

The Importance of Physical Activity and Yoga During Covid-19 Pandemic

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Abstract

Current pandemic coronavirus that is also known as COVID-19 or coronavirus disease 2019 is a respiratory disease that effects on so many dimensions of human body. From 2019 up to now, more than 154,000 articles have been done to find out disease symptoms, what are those appropriate ways to control the disease or even prevent its expansion. Among different strategies, it is well accepted that individuals with strong immune system and healthy body could handle the disease much better compare to those individuals with heart, kidney, or liver problems due to the virus receptor that are located on those organs. Also, because of its highly contagious infectious and high mortality rate, it causes so many anxiety. Accordingly, it disrupts health, cause sense of fear and lead to depression and distress. All of these could increase proinflammatory cytokines, stimulate hypothalamic-pituitary-adrenal axis and increase cortisol, reduce natural killer cells, diminish the immune system and make it much poor to even handle flue. Physical activity and yoga are those well accepted strategies that could control stress and save immune system proper work. They could control metabolic syndrome and guarantee cardiorespiratory fitness that ameliorate the COVID-19 side effects on body and have so many benefits on mental health.

In this review, we try to precisely discuss the physical activity and yoga and their health-benefit, immune system, stress, and COVID-19 and finally the beneficial and vital effects of physical activity and yoga on human health and their effects on immune system regard to control COVID-19.

Keywords: COVID-19; Immune System; Physical Activity; Yoga; Depression

Abbreviations

TLR: Toll-like Receptor; MHC-1: Major Histocompatibility Complex Class I; IL: Interleukin; NK: Natural Killer; Ig: Immunoglobulin; HPA: Hypothalamic-pituitary-adrenal Axis; ACE2: Angiotensin Converting Enzyme 2; COVID-19: Coronavirus Disease of 2019; BDNF: Brain Derived Neurotrophic Factor; TGF-beta1: Transforming Growth Factor-beta1; CRF: Corticotrophin-releasing Factor;

ACTH: Adrenocorticotrophic Hormone; GABA: Gammaaminobutyric Acid; DHEA: Dehydroepiandrosterone

Introduction

Physical activity and yoga have inevitable beneficial effects on human health that they have been well studied and also they work as super effective disease preventive strategies [1-4]. The definition

and details about physical activity and yoga goes back to 1980s. Most of the today's article that report their valuable effects skip their foremost introduction and mostly focus on their outcomes. In this review, we not only discuss disease-related outcomes of physical activity and yoga, but also we deliberate physical activity and yoga in important details [e.g. COVID-19]. Moreover, disease-related stress is important items that could highly affect immune system and increase disease-induced consequences. So we decide to define physical activity and yoga and also discuss their health-related effects and stress-induced responses on COVID-19 as highly contagious disease that threat world health.

In current study, we focused on COVID-19 and strategies that could help to control this disease. PubMed was used to search articles that cover the definition, explanation, and beneficial effects of physical activity and yoga. Also, immune system, its changes and responses to stress and stress-derived changes was studied. Finally, their relationship with COVID-19 was searched and discussed.

Physical activity

Physical activity is well-known and old word. Search "physical activity" in PubMed shown the most first articles are refer to 1800s. Physical activity is defined as any skeletal muscle induced-movement that increase and required continuously energy expenditure and positively correlated with physical fitness [3]. To express the amount of energy required technically kilojoules [kJ] and historically kilocalories [kcal] are used. Each kcal equal to 4.184 kJ and kcal is a measure of heat and kJ is a measure of energy expenditure but kcal is most often be used. There is a considerable differences between physical activity and exercise and there are not exchangeable. First, there is a need to mentioned physical fitness components. There are two categories for physical fitness that each of them are subdivided into more branches. Health-related fitness and skill-related fitness are physical fitness components. The former one consists of cardiorespiratory endurance, muscular endurance, muscular strength, body composition, and flexibility. The later one consists of agility, balance, coordination, speed, power, and reaction time [3]. Exercise is those body movement that results in increase energy expenditure, highly positively correlated with physical fitness, it is planned, structured, and purposeful [to improve or maintain physical fitness components] [3].

