

Effects of intermittent aerobic training on exercise capacity, pulmonary functions, and gait parameters in asthmatic children with cerebral palsy: a randomized controlled trial

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Abstract. – OBJECTIVE: There is no evidence that exercise training program is effective in improving aerobic capacity, musculoskeletal abnormalities, and quality of life in asthmatic children with cerebral palsy (CP). Therefore, the effects of intermittent aerobic training on exercise capacity, pulmonary function, and gait parameters in asthmatic CP children have been evaluated in the current study.

PATIENTS AND METHODS: This clinical trial included thirty-six asthmatic CP children between January and December 2021. Their ages were between 7 and 12 years old. They were randomly allocated to the intermittent aerobic exercise group (IAEG) and a control group (CG), with 18 per each group. The children have been recruited for the 10-week interventional program. The 6-minute walk test (6MWT), forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), stride length, cadence, gait speed, and pediatric asthma quality of life (PAQLQ) were all measured before and after treatment.

RESULTS: Pre-post analysis in the IAEG showed noteworthy changes (6MWT, $p=0.005$; FVC, $p=0.002$; FEV₁, $p<0.001$; overall score of PAQLQ, $p<0.001$; stride length, $p<0.001$; cadence, $p<0.001$; and gait speed, $p<0.001$), while the control group showed non-significant changes ($p>0.05$). There were noteworthy differences between IAEG and CG post-treatment (6MWT, $p=0.019$; FVC, $p=0.031$; FEV₁, $p<0.001$; overall score of PAQLQ, $p=0.031$; stride length, $p<0.001$; cadence, $p=0.009$; and gait speed, $p<0.001$) in favor of the IAEG.

CONCLUSIONS: Depending on the study findings, 10 weeks of intermittent aerobic exercise may improve exercise capacity, pulmonary function, gait parameters, and quality of life in asthmatic CP children. Based on what we found, this protocol should be used in pulmonary rehabilitation programs for children with CP who have breathing problems.

Key Words:

Cerebral palsy, Asthma, Intermittent aerobic exercise, 6MWT, Gait, PAQLQ.

Introduction

Cerebral Palsy (CP) is a heterogeneous disorder group including postural and movement issues that are due to a non-progressive developmental brain damage. The developing musculoskeletal abnormalities occur in most of the CP children. The primary problems include changing in the muscle strength, tone, and balance, associated with central nervous system injuries. The derivative alterations, such as skeletal deformities and muscular contractures, expand in the long run because of the principal issues and abnormal development of musculoskeletal system¹. CP is identified as the commonest disability reason among children. Pulmonary disorders caused by many combined factors are considered to be the primary reason of impaired life quality, morbidity and mortality in several different children who have suffered from CP. The clinical motor disorder of the affected CP children includes impaired fitness, breathing issues and scoliosis; therefore, the intervention is urgent to maximize the physical and musculoskeletal functions. At birth, most of the children experiencing CP do not suffer from musculoskeletal impairments, but the abnormalities appear over the time. The CP children complain about disturbances in different aspects, like sensation, perception, cognition, and behavior. Adult CP individuals suffer fourteen times of elevated mortality rate from pulmonary disorders when compared to the general population. Several studies²⁻⁵ have reported that the death in CP individuals has resulted from pulmonary failure. There are many types of CP, but the most common types are hemiplegia and diplegia⁶.

Pain and admission to hospitals are identified as the main indicators of impaired life quality in severe CP individuals and the most common cause of medical

hospitalization with pulmonary issues; in fact, severe physical disability increases the frequency of hospital admissions in CP individuals⁷. CP Children have poorer lung function when compared with matched children of the same age. Skeletal deformities, like scoliosis, decrease the vital capacity and affect the gait pattern in spastic CP children^{8,9}. The prevalence of skeletal deformities affects 20-25% of non-ambulant CP children¹⁰. The prevention of pelvic and hip deformity decreases the spinal deformity that leads to gait pattern improvement. Several studies¹¹ have found that childhood skeletal deformities can progress into adulthood, affecting pulmonary function through restricted chest expansion.

