The Relationship between Exercise and Medication in Preventing Severe forms of COVID-19 Infection

Bogdan-Alexandru Hagiu1*

1Faculty of Physical Education and Sports, “Alexandru Ioan Cuza” University, Iasi, Romania.

Author’s contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/JPRI/2020/v32i1430616

targeting dysfunctions of these cellular organs can be a therapeutic pathway [1]. Experimental research (performed on rats) suggests the possibility of prophylaxis of severe forms of the disease, because endurance exercises, respectively swimming, have the effect of adapting liver mitochondria to oxidative stress [2]. The same effect of exercise was found in terms of muscle mitochondria [3]. Both resistance and endurance exercises stimulate the biogenesis and respiratory functions of skeletal muscle mitochondria [4]. This restoration of

ABSTRACT

Prophylaxis of severe forms of COVID-19 infection can be achieved by exercising, especially endurance, which stimulates mitochondrial biogenesis and improves their functionality, these organelles having a key role in the pathogenesis of the disease. Some drugs and supplements that stimulate mitochondrial biogenesis through exercise (6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid (Trolox), ω3 fatty acids, vitamin C, zinc, vitamin B12, folic acid, magnesium, MitoQ) and others that inhibit it (acetylsalicylic acid, ibuprofen, acetaminophen).

Keywords: Exercise; medication; COVID-19.

1. INTRODUCTION

It is known that mitochondrial lesions occur in the pathogenesis of COVID-19, and targeting dysfunctions of these cellular organs can be a therapeutic pathway [1]. Experimental research (performed on rats) suggests the possibility of prophylaxis of severe forms of the disease,
mitochondrial function through exercise can also occur in old age [5], the elderly being considered a risk category for COVID-19 infection.

Of course, the possibility of pharmacological protection of mitochondria, with the prophylactic and therapeutic role of severe clinical manifestations of COVID-19 infection, must also be discussed. From this point of view, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox) has proven effective in restoring mitochondrial membrane potential [6]. Protection of mitochondrial functions can be achieved including with ω3 fatty acids, antioxidants (vitamin C and zinc), members of the vitamin B family (Vitamin B12 and folic acid) and magnesium [7].

A mitochondrial-targeted antioxidant (MitoQ) also has a special potential, which improves the carotid-femoral pulse wave velocity, the mechanism being represented by the amelioration of mitochondrial reactive oxygen species-related suppression of endothelial function [8].

However, excessive doses of antioxidants are detrimental to muscle adaptation to exertion [9]. Thus, supplementation with vitamins C and E stops the adaptation of muscle mitochondria to endurance exercises [10]. Hence, a potential conflict between the desire to improve mitochondrial function with antioxidants and that of multiplying them through exercise. On the other hand, there is a study that shows that high dosages of vitamin C (1000 mg/day) and E (235 mg/day) have negative effects on adaptation to resistance exercise and training in young, but positive effects in older men [11]. Future research may determine the recommended doses for young people and the recommended doses for the elderly in order to optimize mitochondrial numbers and functions.

Zn excess must also be avoided, knowing that it has the effect of increasing the amount of free radicals produced by mitochondria; this mineral can act as both an antioxidant and a prooxidant [12].

Regarding supplementation with ω3 fatty acids, it should be borne in mind that excessive use of n-3 PUFAs can alter platelet function [13], which is unfavorable in COVID-19 infection, as platelets are mitochondrial transporters and lesions of these organelles contribute to the formation of thrombi [1].

Medications that negatively interfere with muscle adaptation to exercise remain to be discussed.

Co-administration of anti-inflammatory drugs (acetylsalicylic acid, ibuprofen) with resistance training results in reduced mitochondrial function [14]. It is reasonable to assume that these organelles become more vulnerable to COVID-19 damage. Along with ibuprofen, acetaminophen reduces muscle protein synthesis after exercise [15], thus implicitly mitochondrial biogenesis.

It should be noted that in order to avoid a decrease in immunity, especially in the elderly, regular bouts of short-lasting (up to 45 minutes) moderate intensity exercise [16]. Nutritional and psychosocial factors also intervene to increase immunity. Studies have shown that a healthy lifestyle, regular exercise, balanced nutrition, quality sleep and a strong connection with their families and communities are all associated with a boost to the immune system [17,18]. Of course, there are many unknowns in the evolution of COVID-19 infection, but given that serious complications include heart disease, we must remember a study that shows that exercise stimulates the biogenesis of cardiac mitochondria [19].

Table 1. Co-administration of anti-inflammatory drugs

| Drugs or supplements that have a synergistic effect with exercise on the biogenesis and improvement of mitochondrial functions | Drugs that affect muscle adaptation to exercise (mitochondrial functionality, muscle protein synthesis) |
|---|---|
| 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox) [6] | acetylsalicylic acid [14] |
| ω3 fatty acids [7] | ibuprofen [14] |
| vitamin C [7] | acetaminophen [15] |
| zinc [7] | |
2. CONCLUSION

In conclusion, the prophylaxis of severe forms of COVID-19 infection can be achieved by practicing exercise, especially endurance, the goal being to stimulate mitochondrial biogenesis and improve the functionality of these cellular organs. This is because mitochondria are involved in triggering the cytokine storm and thrombus formation, serious phenomena of the disease [1]. There are drugs and supplements that stimulate mitochondrial biogenesis through exercise (especially antioxidants) and others that inhibit it (anti-inflammatory).

