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High intensity interval training (HIIT) as a viable alternative to induce the prevention of respiratory diseases: a point of view of exercise immunology during COVID-19 outbreak

Treinamento intervalado de alta intensidade (HIIT) como alternativa viável para induzir a prevenção de doenças respiratórias: um ponto de vista da imunologia do exercício durante o surto de COVID-19

El entrenamiento en intervalos de alta intensidad (HIIT) como alternativa factible para inducir la prevención de enfermedades respiratorias: una vista de inmerología del ejercicio durante el brote de COVID-19

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Abstract

The immune system's response against SARS-Cov-2 seems crucial to control viral infection, since this system is homeostatic, dynamic and promotes immunoprotection of the organism through the activation of the innate and adaptive immune system via activation of cellular and chemical complexes that recognize, neutralize, metabolize and eliminate heterologous substances, with or without tissue damage. An obesogenic microenvironment can further increase the risk of disease complications, and cause a more virulent viral strain and a more lethal virus. Moreover, physical inactivity as well as poor eating habits impairs the body's energy metabolism and immune cells due to low-grade chronic inflammation. Studies suggest that light to moderate exercise, as well as mild calorie restriction, as an effective approach to relieve obesity and therefore an interesting strategy to strengthen the immune response during the outbreak of COVID-19, while a vaccine is not developed. Some studies have been shown significant findings in favor of High intensity interval training (HIIT) protocols when compared to moderate intensity exercise, showing how immunological system responds to vigorous to high intensity training. However, HIIT has a lower cost of time, reducing the

time/efficiency ratio, that is, a lower cost of time with similar or even better benefits to higher volume exercise programs. Let us not forget: "time is the most precious asset we have".

Keywords: Immune Complex; Exercise; Severe acute respiratory syndrome related coronavirus; High-Intensity Intermittent Exercise.

Resumo

A resposta do sistema imune contra o SARS-Cov-2 parece fundamental para o controle da infecção viral, uma vez que este sistema é homeostático, dinâmico e promove imunoproteção do organismo por meio da ativação do sistema imune inato e adaptativo via acionamento de complexos celulares e químicos, que reconhecem, neutralizam, metabolizam e eliminam substâncias heterólogas, com ou sem lesão tecidual. Um microambiente obesogênico pode aumentar ainda mais o risco de complicações da doença e também causar uma cepa viral mais virulenta e um vírus mais letal. Além disso, a inatividade física, bem como hábitos alimentares inadequados, prejudicam o metabolismo energético do corpo e também das células imunológicas devido à inflamação crônica de baixo grau. Estudos sugerem que exercícios leves a moderados, bem como restrição calórica leve, são uma abordagem eficaz para atenuar a obesidade e, portanto, uma estratégia interessante para fortalecer a resposta imunológica durante o surto de COVID-19, enquanto uma vacina não é desenvolvida. Alguns estudos têm mostrado achados significativos a favor dos protocolos de treinamento intervalado de alta intensidade (HIIT) quando comparados ao exercício de intensidade moderada, mostrando como o sistema imunológico responde ao treinamento vigoroso ao de alta intensidade. Porém, o HIIT tem um custo de tempo menor, reduzindo a relação tempo/eficiência, ou seja, um custo de tempo menor com benefícios semelhantes ou até melhores aos programas de exercícios de maior volume. Não esqueçamos: “o tempo é o bem mais precioso que possuímos”.

Palavras-chave: Complexo imunológico; Exercício; Coronavírus relacionado à síndrome respiratória aguda grave; Exercício intermitente de alta intensidade.

Resumen

La respuesta del sistema inmunológico frente al SARS-Cov-2 parece fundamental para el control de la infección viral, ya que este sistema es homeostático, dinámico y favorece la inmunoprotección del organismo mediante la activación del sistema inmunológico innato y adaptativo mediante la activación de complejos celulares. y productos químicos, que reconocen, neutralizan, metabolizan y eliminan sustancias heterólogas, con o sin daño tisular.

Un microambiente obesogénico puede aumentar aún más el riesgo de complicaciones de la enfermedad y también causar una cepa viral más virulenta y un virus más letal. Además, la inactividad física, así como los hábitos alimenticios inadecuados, perjudican el metabolismo energético del cuerpo y también las células inmunes debido a la inflamación crónica de bajo grado. Los estudios sugieren que el ejercicio ligero a moderado, así como la restricción calórica leve, son un enfoque eficaz para aliviar la obesidad y, por lo tanto, una estrategia interesante para fortalecer la respuesta inmune durante el brote de COVID-19, mientras no se desarrolle una vacuna. Algunos estudios han mostrado hallazgos significativos a favor de los protocolos de entrenamiento en intervalos de alta intensidad (HIIT) en comparación con el ejercicio de intensidad moderada, mostrando cómo el sistema inmunológico responde al entrenamiento vigoroso y de alta intensidad. Sin embargo, HIIT tiene un menor costo de tiempo, reduciendo la relación tiempo / eficiencia, es decir, un menor costo de tiempo con beneficios similares o incluso mejores a los programas de ejercicio de mayor volumen. No olvidemos: “el tiempo es el bien más preciado que tenemos”.