CP hemiplegic children are suffering from impaired gait parameters, such as longer duration of stance phase and gait cycle, lower gait speed and shorter duration of swing phase compared to their normal peers. It has also been reported¹² that noteworthy angle differences in the lower extremity joints between CP and healthy matched peers can be observed during ground weight bearing. CP children have a decreasing aerobic capacity and a higher oxygen consumption for daily activities that increases with disability. When compared with normal developing children, modalities that improve peak oxygen uptake may lead to decreased oxygen consumption in activities of daily living¹³. The musculoskeletal abnormalities of CP children may affect activities of daily living, such as dressing and walking, which decreases the overall dimensions of quality of life. Therefore, optimizing the muscle function is very important to performing activities of daily living and improving the quality of life¹⁴⁻¹⁶.

There is no evidence about which exercise training program is effective in improving aerobic capacity, musculoskeletal abnormalities, quality of life and body composition in CP children¹⁷. Therefore, the current study examined the effects of intermittent aerobic training on exercise capacity, pulmonary function, and gait parameters in asthmatic CP children, with the hypothesis that intermittent aerobic exercise may be beneficial in those children.

Patients and Methods

Study Design

This prospective randomized clinical trial has been carried out in the outpatient physiotherapy clinic between January and December 2021 after obtaining the Ethical Committee approval from the Ethics Physiotherapy Committee department [RHPT/020/066]. The study has been conducted after explaining the procedures of the study to par-

ents and caregivers of the children. Written consent forms have been signed before starting the program of the study.

Participants

This clinical trial included thirty-six CP children after their eligibility to be enrolled in the study according to the inclusion criteria and the calculation of the required sample for the study. The children have been enrolled in this trial according to the following criteria: diagnosis of hemiplegic CP by pediatric physicians; both genders; age between 7-12 years; capability of independently walking; capability of understanding the instructions of the study program. The children who experienced uncontrolled seizures, post-six-month Botulinum toxin injections, post-one-year orthopedic surgeries, inability to understand the instructions of the study have been excluded.

Sample Size Calculation

Using G*Power 3.1.5, the sample size has been estimated. Using significant data that were obtained from a prior preliminary study with an effect size of up and go test of |6.58|, two-tailed, 95% power, and 0.05 alpha error, the sample size that provided an efficient power to identify noteworthy findings was 14 children per each group. To avoid the dropout rate, 36 children have therefore been enrolled in the study.

Allocation and Randomization

After checking the eligibility and initial assessment, the children have been randomly allocated to traditional physiotherapy program (controls) and intermittent aerobic exercise program plus traditional physiotherapy program (study group). The randomization has been performed by a blind examiner using 36 opaque and sealed envelopes that contained colored and uncolored cards. The children have been instructed to select envelopes. Colored cards have been assigned to controls, while uncolored ones have been assigned to the study group. The consort flowchart of the study is described in Figure 1.

Outcome Measures

Exercise capacity using the 6-minute walk test (6MWT), pulmonary functions including the predicted values of forced vital capacity (FVC) and forced expiratory volume in one second (FEV₁), quality of life using the pediatric asthma quality of life questionnaire (PAQOLQ), and gait parameters (stride length, cadence, and speed) have been assessed on two occasions: pre- and post-treatment.

