Palliative Radiotherapy and Palliative Chemotherapy

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Introduction

Palliative care is defined by the World Health Organization as the active total care of patients whose disease is not responsive to curative treatment [1]. The goals of the treatment in the palliative care phase are mainly to control the symptoms, to enhance the quality of life, and to optimize the patient's limited remaining time. For palliative treatment of cancer patients, anti-cancer treatments such as radiotherapy, chemotherapy, molecular targeted therapy and hormonal therapy can help in achieving these goals.

Palliative Radiotherapy

About 34–50% of patients receiving radiotherapy are of palliative intent [2-4]. Similar to other clinical domains, the practice of palliative radiotherapy is always guided by basic ethical principles and available clinical evidence. It requires sophisticated assessment to balance the potential benefits and burdens to the patients with respect to patient's autonomy and expectations, and consideration of logistical factors.

Benefits and Burdens

Palliative radiotherapy is mainly indicated to relieve various local symptoms in cancer patients; to prevent debilitation such as spinal cord compression and pathological fracture; and to achieve durable locoregional control [5] (table 1). The effectiveness has been confirmed by cumulative clinical evidence. For metastatic bone pain, palliative radiotherapy can achieve an overall pain response rate of 59–62%, and a complete pain response rate of 32–34% [6]. For multiple brain metastases, the overall response rate to external irradiation is around 60% with 30–40% achieving marked neurological improvement [7].

On the other hand, palliative radiotherapy may sometimes cause significant burdens to the patient such as acute side effects, hospitalization, multiple visits to the treatment machine with associated discomfort in transport, and loss of opportunity cost [8].

Patient's Factors and Logistical Factors

Some studies have demonstrated that the practice of palliative radiotherapy would vary markedly among oncologists [9-11] and would be influenced by factors unrelated to the patients' needs such as resource limiting, oncology training of the attending doctors, access to the radiotherapy facilities, waiting time for radiotherapy, patients' age and patients' household income [4, 12-13].

Poor performance status, short predicted life expectancy, perception of slow onset of therapeutic effects and overly burdensome of palliative radiotherapy often preclude palliative radiotherapy as a tool for symptom relief in terminal cancer patients [14]. However, it is noted that physicians' estimation of the life expectancy of the patients may not be accurate [15], the poor performance status may be related to the uncontrolled symptoms and the onset of the therapeutic effect of radiotherapy to some common symptoms such as metastatic bone pain and bleeding caused by cancer can be rapid. With appropriate patient selection, palliative radiotherapy can have a significant role in symptom control in end of life care of cancer patients. "One-shop approach" with the patient assessed, radiotherapy planned and delivered by a single fraction on the same day will be very useful in this group of patients [16].

Fractionation

In the past two decades, there has been increasing clinical evidence suggesting that shorter fractionation schedules and more protracted schedules have the same effectiveness in symptom control of incurable cancer patients, particularly, for metastatic bone pain [17-19] and multiple brain metastases [20-22]. Short fractionation schedules or a single dose can avoid multiple visits to treatment facilities and prolonged hospitalization. The waiting time for radiotherapy can be shortened. External irradiation using a single dose of 8Gy has been recommended as an effective and appropriate treatment for palliation of metastatic bone pain unassociated with spinal cord compression or pathological fracture [19]. Up to the date of writing this article, the optimal fractionation for the neuropathic pain complicating bone metastases, and that for pathological fracture has not been established. It has also been reported that a single dose has inferior effectiveness to a fractionated course in preventing pathological fracture [19].

In some clinical situations, protracted fractionated course of palliative radiotherapy will be more favorable than shorter hypofractionated schedule. Patients who have advanced locoregional cancers with good performance status and long life expectancy are preferably treated by protracted

fractionated schedule with higher total dose and small dose per fraction to achieve durable local control. For lesions inside the pelvis or abdomen, radiation with large dose per fraction will lead to severe acute enteritis and hence relatively protracted course with lower dose per fraction will be more favourable.

Table 1: Indications of Palliative Radiotherapy

Pain relief:
- Metastatic bone pain
- Painful lymphadenopathy
- Pain due to soft tissue infiltration by cancers
- Neuropathic pain due to nerve compression and infiltration

Rescue of neurological deficit
- Spinal cord compression
- Brain metastases

Relief of pressure symptoms
- Thoracic tumours:
  - SVCO
  - Upper airway obstruction
  - Dysphagia
  - Collapse of lung
- Reduced the increased intracranial pressure secondary to brain metastases
- Retroperitoneal tumours
  - Relief of hydronephrosis
- Pelvic tumours
  - Relief of hydronephrosis
  - Urinary retention
  - Intestinal obstruction

Control of fungation and ulceration of metastatic or primary skin cancers

Haemostasis:
- Haemoptysis
- Bleeding rectal or gynaecological cancers
- Bleeding skin cancers

Prophylaxis of impending symptoms
- Prevention of spinal cord compression
- Prevention of pathological fracture
- Prevention of pending pressure symptoms

Durable control of advanced locoregional disease beyond cure.

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Palliative Chemotherapy

Chemotherapy was once commonly regarded as an often futile and always dangerous type of therapy by both public and many palliative physicians and nurses [23]. In the last two decades, there has been a gradual but important change in the perceived role of chemotherapy in the treatment of advanced cancers [24]. In the past, most studies reported the efficiency of palliative chemotherapy in terms of tumor response rate, duration of response and survival benefit. Nowadays, the issue of symptom control and quality of life are usually addressed in clinical studies on palliative chemotherapy. Similar to the practice of palliative radiotherapy, the practice of palliative chemotherapy is always guided by basic ethical principles and available clinical evidence.