Abundance of evidence confirm the health benefits of regular physical activity, that associated with remarkable decrease in the

risk of more than 25 chronic medical conditions and their related mortality [1,2]. Following the approve of beneficial effects of physical activity and due to dose-response relationship between physical activity and health there is a guideline recommendation that the time goal which should be meet is 150 min per week doing moderate to vigorous physical activity. Also physical activity can be measurable using variables such as how hard the work should be, how long does is take, and how often should it be done which there are intensity, duration, and frequency, respectively [2].

Yoga

Yoga is old in India and is part of Indian spiritual practice which could be translated as union or conjunction. It is describe as controlling mental, silencing of the mind and communion with the universe to unit body, mind, and soul [5,6]. Nowadays, yoga becomes a mean for health and is so popular practice in Western societies. Yoga consists of components such as physical posture [asanas], regulated breathing [pranayama], and meditation. With regard to asanas, yoga is much similar to physical exercise and breath regulation and posture maintenance is those differences [6]. Precisely, having rhythmic breath and fix posture are also important in so many exercises and physical activities to keep metabolic system work properly and maintain balance and coordination while performing [7].

There are many classification and styles for yoga which could be studied in details elsewhere [6]. Although yoga is mostly focus on communion and spiritual but most people look at it as physical activity and physical exercise which is not far away of reality. While doing physical activity if it performed mindfully can also cover both physical and spiritual aspects [6]. It has been shown that doing yoga could increase energy, improve immune system function, and prevent disease. Besides, yoga is one of those approved safe practice that health care providers also use it to work on musculoskeletal pain such as low back pain [4,5]. Also, yoga could improve some physical fitness components such as flexibility, muscular endurance [while comparing to sedentary individuals], and ameliorate attention [6]. Yoga was used for type II diabetes, menopausal symptoms, Parkinson's diseases, depression, balance, and even falls in older adults that highlight the importance of doing more research [5]. The effectiveness of yoga be higher while added to daily routine and it should be mentioned that there is no fit yoga program for everyone. In other word, each population need to have their own adapted yoga program that match their needs to find best results

[5]. Yoga also is different from physical activity as it mainly focus on the various layer of consciousness and even if there is movement in the body, it is just look like physical activity. Perform yoga and keep posture maybe could be equal to isometric contraction but truly it is not as it has been shown that isometric contraction could increase heart rate by 32% but heart rate increase by about 6% in yoga. In other hand, some warm up exercises are used in yoga to prevent muscle soreness [6].

Stress and human body systems: immune systems and Covid-19

Immune system could be define as natural [innate] and specific [adaptive] immunity which the former one is body defense against any kind of pathogens that last for short time and the later one is slow and specified immune response [8]. Granulocytes are main cells group that involve in natural immunity. This group contains neutrophil, macrophage, and phagocytic cells. These cells responses mount inflammation. Macrophages could release cytokines that could deliver fever and inflammation. Eosinophil, natural killers, and complement protein are other members of natural immunity. It has been shown that natural killer cells are important to limit viral infection [8]. Lymphocytes is one of the specific immunity component that due to their special receptors on their surface they could attach to special molecules which is called antigen and finally could respond to one kind of invader in body and act as antigen-specific cells that need to proliferate to be enough in number to cope with invader. Among lymphocyte subgroup, B-cells produce antibodies and could bind to free virus by mean to prevent them from enter to the cells. Also, T-cytotoxic cells could lyse virus-infected cells by recognizing the antigen that expressed by those cells [8,9]. Among immune system's components natural killer cells [as natural or innate immunity] and B cells and T-cytotoxic cells [as specific or adaptive immunity] could control virus infection [8,10].

