents, metoclopramide, domperidone and nasogastric intubation; pharyngeal stimulation; elevation of PCO2 by breath holding and rebreathing; central suppression of hiccup reflex by chlorpromazine; and suppression of central irritation from intracranial tension by phenytoin and sodium valproate (14).

iii) Lymphoedema: The causes of lymphoedema include surgery and/or radiotherapy to axilla or groin, post-operative infection and recurrent disease (15,16). The

patient may develop persistent swelling of limb, local tightness, discomfort, pain and subcutaneous thickening. The circumference of the involved part should be serially measured. The aim is to achieve maximum improvement, as once set in, it can't be cured. Stress should be given on skin care with moisturizing lotions, limb exercises, massage from below upward, elastic bandages, stockings and compression pumps (16). Diuretics and steroids may be tried. Bruns et al demonstrated a positive effect of sodium selenite on secondary head and neck lymphedema caused by radiotherapy alone or in combination with surgery (17).

Dev et al studied the prevalence and risk factors for development of lymphedema following breast cancer treatment (15). The prevalence of lymphedema was 13.4 % in patients treated with surgery only where as the prevalence was 42.4% in patients treated with surgery and radiotherapy. Stage of the disease, body surface area greater than 1.5 m<sup>2</sup>, presence of co-morbid conditions, post operative radiotherapy and anthracycline based chemotherapy were significant risk factors in univariate analysis where as axillary irradiation and presence of co-morbid conditions have emerged as independent risk factors in multivariate analysis ( $P < 0.001$ ).

#### B) Gastrointestinal Symptoms

Nearly one-half of the most frequently reported and most distressing symptoms in patients with advanced cancer are gastrointestinal in nature. In one study, Komurcu et al reported dry mouth (84 %), weight loss (76%), early satiety (71%), taste change (60%), constipation (58 %), anorexia (56%), bloating (50 %), nausea (48 %), abdominal pain (42 %), and vomiting (34 %) as the 10 most common gastrointestinal symptoms (18).

i) Vomiting: Nausea and vomiting is a common symptom in patients with advanced cancer, occurring in approximately 21% to 68% of these patients. Nausea and vomiting in a terminally ill cancer patient may result from a variety of causes including gastrointestinal obstruction, infiltration of the wall of the GI tract, liver metastases, brain or meningeal metastases, azotemia, hypercalcemia, electrolyte problems, or from treatment including radiation, chemotherapy, hormonal or biological therapy (19). Clinical consequences of chemotherapy-induced emesis (CIE) include serious metabolic derangements, nutritional depletion and anorexia, risk of aspiration pneumonia, deterioration of patients' physical

and mental status, esophageal tears, fractures, wound dehiscence, withdrawal from potentially useful and curative antineoplastic treatment, and degeneration of self-care and functional ability (20).

Management centers on identifying the underlying causes, addressing these when possible, and controlling the symptoms. Multiple antiemetic regimens have been proposed for the management of chronic nausea in the setting of advanced cancer (21,22). Metoclopramide or domperidone are generally recommended as first-line agents because they improve GI motility and act on the chemoreceptor trigger zone (as a result of their antidopaminergic properties). A continuous parenteral infusion of metoclopramide, at doses of 60 to 120 mg/day, may be helpful for patients with intractable chronic nausea (22). In contrast to radiation therapy- or chemotherapy-induced nausea, the role of 5-HT<sub>3</sub> receptor antagonists (such as ondansetron) is not clear in the setting of chronic nausea in advanced cancer (21). Non-drug measures like reassurance, small frequent feeds and avoidance of nauseating food; correction of reversible causes like hypocalcaemia, increased intracranial tension & constipation; avoidance of gastric irritant drugs; and control of hyperacidity by H<sub>2</sub> receptor blockers.

ii) Anorexia: The loss of appetite may result from fear of vomiting, unappetizing food, dysphagia, uremia, radiotherapy, chemotherapy, or psychogenic in origin. The patient should be informed about the probable mechanism of anorexia and offered psychological support. Small and frequent instalments of palatable and easily digestible food should be recommended. Appetite stimulants may be tried. In advanced cases, hyperalimentation may be offered (23).

iii) Diarrhoea: The causes of diarrhoea in cancer patient are listed in Table-3 (24). The treatment options include identification and elimination of underlying cause like discontinuation of chemotherapy or suspected medication, obtaining stool-assay for *Clostridium difficile* and starting appropriate antibiotics. Bismuth subsalicylate and simethicone help in infectious diarrhoea. Salicylate and indomethacin are helpful in PG-mediated secretory diarrhoea. The supportive measures include intensive oral rehydration with fluids/ ORS, avoiding high fat, high fiber food and taking frequent small meals rich in carbohydrates & proteins. Serious cases may be managed by giving opioid congeners, loperamide, diphenoxylate and octreotide (25).

