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Review Article

Appropriate physical training helps to relieve clinical symptoms of pediatric asthma: a meta-analysis

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Abstract: Objective: Our aim was to investigate the role of appropriate physical training in relieving clinical symptoms of pediatric asthma. Methods: Databases of PubMed, EMBASE, and Cochrane Library were searched using keywords and citation information for collecting potential studies. Reviews were also checked for retrieving some relevant data (studies from January 1st, 1990, to June 30th, 2017, with no language restriction). Two reviewers independently selected randomized controlled trials (RCTs) regarding the effects of physical training on pediatric asthma, according to the inclusion and exclusion criteria, and assessed the quality of papers by using Cochrane's risk of bias assessment tool. The main outcome measures consisted of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), incidence of bronchial hyperresponsiveness (BHR), incidence of exercise-induced bronchoconstriction (EIB), and endurance. RevMan 5.2 software was applied for meta-analysis with either the fixed effects model or random effects model. Categorical data were presented as risk ratios (RRs) while the measurement data were presented as standardized mean difference (SMD) with 95% confidence interval (CI). Results: A total of nine RCTs were included in the present study, involving 881 cases of pediatric asthma. Results of the meta-analysis showed that patients who received appropriate physical training experienced better improvements in the following indices than those who didn't: PEF (pooled SMD=1.50, 95% CI: (0.90, 2.10), P<0.00001), incidence of BHR (pooled RR 0.60, 95% CI: 0.43-0.84, P=0.003), incidence of EIB (pooled RR 0.38, 95% CI: 0.21-0.68, P=0.001), and endurance (pooled SMD=7.86, 95% CI: (7.29, 8.43), P<0.0001). However, the value of FEV1 in patients who received physical training was lower than that in the control group: FEV1 (pooled SMD=-0.31, 95% CI: (-0.53, -0.09), P=0.007). There was no statistical difference between the two groups in FVC (pooled SMD=0.44, 95% CI: (-0.61, -0.09), P=0.41). Conclusion: Appropriate physical training can help to relieve asthma symptoms, decrease incidence of BHR and EIB, and increase endurance but it cannot help in improving FEV1 in asthmatic children.

Keywords: Pediatric asthma, appropriate physical training, pulmonary function, bronchial hyperresponsiveness, meta-analysis

Introduction

Bronchial asthma is a common type of chronic allergic respiratory disease during childhood. It is defined as a chronic inflammatory disorder of the airways which involves various cells and cell components. During the onset of an asthma attack there will often be increased airway responsiveness with clinical symptoms of recurrent wheezing, dyspnea, chest distress, and coughing. The attack often occurs at night or during early morning hours. The incidence and development of asthma can severely affect children's quality of life and can even be life-threatening [1, 2]. According to an epidemiologic survey, asthma morbidity in the USA was 8.4% in 2010 while the morbidity of pediatric asthma in China was 2%-5% [3].

Currently, clinical treatment of acute asthma normally focuses on relieving asthma, reducing inflammatory response, and dilating bronchial smooth muscles. Breathing exercise, as a type of non-drug therapy, is a type of special training for respiratory muscles. Exercise can enhance the force of contraction and efficiency in these muscles and bring about improvements in gas exchange and ventilation function in asthmatic