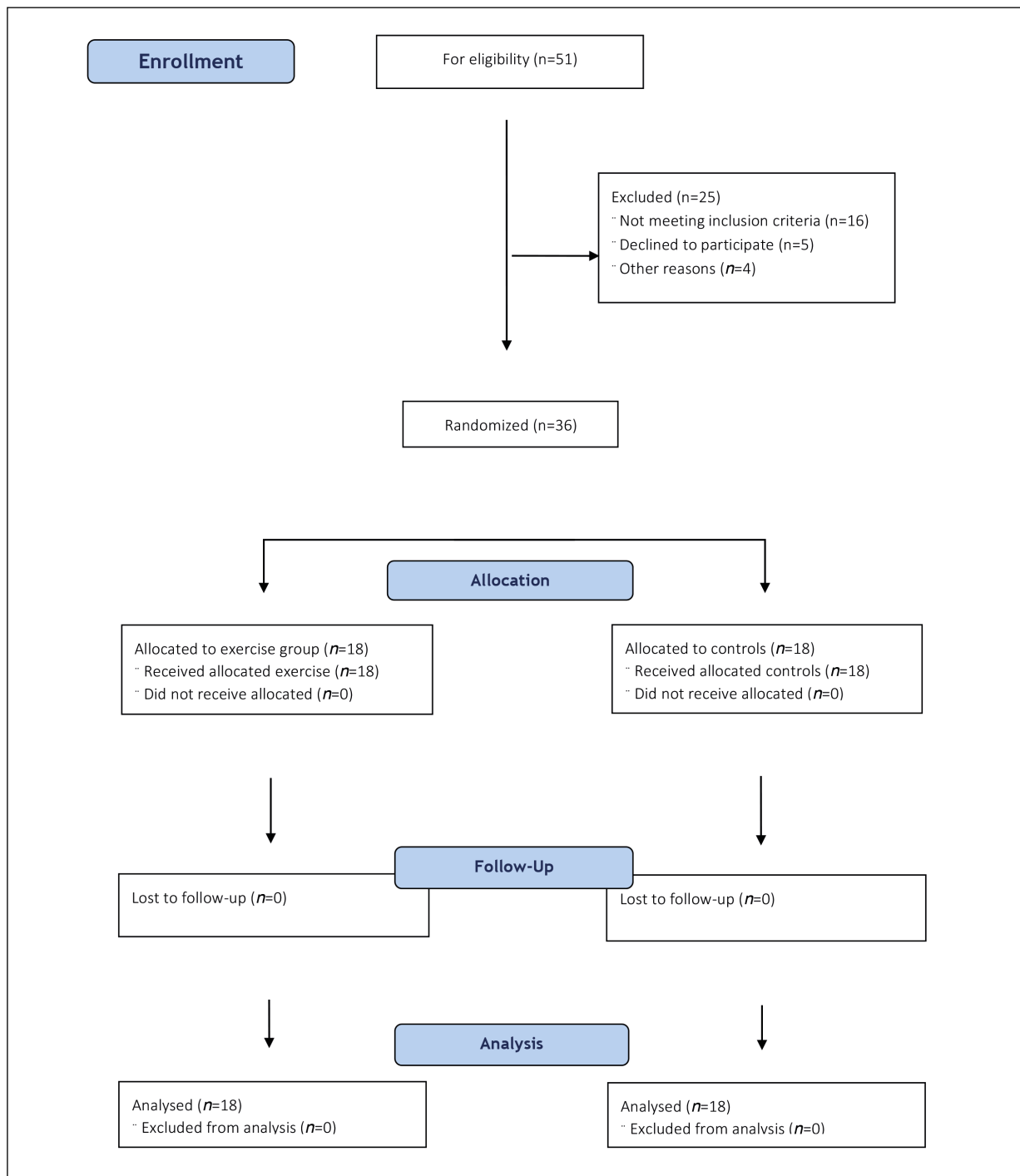


Figure 1. The CONSORT flowchart of the study.

6MWT

The 6MWT has been used to gauge exercise capacity. It is a validated assessment technique for exercise capacity in various pediatric diseases. In addition to showing the beginning and ending points of the test and instructing children and par-

ents on how to avoid hopping, running, or leaping throughout the 6MWT, researchers taught participants and their parents prior to the test. For six minutes, each youngster was asked to walk down a 50-meter straight corridor while a timer was kept near by the examiner's side. Before and after the

twelve-week trial period, the 6MWT distance in meters was measured^{18,19}.

Pulmonary Functions

The predicted values of FVC and FEV₁ have been assessed by conducting a spirometry test. A trained technician used an Autospiro-507 (Minato Medical Science, Osaka, Japan) to assess the pulmonary functions. Each child was asked to inhale and exhale normally, with the lips tightly closed on the mouthpiece and gentle calipers on the noses. Then each one was instructed to inhale deeply and exhale quickly. The FVC and FEV₁ readings from the three experiments have been within 0.150 L or 10% of the best ratings, whichever was greater. Data analysis used the highest values²⁰.

Gait Parameters

The gait parameters have been assessed using the GAITRite system (CIR Systems Inc., Clifton, NJ, USA). There are 13,824 embedded pressure sensors in the GAITRite system that detect each footfall's position and relative pressure. It calculates spatial and temporal factors connected with gait automatically and offers valid and trustworthy measurements. 18Y21 GAITRite creates 20 gait parameters. The stride length, cadence, and gait speed have been assessed and recorded. During clinic appointments, children were asked to walk twice across the computerized GAITRite walkway with bare feet. On the GAITRite mat, there was a meter of space at each end for the subjects to accelerate and decelerate. The child's preferred walking speed was chosen over an imposed speed because it was deemed to be the most efficient for the person²¹.

