Cytokines and exercise: effects of muscle damage, carbohydrate and antioxidants

JONATHAN PEAKE and KATSUHIKO SUZUKI
(School of Human Sciences, Waseda University)

Interest in the effects of exercise on cytokine production has increased dramatically in the past decade. Exercise studies have adopted a variety of experimental approaches to examine the factors affecting cytokine production within skeletal muscle and systemic cytokine concentrations. In particular, research has focused on the influence of exercise–induced muscle damage, carbohydrate ingestion and antioxidant supplementation.

Eccentric exercise has been a popular exercise model to investigate how muscle damage affects cytokine production/release. Eccentric cycling increases the plasma concentration of interleukin (IL)-6, which is described as ‘inflammation responsive’, increased to a greater extent after eccentric cycling compared to concentric cycling. Other studies have reported increased plasma concentrations of IL-6 and IL-1 receptor antagonist (ra) after downhill treadmill running. However, the significance of these findings is unclear for two reasons. Firstly not all of these studies included level treadmill running as a comparison. Secondly, cytokine production in some of these studies may have been influenced more by exercise intensity than muscle damage. We have recently conducted several studies investigating the relationship between exercise–induced muscle damage and plasma cytokine levels. Moderate–intensity downhill running increased the plasma IL-6 concentration, but this increase was not significantly greater than level treadmill running. Furthermore, downhill running did not affect the plasma concentrations of other cytokines such as IL-1ra, IL-8, IL-10 and granulocyte–colony stimulating factor (G-CSF). We have found that despite evidence of severe muscle damage after eccentric contractions of the elbow flexors, changes in plasma cytokine concentrations were relatively minor. Furthermore, large increases in the plasma cytokine concentrations did not correlate with markers of muscle damage after an Ironman triathlon. Therefore, data from our studies suggest that exercise–induced muscle damage is not the major stimulus for cytokine production.

A number of studies have investigated cytokine changes in response to manipulation of dietary carbohydrate and carbohydrate ingestion during exercise. A low carbohydrate diet before exercise enhances the plasma concentrations of IL–1ra, IL–6 and IL–10. Furthermore, consumption of carbohydrate during exercise significantly attenuates skeletal muscle mRNA expression for IL–6 and IL–8, and also the plasma concentrations of IL–1ra, IL–6 and IL–10. It is well–established now that IL–6 is sensitive to changes in muscle glycogen, and during prolonged exercise IL–6 signals the liver to increase glucose output.

More recently, exercise studies have focused on the effects of antioxidant supplementation on cytokine production/release. The rationale for these studies was that reactive oxygen species may stimulate cytokine production during exercise. The results from these studies are conflicting. Some studies have reported that large doses of vitamin C (1500 mg per day) attenuate plasma concentrations of IL–10 and IL–1ra, whereas others have found no effect. Large doses of vitamin E (800 I. U. per day) may actually promote rather than attenuate cytokine production in response to strenuous endurance exercise. A combination of vitamins C and E has reduced cytokine production following exercise in some studies, but not others. These inconsistent findings may have arisen due to variation in the types of antioxidant supplements used, the period of supplementation, the type of exercise and the fitness level of the participants.