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Do Exercises have a Complementary Effect Over Pharmacotherapy in Children with Allergic Asthma?

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Abstract

Aim: To study whether the most frequently prescribed exercises have a complementary effect over that of the most frequently prescribed pharmacotherapy in children with allergic asthma, as there is no consensus on this question.

Material and methods: 24 children (age 9.56 ± 3.29 years) with allergic asthma were studied. They were randomly assigned into two groups of 12 children – "Standard group" and "Exercise group". The "Standard group" was treated for 10 days with the most frequently prescribed pharmacotherapy (low daily doses of inhaled corticosteroids) without exercises. The "Exercise group" received the same treatment combined with the most frequently prescribed exercises (breathing retraining, respiratory muscle training and musculoskeletal flexibility with posture/balance training). Standard spirometry was performed at the beginning and at the end of the 10-day treatment. The best of 3 trials in each spirometry test was recorded. For comparability, the results were analysed as percentages of the actual versus the predicted spirometry values. Multiple variance analysis (MANOVA) with Bonferroni's multiple comparison post-hoc tests were used for the statistical analysis.

Results: At the end of the 10-day treatment course, the most frequently used spirometry parameters ("FEV_1 % Act/Pred" and "FEV_1/FVC % Act/Pred") showed a statistically significant improvement in both groups versus at the beginning of the study ($P<0.05$). At the end of the 10-day treatment course, the same spirometry parameters showed a statistically significant improvement in the "exercise group" versus the "standard group" ($P<0.05$).

Conclusion: The most frequently prescribed exercises have a complementary effect over that of the most frequently prescribed pharmacotherapy in children with allergic asthma.

Keywords: Allergic asthma; Childhood; Complementary therapeutic effect; Exercises; Pharmacotherapy

Introduction

Asthma affects about 300 million people worldwide, making it a serious global health and social problem [1-9]. It is the most common chronic disease in childhood, affecting 7.2% of the children globally [1-11]. Its social significance increases with the constant elevation of the treatment costs [1-8,12]. Other socially significant factors are the temporary disability for the patient or parents of the affected child and the frequent interruptions of the child's educational cycle [1-8,13]. The problem is deepening in the developing countries, as well as in families with low social status, where asthma patients are exposed to additional harmful factors and allergens [1,2,4,5,7,8,11,14-23]. In heavily urbanized and industrialized areas, high air pollution is a leading factor in the initiation, triggering, exaggeration and development of the symptoms [1,2,4,5,7,8,11,14-22,24,25].

There is no consensus about the rational of exercises in children with asthma [1,2,4,5,7,26-35]. Controversies exist between the findings that exercises are associated with improved quality of life and cardiovascular fitness versus the fact that the symptoms could be triggered by exercises, walking, laughter, crying and many other daily living activities [1,2,4,5,7,26,27,29,31-36]. Avoiding strenuous exercises seems to reduce exacerbations of exercise-induced bronchoconstriction [1,4,5,7,26,27,29,31,32,36]. However, exercise avoidance may lead to deconditioning, reduced exercise tolerance, easier fatigue/tiredness, lethargy, higher risk for obesity, increased stress, and increased susceptibility to exacerbations during minimal daily living activities [1,2,4,5,7,26,27,29,31-33,36]. Moreover, breakthrough exercise-related symptoms could be managed by warm-up exercises [1,4,5,7,26,27,29,31,32,36]. Exercise-induced bronchoconstriction may also be related to obesity, lack of fitness, or conditions like inducible laryngeal obstruction [4,35,37-40]. In addition, weight reduction combined with exercises improves better asthma control (lung function, health status and reduced medication needs in obese children with asthma) versus weight reduction alone [4,38,39]. Moreover, training and sufficient warm-up exercises reduce the incidence and severity of exercise-induced bronchoconstriction [4,37,39,40]. Additional factor contributing to inadequate asthma control in adolescents is poor treatment adherence [41].

There is no consensus about the complementary effect of exercises over pharmacotherapy [1,2,4,5,7,26,27,29,32,35]. The aim of our study was to verify whether the most frequently prescribed exercises have a complementary effect over that of the most frequently prescribed pharmacotherapy in children with allergic asthma.

Materials and Methods

This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript is in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals and aim for the inclusion of representative human populations (sex, age and ethnicity) as per those recommendations.