Table. 3 Causes of Diarrhoea in Cancer patients (24)

Specific cause	Comment
Osmotic Diarrhoea	Laxatives, tube-feeding
Surgery	Post-gastrectomy dumping syndrome, short-bowel syndrome, terminal ileum resection
Secretory	Carcinoid tumors, Gastrinomas, Zollinger-Ellison syndrome, Medullary thyroid cancer, Vipomas, Pheochromocytomas
Inflammatory damage	GVHD, Radiotherapy,
Infectious diarrhoea	Clostridium difficile from chemotherapy/ antibiotic use, Methicillin resistant staph aureus
Chemotherapy induced	Cisplatin, 5-FU, Irinotecan, Methotrexate, Interleukin-2
Paraneoplastic syndromes	Autonomic neuropathy, ectopic hormone production

iv) Constipation: The causes of constipation in a cancer patient include mass in anorectal region, neurologic and mechanical changes from surgery, decreased oral intake, decreased mobility and supine positioning, medications like opioids and tricyclic antidepressants, and chemotherapeutic agents like vinca alkaloids. The different treatment options for constipation in cancer patients include encouraging movement and ambulation; maintaining bowel awareness; ensuring adequate hydration and bulk-forming diet; use of laxatives like senna, lactulose and sorbitol; glycerine and bisacodyl suppositories; isotonic saline enemas; small-volume phosphate enemas; and manual evacuation in extreme cases. (26)

v) Ascites: Ascites in a cancer patient is very distressing. Pathogenesis of ascites include peritoneal metastasis, subphrenic lymphatic obstruction due to tumor infiltration, or electrolyte imbalance. Carcinoma ovary, pancreas, gall bladder and colorectum are frequent causes. Treatment options include systemic and intraperitoneal chemotherapy diuretics like spironolactone and frusemide, paracentesis and peritoneovenous shunt (27). Permanent percutaneous drains may prevent the need for repeated paracentesis, although there is potential for infection.

#### C) Respiratory Symptoms

i) Dyspnoea: The causes of dyspnoea in cancer patients include: pleuropericardial effusions, obstruction of a main bronchus, atelectasis, replacement of lung by cancer, superior vena caval compression, abdominal distension, pulmonary embolism, lung fibrosis due to radiotherapy and bleomycin, and concurrent ailments like COPD,

pneumonia, anaemia etc. The treatment options include antibiotics and physiotherapy for infection, bronchodilators to relieve bronchospasm, diuretics and digoxin for cardiac failure, blood transfusion for anaemia, tapping of fluids for effusions, corticosteroids and radiotherapy for obstructed bronchus, breathing exercises and hypnotic relaxation, diazepam to reduce anxiety, morphine to reduce respiratory rate, nebulized bupivacaine to suppress the J- receptors, and oxygen administration for acute severe dyspnoea (28).

ii) Cough: The incidence of cough is 50% of all terminal cancer patients and 80% of bronchogenic carcinoma patients. The main causes of cough in a cancer patient include mechanical irritation of tracheobronchial tree, chest infection, pleural effusion, chronic obstructive airways disease, replacement of lung by cancer, cigarette smoking, and radiation-induced fibrosis. The treatment options of cough include antihistaminics for postnasal drip, bronchodilators for bronchospasm, diuretics for heart failure, antibiotics for infection, radiotherapy or chemotherapy for malignant lesion, resection of respectable lesions, postural drainage and physiotherapy, cessation of smoking, and mucolytics and antitussives as indicated (29).

