



REVIEW ARTICLE

Effect of Physiotherapy Applications on Inflammatory Markers in Asthma Disease

Özden Gökçek^{1*}  and Ufuk Yurdalan² 

¹Physiotherapy and Rehabilitation Department, Ege University, Turkey

²Physiotherapy and Rehabilitation Department, Istanbul Medipol University, Turkey

*Corresponding author: Ozden Gokcek, Physiotherapy and Rehabilitation Department, Health Science Faculty, Ege University, İzmir, Turkey, Tel: 00905066754729



Abstract

It is estimated that there are 300 million individuals diagnosed with asthma worldwide. Asthma is a chronic inflammatory heterogeneous disease with clinical symptoms such as wheezing, nocturnal cough, dyspnea, expiratory airflow limitation, and bronchial spasm.

Chronic systemic diseases associated with asthma cause an increase in the burden of health services, a reduction in the quality of life of individuals, and a decrease in work efficiency. Obesity, which plays a role in the reduction of pharmacological effects in the treatment of asthma, increases with sedentary life. A significant reduction in obesity is observed with exercise applications. Obesity is an important risk factor for asthma and also increases the severity of the disease by causing an increase in inflammation markers. There are contradictions in the literature regarding whether exercise triggers asthma attacks. This review aims to determine the effects of physiotherapy applications on increased inflammatory cytokines that increase asthma symptoms and cause attacks and provide evidence.

In addition to the use of pharmacological drugs, it is seen that alternative and complementary therapy applications are becoming widespread today. In this context, it is clinically important to present evidence that physiotherapy applications provide biochemical improvement.

Keywords

Asthma, Exercise, Inflammation

Introduction

Asthma is a common disease known to have approximately 300 million individuals worldwide [1]. It is seen that 50% of a mild or severe type of asthma, which is an inflammatory disease, has a type 2 inflammatory

response in the airways [2]. The increase in systemic inflammation markers in asthma patients plays a role in the development of hypoxia and dynamic hyperinflation [3]. The presence of inflammatory cells in the airway causes an altered repair response of the airway with the secretion of cytokines and growth factors that induce structural changes in the airways. In the case of airway remodeling, there is an increase in inflammatory cell count, hypertrophy of submucosal glands, hyperplasia of goblet cells and airway smooth muscle, and accumulation of collagen and fibronectin in the subepithelial basement membrane/submucosa around or in airway smooth muscle bundles [4]. Clinical symptoms of asthma are wheezing, nocturnal cough, dyspnea, expiratory airflow limitation, and bronchial spasm [5].

Airway tone is regulated by the autonomic nervous system. The autonomic nervous system acts on mucociliary clearance. Mucociliary clearance; impaired by airway inflammation, excessive mucus production, and changes in mucus viscosity or osmolality [6].

In the pathophysiology of asthma, changes in autonomic, endocrine, immunological, and central nervous system mechanisms and psychosocial factors; motivation, sense of self, lifestyle are negatively affected [7]. Due to the perception of dyspnea and the anxiety of having an attack, asthma patients have a significant limitation in their physical activities compared to healthy individuals. Restriction of physical activity causes deconditioning, the development of deconditioning disease symptoms, resulting in a vicious circle [8].



Citation: Gökçek O, Yurdalan U (2023) Effect of Physiotherapy Applications on Inflammatory Markers in Asthma Disease. Int J Sports Exerc Med 9:252. doi.org/10.23937/2469-5718/1510252

Accepted: May 24, 2023; **Published:** May 26, 2023

Copyright: © 2023 Gökçek O, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

There are studies in the literature that asthma patients are more obese than healthy individuals due to limitations in physical activity [9]. Tumor Necrosis Factor- α (TNF- α) and Interleukin 6 (IL 6) inflammation cytokines secreted from adipose tissue in obese individuals increase the production of C-Reactive Protein (CRP), which is an inflammation mediator, in the liver [10]. Chronic infection and inflammatory response cause lung tissue damage. The aim of the treatment of lung diseases is to prevent or slow the progression of the disease.