During the enrolment process within the paediatric clinic of a Medical University Hospital, 24 children (age 9.56 ± 3.29 years) with allergic asthma were assessed for eligibility. Informed consent was obtained from the parents for experimentation with human subjects/children. The privacy rights of human subjects/children were observed. The eligibility criteria were: age 6-11 years with more than one symptom (wheeze, breath shortness, "Heavy breathing", non-productive cough, chest tightness), variable expiratory airflow limitation (reduced FEV1, reduced FEV_1/FVC below 0.90, positive bronchodilator reversibility test – increased FEV_1 above 12% from predicted), sputum eosinophilic airway inflammation, anamnesis of allergic disease like eczema, allergic rhinitis, drug or food allergy, worsening of the symptoms at night or early morning, variability of the symptoms (in frequency, duration and intensity), initiation/triggering or worsening of the symptoms by viral infections, allergic exposure, smoke, strong smells, contrast temperatures, physical or mental stress [2,4,35,39,40]. The exclusion criteria were: other chronic lung disease, productive cough, chest pain, bleeding, breathe shortness associated with impaired neurological symptoms (including dizziness), severe infections, as well as severe deficiency – cardiovascular, respiratory, hepatic, metabolic or renal [2,4,35,39,40].

These 24 children were randomly allocated into two groups of 12 children – "standard group" and "exercise group". The "standard group" was treated for 10 days (5 days as inpatients and 5 days as outpatients in the same paediatric clinic) with standard pharmacotherapy – low daily doses of inhaled corticosteroids [42-44]. The "Exercise group" received the same treatment with additional standard exercises, including: breathing retraining (exercises manipulating the breathing pattern); respiratory muscle training (exercises increasing the strength and endurance of the respiratory muscles); musculoskeletal flexibility and posture/balance training (exercises increasing the flexibility of the thoracic cage and improving posture by correcting the muscle imbalance) [2,32,45-47].

The 'Breathing retraining' was aiming to correct the abnormal breathing patterns by adopting a slower respiratory rate with longer expiration, reducing hyperventilation, using diaphragmatic type of resting breathing (rather than abdominal or upper-chest one), and using nasal breathing (rather than oral one) [2,32,46]. It was performing 2 times daily with 3 sets of 10 repetitions with a pause of 2 minutes between each set [2,47]. The diaphragmatic inspiration was performing from functional residual capacity to maximum inspiratory lung volume with 2 consecutive breaks, while maintaining a ratio of 2 to 1 breath [2,47].

The 'respiratory muscle training' was performing 2 times daily with 3 sets of 10 repetitions with a pause of 2 minutes between each set [2,47]. Each repetition included a maximal inspiration from residual volume to total lung capacity in sitting position [2,47]. The expiration was performing at the functional residual capacity in order to avoid hyperventilation [2,47]. There were intervals of 60 s between these respiratory manoeuvres [2,47].

The 'musculoskeletal flexibility training' included chest expansions, alt back expansions, side arm rises, arm circles, torso flexion, extension, lateral flexion and rotation [2,32,46,47]. It was performing 2 times daily with 3 sets of 10 repetitions with a pause of 2 minutes between each set [2,32,46,47]. The musculoskeletal posture/balance training was performing 2 times daily with 3 sets of 10 repetitions with a pause of 2 minutes between each set [2,45]. It included correction of the posture and muscle imbalance by relaxation/stretching of the shortened static muscles (pectoral, scapular elevator, upper trapezoidal) and strengthening of the elongated/flabby muscles (lower trapezoidal, rhomboid, serratus anterior) [2,45].

Standard spirometry was performed at the beginning and at the end of the 10-day treatment course [8,48-51]. The best of 3 trials in each spirometry test was recorded [8,48-51]. For statistical comparability, the results were analyzed as percentages of the actual versus the predicted spirometry values. For the statistical analysis was used two-way analysis of variance (ANOVA) – balanced design with 2x2 levels of interaction. The sources of variance were "Group" (with 2 levels - "Standard group" and "Exercise group") and "Treatment" (with 2 levels - "before and after" the 10-day treatment course). To isolate which statistical cluster(s) differed significantly from the other(s), all pair-wise multiple comparison procedures (Bonferroni's post-hoc method) was used.