Natural killer cells could destroy unwanted cells [e.g. tumor, virus] with no previous sensitization and antigen-specific receptors which help natural killer cells as first defense line of body [11]. There are some virus that could interfere with natural killer cells and suppress their works while some other virus could induce natural killer cells proliferation [11]. Natural killer cells control virus through their receptors like natural cytotoxicity receptors that per se is divided into three subgroups [NKp30, NKp44, and NKp46]. Among them NKp46 is the most abundant and known as influenza virus efficient defense but activating natural killers will not happen

with one receptors activity and efficient natural killer cells activation needs cooperation of other receptors which all acting with together [12]. Natural killer-activated-receptors stimulate toll-like receptor [TLR] on natural killer cells. TLR similar to natural cytotoxicity receptors has subgroups that among them, TLR2 is critical for vaccine viral infection control [11,12]. Natural killer cells' activity is controlled by its activating and inhibitory receptors. As natural killer cells work with no previous sensitization, body needs a controlling pathway for natural killer activities. In healthy body expression of major histocompatibility complex class I [MHC-1] molecules inhibit or control natural killer cells activation and even its over-activity [11].

Adaptive immune system or specific immunity consists of two immune responses. First, cellular immune responses against intracellular pathogens like viruses which is mediated by T cells mainly T helper 1 lymphocytes. Second, humoral immune responses against extracellular pathogens like bacteria that is mediated by T helper 2 lymphocyte. T helper lymphocytes secretes cytokines as IL 2 and interferon gamma that these cytokines active T cytotoxic and natural killer cells and also secreted IL4 and IL10 which activate B cells [8,13]. B cells and T cells arise from bone marrow, B cells mature in bone marrow and T cells mature in thymus. B cells and T cytotoxic cells as lymphocyte are a type of white blood cells. They are virus defense in specific or adaptive immunity. They act via their receptors which are located on their surface and only bind to specific antigen and act as antigen-specific cells. Receptors that are inside the cytoplasm bind to virus-induced molecules and detect them as infection. Infection per se stimulates antigen presenting cells and T cells.

Subsequently T cells help B cells to make antibodies and face with infection agent and T cell also could kill infection [13,14]. B cells generate antibodies that could neutralize bacteria-related toxin, opsonization, and bind to free virus to control them. They produce different kinds of antibodies as immunoglobulin [Ig] A, IgE, IgM, IgG, and IgD [8,13]. IgA is secreted by mucous membrane, IgE is evolved as a last line of defense to protect against venoms and involve in allergy, IgM clear antigen from blood, IgG could diffuse into tissue and protect body from infection-induced by virus or bacteria, and IgD is probably secreted by immature B cells [8,13,14]. T cytotoxic express T-cell receptor that recognize specific antigen that is produced by a threat. B cells can only recognize antigen but T cells could recognize antigenic complex that bound to

major histocompatibility complex or MHC. MHC is a large specific site on chromosome 6 of DNA that contain polymorphic genes and essential for adaptive immunity. It presents peptides on cell surface for recognition by T cells. There are two class of MHC; I and II. MHC class I interact with co-receptor CD8 on T cell and MHC class II interact with co-receptor CD4 on T cell. CD8 T cell monitor body cells and destroy threat like virally infected cells [14].

Stress has so many meaning among people but is has been defined as body's homeostasis interruption in response to difficult situation. Also, attempts of pathogens to penetrate into cells is another strong stressor [15]. Stress and psychological anxieties have so various effects on body's physiologic as on immune systems [16]. Stress links to immune system's alteration and could increase the prone of infectious disease. Brain and immune system are two key elements that try to keep body in balance. Stress is mediated through sympathetic pathway and release various substances [16,17]. It increases gastrointestinal symptoms, increases proinflammatory cytokines and results in brain alteration in schizophrenia. Also, stress stimulates neuropeptides and active brain's glial cells which leads to release inflammatory cytokines, causes brain inflammation, and subsequently make brain-related diseases worsen [9]. Also, psychological stress could impair immune system. Each immune cells has receptors for stress-induced hormone secretion. In other word, stress puts body in challenged situation that stimulates autonomic nervous and endocrine system and subsequent epinephrine, norepinephrine, and cortisol secretion [9,18]. It has been shown that during stress immune system's cells changes their signaling to these hormones and increase pro-inflammatory responses [9]. While the stressor situation is too high to perceive the cortisol secretion increases and affects the immune system [18]. Cortisol in short time could limit inflammation and acts as anti-inflammatory agent but its chronic elevation suppresses immune system and increases inflammatory cytokines [9]. Stress also increase the rate of illness, change the function of immune system cells [17] and emotional stress could reduce natural killer cells even in person with benign symptoms [10]. It is documented that T-cell and natural killer have antitumor activity [19] and stress and psychological stress could reduce natural killer cells function and body losses its early antiviral immune response [8,10]. Stress mainly chronic one [lasted more than days] activates the HPA or hypothalamic-pituitary-adrenal axis and increases glucocorticoid [e.g. cortisol] and mediates apoptosis of pre-mature B

