Commentary

Cancer-related fatigue (CRF) is one of the most common problems facing patients both during and after completion of treatment. Overall 50%–90% of cancer patients experience fatigue the latter number corresponding with those undergoing active anticancer chemotherapy or radiotherapy and around 30% of patients continue to have moderate to severe fatigue 6 months after completion of treatment.[1,2] According to the National Comprehensive Cancer Network (NCCN) CRF is defined as "a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning."[3] The pathophysiology of CRF has not been adequately elucidated, and multiple mechanisms have been proposed in its causation. Some of the factors include activation of proinflammatory cytokines (tumor necrosis factor alpha, interleukin 1, interleukin 6), dysregulation of serotoninergic system, hypothalamic pituitary–adrenal axis or circadian rythm, defective adenosine triphosphate (ATP) regeneration, cancer cachexia-anorexia syndrome, anemia, depression, insomnia, chemotherapy and radiotherapy and concurrent comorbidities such as hypothyroidism, infections, and organ failures. Multiple mechanisms have been proposed, and therapeutics are being investigated implying a multimodal approach for the management of fatigue.[4]

The authors in the present study[5] have highlighted a very important aspect of cancer care that is often under-recognized, under-reported, and under-treated resulting in a debilitating quality of life. The major challenge in the management of fatigue is identifying fatigue as a significant problem and nonavailability of objective assessment tool. Although the effort is being directed at developing an objective tool for measuring the physical and cognitive changes caused by fatigue, there is no validated tool for diagnosing fatigue and oftentimes objective assessment is clouded by behavioral manifestations as may be reported by family.[6] Visual analog scale (VAS) for the assessment of severity of fatigue may be used as an initial tool followed by detailed clinical examination and investigations commensurate with the clinical suspicion. The management of fatigue often necessitates a multimodal approach. For mild fatigue on a VAS of 1–3 nonpharmacological techniques such as exercise, yoga, cognitive-behavioral therapy, and sleep therapy can be used.[7] However, patients with moderate-to-severe fatigue with a VAS score of ≥4 may benefit from pharmacological intervention although the evidence to support the benefit of pharmacological intervention is low.

Many studies have proven the beneficial effects of exercise in patients with fatigue with a demonstrable improvement in quality of life. The current NCCN guidelines recommendation is to begin with low intensity and short duration exercise with modification of exercise plan depending on patient's response and severity of fatigue. An exercise plan that includes 20–30 min duration, three to five times a week may have a beneficial effect on patient's fatigue.[3] However, cancer patients who exercised more than 60 min reported an increase in fatigue. Interesting piece of work by Dimeo *et al*. reported endurance training-related decreases in both heart rate and blood lactate concentrations at submaximum intensities reflecting improved functional status and increased metabolic efficiency for a given workload. Endurance training induces improved metabolic efficiency. This could be explained by the fact that there is increased recruitment of the oxidative fibers and decrease in the glycolytic fibers. The oxidative fibers produce less lactate, metabolize the lactate, and oxidize them for fuel generation. Furthermore, oxidative fibers are more resilient to stress as compared to glycolytic fibers. Endurance training improves oxygen uptake by the exercising muscles, improve the cardiorespiratory function, blood oxygen transport, and muscle aerobic capacities (mitochondrial density or capillarization of muscle fibers). Exercise can attenuate cardiac and skeletal toxicities of certain chemotherapies such as anthracyclines and myeloablative therapies. It triggers erythropoeisis and attenuates skeletal atrophy by suppressing the inflammatory response, enhancing the rate of protein synthesis, and antioxidant enzyme activities.[8] Exercise training has proven manifold benefits in the management of fatigue, thus, early institution of fatigue management program right from the point of initiating the disease directed treatment may help in obtaining better outcomes with respect to patient quality of life and physical functioning. This will also prevent premature discontinuation of the disease directed treatment, keep a check on patient adherence, and prevent drop outs from treatment.

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