Results

Regarding the spirometry parameter "forced expiratory volume for one second calculated as a percentage of the actual versus the predicted value" ("FEV_1 % Act/Pred"), ANOVA showed that the effect of different levels of "group" did not depend on what level of "treatment" is present – there was not a statistically significant 2x2 interaction between "group" and "treatment" ($P=0.855$) (Figure 1). The difference in the mean values among the different levels of "group" were greater than would be expected by chance after allowing for effects of differences in "treatment" – there was a statistically significant "group" difference ($P<0.05$), combined with high level of the calculated statistical power (Power=0.858), at the standard level of alpha ($\alpha=0.05$), normality test passed ($P=0.0258$) and equal variance test passed ($P=0.2308$) (Figure 1). Regarding the same spirometry parameter ANOVA showed that the difference in the mean values among the different levels of "Treatment" were greater than would be expected by chance after allowing for effects of differences in "group" – there was a statistically significant "treatment" difference ($P<0.05$), combined with very high level of the calculated statistical power (Power=0.931), at the standard level of alpha ($\alpha=0.05$), normality test passed ($P=0.0258$) and equal variance test passed ($P=0.2308$) (Figure 1). To isolate which statistical cluster(s) differed significantly from the other(s), all pair-wise multiple comparison procedures (Bonferroni's post-hoc test) was used (Figure 1). According to this multiple test, the same spirometry parameter showed a statistically significant improvement in both groups at the end versus at the beginning of the 10-day treatment course ($P<0.05$) (Figure 1). At the end of the 10-day treatment course, the same spirometry parameter showed a statistically significant better effect in the "Exercise group" versus the "standard group" ($P<0.05$), while at the beginning there was no difference between them ($P>0.05$) (Figure 1):

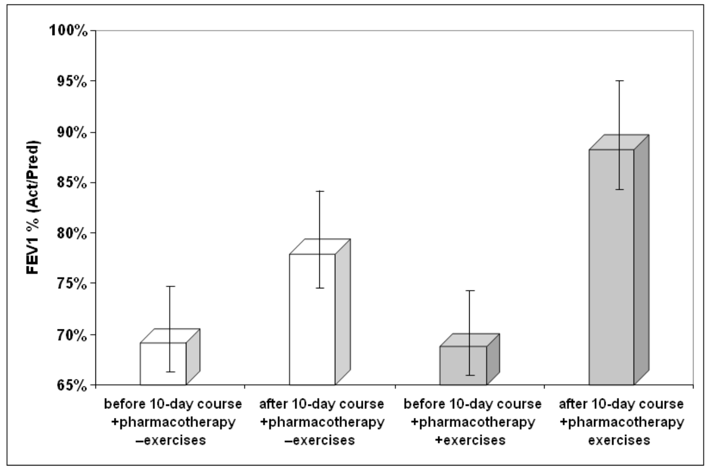

Figure 1: Results from the spirometry parameter "Forced Expiratory Volume for one second calculated as a percentage of the Actual versus the Predicted value" ("FEV_1 % Act/Pred"), recorded before and after the 10-day treatment course from the "standard group" (with/+pharmacotherapy without/- exercises), and from the "Exercise group" (with/+pharmacotherapy and with/+ exercises). The plus-minus error bars (⊥) represent the standard deviations from the average values.

Regarding the spirometry parameter "Forced expiratory volume for one second calculated as a percentage of the actual versus the predicted value divided by the forced vital capacity calculated as a percentage of the actual versus the predicted value" (FEV_1/FVC % Act/Pred), ANOVA showed that the effect of different levels of "group" did not depend on what level of "treatment" is present – there was not a statistically significant 2x2 interaction between "group" and "Treatment" ($P=0.369$) (Figure 2). The difference in the mean values among the different levels of "group" were greater than would be expected by chance after allowing for effects of differences in "treatment" – there was a statistically significant "group" difference ($P<0.05$), combined with very high level of the calculated statistical power (Power=0.956), at the standard level of alpha ($\alpha=0.05$), normality test passed ($P=0.1061$) and equal variance test passed ($P=0.9562$) (Figure 2). Regarding the same spirometry parameter ANOVA showed that the difference in the mean values among the different levels of "treatment" were greater than would be expected by chance after allowing for effects of differences in "group" – there was a statistically significant "treatment" difference ($P<0.05$), combined with very high level of the calculated statistical power (Power=0.99), at the standard level of alpha ($\alpha=0.05$), normality test passed ($P=0.1061$) and equal variance test passed ($P=0.9562$) (Figure 2). To isolate which statistical cluster(s) differed significantly from the other(s), all pair-wise multiple comparison procedures (Bonferroni's post-hoc test) was used (Figure 2). According to this multiple test, the same spirometry parameter showed a statistically significant improvement in both groups at the end versus at the beginning of the 10-day treatment course (P<0.05) (Figure 2). At the end of the 10-day treatment period, the same spirometry parameter showed a significantly better effect in the "exercise group" versus the "standard group" (P<0.05), while at the beginning there was no difference between them (P>0.05) (Figure 2):