Quality of Life (QOL)

The QOL has been assessed using a validated Arabic version of the pediatric asthma quality of life questionnaire (PAQLQ). It is a multidimensional respiratory problem and an age-appropriate measure for assessing quality of life in children and adolescents. It has 23 questions spanning 3 domains: activity limits, symptoms, and more (emotional function). The PAQLQ rates items on a 7-point Likert scale, with 1 indicating "the worst" and 7 indicating "the best" life quality. Each domain's score is the mean reaction to all items. The aggregate score is the sum of the three domains' mean scores. A higher score corresponds to a better sense of health²². The overall score was recorded and analyzed.

Treatment Program

The group of intermittent aerobic exercise conducted exercise training based on the maximal heart

rate (MHR). The duration of the exercise program ranged from forty to fifty minutes, depending on the child's ability. Each exercise included a short period of warming and a short period of cooling for five to ten minutes, while the exercise session intensity was high-intensity exercise >80% of MHR and moderate exercise 60-70% of MHR. The frequency of the exercise program was 4 sessions a week for 10 alternate weeks.

Statistical Analysis

Baseline demographic and clinical characteristics have been curated and analyzed before starting the study program. The Shapiro-Wilk test has been used to assess the normal distribution of data. Pre- and post-treatment changes have been assessed between and within groups using the Student's *t*-test in normally distributed data. The Chi-square and Mann-Whitney U tests have been performed and used to assess the differences in non-normally distributed data. Data have been analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The significance level has been accepted at $p < 0.05$.

Results

Thirty-six asthmatic children with hemiplegic CP (16 girls and 20 boys) were recruited for this randomized controlled study. They were randomly allocated into the intermittent aerobic exercise group (IAEG) and controls (CG). As detailed in Table I, IAEG and CG showed no significant differences in baseline demographic and clinical characteristics ($p > 0.05$; age, $p = 0.796$; gender, $p = 0.502$; BMI, $p = 0.554$; FEV₁ %, $p = 0.689$; asthma duration, $p = 0.711$; and medications including long-acting β_2 -agonist, $p = 0.809$, and corticosteroids, $p = 0.419$).

At baseline, there was no statistical difference in exercise capacity, pulmonary functions, quality of life, and gait parameters between IAEG and CG (6MWT, $p = 0.884$; FVC, $p = 0.872$; FEV₁, $p = 0.689$; overall score of PAQLQ, $p = 0.727$; stride length, $p = 0.648$; cadence, $p = 0.629$; and gait speed, $p = 0.648$). Controversy, there were noteworthy differences between the two groups post-treatment (6MWT, $p = 0.019$; FVC, $p = 0.031$; FEV₁, $p < 0.001$; overall score of PAQLQ, $p = 0.031$; stride length, $p < 0.001$; cadence, $p = 0.009$; and gait speed $p < 0.001$) in favor of the IAEG, as illustrated in Table II.

Pre- and post-analysis in the IAE group showed noteworthy changes (6MWT, $p = 0.005$; FVC, $p = 0.002$; FEV₁, $p < 0.001$; overall score of PAQLQ, $p < 0.001$; stride length, $p < 0.001$; cadence, $p < 0.001$;

Table I. Baseline demographic and clinical characteristics.

| | IAEG (n=18) | CG (n=18) | p-value |
|---|--------------------|---------------|---------|
| Age, yrs | 9.5 ± 2.4 | 9.3 ± 2.2 | 0.796 |
| Gender, B/G, n (%) | 11 (61.1)/7 (38.9) | 9 (50)/9 (50) | 0.502 |
| BMI, Kg/m ² | 19.82 ± 1.4 | 19.56 ± 1.2 | 0.554 |
| FEV ₁ , % pred. | 67.4 ± 5.8 | 68.2 ± 6.1 | 0.689 |
| Asthma duration, yrs | 4.2 ± 1.5 | 4.4 ± 1.7 | 0.711 |
| Medications | | | |
| long-acting β ₂ -agonist, µg | 381.4 ± 45.1 | 377.8 ± 43.5 | 0.809 |
| Corticosteroids (Budesonide), mg/d | 0.69 ± 0.11 | 0.66 ± 0.11 | 0.419 |

IAEG: intermittent aerobic exercise group; CG: control group; BMI: body mass index; FEV₁: forced expiratory volume in one second.

and gait speed, $p < 0.001$), while the control group showed non-significant changes in all outcome measures (6MWT, $p = 0.612$; FVC, $p = 0.289$; FEV₁, $p < 0.321$; overall score of PAQLQ, $p < 0.192$; stride length, $p < 0.071$; cadence, $p < 0.286$; and gait speed, $p < 0.148$), as displayed in Table II.