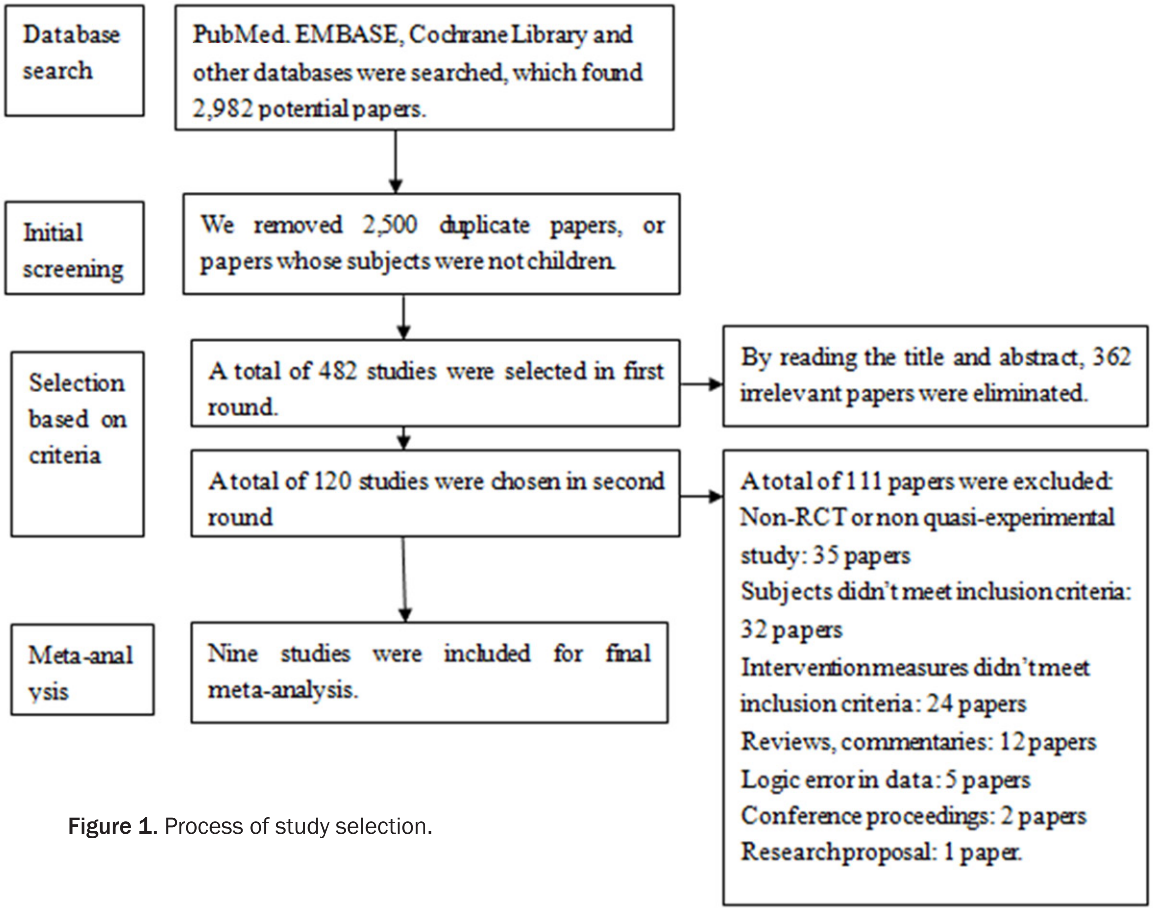

Figure 1. Process of study selection.

children [4-6]. However, it has been reported that physical exercise during acute attacks of asthma can aggravate patient clinical symptoms and as a result, there remain controversies over non-drug therapy such as physical exercise. At present, drug therapy is a quite common way of treating asthma in clinic. It is still unclear whether appropriate physical training can truly bring improvement on the prognosis of pediatric asthma. Therefore, the present study adopted evidence-based meta-analysis to investigate the role of appropriate physical training in improving respiratory function in asthmatic children with the aim of obtaining some useful information for clinical intervention for this disease.

Materials and methods

The reporting of this meta-analysis complies with PRISMA reporting standards [7].

Database

Databases of PubMed, EMBASE, MEDLINE, and Cochrane Library were searched in this study.

Keywords

The following terms were used to search for studies: (asthma* OR ((airway OR respiratory OR bronchial) AND (bronchoconstrict* OR bronchospas* OR hyperreact* OR hyperresponsiv*))) AND (training OR conditioning) AND (endurance OR strength OR exercise OR sport* OR "physical activity" OR run* OR swim* OR row* OR gymnastic OR (hyperpnoea OR hyperpnea) OR ventilatory OR threshold OR inspiratory OR expiratory OR respiratory). Studies were retrieved from January 1st, 1990, through June 30th, 2017.

Selection of studies

Studies were searched using the aforementioned keywords and were selected based on the inclusion and exclusion criteria.

Inclusion criteria: Inclusion criteria: 1) The research was a type of randomized controlled trial (RCT) for analyzing the effects of appropriate physical training versus non-physical training on relieving symptoms of pediatric asthma

Table 1. Basic information of included studies

Included studies	Type of research	Experiment group/control group	Sample size	Nation	Outcome indices
Aranelovic, M 2007 [13]	RCT	45/40	85	USA	FEV1, BHR, PEF, FVC
Bonsignore, M.R 2008 [14]	RCT	25/30	55	USA	FEV1, BHR, PEF, FVC
Moreria, A 2008 [15]	RCT	59/61	120	USA	BHR, PEF, endurance
Cevik Guner, U 2015 [8]	RCT	55/55	110	USA	PEF
Lin, H.C. 2017 [11]	RCT	29/32	61	China	FEV1, PEF, FVC
Santos-Silva, R 2014 [9]	RCT	44/46	90	USA	Endurance, EIB
Nnodum, BN 2017 [12]	RCT	54/46	100	USA	PEF, endurance, EIB
Kováčiková, Z 2017 [10]	RCT	55/55	110	South Korea	FEV1, PEF, FVC, EIB
Rezink, M 2017 [17]	RCT	55/65	120	USA	Endurance

Note: RTC, randomized controlled trial; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; BHR, bronchial hyperresponsiveness; PEF, peak expiratory flow; EIB, exercise-induced bronchoconstriction; endurance, duration of physical exercise.

with no restriction on blind method, follow-up period, and language; 2) Study subjects were children with asthma, with no restriction on gender, severity of disease, and other underlying diseases; 3) The study had one of the following clinical indices: bronchial hyperresponsiveness (BHR), forced expiratory volume in one second (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), exercise-induced bronchoconstriction (EIB), and endurance.