In addition to medical treatment, alternative treatment methods (yoga, Tai Chi, exercise, etc.) are also frequently used in asthma [11]. It has been determined that exercise has an effect on the nervous and immune systems with its endocrine activity, thus activating various complex interacting mechanisms in the psycho-neuro-immune-endocrine pathways [12].

Exercise provides an increase in plasma anti-inflammatory cytokine concentration and receptor antagonists. Exercise has a significant contribution to the reduction of IL6 and TNF- α [13]. Regular physical training can alter the autonomic balance and accelerate the physiological recovery of vagal sympathetic interaction [14]. Physiotherapy is thought to help clear inflammatory exudates, tracheobronchial secretions, airway obstructions and reduce airway resistance to improve respiration and increase gas exchange [15].

It is known that regular exercise in patients with asthma has positive effects on improvement in clinical symptoms, functional capacity, and quality of life in patients [16]. This review aims to determine the effects of physiotherapy applications on adipose tissue, which causes an increase in inflammation markers and inflammatory cytokines, which increase asthma symptoms and cause attacks, and present evidence.

Aerobic Exercise and Inflammation

Aerobic exercise appears to reduce airway remodeling with reduced airway smooth muscle hypertrophy and hyperplasia, reduction in leukocyte infiltration, proinflammatory cytokine production, adhesion molecule expression, and enhanced regulatory T cell (Treg) responses [17]. Regular exercises to increase aerobic condition (swimming etc.) increase the ventilatory threshold and decrease the minute volume. As a result, the feature of exercise as a trigger for symptoms disappears [18].

It has been determined that exercise training mediates the activity of immune and metabolomic pathways as a beneficial effect on asthma [19].

Airway inflammation is one of the main factors that increase the risk of exacerbation and severity of asthma in asthma. Potential mediator mechanisms by exercise include reductions in serum Th2 proinflammatory

cytokines, interleukin (IL)-4, IL-5 and IL-6, IL-13-16, monocyte chemoattractant protein 1, and keratinocyte chemoattractant protein (mouse homolog human IL-8) inhibition of nuclear factor kappa B (NF κ B) activation and an increase in the anti-inflammatory cytokines IL-10, IL-1ra and circulating regulatory T cells [20].

Exercise has also been found to improve patency of bronchioles through epithelial stimulation and mucociliary clearance, and smooth muscle function through deep inspiration and sigh rate [21].

Several randomized controlled trials in the literature have found that aerobic exercise training is beneficial for functional capacity, airway inflammation, asthma exacerbation, control, healthcare utilization, psychological state, and quality of life [22].

There is evidence that aerobic exercise training reduces bronchial hyperresponsiveness through a mechanism involving β 2-adrenergic receptors [23].

Physical Activity and Inflammation

Physical activity is effective in preventing the development of chronic diseases and managing disease symptoms [24]. In the literature, it has been proven that good asthma control, a decrease in the number of exacerbations and attacks, and a decrease in the need for health care use are associated with the level of physical activity participation [8].

Sedentary life plays an important role in the development of obesity, which is one of the risk factors for asthma disease in individuals. Obesity causes decreased lung volume, more pronounced asthma symptoms, increased work of breathing, less favorable response to controller medications, and increased airway inflammation [25]. It also has a negative effect on the immune system of individuals. Physical inactivity contributes to poor asthma control and consequent increase in symptoms, risk of exacerbations, and airway inflammation in asthmatics [26]. It is known that an active life provides an increase in the physical fitness level of individuals and a decrease in body mass index. An increase in physical activity is effective in weight loss and reduces sleep disorders [27].

Physical activity causes a decrease in the level of pro-inflammatory mediators and an increase in anti-inflammatory mediators and their mediators. Rahimi, et al. according to their study, it was determined that physical activity reduces CRP concentration and decreases other inflammation markers [28].

Based on cross-sectional data, it is reported that it is effective in increasing physical activity levels, reducing inflammation, and lowering susceptibility to obesity and type 2 diabetes [29].