#### D) Oral Cavity Symptoms

i) Xerostomia: The underlying pathophysiology of dry mouth is diminished secretion of saliva or diseased buccal mucosa. The causes include anxiety, depression, hypercalcemia, invasion of salivary glands by cancer, erosion of buccal mucosa, local radiation, local radical surgery, anticholinergic drugs etc. For treatment, meticulous mouth-care every two hours is indicated by effervescent mouthwash tablets containing peppermint oil, clove oil, spearmint, menthol etc. 0.1% hexidine has got antibacterial activity. Chewing gums, flavored candy and pineapple chunks may be tried. Artificial salivas, plenty of fluid-intake and frequent moistening of lips is also helpful (30).

ii) Oral candidiasis: Oral candidiasis may be a distressing problem in a terminal cancer patient. Dry mouth, corticosteroids and bacterial antibiotics are the common factors implicated (30). Antifungal agents like nystatin, ketoconazole, fluconazole etc provide good symptomatic relief.

iii) Metallic taste: It may be due to decreased sensitivity of taste buds, decreased number of taste buds, toxic dysfunction of taste buds, nutritional deficiencies or poor dental hygiene. Patient should be advised to reduce urea content of diet; to eat white meats, eggs, dairy products;

to drink more liquids; to eat cold food; and to have fresh fruits and vegetables (31).

iv) Halitosis: Many cancer patients develop halitosis i.e. feeling of unpleasant or foul smelling breath. Causes may be any infection, gastric outlet obstruction, smoking, or ingestion of substances like garlic, onion, alcohol. Treatment possibilities include attention to orodental hygiene, adequate fluid intake, treatment of oral candidiasis, use of mouthwashes (30).

E) Psychiatric Symptoms: Any physical ailment must be ruled out before labeling any symptom as psychiatric. The prevalence of anxiety and depression is about 25% in all cancer patients and 77% in those with advanced disease (32). These patients should be treated with supportive therapy, hypnosis, relaxation therapy, and pharmacological drugs. Lorazepam, alprazolam and diazepam are the common anxiolytic drugs. Amitriptyline, imipramine and fluoxetine are the commonly used antidepressants. The evaluation tools to assess psychological distress in cancer patients and their relatives include Hospital Anxiety and Depression Scale (HADS), Cognitive Behavioral Assessment 2.0, the Family Strain Questionnaire and the Satisfaction with Life Scale (33).

#### Role of Radiotherapy in Palliative Care

Radiotherapy is an indispensable modality in the palliation of cancer. All palliative care programs should be acquainted with its indications and have a close working relationship with a radiation oncology department. The main indications are: pain relief (particularly bone pain), control of hemorrhage, fungation and ulceration, dyspnea, blockage of hollow viscera, and the shrinkage of any tumors causing problems by virtue of space occupancy. In addition, it has an important role in the palliation of three oncological emergencies: superior vena caval obstruction, spinal cord compression, and raised intracranial pressure due to cerebral metastases. The doses and schedules applied include 500cGy/fraction, 800cGy/fraction, 20Gy in 5 fractions, 30 Gy in 10 fractions and 40Gy in 20 fractions (34).

#### Medical Education in Palliative Care

There is a continuing need for medical education in palliative care. Particular attention should be paid to the basic medical education of clinical students and the training of junior doctors, especially regarding communication skills and bereavement care (35). Clinicians in India need to be provided focused skills and

training for them to be able deliver quality palliative care to the large number of patients with incurable cancer. The cost of palliative care and the optimum place to deliver it, the symptoms of advanced cancer, pain relief and symptom control methods and quality of life in end-stage cancer patients are some aspects that should be an integral part of clinical residency programs (2).

#### Medicolegal Aspects

Morphine is the gold standard analgesic to control chronic cancer-related pain, but its availability is restricted. The fear of diversion of morphine for non-medical uses has led to severe control on its availability. The courts have issued directives to improve the availability of the drug, yet 97% of Indian patients have very poor access to the drug (36). There is a need to improve access to pain-free end-of-life care. The government should enforce laws necessitating more hospices and palliative care centers to provide free medical care to terminal cancer patients. Public awareness should be created in this regard and concept of palliative care should be included in medical education.

#### Conclusion

About 70% of patients in developing and underdeveloped countries present in advanced stages of disease, where adequate symptom control and comfort of the remaining life should be the aim of treatment. Palliative care should be provided by a dedicated team consisting of doctor, nurse and ancillary staff. Recent developments that are important to oncology practice are: the role of artificial nutrition; management of malignant small bowel obstruction; communication tasks, recognition of patient preferences, advanced-care planning and bereavement care. In India, the standard of palliative care is still disappointing as far as facilities are concerned. This can be primarily attributed to lack of cooperation from surgeons and other specialists who focus mainly on early cases and think that palliation is the concern of only the radiation oncologists. Newer centers for palliative care of cancer patients need to be made available and the public should be made aware in this regard as a form of treatment option.

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