Exclusion criteria: Exclusion criteria: 1) Subjects were not children or animals; subjects did not meet the standards for physical training; 2) No valid data analysis in the study; 3) Non-RCT study; no major index was included in the study; 4) Data were incomplete; 5) Papers were reviews, commentaries, conference proceedings, or lectures. If the study had been published repeatedly, the version with the most complete data was taken for assessment.

Process of selection: One reviewer read the title of the papers to remove any duplicates while the other two reviewers independently read the title and abstract. They selected studies based on the inclusion and exclusion criteria. Afterwards, the two reviewers read the full-text of the eligible studies carefully and extracted clinical indices independently for making data extraction tables. Discussions were carried out to resolve any disagreement by consensus.

Data extraction

The following information was extracted: publication date of the study, number of patients, random method, blind method, age, incidence of BHR, FEV1, FVC, PEF, incidence of EIB, and endurance. In order to ensure reliability of the extraction process, the two main reviewers adopted the double blind method to select indices in the included papers independently. Disagreement was resolved whenever possible by discussion. The process of study selection is presented in **Figure 1**.

Quality assessment of the study

Cochrane's risk of bias assessment tool was used to assess the quality of our study. The tool included the following seven items for evaluating the risk of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Based on the risk of bias assessment criteria, each item was rated as "low risk of bias", "high risk of bias", or "unclear risk of bias". If the paper had a clear description for each index, it was rated as "low risk of bias". If the paper claimed that the experiment was not conducted according to the above seven items, it was rated as "high risk of bias". If the paper had no description about the relative risks of bias, it was rated as "unclear risk of bias".

Outcome measures and statistical analysis

Outcome measures: Main outcome measures were indices that could reflect the changes of pulmonary function after physical training including BHR, FEV1, FVC, PEF, EIB, and endurance.

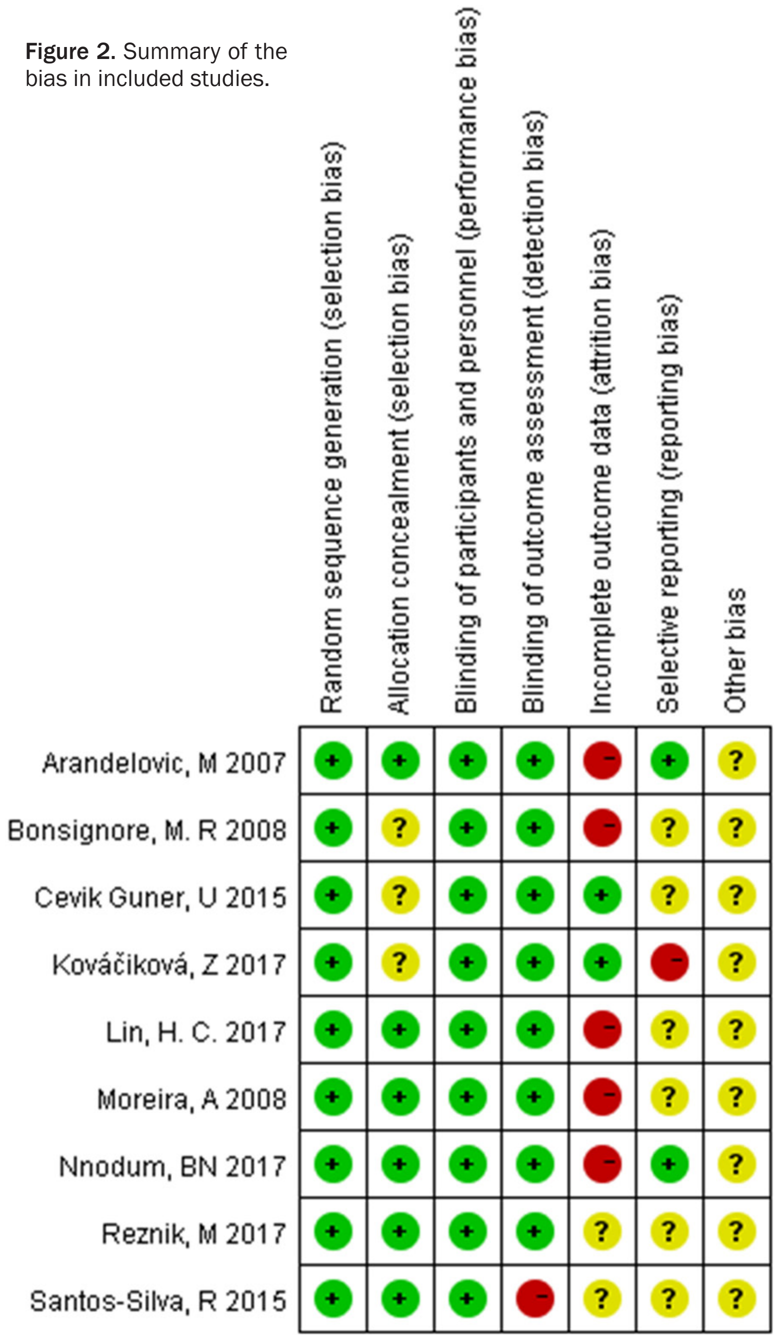

Figure 2. Summary of the bias in included studies.