Discussion

This study has been designed to assess the effects of intermittent aerobic training on exercise capacity, pulmonary function, and gait parameters in asthmatic CP children, theorizing that intermittent aerobic exercise may have beneficial effects in those children. The results showed that 6MWT, FVC, FEV₁, and gait parameters had improved in the study group when compared with controls.

The 6MWT correlates well with the pulmonary function parameters, as shown in a previous publication²³ that looked at how the pulmonary function parameters and physical activity of people with chronic obstructive pulmonary disease changed over time. Correlational analysis results confirmed the findings of the previous literature concerning asthma, which affirms that a decline in inspiratory capacity also shows a statistically significant correlation between FEV₁, FVC, and 6MWT. The association between 6MWT and spirometry parameters was established to assess the ability of a patient with asthma to increase ventilation and diffuse capacity in response to the increasing metabolic demands of exercise²⁴.

A previous study done by Marin et al²⁵, who studied the inspiratory capacity, dynamic hyperinflation, breathlessness, and exercise performance during the 6MWT, found that the 6MWT and the spirometry parameters were changed in response to an aerobic exercise program. Further studies performed by Wibmer et al²⁶, who investigated on the relationship between exercise capacity and lung volumes before

and after 6MWT, supported these results by showing significant improvements in post-6MWT spirometry measures when compared to pre-6MWT measures. Both pre- and post-6MWT parameters were measured in this study.

These findings back up to previous findings²⁷ which determined spirometry parameters and diffusion capacity in COPD active smokers after exercise and demonstrated an improvement in spirometry parameters after aerobic exercises that improved gas transfer and diffusing capacity of the lungs, which were altered secondary to impairment in small airways. Study results obtained by Zeng et al²⁸ suggested that total lung capacity was only mildly elevated. Even so, the improvement in FVC, FEV₁, and QOL was significantly linked to 6MWT in our study.

QOL questionnaires are generally used in QOL assessment after therapeutic intervention in asthmatic patients. The present study results have demonstrated that the improvement in 6MWT, FVC, and FEV₁ was closely correlated with the score of PAQLQ as an indicator of quality of life due to an improvement in ventilation, perfusion, and diffusing capacity²⁹.

In asthmatic patients, the swing time and gait parameters, such as stride length, cadence, and speed, were significantly affected. The gait alteration may be due to decreased physical activity in daily life, muscle weakness, abnormal breathing patterns, a rise in respiratory demand and altered balance. Reduced levels of physical activity led to decreased muscle fiber cross-sectional area and reduction of mitochondrial density, resulting in skeletal muscle dysfunction. These dysfunctions may affect walking patterns³⁰. The results of our study come in agreement with the results of a previous study³¹, which found that biomechanical gait alterations and walking abnormalities in asthmatic patients improved after exercise training. The study conducted by Annegarn et al³² showed that subjects with asthma

Table II. Baseline and 10-week differences between and within IAE and control groups.

