

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

ELSEVIER

#### Contents lists available at ScienceDirect

# **Medical Hypotheses**

journal homepage: www.elsevier.com/locate/mehy



### Letter to Editors

# Can moderate intensity aerobic exercise be an effective and valuable therapy in preventing and controlling the pandemic of COVID-19?



A novel contagious virus with the ability to quickly transmit and cause pneumonia like symptoms came into light on December 2019 in Wuhan, Hubei Province of China. World health organization quickly came up with the nomenclature of 2019 novel coronavirus (COVID-19) and promptly declared it as a pandemic, a potential threat to the world population [1].

The median age of people getting affected with the lethal virus appears to be 47 years. The respiratory symptoms have an incubation period of 4 days with or without radiological abnormalities [2]. Moreover, it is observed from the current clinical scenario that immunosuppressed or weak immune defense mechanism individuals are more susceptible to COVID 19 fatalities.

There are quite number of researches which states that moderate intensity aerobic training modulates the immune system. Exercise training is safe and beneficial. Studies on the impact of moderate exercise training on immune functions have shown that even activities like daily brisk walking can be superior to sedentary lifestyles and individuals are reported to have lesser number of sick days almost half with training over a period of 8 to 15 weeks. The immuno-protective effects that come with moderate exercise training are mostly associated with the cumulative effects of daily acute positive changes that occur during each exercise bout [3]. (refer Table 1)

The immunoprotective effects of aerobic training is also seen in acquired immunodeficiency syndrome (AIDS) where the immunity gets compromised gradually and exercise are an imperative tool to enhance immunity in the body. Exercises can be given in stages as suggested by American college of sports medicine (ACSM) by stratifying the population to measure the effects of the treatment [4].

Stage 1 (mild stage)

- a. Increase in CD4 cell counts
- b. Possibly delay in onset of symptoms
- c. Increase in muscle function and size

Stage 2 (moderate stage)

- a. Increase in CD4 cell counts (lesser extent than that of stage 1)
- b. Possible diminished severity and frequency of symptoms

Stage 3 (severe stage)

- a. Unknown effects on CD4 cells
- b. Inconclusive effects on symptoms

In addition, systematic training program can also result in increase in natural killer cells (NK), downregulation of inflammation and Tumor Necrosis Factor (TNF) in the body [5] and may also play a role in modulating the risk factors of diabetes, hypertension and chronic smoking.

The hypothesis for the current article is whether moderate intensity aerobic exercises can prevent the new incidence of COVID-19 among sedentary healthy individuals, population afflicted with non-communicable diseases, and persons with the habbit of chronic smoking.

Moderate intensity exercise can definitely act as a preventive therapy to bring down further incidence of COVID-19. A randomized controlled trial evaluating the preventive effect of aerobic exercises on acute respiratory illness found that participants in exercise group reported lesser episodes of illness compared to participants with sedentary lifestyles. The severity index and total days of illness (duration) showed a lower trend for the exercise group as compared to control [6]. The trial also revealed a decrease in interleukin-8 factor and increase in mean levels of neutrophils in the exercise group. It was also reported that the immunoprotective effect of aerobic exercise can also improve antibody responses to influenza vaccination in sedentary elderly [6] (refer Table 1).

Mode of exercise can be aerobic exercise for large muscles with the goal to increase aerobic and work capacity. Flexibility training can also be incorporated to increase range of motion, neuromuscular excitability, and decrease the risk of injury during training. Moreover, functional activities can also be used to maintain activity of daily living. However, intensity of exercise can be 60–75% of heart rate maximum, 50–60% of VO<sub>2</sub> maximum, 40–60% heart rate reserve, with rating of perceived exertion (RPE) of 10–14/20, frequency of exercise being 3–5 days/week and sessions ranging from 20 to 60 min (table 1). Especially RPE may be useful to determine the intensity of the exercises for healthy sedentary population at home in the current situation of partial or complete lockdown.

