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INTERLEUKIN-6 KINETICS IN BLOOD AFTER ACUTE EXERCISE: MECHANISMS AND CLINICAL IMPLICATIONS

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Abstract: Interleukin-6 (IL-6) is a multifunctional cytokine that plays a central role in regulating immune and metabolic responses to exercise. This literature review examines the kinetics of IL-6 in the blood after acute exercise sessions, highlighting the main factors that influence its release, such as the type of exercise, intensity, duration and energy supplementation. The studies reviewed indicate that long-term aerobic exercise tends to cause more significant increases in IL-6 levels compared to resistance exercise. In addition, carbohydrate ingestion during exercise can attenuate IL-6 elevation, while fasted exercise amplifies this response. The clinical implications of these findings are discussed, especially in relation to the use of exercise as a therapeutic strategy to modulate the inflammatory state in individuals with chronic conditions. The review concludes that IL-6 is an essential mediator of adaptations to exercise and suggests directions for future research in the area.

Keywords: Interleukin-6, physical exercise, immune response, cytokine kinetics, energy supplementation, metabolic adaptation, inflammation.

INTRODUCTION

Interleukin-6 (IL-6) is a multifunctional cytokine that plays a central role in both the immune system and energy metabolism. During exercise, IL-6 is one of the main cytokines released by skeletal muscle, functioning as a “myokine” that mediates various biological responses. Its release is influenced by various factors, such as the intensity, duration and type of exercise, as well as the individual's nutritional status and physical condition (PEDERSEN; FEBBRAIO, 2008) (FISCHER, 2006).

Studies indicate that physical exercise can cause a significant increase in circulating IL-6 levels, with a peak shortly after the activity

and a subsequent gradual reduction. This transient increase in IL-6 plays a crucial role in mediating metabolic and immunological adaptations to exercise, promoting an anti-inflammatory response and facilitating the mobilization of energy substrates. However, the impact of exercise on IL-6 kinetics is complex and depends on a multifactorial interaction that includes the type of muscle contraction, the amount of muscle mass recruited and the availability of energy substrates (STEENSBURG et al., 2001) (NORTHOFF; BERG, 1991).

Given the relevance of IL-6 in the context of exercise, it is essential to understand the variations in its kinetics in response to different exercise modalities. This review seeks to synthesize the current evidence on the dynamics of IL-6 in the blood after an acute exercise session, highlighting the main factors that influence its release and the clinical implications of these responses (PEDERSEN; FEBBRAIO, 2008) (OSTROWSKI et al., 1998).

METHODOLOGY

This literature review was carried out with the aim of compiling and analyzing studies investigating the kinetics of interleukin-6 (IL-6) in the blood after acute exercise sessions. The search for relevant articles was conducted in the PubMed, Scopus, Embase, Web of Science, Cochrane, CINAHL and ScienceDirect databases, covering publications up to May 2024.

SEARCH STRATEGY

- Search terms related to IL-6, physical exercise and cytokine kinetics were used, combining keywords such as “Interleukin-6”, “Exercise”, “Cytokine Kinetics”, “Acute Exercise”, and “Blood IL-6”. The Boolean operators “AND” and “OR” were used to refine the search and ensure that relevant studies were

included.

INCLUSION AND EXCLUSION CRITERIA

- The inclusion criteria for selecting the studies were as follows:
 - Studies evaluating the IL-6 response in the blood of humans after an acute exercise session.
 - Studies that included pre- and post-exercise IL-6 measurements at different time intervals.
 - Publications in English, Portuguese or Spanish.
- The exclusion criteria were:
 - Studies carried out on animal models.
 - Studies that did not report quantitative data on IL-6 in the blood.
 - Peer-reviewed studies, but no access to the full text.

STUDY SELECTION AND ANALYSIS

- After removing duplicates, the titles and abstracts of the identified articles were reviewed to determine their eligibility based on the above criteria. The selected studies were analyzed in depth, and their results were organized and synthesized in this review, focusing on the factors that influence IL-6 kinetics after exercise, such as type of exercise, intensity, duration and energy supplementation.

RESULTS

This literature review analyzed several studies that explored the response of interleukin-6 (IL-6) in the blood after acute sessions of physical exercise. The results indicate that the kinetics of IL-6 are largely dependent on variables such as the type of exercise, the intensity, the duration of the activity and the nutritional status of the participants.

TYPE OF EXERCISE

- The studies reviewed show that aerobic exercise, particularly long-duration exercise, tends to cause more significant increases in IL-6 levels compared to resistance exercise. For example, modalities such as running and cycling, performed at moderate to high intensities, often result in substantial increases in IL-6, with peaks observed shortly after the end of the exercise. In contrast, resistance exercise, especially when performed at a lower volume or in short duration protocols, shows a less pronounced IL-6 response (HELGE et al., 2003) (NINDL et al., 2009).

INTENSITY AND DURATION OF EXERCISE

- The intensity and duration of exercise are critical factors that modulate the release of IL-6. High-intensity, longer-duration exercise is consistently associated with greater elevations in circulating IL-6 levels. The literature suggests that prolonged exercise, such as marathons or endurance sessions lasting several hours, can result in IL-6 increases of up to 100 times baseline values. In contrast, short-term exercise, even if intense, tends to generate smaller and more transient responses (PETERSEN; PEDERSEN, 2005) (OSTROWSKI et al., 1999).

