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REVIEW

Supportive Care in Cancer Cachexia: Meeting the Unmet Need

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Abstract

Cachexia is characterized by loss of appetite, weight loss and tissue wasting, accompanied by a decrease in muscle mass and adipose tissue, affecting approximately 50% of cancer patients and contributes to decreased quality of life of patients, reduced tolerance to chemotherapy, and decreased survival. Current therapies focus on maintenance of physical function, quality of life, and reduction of distress in patients and their families rather than definitive treatment for the underlying pathophysiology. Consistent with evolving guidelines for the treatment of cachexia, current models take a multidisciplinary approach, with patients generally seeing a physician, nutritionist or dietician, and physiotherapist sequentially. This is routinely supplemented by psychosocial support, whether within the program or via referral. Early intervention and attention to nutritional status are essential in patients with anorexia-cachexia syndrome. Pharmacological interventions for neoplastic cachexia include drugs that stimulate the appetite: megestrol acetate (MA) and dronabinol; cytokine inhibitors (such as cyproheptadine, thalidomide, pentoxifylline and an eicosapentaenoic acid (EPA)); and anabolic agents such as nandrolone decanoate, oxandrolone and corticosteroids. This review will discuss about the role of supportive care in cancer cachexia with a special emphasis on nursing oncology perspective.

Keywords: Supportive Care- Cancer Cachexia- Nutrition- Psychological Care

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Introduction

Cachexia is characterized by loss of appetite, weight loss and tissue wasting, accompanied by a decrease in muscle mass and adipose tissue, affecting approximately 50% of cancer patients and contributes to decreased quality of life of patients, reduced tolerance to chemotherapy, and decreased survival rates [1]. Cancer cachexia is characterised by the clinical presentation of a complex metabolic profile and loss of lean body mass accompanying malignant disease [2]. An international consensus statement defines cachexia as weight loss greater than 5%, or weight loss greater than 2% in individuals already showing depletion according to current body weight and height (body mass index (BMI) < 20 kg/m^2) or skeletal muscle mass (sarcopaenia) [2].

Cachexia affects about 50-80% of cancer patients [3, 4]. Approximately 20% of all cancer deaths are due to Cachexia. A weight loss of equal or more than 30% can cause death of the patient [5, 6]. The prevalence of cancer cachexia may vary as per the cancer site and stage. Highest prevalence has been seen in pancreatic cancer (89%), followed by gastric cancer (76%) and esophageal cancer (53%) in various studies [7, 8].

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Clinical features of Cachexia includes weight loss, anorexia, fatigue, muscle loss, pallor, peripheral edema and generalized weakness. Current therapies focus on maintenance of physical function, quality of life, and reduction of distress in patients and their families rather than definitive treatment for the underlying pathophysiology [9, 10]. Pathophysiology behind the Cachexia metabolic syndrome is multifactorial and complex. Both central and peripheral pathways contribute towards the proinflammatory and procachetic factor stimulation. This in turn generates a host response in terms of weight loss, muscle loss and fat loss.

The complex interplay between systemic inflammation and metabolic disruption associated with cachexia makes it unlikely that a single therapy could effectively combat the condition [11]. Rather, multidisciplinary and multitherapy approaches need be considered when developing treatment plans for cachectic patients.

Recent literature has seen the emergence of dedicated multimodal clinical programs in response to the impact of cancer cachexia in oncological and palliative care communities [12]. Consistent with evolving guidelines for the treatment of cachexia, current models take a multidisciplinary approach, with patients generally seeing a physician, nutritionist or dietician, and physiotherapist sequentially. This is routinely supplemented by psychosocial support, whether within the program or via referral [13-15, 16].

Due to the nature of cachexia, most cohort studies of these programs are small and short term, with long-term follow-up or studies detailing refinement of cachexia care delivery rarely reported [17]. Early intervention and attention to nutritional status are essential in patients with anorexia-cachexia syndrome. Pharmacological interventions for neoplastic cachexia include drugs that stimulate the appetite: megestrol acetate (MA) and dronabinol; cytokine inhibitors (such as cyproheptadine, thalidomide, pentoxifylline and an eicosapentaenoic acid (EPA)); and anabolic agents such as nandrolone decanoate, oxandrolone and corticosteroids [18]. This review will discuss about the role of supportive care in cancer cachexia with a special emphasis on nursing oncology perspective.