Statistical analysis: RevMan 5.2 from Cochrane Collaboration was used for statistical analysis of the effect size. The count data, such as incidences of BHR and EIB, were presented as risk ratios (RRs) with 95% confidence intervals (CI) while the value of FEV1, FVC, PEF, and endurance were expressed as standard mean difference (SMD), since different studies may use different measuring tools with various units. The effect size was expressed as 95% CI. I^2 statistics were used to determine the level of heterogeneity. An I^2 of 0-25% indicated no heterogeneity, an I^2 of 25-50% indicated mild heterogeneity, an I^2 of 50-75% indicated moderate heterogeneity, and an I^2 of 75-100% indicated high heterogeneity. If the heterogeneity was not significant in studies ($P \geq 0.1$, $I^2 < 50\%$), the fixed effects model (FEM) was adopted for analysis. Otherwise ($P < 0.1$, $I^2 > 50\%$), the random effects model (REM) was used. Sensitivity analysis was performed to investigate the possible source of heterogeneity. The possible source may include year of study, multi/single-center, author, and small sample size. The significance level of α was 0.05.

Results

Study selection and basic information

After selection based on the inclusion and exclusion criteria, a total of 9 studies was finally included. They involved 421 asthmatic children who received appropriate physical training and 430 cases as control [8-17]. The selection process and its results are shown in **Figure 1** and **Table 1**.

Bias in included studies

Evaluation of bias in the included studies was conducted based on the risk of bias table from Cochrane Collaboration (**Figures 2** and **3**). The result showed that each study had some level of bias mainly in allocation concealment, selective reporting, and incomplete outcome data.

Results of meta-analysis

Incidence of BHR: BHR was taken as one of the outcome indices in three included studies, involving 260 cases. All three papers reported

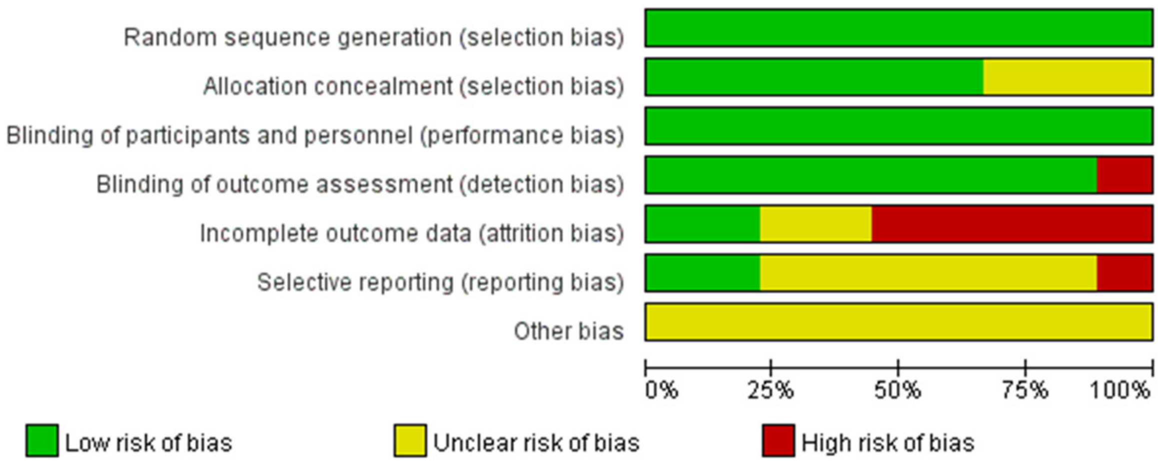

Figure 3. Bias of the included studies.

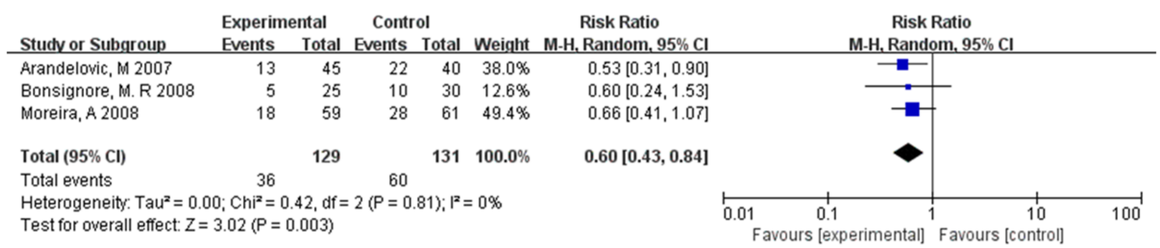

Figure 4. Forest plot of BHR. Experimental: appropriate training group.