ENERGY SUPPLEMENTATION

- The presence or absence of energy supplementation during exercise also influences IL-6 kinetics. Studies indicate that ingesting carbohydrates during exercise can attenuate the rise in IL-6 in the blood, probably due to the maintenance of adequate glucose levels, which reduces the body's need to mobilize alternative energy substrates. On the other hand, fasted exercise tends to amplify the IL-6 response, due to the greater metabolic stress imposed on the body (FEBBRAIO et al., 2003) (NIEMAN et al., 2003).

CLINICAL IMPLICATIONS

- The findings of this review suggest that IL-6 plays a crucial role in both the inflammatory response and metabolic adaptation to exercise. The transient elevation of IL-6 after exercise is considered beneficial, promoting an anti-inflammatory environment and facilitating muscle recovery. However, variations in the IL-6 response can have important clinical implications, especially in individuals with chronic inflammatory conditions or other comorbidities (VILLAR-FINCHEIRA et al., 2021).

DISCUSSION

The results of this literature review reinforce the complexity of the IL-6 response to physical exercise and its importance as a mediator of immunological and metabolic adaptations. IL-6 is a multifunctional cytokine that performs paradoxical functions in the body, acting as both a pro-inflammatory and anti-inflammatory agent, depending on the physiological context. During exercise, its release is influenced by a variety of factors, including the type, intensity and duration of exercise, as well as the individual's nutritional condition.

COMPARING TYPES OF EXERCISE

- The review showed that long-term aerobic exercise generally causes more pronounced increases in IL-6 levels compared to resistance exercise. This difference can be attributed to the greater recruitment of muscle fibers and the increase in energy demand during aerobic exercise, which stimulates the production of IL-6 to meet metabolic needs. In addition, aerobic exercise promotes greater mobilization of energy substrates such as glucose and fatty acids, which may explain the higher IL-6 levels observed. On the other hand, although resistance exercise also raises IL-6 levels, it tends to generate less pronounced responses, especially when performed at a lower volume or intensity. However, in high-intensity protocols with greater muscle involvement, resistance exercise can result in significant increases in IL-6, suggesting that the magnitude of the response is more related to intensity and metabolic stress than to the type of exercise itself (KELLER et al., 2001).

INFLUENCE OF ENERGY SUPPLEMENTATION

- The literature reviewed highlights the modulating role of energy supplementation in the IL-6 response to exercise. Carbohydrate ingestion during exercise appears to attenuate IL-6 elevation, which can be explained by maintaining adequate blood glucose levels and reducing the need to mobilize other energy sources. In contrast, exercise performed in a fasted state results in an amplified IL-6 response, reflecting the greater metabolic stress and the greater need to mobilize alternative energy substrates (TOMINAGA et al., 2019) (ADEVA-ANDANY et al., 2016).

PHYSIOLOGICAL AND CLINICAL IMPLICATIONS

- The transient IL-6 response to exercise is widely considered to be beneficial, promoting anti-inflammatory adaptations and facilitating muscle recovery. However, it is important to consider that variations in IL-6 kinetics may have different clinical implications, especially in specific populations, such as individuals with chronic inflammatory diseases, obesity or diabetes. Exercise can act as a crucial modulator of the inflammatory state in such populations, and manipulating intensity, duration and supplementation during exercise can be a useful strategy to optimize therapeutic benefits (PEDERSEN; FEBBRAIO, 2012) (BROHOLM; PEDERSEN, 2010).

FUTURE DIRECTIONS

- Despite progress in understanding IL-6 kinetics in response to exercise, there are still gaps to be explored. Future studies should focus on the interaction between different types of exercise and nutritional interventions, as well as investigating the role of IL-6 in populations with specific health conditions. Additionally, investigating the molecular mechanisms underlying IL-6 release and its autocrine and paracrine function in muscle tissue may offer new perspectives on exercise-mediated metabolic and immune regulation (GIUDICE; TAYLOR, 2017).

CONCLUSION

The kinetics of interleukin-6 (IL-6) after exercise is a complex and multifaceted phenomenon, influenced by several factors, including the type of exercise, intensity, duration and nutritional status. The IL-6 response to exercise plays a crucial role in mediating immunological and metabolic adaptations, and is an important regulator of the interaction between exercise and the immune system.

This review highlights that long-term aerobic exercise tends to cause more significant increases in IL-6 levels compared to resistance exercise. In addition, energy supplementation, especially with carbohydrates, can attenuate the rise in IL-6, while fasted exercise tends to amplify this response. These findings have important clinical implications, especially for populations with chronic inflammatory

conditions, in which exercise can be used as a therapeutic strategy to modulate the inflammatory state.

Although considerable progress has been made in understanding IL-6 kinetics in response to exercise, there is a need for further research to clarify the mechanisms underlying this response and its long-term implications for health. Future studies should focus on how different exercise interventions and nutritional strategies can be optimized to maximize the benefits of IL-6 in the context of exercise.

In summary, IL-6 has emerged as an important mediator of exercise responses, with significant therapeutic potential. A better understanding of its kinetics and the factors that influence it could open up new possibilities for personalized interventions in the field of health and well-being.

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