cells, decreases them in number, and impairs antibody response that affect more than 60% of them and eliminate them in 36 hours [20]. Stress decreases the T cells proliferative response, drop them in number, decrease the sensitivity of T cells receptors [beta2-adrenergic receptors] that result in low sympatho-adrenergic-induced immune response [8,15].

Acute stress [which lasting for minutes] eliminate pathogens and increase proinflammatory cytokines while chronic stress [that lasting from days to years] increase the susceptibility to infectious, highly increase pro-inflammatory cytokines, disable immune system to control latent virus and activate latent virus [9,15]. It is unclear if pandemic Covid-19 is a latent virus that could be lytic form in the absence of immune system's proper function due to stress of Covid-19-infection [21].

Covid-19: pandemic, structure, immune system and vaccine

Pandemic infectious diseases are mostly dangerous historical events that spread worldwide and affect countries [22]. History witnesses various pandemics that expand and pass country by country. Spanish flu in 1918 and Asian flu in 1957 are pandemic diseases that affect about 50 % of people around the world [22]. COVID-19 is one of the current pandemic disease that similar to previous diseases affects many dimensions such as socioeconomics, health, and politics of worldwide [22].

Coronavirus first discover refer to about 60 years ago. It is a single strand RNA that act through its matched receptor in host. COVID-19 has an spike or S protein part that latch to angiotensin converting enzyme 2 or ACE2 which is COVID-19's receptor and found in the lungs, heart, kidney, and liver. The S protein of this virus has two domains as S1 and S2. S2 domain mediates coronavirus entry that attachment of S protein by ACE2 mount the virus-related effects on body-related organs [23]. Coronavirus generate a sequence of immune system responses and stimulate lymphocytes. In most patient the number of T lymphocyte decrease and it could be a possible factor that complicate the situation for COVID 19 patients as it is one of the body virus defense strategy [24]. Presence of COVID19 in lung stimulate its macrophage. Macrophage is member of granulocyte -the largest group of cells in natural immunity-that attack to invader and phagocytose invader and damage tissue [8]. In the next stage of immune response, the T and B lymphocyte are involved. Virus present provokes strong immune response that

several immune pathways are activated. Neutrophils move to infection sites and kill virus. Subsequent of these events, antigens present and stimulate adaptive or specific immunity that need seven to fourteen days following virus infection and activate B cells which induce virus-specific antibodies and T cytotoxic cells kill virus-infected cells [23]. It is well documented that, virus existence and chronic stimulation of T cells could result in body defense weakness due to T cell exhaustion and lower the proliferative capacity. T cell exhaustion stimulate inhibitory receptors and by affecting various regulators could affect T cells, B cells, and natural killer cells and subsequently suppress the immune system [23]. It has been proposed that CD147 could have a role in facilitating SARS-CoV entering for host cells [25]. CD147 that is known as Basigin or extracellular matrix metalloproteinase inducer or EMMPRIN is a transmembrane protein of the immunoglobulin that is a stimulator of matrix metalloproteinase. It has been shown that CD147 expression is often increase in inflammatory process such as cancer, influenza A, and even in high glucose [26]. CD147 is probably another receptor for COVID19 that mediate virus invasion into host cells [25], but as there is one study which work on effect of Meplazumab, as an anti-CD147 antibody, in China maybe it would be better to have more research to have finalize decision about the role of CD147 on COVID19.

The role of vaccine in containment of COVID-19 is globally studied. Vaccine progress is a complicated process that need considerable amount of time. Vaccine help immune system with essential instructions to recognize disease and could create antibodies [27]. According to a published study about the effectiveness of vaccination, it is shown that it could reduce virus attack rate from 9% to about 4.5% which is more dominant in old people [28]. COVID-19 vaccines is a new and challengeable process to could find the best one and need more studies to have final conclusion.