Palabras clave: Complejo inmunológico; Ejercicio; Coronavirus relacionado con el síndrome respiratorio agudo severo; Ejercicio intermitente de alta intensidade.

1. Introduction

In 2020, the coronavirus pandemic was officially declared by the World Health Organization (WHO), which by scientific definition was called Coronavirus disease 2019 (COVID-19). After an outbreak of infections caused by a new coronavirus, a member of the betacoronavirus family, which causes excessive production of pro-inflammatory cytokines, affecting lung cells via endocytosis and the Angiotensin-converting enzyme 2 (ACE-2) receptor, and generates severe acute respiratory syndrome to coronavirus-2 (SARS-CoV-2) (Valencia, 2020). The immune system's response against SARS-Cov-2 seems crucial to control viral infection, since this system is homeostatic, dynamic and promotes immunoprotection of the organism through the activation of the innate and adaptive immune system via activation of cellular and chemical complexes, that recognize, neutralize, metabolize and eliminate heterologous substances, with or without tissue damage (Horiguchi et al., 2018).

The incubation time for COVID-19 viral infection varies from 5.1 to 11.5 days, and can present mild to severe symptoms, mainly affecting the elderly and individuals with pre-existing chronic medical conditions (Horiguchi et al., 2018; Luzi & Radaelli, 2020). An

obesogenic microenvironment can further increase the risk of disease complications, and also cause a more virulent viral strain and a more lethal virus (Luzi & Radaelli, 2020).

Moreover, physical inactivity as well as poor eating habits impairs the body's energy metabolism and also immune cells due to low-grade chronic inflammation (Simpson et al., 2020). Luzi and Radaelli (Luzi & Radaelli, 2020) suggest that light to moderate exercise, as well as mild calorie restriction, as an effective approach to relieve obesity and therefore an interesting strategy to strengthen the immune response during the outbreak of COVID-19, while a vaccine is not developed. Furthermore, patients with chronic obstructive pulmonary disease (COPD) who also have difficulty breathing due to the blockage of airflow, similar to that observed in SARS-CoV-2, frequently present overweight or obesity (James et al., 2018), and physical exercise can also reduce cardiometabolic risk and future mortality assisting in the treatment of COPD (James et al., 2018).

2. Methodology

A narrative review was conducted. Cross-sectional studies and clinical trials that explore the role of HIIT on markers of the immune system were included, such as: natural killer cells, neutrophils, antibodies, nuclear factor-erythroid 2-related factor-2, NF-κB, TNF-α, IL-1b and IL-6, T, B cells and immunoglobulin. The electronic search was carried out in the following databases: SCOPUS, PubMed, Science Direct, Lilacs, SciELO, Google Scholar and Web of Science. No language or year of publication restrictions were imposed. We analyzed titles and abstracts to decide whether a study could be included in our review. Articles were included if they met the following criteria: having undergone peer review and/or research-based. Studies with incomplete data were excluded.

3. Exercise Approach and Immune Responses

Physical exercise, seems to be an excellent immune regulator capable of improving the responses of both the innate and adaptive immune systems with increased blood concentrations of natural *killer cells* (NK), neutrophils and antibodies (Wells et al., 2016) and represents a non-pharmacological therapeutic strategy for different pathophysiology such as obesity, for example (Pedersen & Saltin, 2015). The skeletal muscle acts as an endocrine organ and is adequate of causing an immunomodulation and activation of the immune response (Pedersen & Saltin, 2015) and the immune system, in turn, is able of causing the

functional remodeling of the skeletal muscle and adaptations after the mechanical stress arising from the training (Wells et al., 2016).

Directly, physical exercise seems upregulates the nuclear factor-erythroid 2-related factor-2 (Nrf2). Nrf2 has been associated with an improvement in the inflammatory profile because of its ability to antagonize NF-κB. Mao et al. (Mao et al., 2010) using an Nrf2 (-/-) model, observed increased activation and expression of NF-κB and TNF-α. In addition, Jin et al. (Jin et al., 2008) observed that knockout mice (KO) for Nrf2 presented greater activation of NF-κB, inflammatory cytokines TNF-α, IL-1b and IL-6. Thus, as physical exercise results in an increase in Nrf2 and this in turn reduce the inflammatory response. Therefore, it is reasonable to infer that there are likely positive effects of exercise on the immune system in individuals with different health complications (James et al., 2018; Luzi & Radaelli, 2020), autoimmune patients and also healthy individuals (Richard J Simpson et al., 2020; Wells et al., 2016).