Chest Physiotherapy and Inflammation

The inflammatory process clogs the bronchial lumen

and causes the accumulation of secretions [30]. The primary purpose of chest physiotherapy is to help clear accumulated secretions, restore respiratory condition, thereby lowering airway resistance, increasing gas exchange, and facilitating breathing [15].

Chest physiotherapy is an important aid in the treatment of respiratory diseases. Chest physiotherapy techniques can be classified as traditional, modern, and instrumental techniques [31].

Postural drainage, vibration, percussion, huffing, and coughing are traditional techniques aimed at facilitating mucociliary clearance [32].

Modern techniques; exercises include forced expiration, active respiratory cycle, autogenic drainage, assisted autogenic drainage, prolonged expiration, increased expiratory flow, total slow expiration with glottis open in lateral posture, and inspiratory controlled flow exercises [33]. In addition to clearing secretions in respiratory tract diseases, the positive contributions of exercise and breathing exercise are stated in increasing mucus viscosity and elasticity [21].

El Dein, et al. in a study conducted, applied conventional chest therapy applications and pneumatic compression to the study group of fifteen children aged 6-12 years, who were diagnosed with thirty pneumonia, while they applied only conventional chest physiotherapy to the control group of fifteen people. When they compared the study group and the control group, they found that the study group had more decreases in inflammation markers. However, it was observed that the patients in the control group had a decrease in inflammation markers (CRP, WBC, etc.) after treatment compared to before treatment [34].

Respiratory Muscle Training and Inflammation

Inspiratory muscle training (IMT) affects the autonomic nervous system and provides adaptation by stimulating stretch receptors in the lung, thus taking an active role in inflammation [35]. Inspiratory muscle training weakens the chemoreceptor activities in the diaphragm and has a positive effect on the immune system [36]. There are studies on the effectiveness of IMT in improving functional capacity [37]. In the literature, it is stated that IMT is effective in reducing IL6 [38].

Figueiredo, et al. followed thirty-seven hemodialysis patients in three groups as IMT, aerobic training, and combined training, for initial, 8-week, and 16-week periods. In conclusion, they concluded that eight weeks of IMT improved the functional and inflammatory parameters of patients on hemodialysis treatment, similar to the effect of low-intensity aerobic training [39].

Pellizzaro, et al. in a randomized controlled study, thirty-nine hemodialysis patients were evaluated in

three groups during the 10-day dialysis process. They divided the first group as respiratory muscle training (n = 11), the second group as peripheral muscle training (n = 14), and the third group as control (n = 14). Compared with the control group, the group that received respiratory muscle training and the group that received peripheral muscle training had a significant decrease in CRP levels [40].

As a result, it is stated in our review that physiotherapy applications in asthma patients reduce the inflammation markers that cause an increase in the symptoms of the disease and the number of attacks, and also have an important role in the reduction of adipose tissue, which causes the increase in inflammation markers. In this respect, it is important to include physiotherapy applications in the treatment process of patients, both in terms of clinical and future research.

Ethics

No ethics committee approval was required for the review.

Contributed by Author

Concept: Ozden Gokcek; Design: Ozden Gokcek, Ufuk Yurdalan; Literature Search: Ozden Gokcek, Ufuk Yurdalan; Writing: Ozden Gokcek; Consultancy: Ozden Gokcek; Critical review: Ufuk Yurdalan.

Financial Disclosure

No financial support for review.

Conflict of Interest

None declared.

References

1. GBD 2015 Chronic Respiratory Disease Collaborators (2017) Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: A systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med* 5: 691-706.
2. Fajt ML, Gelhaus SL, Freeman B, Uvalle CE, Trudeau JB, et al. (2013) Prostaglandin D2 pathway upregulation: Relation to asthma severity, control, and TH2 inflammation. *J Allergy Clin Immunol* 131: 1504-1512.
3. Pini L, Valsecchi A, Boni E, Guerini M, Tantucci C (2010) Acute dynamic hyperinflation and systemic inflammation in stable COPD patients. *Am J Respir Crit Care Med* 181: A 2907.
4. Royce SG, Lim CXF, Patel KP, Wang B, Samuel CS, et al. (2014) Intranasally administered serelaxin abrogates airway remodelling and attenuates airway hyperresponsiveness in allergic airways disease. *Clin Exp Allergy* 44: 1399-1408.
5. Kim DY, Park JW, Jeoung D, Ro JY (2009) Celestrol suppresses allergen-induced airway inflammation in a mouse allergic asthma model. *Eur J Pharmacol* 612: 98-105.
6. Nawroth JC, Does AM, Firth AR, Kanso E (2020) Multiscale mechanics of mucociliary clearance in the lung. *Philos Trans R Soc Lond B Biol Sci* 375: 20190160.