It has been previously observed in researches that acute phase of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome CoronaVirus (MERS-CoV) is associated with severe reduction in T cells count in the blood [7] and moreover initial invasion of COVID-19 may affect the organs and cause inflammation of the lungs, which the body immune system responds preliminary to prevent the virus spread from its incubation phase to more severe phase. Hence it is foremost important that strategies which boost the immune system may play a vital role in preventing the world-wide spread.

It's now proven that moderate intensity aerobic exercise sessions of less than 60 min duration has antipathogen activity with an improved recirculation of immunoglobulins, anti-inflammatory cytokines, neutrophils, NK cells, cytotoxic T cells, and immature B cells [5,8], which play a vital role in the defense of the body. Acute exercise sessions helps

Nieman et al RCT 55 Moderate intensity exercise, 60% d HRR 30-40 min duration, 5 days/wk. for 12 wks.  Nieman et al RCT 36 Moderate intensity exercise, 60% d HRR 45 min duration, 5 days/wk. for 12 wks.  Nieman et al RCT 36 Moderate intensity exercise, 60% of HRR 45 min duration, 5 days/wk. for 12 wks.  Nieman et al RCT 36 Moderate intensity exercise, 60% of HRR 45 min duration, 5 days/wk. for 12 months  Abobe (12) Cabbe (12) RCT 115 Moderate intensity exercise, 60-70% maximal approximately 45-60 min for 10 months  Woods et al 2009 [13] RCT 154 Moderate intensity exercise, 60-70% maximal approximately 45-60 min for 10 months  Woods et al 2009 [13] RCT 154 Moderate intensity sustained exercise, with a target 2019 [14] RCT 154 Moderate intensity sustained exercise, with a target 2019 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [14] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise, with a target 2015 [15] RCT 155 Moderate intensity sustained exercise (150 min session consisted of 30-min brisk walking at a session consisted of 30-min brisk walking at a received intensity and received intensity						
RCT       35       Moderate intensity exercise, 60% of HRR       30–40 min duration, 5 days/wk. for 12 wks.         RCT       115       Moderate intensity exercise, 60–70% maximal       45 min duration, 5 days/wk for 12 weeks         RCT       115       Moderate intensity exercise, 60–70% maximal       3 days/wk, and the duration of each session oxygen uptake         RCT       154       Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs       120 min session/wk followed 45 min home exercise rating of 12–16 points on the 6 to 20-point Borgs         RCT       32       Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual age predicted Heart rate maximum       Exercise training corresponding to 75% of individual HR max Heart rate maximum	Study	Design	Sample size	Intervention type	Duration/Frequency of intervention	Major findings
RCT       36       Moderate intensity exercise, 60% of HRR       45 min duration, 5 days/wk for 12 weeks         RCT       115       Moderate intensity exercise, 60–70% maximal       45 min, 5 days/wk for 12 months         RCT       144       Moderate Intensity exercise, 60–70% maximal       3 days/wk, and the duration of each session oxygen uptake         RCT       154       Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs scale       120 min session/wk followed 45 min home exercise program for 8 weeks.         RCT       32       Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise exercise exercise exercise exercise exercise exercise intensity corresponding to 75% of individual HR max Heart rate maximum       Exercise training to 75% of individual HR max Heart rate maximum	Nieman et al 1993 [10]	RCT	55	Moderate intensity exercise, 60% HRR	30-40 min duration, 5 days/wk. for 12 wks.	NK activity, T cells functions improved with lower incidence of URTI in the exercise group
RCT       115       Moderate intensity exercise       45 min, 5 days/wk for 12 months         RCT       144       Moderate Intensity exercise, 60–70% maximal oxygen uptake       3 days/wk, and the duration of each session approximately 45–60 min for 10 months         RCT       154       Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs       120 min session/wk followed 45 min home exercise program for 8 weeks.         RCT       32       Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise exercise session consisted of 30-min brisk walking at a a prescribed moderate aerobic exercise intensity corresponding to 75% of individual age predicted Heart rate maximum       Exercise training of 25% of individual HR max Heart rate maximum	Nieman et al 1990 [11]	RCT	36	Moderate intensity exercise, 60% of HRR	45 min duration, 5 days/wk for 15 weeks	Reduction in URTI symptoms, increased NK cell activity
RCT 144 Moderate Intensity exercise, 60–70% maximal adays/wk, and the duration of each session approximately 45–60 min for 10 months  RCT 154 Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs scale  RCT 32 Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual HR max Heart rate maximum	Chubak et al 2006 [12]	RCT	115	Moderate intensity exercise	45 min, 5 days/wk for 12 months	Risk of colds decreased in exercisers
RCT 154 Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs scale  RCT 32 Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise session consisted of 30-min brisk walking at a a prescribed moderate aerobic exercise intensity corresponding to 75% of individual HR max Heart rate maximum	Woods et al 2009 [13]	RCT	144	Moderate Intensity exercise, 60–70% maximal oxygen uptake	3 days/wk, and the duration of each session approximately 45–60 min for 10 months	Participants in the exercise group experienced improvements in influenza seroprotection throughout the entire influenza season, exercise group experienced reduced overall illness severity and sleep disturbance
RCT 32 Exercise training was comprised of a 16-week, 5 days/ 5 days/week, home-based walking program. Each exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual age predicted  Exercise training comprised of a 16-week, 5 days/ week, home-based walking program. Each exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual HR max Heart rate maximum	Barrett 2012 [14]	RCT	154	Moderate-intensity sustained exercise, with a target rating of 12–16 points on the 6 to 20-point Borgs scale	120 min session/wk followed 45 min home exercise program for 8 weeks.	Reduced URTI episodes and severity of Illness
	Sloan 2012 [15]	RCT	32	Exercise training was comprised of a 16-week, 5 days/week, home-based walking program. Each exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual age predicted Heart rate maximum	Exercise training comprised of a 16-week, 5 days/ week, home-based walking program. Each exercise session consisted of 30-min brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual HR max	16-week moderate intense walking program can increase the secretion of salivary immunoglobulin A, which constitutes the main specific immune defense mechanism in saliva