| Outcome measures | IAEG (n=18) | CG (n=18) | p-value |
|----------------------------|----------------|--------------|---------|
| 6 MWT, m | | | |
| Pre-treatment | 365.7 ± 89.3 | 371.5 ± 74.4 | 0.884 |
| Post-treatment | 445.5 ± 71.4 | 384.2 ± 77.3 | 0.019 |
| p-value | 0.005 | 0.612 | |
| FVC, % pred. | | | |
| Pre-treatment | 78.2 ± 7.5 | 78.6 ± 7.3 | 0.872 |
| Post-treatment | 87.4 ± 9.3 | 81.2 ± 7.1 | 0.031 |
| p-value | 0.002 | 0.289 | |
| FEV ₁ , % pred. | | | |
| Pre-treatment | 67.4 ± 5.8 | 68.2 ± 6.1 | 0.689 |
| Post-treatment | 79.6 ± 6.2 | 70.3 ± 6.4 | <0.001 |
| p-value | <0.001 | 0.321 | |
| PAQLQ, overall score | | | |
| Pre-treatment | 5.4 ± 0.8 | 5.5 ± 0.9 | 0.727 |
| Post-treatment | 6.7 ± 1.2 | 5.9 ± 0.9 | 0.031 |
| p-value | 0.002 | 0.192 | |
| Gait parameters | | | |
| Stride length, m | | | |
| Pre-treatment | 0.41 ± 0.06 | 0.42 ± 0.07 | 0.648 |
| Post-treatment | 0.72 ± 0.08 | 0.47 ± 0.09 | <0.001 |
| p-value | <0.001 | 0.071 | |
| Cadence, steps/min | | | |
| Pre-treatment | 111.4 ± 7.5 | 110.2 ± 7.3 | 0.629 |
| Post-treatment | 101.5 ± 6.2 | 107.6 ± 7.1 | 0.009 |
| p-value | <0.001 | 0.286 | |
| Speed, m/s | | | |
| Pre-treatment | 0.44 ± 0.06 | 0.45 ± 0.07 | 0.648 |
| Post-treatment | 0.73 ± 0.07 | 0.48 ± 0.05 | <0.001 |
| p-value | <0.001 | 0.148 | |

Significant difference at $p < 0.05$; IAEG: intermittent aerobic exercise group; CG: control group; 6MWT: six-minute walk test; FVC: forced vi-tal capacity; FEV₁: forced expiratory volume in one second; PAQLQ: pediatric asthma quality of life questionnaire.

walked at a decreased speed, decreased cadence, and greater medium-lateral variability during 6MWT when compared with healthy subjects.

Our study findings came in agreement with another previous study³³ that showed significant improvements in VO_{2peak} and lower percent utilization on a submaximal effort test in children with CP. This means that these children showed an improvement in exercise capacity and an increase in energy reserves after the intervention. It has been mentioned that VO_{2peak} has improved by 8-10% after an aerobic exercise training program³⁴. Nseniga et al³⁵ demonstrated that there was a significant improvement in VO_{2peak} by 22% after eight weeks of aerobic exercise training on a cycle ergometer (30 min with an exercise intensity of 50-65% of estimated VO_{2peak}, three sessions a week). Unnithan et al³⁶ showed an 18% increase in the VO_{2peak} after three months of combined endurance and strength training (3 sessions/week of 70 min with an exercise intensity of 65-75% of predicted HRmax). Also, during the

last test, the heart rate during the submaximal effort test decreased significantly, indicating that their relative exhaustion had decreased. During follow-up, we found that the oxygen cost at a submaximal effort also decreased due to a longer training period of walking or running³⁷.

Conclusions

Depending on the study findings, 10 weeks of intermittent aerobic exercise may improve exercise capacity, pulmonary function, gait parameters, and quality of life in asthmatic CP children. Our results recommended this protocol to be used in the pulmonary rehabilitation programs for CP children with respiratory disorders.

Conflict of Interest

The authors declare that they have no competing interests.

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Ethics Approval

The trial has been carried out in the outpatient physiotherapy clinic after obtaining the Ethical Committee approval from the Ethics Physiotherapy Committee department [RHPT/020/066].

Informed Consent

Written consent forms have been signed before starting the program of the study.