Physical activity and yoga on controlling stress and cope with Covid-19

Stress and psychological stress disable immune system and prone body for different diseases. COVID-19-induced social and health stress encourage depression, the fear of disease lead to considerable amount of stress on mind and body immune system. Current public health recommendation and staying home lead to physical inactivity that make immune system weak and make individual vulnerable for COVID-19. Performing exercise ameliorate

the immune system and anti-viral defense [29,30]. Also, COVID-19 induced social distancing lead to grow depression and doing physical activity and stay away of sedentary life style is so helpful to prevent depression and its derived immune system deficiency [13,31]. Performing physical activity cause multi-dimensional positive effects to cope with COVID-19 such as anti-inflammatory, antioxidant, strengthen immune system, neurogenesis and neuroprotection effects due to the brain derived neurotrophic factor or BDNF [29]. It is recommended that if an individual shown the COVID-19 symptom, should cease physical activity for about two weeks and if the symptoms are sever cease physical activity for about six weeks, otherwise continue to be active [29,32]. It has been reported that stop doing physical activity in just two week could negatively affect cardiorespiratory system and decrease insulin sensitivity. Being physically active positively control metabolic syndrome and guarantee cardiorespiratory fitness that ameliorate the COVID-19 side effects on body and also have so many benefits on mental health [29,31].

Yoga could regulate homeostatic responses of nervous, endocrine and immune systems. In other word doing yoga help to modulate nervous system responses [afferent and efferent signals] and regulate body posture and breath which promote physical and mental health [7,16]. According to published reports yoga could control risk factor that are associated with diseases conditions such as diabetes. Strong immune system could control the levels of CRP as an essential clinical characteristics of COVID-19 [7]. As it has been written before, stress could widely affect immune system and cause immunosuppression. Stress not only have negative effects on nervous system but also affects HPA. Modulation HPA axis with yoga could relieve stress and help antiviral immune responses [7,33]. It is reported that yoga and slow breathing techniques may be deliver complementary process for the management of hypertension in COVID-19 patients as most of COVID-19 patient have hypertension [7]. In other study, it is stated that yoga may help treating or even preventing SARS-CoV-2 [34]. But there is so limited evidence to could have final decision and need to be aware and it would be more wisely to stop it for about six weeks like what is recommended for physical activity [29].

Lactoferrin which is found in mammalian milk has antibacterial and antiviral properties and it has been documented lactoferrin could bind to ACE2 and may be preventive strategies for COVID-19.

It is documented that moderate exercise increase lactoferrin for about two hours following exercise [29]. As COVID-19 affect the lung, have strong respiratory system and doing endurance training could create beneficial adaptation to cope with this virus-related outcomes [29]. ACE2 is a regulator of renin-angiotensin system [RAS] and metabolize angiotensin II into angiotensin 1-7. Angiotensin 1-7 has anti-inflammatory effects [35]. ACE2 acts as COVID19 receptor, it has been proposed that using angiotensin converting-enzyme inhibitors and angiotensin II receptor blockers may manage.

COVID-19 in hypertension patient. In contrast, animal studies show that these two inhibitors and blockers may increase ACE2 expression and may encourage the risk for COVID-19 [35]. The presence of ACE2 is necessary for producing angiotensin1-7 and its anti-inflammatory effects but ACE2 is also COVID-19's receptor that while this virus bind to it, ACE2 cannot use for anti-inflammatory role. There are two axis as ACE2-angiotensin 1-7-Mas receptor axis and ACE-angiotensin II-angiotensin receptor type 1 axis. The former one is necessary for presence of ACE2 and producing angiotensin1-7 -related anti-inflammation results. The later one related to inflammation. Body need balance between these two axes to use ACE2 without encouraging COVID-19. The simple way to create this balance is doing exercise. Training and physical activity increase the ACE2-angiotensin 1-7-Mas receptor axis and simultaneously inhibit the ACE-angiotensin II-angiotensin receptor type 1 axis and control the inflammation [35]. It has been shown that, by doing exercise and activating ACE2-angiotensin 1-7-Mas receptor axis pulmonary fibrosis could be reduce due to transforming growth factor-beta1 [TGF-beta1] reduction. TGFbeta1 is the most potent inducer of pulmonary diseases [35].