Supportive care in Cancer Cachexia

The management of cancer cachexia requires a multimodal approach with a dedicated interdisciplinary team of physicians, oncologists, anesthesiologists, psychiatrists, psychologists, physiotherapists, nurse specialists, counsellors and dieticians. Physical, social, mental, emotional and financial aspects need to be assessed and all the domains need adequate focus [19]. Patients with cachexia-anorexia syndrome generally presents with weight loss, anorexia, fatigue, muscle loss, pallor, peripheral edema and generalized weakness.

The goal of diagnosing and treating cancer cachexia is to improve the quality of life, increase the treatment tolerance and therefore improving the disease prognosis. Early recognition of cachexia at precachexic phase has more chances of reversal with the help of nutritional supplementation than trying to reverse an advance situation [20].

A detailed and thorough evaluation of all the dimensions is important to treat this syndrome. Patients at risk for developing cancer cachexia and patients with the presenting features are assessed with use of validated tools and evaluation instruments.

Physical Management

Chemotherapy drugs contain cytotoxic metallic compounds that can cause alteration of taste receptors on tongue. As chemotherapy induced dysgeusia causes alteration in food habits, meal preparation without extreme smell or taste has shown to be accepted by the patients. Patients with loose fitting dentures are unable to eat in view of pain and difficulty in eating. Dental consultations are required to improve patient's ability to chew and swallow.

Radiation and Chemotherapy induced Mucositis and ulceration are major causes of pain and difficulty in patient feeding. Bicarbonate soda gargles and local anesthetic oral gel improve the oral pain and improve swallowing with semisolid and liquid food. Chemotherapy induced nausea and vomiting affects food intake in cancer patients that is managed with antiemetics, nasogastric tube insertion or stent placement.

Poor nutrition causes decrease in blood indices, can lead to severe anemia. Iron based dietary supplement can improve anemia and fatigue. Lack of protein causes the collection of extracellular fluid in the dependent parts of the body. Cachexia can cause loss of adipose tissue and muscle mass.

Patients become less mobile as the disease progresses. Loss of fat pad in the gluteal region and the pressure part can give rise to pressure ulcers or bed sores after prolonged immobilization. Frequent change in position and passive movement of the patient can prevent the ulcers and bed sores. Water beds or air mattress is another way to reduce the pressure on areas like lower back, gluteal region, and upper back.

Psychological Management

Cachexic syndrome has direct impact on patient's self-image and social relationships. Multiple challenges faced by the cancer patients include visible skeleton, feeling different, unable to stop the weight loss, restricted life, exhaustion leading to loss of hope, change in body image causing personal discomfort and loss of self-esteem, decline in sexual health affecting relationship with the partner [21-23].

Symptoms like chronic pain, change in taste receptors due to chemotherapy, disturbed sleep cycle and fatigue due to radiotherapy can affect the feeding ability of the patient. The treatable factors should be taken into account and appropriate therapy should be initiated to relieve the symptoms and better quality of life [24].

Nutrition and Psychological Care

Anorexia presents as an interdependent situation with cachexia. Lack of appetite and weight loss impact the physical condition of the patients and causes mental

stress to caregivers. Many of the times, caregivers are blamed for patient's inability to eat and drink. Strategies to improve eating in cancer patients must be planned in consultation with caregivers or family members [25-26]. Counselling regarding the eating habits should be done after initial assessment.

The timing for breakfast, lunch and dinner should be kept fixed to encourage the psychological urge to eat [27, 28]. Meals should be prepared as per the likes and dislikes of the patient. Meals size should be kept small and at frequent intervals to increase the acceptability. Energy dense foods are generally recommended to increase the calorie intake [29, 30].

Providing calorie rich diet and extra supplementation might not improve the patient's condition and weight might not improve if patient is already at advanced stage. Forcing the patient to eat can prove counterproductive at this stage and the patient may completely refuse to eat and avoid the instructions of caregivers. Dietary counselling and nutritional supplements have not been found beneficial in advanced stage cancer patients. Cancer progression is the major cause of cancer cachexia. Nutrition supplements through nasogastric tube or intravenous route have not shown to improve the cachexic syndrome [31-33]. Option of gastrostomy and Total Parental Nutrition can be given to patients with esophageal or stomach cancer or nonfunctioning alimentary canal, in view of existing mechanical obstruction to food intake. Total Parenteral Nutrition (TPN) can be started after discussion with the family members regarding the prognosis of the disease and the expected survival of the patient [34].