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References

- 1) Berker N, Yalcin S, editors. *The Help Guide to Cerebral Palsy*. 2nd ed. Seattle (WA): Global Help 2010; 5-32
- 2) Blair E, Langdon K, McIntyre S, Lawrence D, Watson L. Survival and mortality in cerebral palsy: observations to the sixth decade from a data linkage study of a total population register and national death index. *BMC Neurol* 2019; 19: 1-11.
- 3) Ryan JM, Peterson MD, Ryan N, Smith KJ, O'connell NE, Liverani S, Nana Anokye N, Victor C, Allen E. Mortality due to cardiovascular disease, respiratory disease, and cancer in adults with cerebral palsy. *Dev Med Child Neurol* 2019; 61: 924-928.
- 4) Brooks JC, Strauss DJ, Shavelle RM, Tran LM, Rosenbloom L, Wu YW. Recent trends in cerebral palsy survival. Part I: Period and cohort effects. *Dev Med Child Neurol* 2014; 56: 1059-1064.
- 5) Himmelmann K, Sundh V. Survival with cerebral palsy over five decades in western Sweden. *Dev Med Child Neurol* 2015; 57: 762-767.
- 6) Himmelmann K, Hagberg G, Uvebrant P. The changing panorama of cerebral palsy in Sweden. X. Prevalence and origin in the birth year period 1999-2002. *Acta Paediatr Int J Paediatr* 2010; 99: 1337-1343.
- 7) Elema A, Zalmstra TA, Boonstra AM, Narayanan UG, Reinders-Messelink HA, V D Putten AA. Pain and hospital admissions are important factors associated with quality of life in nonambulatory children. *Acta Paediatr* 2016; 105: e419-e425.
- 8) Kwon YH, Lee HY. Differences of respiratory function in children with spastic diplegic and hemiplegic cerebral palsy, compared with normally developed children. *J Pediatr Rehabil Med* 2013; 6: 113-117.
- 9) Lampe R, Blumenstein T, Turova V, Alves-Pinto A. Lung vital capacity and oxygen saturation in adults with cerebral palsy. *Patient Prefer Adherence* 2014; 8: 1691-1697.
- 10) Toovey R, Harvey A, Johnson M, Baker L, Williams K. Outcomes after scoliosis surgery for children with cerebral palsy: a systematic review. *Dev Med Child Neurol* 2017; 59: 690-698.
- 11) Graham HK, Rosenbaum P, Paneth N, Dan B, Lin JP, Damiano DL, Becher JG, Gaebler-Spira D, Colver A, Reddihough DS, Crompton KE, Lieber RL. Cerebral palsy. *Nat Rev Dis Primers* 2016; 2: 15082.
- 12) Wang X, Wang Y. Gait analysis of children with spastic hemiplegic cerebral palsy. *Neural Regen Res* 2012; 7: 1578-1584.
- 13) Tsoi WS, Zhang LA, Wang WY, Tsang KL, Lo SK. Improving quality of life of children with cerebral palsy: a systematic review of clinical trials. *Child Care Health Dev* 2012; 38: 21-31.
- 14) Wang HY, Chen CC, Hsiao SF. Relationships between respiratory muscle strength and daily living function in children with cerebral palsy. *Res Dev Disabil* 2012; 33: 1176-1182.
- 15) Kwon YH, Lee HY. Differences of respiratory function in children with spastic diplegic and hemiplegic cerebral palsy, compared with normally developed children. *J Pediatr Rehabil Med* 2013; 6: 113-117.
- 16) Kwon YH, Lee HY. Differences of respiratory function according to level of the gross motor function classification system in children with cerebral palsy. *J Phys Ther Sci* 2014; 26: 389-391.
- 17) Hwang CL, Wu YT, Chou CH. Effect of aerobic interval training on exercise capacity and metabolic risk factors in people with cardiometabolic disorders: a meta-analysis. *J Cardiopulm Rehabil Prev* 2011; 31: 378-385.
- 18) Li AM, Yin J, Yu CC, Tsang T, So HK, Wong E, Chan D, Hon EKL, Sung R. The six-minute walk test in healthy children: reliability and validity. *Eur Respir J* 2005; 25: 1057-1060.
- 19) Abdelbasset WK, Alsabaie SF, Tantawy SA, Abo Elyazed TI, Kamel DM. Evaluating pulmonary function, aerobic capacity, and pediatric quality of life following a 10-week aerobic exercise training in school-aged asthmatics: a randomized controlled trial. *Patient Prefer Adherence* 2018; 12: 1015-1023.
- 20) Lahm T, Douglas IS, Archer SL, Bogaard HJ, Chesser NC, Haddad F, Hemnes AR, Kawut SM, Kline JA, Kolb TM, Mathai SC, Mercier O, Michelakis ED, Naeije R, Tuder RM, Ventetuolo CE, Vieillard-Baron A, Voelkel NF, Vonk-Noordegraaf A, Hassoun PM; American Thoracic Society Assembly on Pulmonary Circulation. Assessment of Right Ventricular Function in the Research Setting: Knowledge Gaps and Pathways Forward. An Official American Thoracic Society Research Statement. *Am J Respir Crit Care Med* 2018; 198: e15-e43.
- 21) Van der Linden ML, Kerr AM, Hazlewood ME, Hillman SJ, Robb JE. Kinematic and Kinetic Gait Characteristics of Normal Children Walking at a Range of Clinically Relevant Speeds. *J Pediatr Orthop* 2002; 22: 800-806.
- 22) Abdel Hai R, Taher E, Abdel Fattah M. Assessing validity of the adapted Arabic Paediatric Asthma Quality of Life Questionnaire among Egyptian chil-