URTI: Upper Respiratory Tract Infection, RCT: Randomized controlled Trial, HRR: Heart Rate Reserve, wk: Week, HR max: Heart Rate Maximum, Borgs Scale: Rating of Perceived Exertion, nk cells: natural killer cells.

#### Moderate intensity aerobic exercise

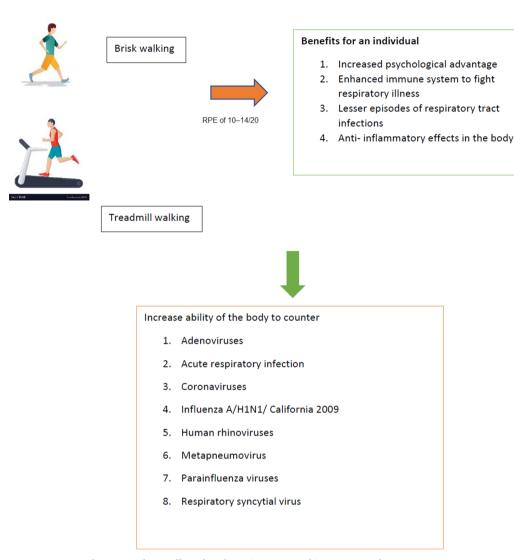


Fig. 1. Cumulative effect of moderate intensity aerobic exercise on the immune system.

in mobilizing NK cells, CD8<sup>+</sup> and T lymphocytes that exhibit high cytotoxicity and tissue migrating potential [5].