It seems that the influence of physical exercise on the immune system is dose-dependent in relation to its intensity and volume (Khammassi et al., 2020; D. C. Nieman et al., 1990; Simpson et al., 2020; Valencia, 2020). Nieman et al. (D. C. Nieman et al., 1990) proposes an open window of alteration of the immune system after physical exercise, and such manifestation would occur with significant magnitude in the face of long-lasting endurance, such as in a marathon, or also in the face of extremely heavy efforts. So, running a marathon suppresses immune function (David C Nieman, 2007) through transient leukocytosis and immunodepression by activating the sympathetic nervous system , releasing catecholamines and glucocorticoids. Thus, elevated cortisol is associated with inhibition of NK cell function and can also depress both the production and function of T, B cells and immunoglobulin A (IgA), and thus corroborate the increased risk of impairment of upper respiratory tract infections (ITRS) during the subsequent days. In addition to the studies already mentioned with aerobic scope, Wells et al. (Wells et al., 2016)evaluated resistance training protocols of high volume and moderate intensity (10 – 12 repetitions with a load equating to 70% of their 1RM) *versus* high intensity and low volume (3 – 5 repetitions with a load equating to 90% of their 1RM). Was observed that markers of muscle damage were significantly higher in the protocol of high intensity and low volume, however both training induce a pro-inflammatory response similar without difference between the types of training, inferring that the likely modulation of the immune system could be dependent on the intensity of the training.

Based on a consensus then, it was suggested that only exercises of moderate intensity and short duration (up to 45 minutes) would cause positive effects with reduced inflammation (Simpson et al., 2020) while intense exercises would increase the risk of infection. It is worth mentioning that athletes are more susceptible to ITRS due to changes in mucosal immunity (James et al., 2018; Simpson et al., 2020).

Although, more recent studies demonstrate that physical exercise is associated with an anti-inflammatory state and only a transient suppression of immunological components. Endurance athletes, for example, they can neutralize the effects of post-exercise immune suppression with exercise-adaptive lymphocytic homeostasis and positive regulation of anti-apoptotic proteins to the detriment of pro-apoptotic proteins. Prolonged and exhausting exercise usually reduces T lymphocytes and pro-inflammatory cytokine, interferon-γ (IFN-γ) in the blood, in addition to elevating cytokines and anti-inflammatory mediators such as interleukin-4 (IL-4) and interleukin-10 (IL -10), thus, an anti-inflammatory state induced by strenuous exercise or heavy exercise (Shaw et al., 2018). An example of this statement is presented by Born, Zinner, Sperlich (Born et al., 2017) and Khammassi et al., (Khammassi et al., 2020) who found an improvement in immune function with high-intensity interval training (HIIT) and observed improvements in immune functions, less risk of infection and inflammation, functional adaptation of the immune system in response to increased stress and training load.

Recently, Netea et al., (Netea et al., 2016) demonstrated that the innate immune system can present "trained immunity" or "innate immune memory" a characteristic of the adaptive immune system after being challenged by pathogens, expanding the possibility of changes in immune self regulation, the which causes an increase in inflammatory mediators and improves the response after stimulus to eliminate the infection. This "trained immunity" is based on intracellular and metabolic epigenetic changes in the innate immune system with changes in histones, chromatin reconfiguration, DNA methylation and / or the action of microRNAs (Netea et al., 2016). Therefore, this change in the pattern of classical immunological memory and the activation of trained immunity, require further research to better explore this new immune pattern.

4. Final Considerations

In summary, some studies have been shown significant findings in favor of HIIT protocols when compared to moderate intensity exercise, showing how immunological system

responds to vigorous to high intensity training. Both in the disease, with greater activation of the inflammatory profile, or in face of physical exercise, describing the mechanisms involved in trained immunity, would provide new therapeutic advances with the training prescription, with an emphasis on positive effects on the immune system, and consequently for the prevention of respiratory diseases. However, HIIT has a lower cost of time, reducing the time/efficiency ratio, that is, a lower cost of time with similar or even better benefits to higher volume exercise programs. Let us not forget: "time is the most precious asset we have".