- dren with asthma. *East Mediterr Health J* 2010; 16: 274-280.
- 23) Waschki B, Kirsten AM, Holz O, Mueller K, Schaper M, Sack A, Meyer T, Rabe KF, Magnussen H, Watz H. Disease progression and changes in physical activity in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2015; 192: 295-306.
 - 24) o'Donnell DE, Guenette JA, Maltais F, Webb KA. Decline of resting inspiratory capacity in COPD: the impact on breathing pattern, dyspnea, and ventilatory capacity during exercise. *Chest* 2012; 14: 753-762.
 - 25) Marin JM, Carrizo SJ, Gascon M, Sanchez A, Gallego B, Celli BR. Inspiratory capacity, dynamic hyperinflation, breathlessness, and exercise performance during the 6-minute-walk test in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001; 163: 1395-1399.
 - 26) Wibmer T, Rüdiger S, Kropf-Santhen C, Stoiber KM, Rottbauer W, Schumann C. Relation of exercise capacity with lung volumes before and after 6-minute walk test in subjects with COPD. *Respir Care* 2014; 59: 1687-1695.
 - 27) Harvey BG, Strulovici-Barel Y, Kaner RJ, Sanders A, Vincent TL, Mezey JG, Crystal RG. Risk of COPD with obstruction in active smokers with normal spirometry and reduced diffusion capacity. *Eur Respir J* 2015; 46: 1589-1597.
 - 28) Zeng S, Tham A, Bos B, Jin J, Giang B, Arjomandi M. Lung volume indices predict morbidity in smokers with preserved spirometry. *Thorax* 2019; 74: 114-124.
 - 29) Esteban C, Quintana JM, Aburto M, Moraza J, Egurrola M, Pérez-Izquierdo J, Aizpiri S, Aguirre U, Capelastegui A. Impact of changes in physical activity on health-related quality of life among patients with COPD. *Eur Respir J* 2010; 36: 292-300.
 - 30) Yentes JM, Sayles H, Meza J, Mannino DM, Rennard SI, Stergiou N. Walking abnormalities are associated with COPD: an investigation of the NHANES III dataset. *Respir Med* 2011; 10: 80-87.
 - 31) Yentes JM, Schmid KK, Blanke D, Romberger DJ, Rennard SI, Stergiou N. Gait mechanics in patients with chronic obstructive pulmonary disease. *Respir Res* 2015; 16: 31.
 - 32) Annegarn J, Spruit MA, Savelberg HH, Willems PJ, van de Boven C, Schols AM, Wouters EF, Meijer K. Differences in walking pattern during 6-min walk test between patients with COPD and healthy subjects. *PLoS One* 2012; 7: e37329.
 - 33) Lauglo R, Vik T, Lamvik T, Stensvold D, Finbråten AK, Moholdt T. High-intensity interval training to improve fitness in children with cerebral palsy. *BMJ Open Sport Exerc Med* 2016; 2: e000111.
 - 34) Baquet G, van Praagh E, Berthoin S. Endurance training and aerobic fitness in young people. *Sports Med* 2003; 33: 1127-1143.
 - 35) Nsenga AL, Shephard RJ, Ahmaidi S. Aerobic training in children with cerebral palsy. *Int J Sports Med* 2013; 34: 533-537.
 - 36) Unnithan VB, Katsimanis G, Evangelinou C, Kosmas C, Kandrali I, Kellis E. Effect of strength and aerobic training in children with cerebral palsy. *Med Sci Sports Exerc* 2007; 39: 1902-1909.
 - 37) George CL, Oriol KN, Blatt PJ, Marchese V. Impact of a community-based exercise program on children and adolescents with disabilities. *J Allied Health* 2011; 40: e55-e60.