Pharmacological Treatment

The decision to use pharmacotherapy for the treatment of cachexia is personalized based on the patient's presentation and disease syndrome.

Progesterone Analogues

Usage of Megestrol acetate medroxyprogesterone (MA) to improve appetite and body weight has been proven used in various trials [35, 36]. This drug acts via central stimulation of appetite via release of neuropeptide. Dose of MA ranges from 160 mg to 800 mg per day. Liquid suspension form is better than tablet form in term of bioavailability and is more cost effective. These drugs can cause increase in calorie intake and weight gain in up to 20% of the patients [37-39]. The weight gain due to these agents is due to water retention and fat deposition, but it does not increase lean body mass. Adverse effects include thromboembolic events, hypothalamic pituitary adrenal axis suppression and edema [40, 41]. Progesterone analogues have not resulted in increased survival rates despite improved appetite and weight gain, rather an increased risk of death has been observed with doses more than 800mg/day [42, 43].

Anabolic agents

Anabolic steroids have shown to increase the lean body mass but the overall weight can be decreased. Steroids induce the appetite by generating a euphoric and anti-inflammatory effect. The dose used for dexamethasone is 4 mg/day. The duration of appetite simulation with glucocorticoids is short lived [44, 45]. Antiandrogen therapy leads to increase in lean body mass. Nandrolone decanoate promotes protein nitrogen accumulation [46]. Use of growth hormones and ghrelin analogues have not been suggested in view of insufficient evidence and data.

Dietary Supplementation

Use of omega 3 fatty acid has been correlated with weight gain and increase in lean body mass. It can be used as a good source of calories for cachexic patients. Natural source of omega 3 fatty acids includes fish and salmon [47]. Use of specific amino acids like arginine and glutamine, carnitine supplements and methybutyrate has been used in combination with vitamins and minerals including magnesium, vitamin C, vitamin D and vitamin E in various trials [48].

Non-Steroidal Anti-inflammatory Drugs (NSAID)

NSAIDs down regulate the inflammatory response caused by disease progression in cancer patients. NSAIDs have shown to reduce the levels of inflammatory markers, along with reduced expenditure of energy in resting state. There are insufficient evidence to support its usefulness although it improved body weight and quality of life in some studies [49].

Eicosapentaenoic acid (EPA)

In vitro studies have proven that EPA attenuates the process of lipolysis and also improves the lean body mass. In Cochrane meta-analysis, EPA did not prove to be superior to placebo though in subgroup analysis, EPA has shown benefit in improving lean body mass [47, 50].

Table 1. Nursing Checklist

1	Serial weight and BMI monitoring and documentation at every visit	Weight (kg), BMI
2	Measurement of anthropometrical data	Waist (cm)
3	MST and documentation of calorie intake	Calorie/day , MST score
4	Nutritional & food counselling	Food Sources of vitamins, minerals
5	Checking medication compliance	Antiemtics, supplements, Analgesics
6	Understanding Psychosocial concerns	Refusal to eat, family concerns, neglect
7	Physical discomfort/ treatment side effects	Mucositis, ulceration, dental issues
8	Feeding assistance	Swallowing exercises, options of liquid food, nasogastric feeding.

Cyprohepatidine

This is a serotonin antagonist and has antihistaminic properties. It has shown to have mild stimulatory effect on appetite but fails to cause a significant weight gain. Patients of carcinoid syndrome with cachexia can be advised cyprohepatidine to increase appetite [51].

Thalidomide

It is an immunomodulatory drug with a potent anti TNF alpha action. It has been associated with gain of lean body mass. The dose ranges from 150 mg to 200 mg/day and has shown to improve body weight [52, 53].

Nursing Checklist

Nursing staffs have a critical responsibility in the management of cancer patients with cachexia. This checklist can be helpful for assessment of cancer cachexia patients who is visiting hospital for supportive care (Table 1).

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