Figure 5. Forest plot of EIB. Experimental: appropriate training group.

a lower incidence rate of BHR in patients who received appropriate physical training (physical training group) than those who didn't (control group). Heterogeneity of the three reports was low (I^2=0). Meta-analysis showed that appropriate physical training could significantly lower the occurrence of BHR (pooled RR 0.60, 95% CI: 0.43-0.84, P=0.003, **Figure 4**).

Incidence of EIB: Three studies used EIB as one of the outcome indices, involving 300 cases. All three papers reported a lower incidence rate of EIB in the physical training group as opposed to the control group. Heterogeneity among the studies was low (I^2=0). Meta-analysis indicated that appropriate physical training could reduce the incidence of EIB (pooled RR 0.38, 95% CI 0.21-0.68, P=0.001, **Figure 5**).

Pulmonary function: The value of FEV1 in the physical training group was much lower than that in control group: FEV1 (pooled SMD= -0.31, 95% CI (-0.53, -0.09), P=0.007). There was no statistical difference between the two groups in FVC: FVC (pooled SMD=0.44, 95% CI (-0.61, -0.09), P=0.41). The value of PEF in the physical training group increased more significantly as compared to the control group: PEF (pooled SMD=1.50, 95% CI (0.90, 2.1), P<0.00001). See **Figures 6-8**.

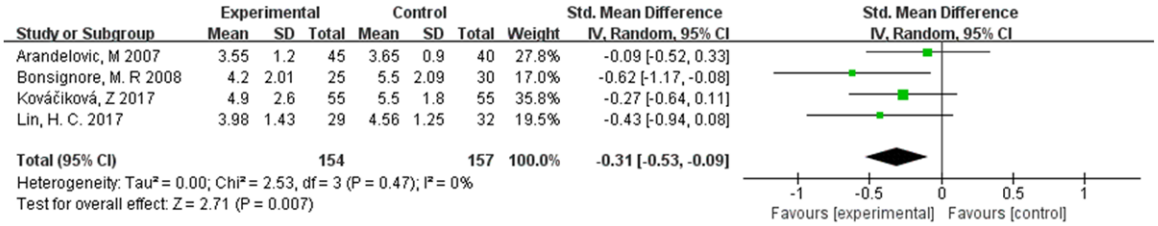

Figure 6. Forest plot of FEV1. Experimental: appropriate training group.

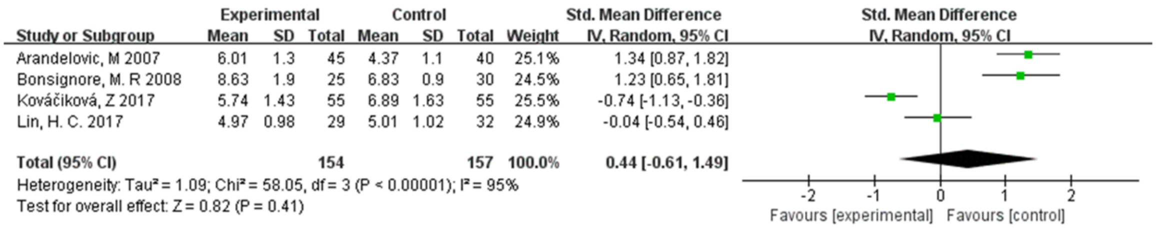

Figure 7. Forest plot of FVC. Experimental: appropriate training group.

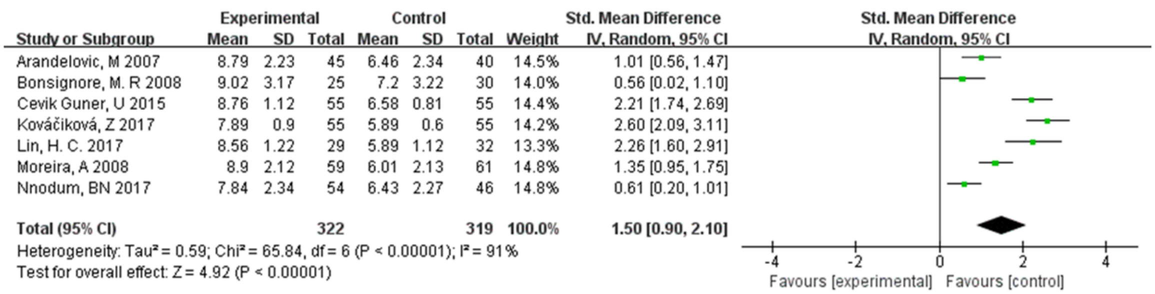

Figure 8. Forest plot of PEF. Experimental: appropriate training group.