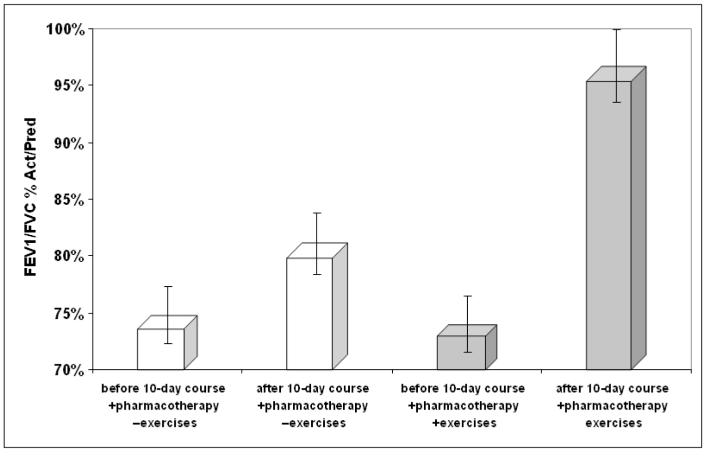

Figure 2: Results from the spirometry parameter "Forced Expiratory Volume for one second (FEV_1) calculated as a percentage of the Actual (Act) versus the Predicted (Pred) value divided by the Forced Vital Capacity (FVC) calculated as a percentage of the Actual (Act) versus the Predicted (Pred) value" (FEV_1/FVC % Act/Pred), recorded before and after the 10-day treatment course from the "standard group" (with/+pharmacotherapy without/- exercises), and from the "Exercise group" (with/+pharmacotherapy and with/+ exercises). The plus-minus error bars (⊥) represent the standard deviations from the average values.

No exercise-related exaggeration, exercise-induced bronchoconstriction, or other exercise-triggered symptom, was reported during the two-week period of the study in both groups.

Discussion

The effect of different levels of "group" did not depend on what level of "treatment" is present and vice versa. Therefore, the improvement in both groups (at the end versus at the beginning of the 10-day treatment course) did not depend on the "inter-group" difference and vice versa. Moreover, at the beginning there was no difference between the "groups". From these results it could be concluded that both treatments (pharmacotherapy with or without exercises) were successful, but the combined treatment (pharmacotherapy with exercises) was more successful versus pharmacotherapy without exercises. Therefore, the exercises had a statistically significant complementary effect over pharmacotherapy. These results were confirmed not only by the statistical significance of the P-value, but also by the high power of the performed statistical test, the passed normality test and the passed equal variance test. Therefore, it seems advisable for children with allergic asthma to use the most frequently prescribed exercises (breathing retraining, respiratory muscle training and musculoskeletal flexibility with posture/balance training) in addition to the most frequently prescribed pharmacotherapy (low daily doses of inhaled corticosteroids). This advice seams advisable for children at the age of 6-11 years with more than one symptom (wheeze, breath shortness, "Heavy breathing", non-productive cough, chest tightness), variable expiratory airflow limitation (reduced FEV_1, reduced FEV_1/FVC below 0.90, positive bronchodilator reversibility test – increased FEV_1 above 12% from predicted), sputum eosinophilic airway inflammation, anamnesis of allergic disease like eczema, allergic rhinitis, drug or food allergy, worsening of the symptoms at night or early morning, variability of the symptoms (in frequency, duration and intensity), initiation/triggering or worsening of the symptoms by viral infections, allergic exposure, smoke, strong smells, contrast temperatures, physical or mental stress. The level of evidence of this advice could be estimated as follows:

- Level I (RCT with proper randomization) according to the Canadian Task Force on the Periodic Health Examination's Levels of Evidence [52]
- Level I (RCT with clear cut results) according to Sackett DL [52]
- Level 1-B (RCT with narrow confidence intervals) according to the Centre for Evidence-Based Medicine [52]
- Grade-A (Level I evidence – strong recommendation) according to the Grade Practice Recommendations [52]
- Step 1 (Level 1) – random sample survey (Question: How common is the problem?) or Step 2 (Level 2) – randomized trial with dramatic effect (Question: Does this intervention help? (Treatment Benefits)? [53]

The lack of any exercise-related exaggeration, exercise-induced bronchoconstriction, or other exercise-triggered symptom during the two-week period of the study in both groups, most probably is a result of the adequate pharmacotherapy. Due to the limitation of this study, further studies are need addressing the protection effect of the adequate pharmacotherapy over the exercise-induced/triggered symptoms. In addition, for children with different age periods (less than 6 years or more than 11 years) and different eligibility criteria (from the listed above), further studies in these directions are need. Also, it is necessary to study the statistical significance/strength and/or the complementary effect of the separate exercise elements (frequency, duration and/or intensity) in children with different age periods and different asthma variations.

Conclusion

Exercises have a complementary effect over pharmacotherapy in children with allergic asthma.

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