7. Ritz T, Meuret AE, Trueba AF, Fritzsche A, Leupoldt A (2013) Psychosocial factors and behavioral medicine interventions in asthma. *J Consult Clin Psychol* 81: 231-250.
8. Nyenhuis SM, Dixon AE, Ma J (2018) Impact of lifestyle interventions targeting healthy diet, physical activity, and weight loss on asthma in adults: What is the evidence? *J Allergy Clin Immunol Pract* 6: 751-763.
9. Hampton T (2014) Studies probe links between childhood asthma and obesity. *JAMA* 311: 1718-1719.
10. Unek IT, Bayraktar F, Solmaz D, Ellidokuz H, Sisman AR, et al. (2010) The levels of soluble CD40 ligand and C-reactive protein in normal weight, overweight and obese people. *Clin Med Res* 8: 89-95.
11. Wang C, Preisser J, Chung Y, Li K (2018) Complementary and alternative medicine use among children with mental health issues: Results from the national health interview survey. *BMC Complement Altern Med* 18: 241.
12. Verratti V (2009) Neuroimmune biology of physical exercise. *J Biol Regul Homeost Agents* 23: 203-206.
13. Amin MN, Mowafy ME, Mobark A, Abass N, Elgami A (2021) Exercise-induced downregulation of serum interleukin-6 and tumor necrosis factor-alpha in Egyptian handball players. *Saudi J Biol Sci* 28: 724-730.
14. Pierpont GL, Adabag S, Yannopoulos D (2013) Pathophysiology of exercise heart rate recovery: A comprehensive analysis. *Ann Noninvasive Electrocardiol* 18: 107-117.
15. Chaves GS, Freitas DA, Santino TA, Nogueira PAM, Fregonezi GA, et al. (2019) Chest physiotherapy for pneumonia in children. *Cochrane Database Syst Rev* 1: CD010277.
16. Yüksel H, Söğüt A, Yılmaz Ö, Günay Ö, Tıkız C, et al. (2009) Effects of physical exercise on quality of life, pulmonary function and symptom score in children with asthma. *Asthma Allergy Immunol* 7: 58-65.
17. Lowder T, Dugger K, Deshane J, Estell K, Schwiebert LM (2010) Repeated bouts of aerobic exercise enhance regulatory T cell responses in a murine asthma model. *Brain Behav Immun* 24: 153-159.
18. Wang JS, Hung WP (2009) The effects of a swimming intervention for children with asthma. *Respirology* 14: 838-842.
19. Panagiotou M, Koulouris NG, Rovina N (2020) Physical Activity: A Missing Link in Asthma Care. *J Clin Med* 9: 706.
20. Scott JPR, Sale C, Greeves JP, Casey A, Dutton J, et al. (2011) Effect of exercise intensity on the cytokine response to an acute bout of running. *Med Sci Sports Exerc* 43: 2297-2306.
21. Rivera LC, Gibson PG, Gardiner PA, McDonald VM (2018) A systematic review of associations of physical activity and sedentary time with asthma outcomes. *J Allergy Clin Immunol Pract* 6: 1968-1981.
22. Hewitt M, Estell K, Davis IC, Schwiebert LM (2010) Repeated bouts of moderate-intensity aerobic exercise reduce airway reactivity in a murine asthma model. *Am J Respir Cell Mol Biol* 42: 243-249.
23. Thornton JS, Fremont P, Khan K, Poirier P, Fowles J, et al. (2016) Physical activity prescription: A critical opportunity to address a modifiable risk factor for the prevention and management of chronic disease: A position statement by the Canadian academy of sport and exercise medicine. *Br J Sports Med* 50: 1109-1114.