References

Born, D.-P., Zinner, C., & Sperlich, B. (2017). The Mucosal Immune Function Is Not Compromised during a Period of High-Intensity Interval Training. Is It Time to Reconsider an Old Assumption? Frontiers in Physiology, 8. https://doi.org/10.3389/fphys.2017.00485

Horiguchi, H., Loftus, T. J., Hawkins, R. B., Raymond, S. L., Stortz, J. A., Hollen, M. K., Weiss, B. P., Miller, E. S., Bihorac, A., Larson, S. D., Mohr, A. M., Brakenridge, S. C., Tsujimoto, H., Ueno, H., Moore, F. A., Moldawer, L. L., & Efron, P. A. (2018). Innate Immunity in the Persistent Inflammation, Immunosuppression, and Catabolism Syndrome and Its Implications for Therapy. Frontiers in Immunology, 9. https://doi.org/10.3389/fimmu.2018.00595

James, B. D., Jones, A. v, Trethewey, R. E., & Evans, R. A. (2018). Obesity and metabolic syndrome in COPD: Is exercise the answer? Chronic Respiratory Disease, 15(2), 173–181. https://doi.org/10.1177/1479972317736294

Jin, W., Wang, H., Yan, W., Xu, L., Wang, X., Zhao, X., Yang, X., Chen, G., & Ji, Y. (2008). Disruption of Nrf2 Enhances Upregulation of Nuclear Factor-B Activity, Proinflammatory Cytokines, and Intercellular Adhesion Molecule-1 in the Brain after Traumatic Brain Injury. Mediators of Inflammation, 2008, 1–7. https://doi.org/10.1155/2008/725174

Khammassi, M., Ouerghi, N., Said, M., Feki, M., Khammassi, Y., Pereira, B., Thivel, D., & Bouassida, A. (2020). Continuous Moderate-Intensity but Not High-Intensity Interval Training Improves Immune Function Biomarkers in Healthy Young Men. Journal of Strength and Conditioning Research, 34(1), 249–256. https://doi.org/10.1519/JSC.0000000000002737

Luzi, L., & Radaelli, M. G. (2020). Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. Acta Diabetologica, 57(6), 759–764. https://doi.org/10.1007/s00592-020-01522-8

Mao, L., Wang, H., Qiao, L., & Wang, X. (2010). Disruption of Nrf2 Enhances the Upregulation of Nuclear Factor-kappaB Activity, Tumor Necrosis Factor and Matrix Metalloproteinase-9 after Spinal Cord Injury in Mice. Mediators of Inflammation, 2010, 1–10. https://doi.org/10.1155/2010/238321

Netea, M. G., Joosten, L. A. B., Latz, E., Mills, K. H. G., Natoli, G., Stunnenberg, H. G., ONeill, L. A. J., & Xavier, R. J. (2016). Trained immunity: A program of innate immune memory in health and disease. Science, 352(6284), aaf1098–aaf1098. https://doi.org/10.1126/science.aaf1098

Nieman, D. C., Johanssen, L. M., Lee, J. W., & Arabatzis, K. (1990). Infectious episodes in runners before and after the Los Angeles Marathon. J Sports Med Phys Fitness, 30(3), 316–328.

Nieman, David C. (2007). Marathon Training and Immune Function. Sports Medicine, 37(4), 412–415. https://doi.org/10.2165/00007256-200737040-00036

Pedersen, B. K., & Saltin, B. (2015). Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. Scandinavian Journal of Medicine & Science in Sports, 25, 1–72. https://doi.org/10.1111/sms.12581

Shaw, D. M., Merien, F., Braakhuis, A., & Dulson, D. (2018). T-cells and their cytokine production: The anti-inflammatory and immunosuppressive effects of strenuous exercise. Cytokine, 104, 136–142. https://doi.org/10.1016/j.cyto.2017.10.001

Simpson, Campbell, J. P., Gleeson, M., Krüger, K., Nieman, D. C., Pyne, D. B., & Walsh, N. P. (2020). Can exercise affect immune function to increase susceptibility to infection? Exercise Immunology Review, 26, 8–22.

Valencia, D. N. (2020). Brief Review on COVID-19: The 2020 Pandemic Caused by SARS-CoV-2. Cureus. https://doi.org/10.7759/cureus.7386

Wells, A. J., Hoffman, J. R., Jajtner, A. R., Varanoske, A. N., Church, D. D., Gonzalez, A. M., Townsend, J. R., BOONE, C. H., Baker, K. M., Beyer, K. S., Mangine, G. T., Oliveira, L. P., Fukuda, D. H., & Stout, J. R. (2016). Monocyte Recruitment after High-Intensity and High-Volume Resistance Exercise. Medicine & Science in Sports & Exercise, 48(6), 1169–1178. https://doi.org/10.1249/MSS.0000000000000878

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