

Promotion of case management with coordinated care for fatigued patients with advanced cancer

Jaw-Shiun Tsai¹, Ching-Yu Chen^{1,2}

¹Hospice and Palliative Care Unit, Department of Family Medicine, College of Medicine and Hospital, National Taiwan University, Taipei, Taiwan;

²Division of Geriatric Research, Institute of Population Health Science, National Health Research Institutes, Ju-Nan, Taiwan

Corresponding to: Ching-Yu Chen, MD. Department of Family Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan. Email: chency@nhri.gov.tw.



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Since advanced cancer patients suffer from physical, psychosocial, and spiritual distress as a result of multiple organ failure, the symptom burden is so heavy that one of their main wishes is to be comfortable and symptom-free at the end stage of their lives (1). Thus, tailored symptom management is the basis to improve the quality of life in their last period of life. The overall prevalence of fatigue in patients with advanced cancer is 74% (2). It appears to be more severe in patients who have worse performance status or more extensive disease (3). Thus, fatigue is one of the most pervasive symptoms experienced by patients with advanced cancer. In addition, it has a great impact on cancer patients' quality of life, and may even increase the risk of suicide (4). Therefore, it is an urgent issue to alleviate fatigue of patients with advanced cancer.

Symptoms of advanced cancer patients do not result from physical deterioration alone. Fatigue has been known as a multidimensional phenomenon (5), a subjective sensation attributable to disease progression and a host of secondary psychosocial and spiritual stresses in advanced cancer patients (6). Cancer cachexia, malnutrition, muscle wasting and complications from cancer therapy are some of the biological factors resulting in fatigue (7). In addition, several lines of evidence demonstrate a variety of terminal symptoms associated with fatigue in cancer patients, such as pain, dyspnea, lack of appetite and nausea, which significantly limit patients' daily activities (8). Psychologically, prolonged stressful symptoms and sufferings result in exhaustion (9). Decreased social activities and poor family support and interpersonal relationship further aggravate the fatigue (10,11). Spiritual distress and needs, such as death fear and

urgency to fulfill their will also raise the fatigue intensity (6). Therefore, physical deterioration and suffering, psychological distress, changes in interpersonal relationships, and needs to pursue the purpose and meaning of life may all be the underlying causes of their fatigue (12-14).

Fatigue is still a critical issue in the care of cancer patients; there are several guidelines developed for management of cancer-related fatigue. Treatment with dexamethylphenidate, exercise, and psychosocial interventions are reported to be significantly beneficial for fatigue relief in patients with cancer (15-17). In addition, optimizing management of associated symptoms of fatigue has also been recommended in the care of patients with cancer (18). However, evidence-based interventions have not yet established, especially for fatigued patients with advanced cancer.

A randomized controlled trial by de Raaf *et al.* suggests that nurse-led monitoring and protocolized management of physical symptoms is effective in alleviating fatigue in patients with advanced cancer. Although the participants in that study were patients with advanced cancer, they relatively had better performance status [Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2] and longer survival (life expectancy ≥ 4 months). In addition, the study did not find the effect of the intervention on some essential components of patients' suffering, such as physical senses of tiredness, difficulties with concentrating, depressed mood, and other aspects of quality of life. However, the study is very important to demonstrate a case management with coordinated care model to alleviate fatigue of advanced cancer patients, consisting of symptom monitoring, protocolized treatment, patient education,

adjustment of symptomatic medication, nonpharmacologic interventions, referral to other specialists, and so on. In addition, the participants in the intervention group received extra attention from the health care providers, which should contribute to the positive results. Thus, such a comprehensive multidisciplinary care should be promoted to alleviate fatigue of advanced cancer patients, who have better functional performance and longer survival (19).

On the other hand, in the setting of hospice and palliative care, the symptom management for patients with far advanced cancer, with a mean life expectancy of 2-3 weeks, has certain identifiable patterns. A study shows that patients averaged 9.1 symptoms at the time of admission to a palliative care unit. While a majority of symptoms improved a week after admission, many symptoms worsened before passing (20). Disease progression will cause an increase in symptom intensity and the emergence of new symptoms (19). A prospective and longitudinal study has showed that the changes of subjective symptoms and objective signs are parallel to each other, indicating improvement during initial 1-2 weeks after admission and significant deterioration at 2 days before death. This finding suggests that physical distress may not improve for long due to the rapid progression of disease status near the end of life (6). In addition, at the advanced stage, severe psychosocial and spiritual distress will accelerate the symptom intensity, resulting in symptoms that are multiple, concurrent, moderate-severe in intensity, and very challenging to treat.

The management of fatigue in the care of patients with advanced cancer is also a complex problem. The study by de Raaf *et al.* demonstrates that the intervention is effective when administered frequently, whereas symptom scores start increasing again when the intervention is completed (19). Another study demonstrates the pattern of fatigue intensity during admission in a palliative care unit is stationary-increase, suggesting fatigue being a poorly controllable symptom in advanced cancer patients (21). Fatigue may be associated with the cancer anorexia-cachexia syndrome, which is an irreversible condition, and whose clinical manifestations include muscle wasting and other metabolic disturbances (22). This syndrome is caused mainly by pro-inflammatory cytokines, such as TNF α , IL-1, IL-6, and prostaglandins secreted by both cancer and inflammatory cells (23). As these mediators could not be completely blocked by therapeutic agents, especially in the far advanced stage, the associated symptoms progress with time (21).

It is very important to develop effective interventions for fatigue of advanced cancer patients. As defined by

the World Health Organization, palliative care is to improve quality of life of patients and families who face life-threatening illnesses by providing pain and symptom relief, spiritual and psychosocial support to them from diagnosis to the end of life and bereavement. It has been proved that comprehensive palliative care can facilitate terminal cancer patients to have good quality of life and experience a good death (24). The palliative care team consists of members with medical, psychological, and spiritual backgrounds, including physicians, nurses, clinical psychologists, chaplains, and social workers. Once cancers become refractory to curative therapy, symptoms from multiple organ failures inevitably develop and physical conditions deteriorate. At the end stage of cancer patients' lives, palliative care provides total care to modify the natural course of symptom progression, leading to a peaceful death for them (21).

There are several tips on relieving fatigue and promoting their quality of life. Early referral to palliative care, optimal pharmacological and non-pharmacological management, quick establishment of warm emotional attachment among peer patients, family, and health professionals are some of those tips (21). Psycho-social-spiritual care should be given precedence, especially during the last a few days of life. Particularly, fatigue is a multidimensional phenomenon with different connotations in different societies and cultures (6). As hospice professionals, we have to understand the importance of psychological and spiritual support in promoting patients' quality of life, especially in the management of intractable fatigue (6).

Terminal patients may require different strategies of symptom control, even in the same stage in the dying process. Upon entering the palliative ward, patients with an estimated survival time of 3 weeks may find their physical symptoms alleviated due to the hospice care; in the middle stage, however, the symptoms aggravate as the organs and physical systems start to fail; psychological adjustments and social supports may help ease the symptom at this stage. By the end stage, since patients are literally at the door of death, only spiritual enlightenment, not medical treatment, can help them manage the fear of dying (25).

In conclusion, holistic care that encompasses physical, psychosocial and spiritual aspects represents a rational approach for the relief of incurable symptoms at the end stage of life for advanced cancer patients. So far, accumulated knowledge suggests that comprehensive care through a multidisciplinary team is the best intervention to relieve fatigue for these patients.

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