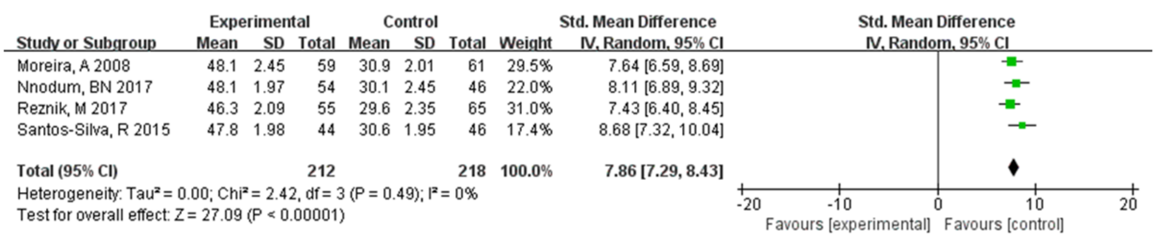

Figure 9. Forest plot of endurance. Experimental: appropriate training group.

Endurance: Four studies included endurance as one of the outcome indices, involving 430 patients. All four studies reported longer endurance in the physical training group than that in the control group. Heterogeneity in these reports was low ($I^2=0$). Analysis showed that the physical training group had much longer endurance than the control group: endurance (pooled SMD 7.86, 95% CI: (7.29, 8.43), P< 0.0001). See **Figure 9**.

Publication bias

Publication bias was assessed for studies that contained PEF as one of the outcome measures. The funnel plot for papers included was symmetrical, indicating no bias. See **Figure 10**.

Discussion

Results of the meta-analysis show that appropriate physical training can help to reduce inci-

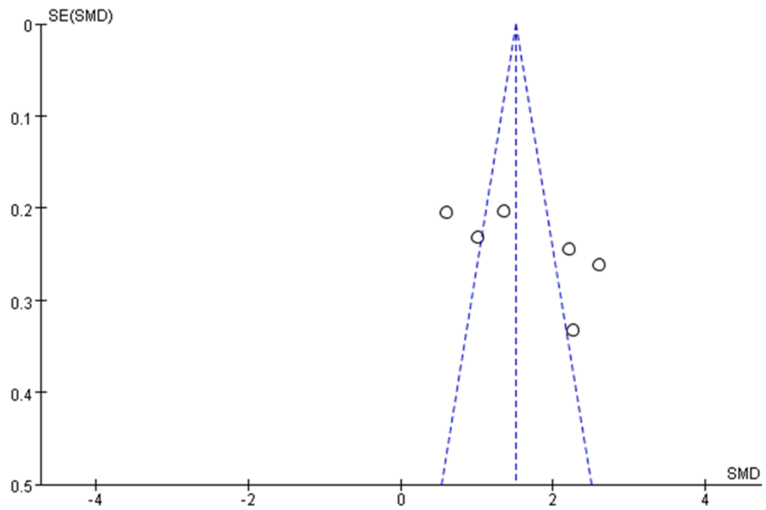

Figure 10. Funnel plot of PEF. PEF: peak expiratory flow.

dence of BHR and EIB, as well as improve FEV1, PEF, and endurance in asthmatic children.

Appropriate physical training can effectively reduce the incidence of BHR and EIB

Airway hyper-responsiveness refers to the tendency of airways to narrow too much or too easily in response to various stimuli. It is a key factor in the development of asthma and can directly reflect the severity of the disease [18]. BHR can occur when inflammatory cells in the airway increase, leading to intermittent and reversible airflow limitation. Currently, the common way of relieving BHR is to reduce the inflammatory response of the airway. Yarova et al. have reported that BHR can be significantly alleviated when the systematic or local inflammatory response is inhibited [19]. However, Shaaban et al. have documented that functional training could worsen the degree of BHR, contradictory to the results of our meta-analysis [20]. This might be due to the fact that functional training during the acute attacks of asthma can bring about bronchial spasm, induce bronchoconstriction, and aggravate the inflammatory response of airway, thus leading to the increase of BHR. However, since the subjects in our present study were children during the remission stage of asthma, there would be either no such contraction in the bronchial smooth muscle or no airway inflammation, plus, appropriate physical training could relax these smooth muscles. Thus, the value of BHR decreased. EIB refers to dyspnea after physical exercise, which is greatly related to airway constriction. It can cause wheezing and dyspnea, affecting the patient's daily life. Bronchoconstriction caused by excessive physical activity is quite common among asthmatic children, therefore, these patients need to pay attention and take appropriate physical activity [21, 22]. Results of the present meta-analysis demonstrate that appropriate physical training can effectively reduce the incidence of EIB and relieve patient clinical symptoms.

Appropriate physical training cannot improve FVC and FEV1

Pulmonary function testing has been widely applied clinically, as it is a non-invasive and safe test with good diagnostic value. FVC and FEV1 are two of these items that can reflect pulmonary function. FVC refers to the volume of air exhaled with maximum effort and speed after full inhalation. FEV1 refers to the amount of air that can be forcibly exhaled in the first second, which has a wide spectrum of clinical applications [23, 24]. Researchers normally use FEV1 as an index for detecting irreversible pulmonary function deficit in asthma. The index is easy to be measured and can well reflect the changes in patient pulmonary function. Results of the meta-analysis show that appropriate physical training cannot effectively improve FEV1 and FVC. This might be due to the fact that the training time was not long enough to achieve improvements in FEV1 and FVC.

