Does Muscle-Derived Interleukin-6 Mediate Some of the Beneficial Effects of Exercise on Cancer Treatment–Related Fatigue?

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Purpose/Objectives: To review evidence that muscle-derived interleukin-6 (IL-6) mediates some of the beneficial effects of exercise on cancer treatment–related fatigue (CTRF).

Data Sources: Electronic nursing, psychology, and medicine databases.

Data Synthesis: Fatigue is a common and often debilitating symptom associated with cancer treatment. Although the molecular mechanisms underlying CTRF have yet to be fully elucidated, it may be akin to the fatigue associated with "sickness behavior," which is initiated by the production of the proinflammatory cytokines interleukin-1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α). Physical exercise has been shown to decrease fatigue levels in patients with cancer undergoing treatment. Skeletal muscle selectively produces IL-6 during exercise, and muscle-derived IL-6 can decrease the production and activity of IL-1β and TNF-α. Thus, the anti-inflammatory effects of muscle-derived IL-6 may be a mechanism underlying the observed beneficial effects of exercise on CTRF.

Conclusions: Further studies are needed to determine whether the anti-inflammatory effects of exercise underlie its beneficial effects on CTRF.

Implications for Nursing: Nurses have proven to be leaders in the field of cancer symptom management. An understanding of potential mechanisms underlying the beneficial effects of exercise on CTRF may help to fine-tune exercise interventions to maximize symptom control and to identify new treatment strategies for fatigued patients with cancer who are unable to participate in an exercise program.

Fatigue is a common and often debilitating symptom associated with cancer treatment. Although the molecular mechanisms underlying cancer treatment–related fatigue (CTRF) have yet to be fully elucidated, it may be homologous to the fatigue associated with "sickness behavior," a cluster of symptoms caused by the production of the proinflammatory cytokines interleukin-1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α). Physical exercise has been shown to decrease fatigue levels in patients with cancer undergoing treatment. Yet the mechanisms underlying this benefit are unclear. This article discusses recent observations regarding the secretion of interleukin-6 (IL-6) by exercising muscle, its anti-inflammatory effects, and its potential relevance to the beneficial effects of exercise on CTRF.

Overview of Concepts

"Cancer-related fatigue is 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" (National Comprehensive Cancer Network, 2009, p. FT-1). Fatigue often begins at the start of treatment and is the most common symptom experienced by patients undergoing cancer treatment (Irvine, Vincent, Graydon, Bubela, & Thompson, 1994). Given the effect that CTRF has on physical functioning and quality of life, its management is a crucial component of the cancer treatment plan. Although the cause of CTRF remains unclear, it may be the same as sickness behavior, a normal physiologic response to infection or tissue injury that is initiated by the production of IL-1β and TNF-α by immune cells (Dantzer & Kelley, 2007; Wood, Nail, Gilster, Winters, & Elsea, 2006). In a healthy individual, serum levels of IL-1β and TNF-α are low or undetectable (0–10 pg/ml). However, in response to immune challenge (e.g., infection, tissue damage), serum levels of IL-1β and TNF-α increase 10- to 100-fold, depending on the magnitude of the immune stimulus. IL-1β and TNF-α, in turn, trigger the production of IL-6, leading to an increase in serum levels of the cytokines (Mant et al., 2008). Although a direct role for the cytokines in CTRF has yet to be demonstrated, indirect evidence supports the idea. First, patients with cancer undergoing treatment often experience several symptoms, including anorexia, cachexia, pain, sleep disturbance, and depression, which