24. Freitas PD, Silva AG, Ferreira PG, Silva ADA, Salge JM, et al. (2018) Exercise improves physical activity and comorbidities in obese adults with asthma. *Med Sci Sports Exerc* 50: 1367-1376.
25. Scott HA, Wood LG, Gibson PG (2017) Role of obesity in asthma: Mechanisms and management strategies. *Curr Allergy Asthma Rep* 17: 53.
26. Kline CE (2014) The bidirectional relationship between exercise and sleep: Implications for exercise adherence and sleep improvement. *Am J Lifestyle Med* 8: 375-379.
27. Rahimi GRM, Yousefabadi HA, Niyazi A, Rahimi NM, Alikhaje Y (2022) Effects of lifestyle intervention on inflammatory markers and waist circumference in overweight/obese adults with metabolic syndrome: A systematic review and meta-analysis of randomized controlled trials. *Biol Res Nurs* 24: 94-105.
28. Schmidt FM, Weschenfelder J, Sander C, Minkwitz J, Thormann J, et al. (2015) Inflammatory cytokines in general and central obesity and modulating effects of physical activity. *PLoS One* 10: e0121971.
29. Suartawan IP (2019) Pneumonia pada anak usia 20 bulan i putu suartawan. *Jurnal Kedokteran* 05: 198-206.
30. Morrison L, Innes S (2017) Oscillating devices for airway clearance in people with cystic fibrosis. *Cochrane Database Syst Rev* 5: CD006842.
31. Darzi FY, Hasavari F, Khaleghdoost T, Leyli EK, Khalili M (2016) Effects of thoracic squeezing on airway secretion removal in mechanically ventilated patients. *Iran J Nurs Midwifery Res* 21: 337-342.
32. Mckoy NA, Wilson LM, Saldanha IJ, Odelola OA, Robinson KA (2016) Active cycle of breathing technique for cystic fibrosis. *Cochrane Database Syst Rev* 7: CD007862.
33. Grillo LJJ, Housley GM, Gangadharan S, Majid A, Hull JH (2022) Physiotherapy for large airway collapse: An ABC approach. *ERJ Open Res* 8: 00510-2021.
34. Dein MSE, Dein SNE, Hassan A (2021) Effect of lymphatic pump on inflammatory markers and chest expansion in children with community-acquired pneumonia. *Egypt J Hosp Med* 85: 2840-2844.
35. Brilla LR (2012) Perspectives on breathing in sports and health. *J Sport Med Doping Stud* 2: 1000e121.
36. Mehani SHM (2017) Immunomodulatory effects of two different physical therapy modalities in patients with chronic obstructive pulmonary disease. *J Phys Ther Sci* 29: 1527-1533.
37. Montemezzo D, Fregonezi GA, Pereira DA, Britto RR, Reid WD (2014) Influence of inspiratory muscle weakness on inspiratory muscle training responses in chronic heart failure patients: A systematic review and meta-analysis. *Arch Phys Med Rehabil* 95: 1398-1407.
38. Mills DE, Johnson MA, McPhilimey MJ, Williams NC, Gonzalez JT, et al. (2013) The effects of inspiratory muscle training on plasma interleukin-6 concentration during cycling exercise and a volitional mimic of the exercise hyperpnea. *J Appl Physiol* 115: 1163-1172.
39. Figueiredo PHS, Lima MMO, Costa HS, Martins JB, Flecha OD, et al. (2018) Effects of the inspiratory muscle training and aerobic training on respiratory and functional parameters, inflammatory biomarkers, redox status and quality of life in hemodialysis patients: A randomized clinical trial. *PLoS One* 13: e0200727.
40. Pellizzaro CO, Thomé FS, Veronese FV (2013) Effect of peripheral and respiratory muscle training on the functional capacity of hemodialysis patients. *Ren Fail* 35: 189-197.