COVID-19 is new to our immune system and the first line of immune system [as innate immunity] is crucial to cope with new virus and following the virus entrance the body create its antibody and specific immunity will play key role to cope with it [13,29]. It is documented that physical activity less than 60 minutes and acute exercise increase the anti-inflammatory cytokines, natural killer cells, T cytotoxic cells, and immature B cells. Performing exercise could selectively increase lymphocyte and decrease inflammation that is so important to control clinical condition [36]. Prolong and intensive endurance exercise alter natural killer cell, T and B cells function, and other immune function biomarkers. Immune system needs oxygen and energy to generate cells, following prolong and

intensive exercise body's metabolism increase due to recovery and immune system face with transient dysfunction. It has been reported that, have sufficient carbohydrate and polyphenols could counter immune system dysfunction [36]. It is well documented although a bout of intensive exercise transiently decrease immune system responses but in a regular manner exercise decrease illness and control inflammation [36].

Yoga bring peace in life of individual and teach how to be aware about body and mind and how to be careful for other and pray good wishes for them. Yoga is not holding a special posture, in contrast it is a relaxed situation with focusing on infinity [6]. It has been reported that doing yoga could control and decrease pro-inflammatory cytokine in healthy individuals or patients and boost immune system. Yoga affect parasympathetic nervous system and reduce muscles' and joints' tension [6,30]. Continuous stressors lead to sympathetic overdrive and stimulate HPA that per se control wide majority of body systems [e.g. immune function, digestion]. The HPA axis release corticotrophin-releasing factor [CRF] from hypothalamus and subsequent adrenocorticotrophic hormone [ACTH] secretion from pituitary gland and finally release cortisol. Cortisol run gluconeogenesis and increase blood glucose levels, suppress immune system and increase inflammatory cytokines, impair memory and cause depression [16,30]. Being positive and well-wishers encourage the body positive neurotransmitters such as serotonin, gamma-aminobutyric acid [GABA], and dehydroepiandrosterone [DHEA] [30]. Performing yoga not only control the cortisol and its-related dysfunction but also, promote parasympathetic and vagal tone which increase heart rate variability. Low heart rate variability show poor myocardia. Yogic training by releasing prolactin and oxytocin encourage the feeling of calmness, reduced cortisol, control and diminish stress [30]. It has been reported that yoga could decrease inflammatory markers and IL-6, increase immunoglobulin, elevate natural killer cells, increase leptin and adiponectin levels, and control acute and chronic stress [4,30]. Physical activity and yoga are beneficial ways to control stress and help body immune system to work properly.

Conclusion

Stress and fear of COVID-19 could disable immune system and prone body for different diseases. Home-staying and public health recommendation [such as social distancing] lead to depression and physical inactivity that they both make immune system weak. Physical activity and yoga improve this vital system and by creating

balance between ACE2-angiotensin 1-7-Mas receptor axis and ACE-angiotensin II-angiotensin receptor type 1 axis could have anti-viral effects. Performing physical activity and have active life style is so helpful to improve immune system and prevent depression. Doing physical activity and yoga have various positive effects such as anti-inflammatory, antioxidant, neurogenesis and neuroprotection that could consider them as strategies to cope with COVID-19. They could decrease inflammatory markers and IL-6, increase immunoglobulin, elevate natural killer cells, T cytotoxic cells, and immature B cells and consequently control acute and chronic stress, decrease inflammation, and control clinical condition. Also, there are different efforts about vaccination and even though some research show their positive effect to control the COVID-19 expansion but still there are lots of issues to work on them. Generally, more studies need to uncover the COVID-19 secrets and any appropriate ways to control it and its-induced stress, and scrutinized probable effects of different types of physical activities on COVID-19, as well.

Conflict of Interest

Current study authors have no conflict of interest, financial or otherwise.

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