Appropriate physical training can effectively improve endurance

Endurance refers to the duration of physical exercise. Abdominal breathing, a common way of breathing in children, can effectively compensate for some shortcomings of chest breathing during an asthma attack. Abdominal breathing with increased respiratory load can make both inspiratory and expiratory muscles more actively involved in breathing, improve the contraction and relaxation function of the respiratory muscles, promote gas exchange, increase lung volume, and ensure effective ventilation. Pursed lip breathing and deep breathing can increase alveolar ventilation volume and efficiency of respiratory muscles, which can effectively prevent respiratory muscle fatigue and improve respiratory efficiency. Appropriate physical training can not only adjust muscle coordination and function in an effective way but also motivate patients to exercise, which can help improve patient pulmonary function significantly. One study showed that breathing exercise can raise respiratory muscle strength and endurance by 35-55% and 19-55%, respectively [22]. Results of the meta-analysis demonstrate that appropriate physical training can effectively prolong endurance and relieve the clinical symptoms of patients.

Due to the limited inclusion of the papers in this retrospective study and the fact that each included study didn't cover all the outcome measures in this meta-analysis, heterogeneity was high. However, there were some limitations in the quality of the experimental methodologies. For instance, 'other bias' and the details of the blind method were not explained. Nevertheless, the outcome indices in the present study were all objective indices, meaning that they could hardly be affected by whether or not the blind method was conducted. Taking all of these factors into consideration, the study results are reliable and can provide some clinical guidance regarding the role of physical training in treating asthma during the remission stage. However, due to variation in the quality of the included methodologies, the study result may still have some bias.

In conclusion, appropriate physical training can help relieve asthma symptoms, lower incidence of BHR and EIB, improve pulmonary function, and prolong endurance in asthmatic children. Therefore, physical exercise can be recommended as a supplementary therapy for treating pediatric asthma.

Disclosure of conflict of interest

None.

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References

[1] Prasad GK, George PE and Thomas JA. Bronchial asthma. Springer India 2016.

[2] Sears MR, Taylor DR, Print CG, Lake DC, Li QQ, Flannery EM, Yates DM, Lucas MK and Herbison GP. Regular inhaled beta-agonist treatment in bronchial asthma. Lancet 1990; 336: 1391-1396.

[3] Prefontaine D, Nadigel J, Chouiali F, Audusseau S, Semlali A, Chakir J, Martin JG and Hamid Q. Increased IL-33 expression by epithelial cells in bronchial asthma. J Allergy Clin Immunol 2010; 125: 752-754.

[4] Agarwal R, Dhooria S, Aggarwal AN, Maturu VN, Sehgal IS, Muthu V, Prasad KT, Yenge LB, Singh N, Behera D, Jindal SK, Gupta D, Balamugesh T, Bhalla A, Chaudhry D, Chhabra SK, Chokhani R, Chopra V, Dadhwal DS, D'Souza G, Garg M, Gaur SN, Gopal B, Ghoshal AG, Guleria R, Gupta KB, Haldar I, Jain S, Jain NK, Jain VK, Janmeja AK, Kant S, Kashyap S, Khilnani GC, Kishan J, Kumar R, Koul PA, Mahashur A, Mandal AK, Malhotra S, Mohammed S, Mohapatra PR, Patel D, Prasad R, Ray P, Samaria JK, Singh PS, Sawhney H, Shafiq N, Sharma N, Sidhu UP, Singla R, Suri JC, Talwar D and Varma S. Guidelines for diagnosis and management of bronchial asthma: joint ICS/NCCP (I) recommendations. Lung India 2015; 32: S3-S42.

[5] Agarwal R, Dhooria S, Aggarwal AN, Maturu VN, Sehgal IS, Muthu V, Prasad KT, Yenge LB, Singh N, Behera D, Jindal SK, Gupta D, Balamugesh T, Bhalla A, Chaudhry D, Chhabra SK, Chokhani R, Chopra V, Dadhwal DS, D'Souza G, Garg M, Gaur SN, Gopal B, Ghoshal AG, Guleria R, Gupta KB, Haldar I, Jain S, Jain NK, Jain VK, Janmeja AK, Kant S, Kashyap S, Khilnani GC, Kishan J, Kumar R, Koul P, Mahashur A, Mandal AK, Malhotra S, Mohammed S, Mohapatra PR, Patel D, Prasad R, Samaria JK, Sarat P, Sawhney H, Shafiq N, Sidhu UP, Singla R, Suri JC, Talwar D and Varma S. Guidelines for diagnosis and management of bronchial asthma: joint recommendations of national college of chest physicians (India) and Indian chest society. Indian J Chest Dis Allied Sci 2015; 57 Spec No: 5-52.