It is clear that moderate intensity exercises have an enhanced effect on the immune system due to adaptations of training sessions which may have a definitive preventive advantage among healthy sedentary individuals, people with type 2 diabetes and hypertension by preventing new incidence in the current outbreak of Covid-19 (Fig. 1). Non-pharmaceuticals interventions way be an important source of immunoprotection in the current outbreak. A systematic aerobic training program can prevent the quick spread of the virus from one person to other if our immune system is strong enough. This can be an easy and indispensable way to promote a healthy way of living that may not only prevent communicable diseases but also non communicable diseases. There is a definitive need to further increase our understanding regarding the physiological mechanism responsible to induce the change and strengthen the immunity among sedentary population. Moreover, there is also a need for increased prescription of moderate intensity exercises by the specialist under supervision and home-based scenarios (Which can be easily prescribed once the person is free from Diabetes, Hypertension etc. complications, using the Borg's scale of 6-20 for intensity). As active routine not only have psychological benefits but also physiological benefits. An aerobic exercise program of moderate intensity which can be determined using Borg's scale, rating of perceived exertion (RPE) 6–20 (fairly light to somewhat hard) as it has a very good correlation with the physiological measure of exercise intensity [9]. Borg's RPE has a real-world applicability and also seems to be an authentic tool for monitoring and prescribing exercise intensity, which is self-governing in regards of gender, age, previous physical activity level and coronary artery disease [9]. It is also stated in some researches that exercising at an RPE of 11–13 is suggested for sedentary individuals, and an RPE of 13–15 may be recommended for those who have been previously exercising [9].

# **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgement

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2020.109854.

#### References

- [1] Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Vol. 7, Military Medical Research. BioMed Central Ltd.: 2020.
- [2] Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med [Internet]. 2020 Feb 28; Available from: http://www.ncbi.nlm.nih.gov/pubmed/32109013.
- [3] Nieman DC, Pedersen BK. Exercise and Immune Function Recent Developments. Vol. 27, CURRENT OPINION Sports Med. 1999.
- [4] Brill P. ACSM's Exercise Management for Persons With Chronic Diseases and Disabilities, edited by J. Larry Durstine, Geoffrey E. Moore, Patricia L. Painter, and Scott O. Roberts . Act Adapt Aging. 2012;36(2):182–3.
- [5] Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. J Sport Heal Sci 2019;8(3):201–17.
- [6] Barrett B, Hayney MS, Muller D, Rakel D, Brown R, Zgierska AE, et al. Meditation or exercise for preventing acute respiratory infection (MEPARI-2): A randomized controlled trial. PLoS ONE 2018;13(6):1–20.
- [7] Channappanavar R, Zhao J, Perlman S. T cell-mediated immune response to

- respiratory coronaviruses. Immunol Res 2014;59(1-3):118-28.
- [8] Zbinden-Foncea H, Francaux M, Deldicque L, Hawley JA. Does high cardiorespiratory fitness confer some protection against pro-inflammatory responses after infection by SARS-CoV-2? Obesity 2020;0–3.
- [9] Scherr J, Wolfarth B, Christle JW, Pressler A, Wagenpfeil S, Halle M. Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. Eur J Appl Physiol 2013;113(1):147–55.
- [10] Nieman DC, Henson DA, Gusewitch G, Warren BJ, Dotson RC, Butterworth DE N-CS. Physical activity and immune function in elderly women.
- [11] Nieman DC, Nehlsen-Cannarel! SL, Markoff PA, Balk-Lamberton AJ, Yang H, Chritton DBW, et al. The Effects of Moderate Exercise Training on Natural Kifier Cells and Acute Upper Respiratory Tract Infections.
- [12] Chubak J, McTiernan A, Sorensen B, Wener MH, Yasui Y, Velasquez M, et al. Moderate-intensity exercise reduces the incidence of colds among postmenopausal women. Am J Med 2006;119(11).
- [13] Woods JA, Keylock KT, Lowder T, Vieira VJ, Zelkovich W, Dumich S, et al. Cardiovascular exercise training extends influenza vaccine seroprotection in sedentary older adults: the immune function intervention trial. J Am Geriatr Soc 2009;57(12):2183–91.
- [14] Barrett B, Hayney MS, Muller D, Rakel D, Ward A, Obasi CN, et al. Meditation or exercise for preventing acute respiratory infection: a randomized controlled trial. Ann Fam Med 2012;10(4):337–46.
- [15] Sloan CA, Engels HJ, Fahlman MM, Yarandi HE, Davis JE. Effects of exercise on S-IGA and URS in postmenopausal women. Int J Sports Med 2013;34(1):81–6.

Snehil Dixit (Snehil)

Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Saudi Arabia

E-mail addresses: snehildixit83@gmail.com, snehildixit@outlook.com.