CONSENT AND ETHICAL APPROVAL

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the author.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Saleh J, Peyssonaux C, Singh KK, Edeas M. Mitochondria and microbiota dysfunction in COVID-19 pathogenesis. Mitochondrion. 2020;54:1–7.
2. Lima FD, Stamm DN, Della-Pace ID, Dobrachinski F, de Carvalho NR, Royes LF, Soares FA, Rocha JB, González-Gallego J, Bresciani G. Swimming training induces liver mitochondrial adaptations to oxidative stress in rats submitted to repeated exhaustive swimming bouts. PLoS One. 2013;8(2):55668. DOI: 10.1371/journal.pone.0055668. Epub 2013 Feb 6. PMID: 23405192; PMCID: PMC3565999.
3. Lundby C, Jacobs RA. Adaptations of skeletal muscle mitochondria to exercise training. Exp. Physiol. 2016;101:17–22. DOI: 10.1113/EP085319
4. Groennebaek T, Vissing K. Impact of resistance training on skeletal muscle mitochondrial biogenesis, content, and function. Front Physiol. 2017;8:713. DOI: 10.3389/fphys.2017.00713. PMID: 28966596; PMCID: PMC5605648.
5. Carter HN, Chen C, Hood DA. Mitochondria, muscle health, and exercise with advancing age. Physiolology (Bethesda). 2015;30(3):208-223. DOI: 10.1152/physiol.00039.2014
6. Distelmaier F, Visch HJ, SMEITINK JA, MAYATEPEK E, KOOPMAN WJ, Willems PH. The antioxidant Trolox restores mitochondrial membrane potential and Ca2+ -stimulated ATP production in human complex I deficiency. J Mol Med (Berl). 2009;87(5):515-522.
7. Du J, Zhu M, Bao H, Li B, Dong Y, Xiao C, Zhang GY, Henter I, Rudorfer M, Vitiello B. The role of nutrients in protecting mitochondrial function and neurotransmitter signaling: implications for the treatment of depression, PTSD, and suicidal behaviors. Crit Rev Food Sci Nutr. 2016;56(15):2560-2578. DOI: 10.1080/10408398.2013.876960. PMID: 25365455; PMCID: PMC4417658.
8. Rossman MJ, Santos-Parker JR, Steward CAC, Bispham NZ, Cuevas LM, Rosenberg HL, Woodward KA, Chonchol M, Gioia-Ryan RA, Murphy MP, Seals DR. Chronic supplementation with a mitochondrial antioxidant (MitoQ) improves vascular function in healthy older adults. Hypertension. 2018;71(6):1056-1063. DOI: 10.1161/HYPERTENSIONAHA.117.10787.
9. Distelmaier F, Visch HJ, SMEITINK JA, MAYATEPEK E, KOOPMAN WJ, Willems PH. The antioxidant Trolox restores mitochondrial membrane potential and Ca2+ -stimulated ATP production in human complex I deficiency. J Mol Med (Berl). 2009;87(5):515-522.
10. Distelmaier F, Visch HJ, SMEITINK JA, MAYATEPEK E, KOOPMAN WJ, Willems PH. The antioxidant Trolox restores mitochondrial membrane potential and Ca2+ -stimulated ATP production in human complex I deficiency. J Mol Med (Berl). 2009;87(5):515-522.
11. Distelmaier F, Visch HJ, SMEITINK JA, MAYATEPEK E, KOOPMAN WJ, Willems PH. The antioxidant Trolox restores mitochondrial membrane potential and Ca2+ -stimulated ATP production in human complex I deficiency. J Mol Med (Berl). 2009;87(5):515-522.
12. Lee SR. Critical role of zinc as either an antioxidant or a prooxidant in cellular systems. Oxidative Medicine and Cellular Longevity; 2018.

13. Gammone MA, Riccioni G, Parrinello G, D'Orazio N. Omega-3 polyunsaturated fatty acids: Benefits and endpoints in sport. Nutrients. 2018;11(1):46. DOI: 10.3390/nu11010046 PMID: 30591639; PMCID: PMC6357022.

14. Cardinale DA, Lilja M, Mandić M, Gustafsson T, Larsen FJ, Lundberg TR. Resistance Training with co-ingestion of anti-inflammatory drugs attenuates mitochondrial function. Front Physiol. 2017;8:1074. DOI: 10.3389/fphys.2017.01074 PMID: 29311990; PMCID: PMC5742251.

15. Trappe TA, White F, Lambert CP, Cesar D, M. Hellerstein M, Evans WJ. Effect of ibuprofen and acetaminophen on postexercise muscle protein synthesis. American Journal of Physiology-Endocrinology and Metabolism. 2002;282: 3:551-556.

16. Simpson RJ, Campbell JP, Gleeson M, Krüger K, Nieman DC, Pyne DB, Turner JE, Walsh NP. Can exercise affect immune function to increase susceptibility to infection? Exerc Immunol Rev. 2020; 26:8-22. PMID: 32139352.

17. Kim SW, Su KP. Using psychoneuroimmunity against COVID-19. Brain Behav Immun. 2020;87:4-5. DOI: 10.1016/j.bbi.2020.03.025 Epub 2020 Mar 29. PMID: 32234338; PMCID: PMC7194899.

18. Finelli C. Obesity, COVID-19 and immunotherapy: The complex relationship! Immunotherapy. 2020;10.2217/imt-2020-0178. DOI: 10.2217/imt-2020-0178 [Published online ahead of print, 2020 Jul 17].

19. Vettor R, Valerio A, Ragni M, Trevellin E, Granzotto M, Olivieri M, Tedesco L, Ruocco C, Fossati A, Fabris R, Serra R, Carruba MO, Nisoli E. Exercise training boosts eNOS-dependent mitochondrial biogenesis in mouse heart: Role in adaptation of glucose metabolism. Am J Physiol Endocrinol Metab. 2014;306(5):E519-28. DOI: 10.1152/ajpendo.00617.2013 Epub 2013 Dec 31. Erratum in: Am J Physiol Endocrinol Metab. 2014 Dec 1;307(11):E1084. PMID: 24381004.