Benefit and burdens of Palliative chemotherapy

Following tumor shrinkage, control of neoplastic growth and alternation of tumor biology and metabolic activity by palliative chemotherapy, local and systemic symptom control can be achieved. Even without tumor regression, patients will also be clinically benefited [25]. Clinical studies including randomized trials have demonstrated significant improvement in quality of life by palliative chemotherapy in hormonal refractory prostate cancer [26], advanced gastrointestinal cancer [27], metastatic breast cancer [28], small cell lung cancer [29] and non-small cell lung cancer [30]. Some studies can also demonstrate survival benefit of palliative chemotherapy in metastatic colorectal cancer, metastatic breast cancer, ovarian cancers [31] and lung cancers [32-33]. In general, the effectiveness of palliative chemotherapy is related to performance status, age and chemosensitivity of the cancers [23].

On the other hand, palliative chemotherapy will have significant adverse effects common to most chemotherapeutic agents such as nausea, vomiting, alopecia, diarrhoea and myelosuppression, and adverse effects specific to the chemotherapeutic agents used. In addition, chemotherapy will lead to significant psychosocial burdens to the patients and their families such as difficulties in making the decision on commencing, continuing and discontinuing palliative chemotherapy, worries about the effectiveness and side effects of the treatment, frustration when treatment fails, social and financial costing of treatment. Patients and their families may have unrealistic expectations of the survival benefit of palliative chemotherapy.

Commencement

Before commencement of palliative chemotherapy, the potential benefits and risks should be sophisticatedly assessed in respect to the chemosensitivity of the cancer, patient's performance status and age, and the outcome of previous chemotherapy. Any alternatives to achieve the same treatment goals should be carefully considered. The patients and their families should be provided with adequate information. Attending physician should discuss frankly with the patients and their families to get a consensus on treatment goals. This helps to avoid unrealistic expectations. The choice of chemotherapeutic regimens should not only be based on the effectiveness and the possible adverse effects, but also based on the patient's convenience,

administration convenience, psychosocial and financial aspects of the patient. With careful selection of chemotherapeutic agents and dosage, administration schedule and anti-emetic agents, the adverse effects and patient's psychosocial burdens can be minimized.

During Treatment

Unlike palliative radiotherapy, the treatment duration of palliative chemotherapy is much longer. Patients will experience frustrations during the course of the treatment. It is not only that the effectiveness and the adverse effects should be monitored closely, but also the impacts on the quality of life of the patients and their families should be assessed regularly. The chemotherapy schedule and dosage should be adjusted to avoid severe toxicities. Good communication, appropriate counseling and support can help to minimize patients' frustrations during the treatment.

Discontinuation

In general, palliative chemotherapy will be discontinued or regimens switched when there are severe adverse effects, progression of the cancer or the treatment goals achieved. In cases when the patient achieves static disease and the symptoms are under control, "Drug Holiday" with the chemotherapy suspended for a period of time until the diseases progression can be considered. Timely discontinuation is essential to avoid over-treatment by palliative chemotherapy.

Conclusion

Radiotherapy and chemotherapy are both effective palliative treatment modalities in incurable cancer patients. With appropriate fractionation and meticulous planning, the potential burdens of palliative radiotherapy would be minimal. Even in end of life care of terminal cancer patients, palliative radiotherapy has a definite role in symptom control and should not be precluded. With appropriate choice of chemotherapeutic regimens and dosages, and effective treatment and preventive measures of the acute side effects, the adverse effects of palliative chemotherapy can be minimized. The practice of palliative chemotherapy should be well balanced between the potential benefits and risks. Adequate information and good communication are required to avoid unrealistic expectations of palliative chemotherapy.

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Hormonal therapy and targeted therapy in palliative cancer care

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In patients with advanced cancer, chemotherapy, hormonal therapy and targeted therapy are common treatment modalities for systemic palliative treatment. Majority of the chemotherapeutic agents affect cells in proliferative phase (G1 to M phase of cell cycle) and differentiate cancer cells from normal cells by their higher rate of cell proliferation. Therefore normal cells with high proliferation rate are frequently affected by chemotherapy, causing adverse effects such as marrow suppression or alopecia. On the other hand, hormonal therapy and targeted therapy agents usually retain the cancer cells in quiescence state (G0 to G1 phase) and the tumour growth is halted. These two types of agents affect tumour cell through inhibition of specific receptor or the growth factor that stimulate the tumour cells. Hence they are more selective and their adverse effects are more tolerable to fragile patients.

Hormonal Therapy

Breast Cancer

Sex hormonal related cancer, such as breast cancer and prostate cancer, frequently response to hormonal treatment. Estrogen receptor (ER) is commonly present in breast cancer, especially in the elderly. In patients with ER positive advanced breast cancer, hormonal manipulation is an effective treatment. Hormonal manipulation is achieved by either blockade of the ER in cancer cell or removal of hormone production source. Blockade of the ER by tamoxifen is the most common form of hormonal therapy in patients with advanced breast cancer. The overall response rate and duration of response of tamoxifen in patients with ER positive advanced breast cancer is 70-80% and 12-16 months