[6] Tripodi S, Barreto M, Di Rienzo-Businco A, Grossi O, Sfika I, Ragusa G, Campisano M and Miceli-Sopo S. Asthma control test and bronchial challenge with exercise in pediatric zsthma. Front Pediatr 2016; 4: 16.

[7] Zhu C, Feng X, Ye G and Huang T. Meta-analysis of possible role of cadherin gene methylation in evolution and prognosis of hepatocellular carcinoma with a PRISMA guideline. Medicine (Baltimore) 2017; 96: e6650.
[8] Cevik Guner U and Celebioglu A. Impact of symptom management training among asthmatic children and adolescents on self-efficacy and disease course. J Asthma 2015; 52: 858-865.
[9] Santos-Silva R, Melo C, Goncalves D, Coelho J and Carvalho F. Comparison between exercise performance in asthmatic children and healthy controls--physical activity questionnaire application. Rev Port Pneumol 2014; 20: 138-145.
[10] Kovacikova Z, Neumannova K, Rydlova J, Bizovska L and Janura M. The effect of balance training intervention on postural stability in children with asthma. J Asthma 2017; 1-9.
[11] Lin HC, Lin HP, Yu HH, Wang LC, Lee JH, Lin YT, Yang YH, Li PY, Sun WZ and Chiang BL. Tai-Chi-Chuan exercise improves pulmonary function and decreases exhaled nitric oxide level in both asthmatic and nonasthmatic children and improves quality of life in children with asthma. Evid Based Complement Alternat Med 2017; 2017: 6287642.
[12] Nnodum BN, McCormack MC, Putcha N, Hwang S, Paulin LM, Brigham EP, Fawzy A, Romero K, Diette GB and Hansel NN. Impact of physical activity on reporting of childhood asthma symptoms. Lung 2017; 195: 693-698.
[13] Arandelovic M, Stankovic I and Nikolic M. Swimming and persons with mild persistant asthma. Scientific World Journal 2007; 7: 1182-1188.
[14] Bonsignore MR, La Grutta S, Cibella F, Scichilone N, Cuttitta G, Interrante A, Marchese M, Veca M, Virzi M, Bonanno A, Profita M and Morici G. Effects of exercise training and montelukast in children with mild asthma. Med Sci Sports Exerc 2008; 40: 405-412.
[15] Moreira A, Delgado L, Haahtela T, Fonseca J, Moreira P, Lopes C, Mota J, Santos P, Rytila P and Castel-Branco MG. Physical training does not increase allergic inflammation in asthmatic children. Eur Respir J 2008; 32: 1570-1575.
[16] Lin LL, Huang SJ, Ou LS, Yao TC, Tsao KC, Yeh KW and Huang JL. Exercise-induced bronchoconstriction in children with asthma: an observational cohort study. J Microbiol Immunol Infect 2017.
[17] Reznik M, Islamovic F, Choi J, Leu CS and Rowlands AV. Factors associated with in-school physical activity among urban children with asthma. J Asthma 2017; 1-10.
[18] Sin BA, Yildiz OA, Dursun AB, Misirligil Z and Demirel YS. Airway hyperresponsiveness: a comparative study of methacholine and exercise challenges in seasonal allergic rhinitis with or without asthma. J Asthma 2009; 46: 486-491.
[19] Yarova PL, Stewart AL, Sathish V, Britt RD Jr, Thompson MA, P Lowe AP, Freeman M, Aravamudan B, Kita H, Brennan SC, Schepelmann M, Davies T, Yung S, Cholisoh Z, Kidd EJ, Ford WR, Broadley KJ, Rietdorf K, Chang W, Bin Khayat ME, Ward DT, Corrigan CJ, JP TW, Kemp PJ, Pabelick CM, Prakash YS and Riccardi D. Calcium-sensing receptor antagonists abrogate airway hyperresponsiveness and inflammation in allergic asthma. Sci Transl Med 2015; 7: 284ra260.
[20] Shaaban R, Leynaert B, Soussan D, Anto JM, Chinn S, de Marco R, Garcia-Aymerich J, Heinrich J, Janson C, Jarvis D, Sunyer J, Svanes C, Wjst M, Burney PG, Neukirch F and Zureik M. Physical activity and bronchial hyperresponsiveness: European community respiratory health survey II. Thorax 2007; 62: 403-410.
[21] Grzelewski T, Grzelewska A, Majak P, Stelmach W, Kowalska A, Stelmach R, Janas A and Stelmach I. Fractional exhaled nitric oxide (FeNO) may predict exercise-induced bronchoconstriction (EIB) in schoolchildren with atopic asthma. Nitric Oxide 2012; 27: 82-87.
[22] Norqvist J, Eriksson L, Soderstrom L, Lindberg A and Stenfors N. Self-reported physician-diagnosed asthma among Swedish adolescent, adult and former elite endurance athletes. J Asthma 2015; 52: 1046-1053.
[23] Barochia AV, Kaler M, Cuento RA, Gordon EM, Weir NA, Sampson M, Fontana JR, MacDonald S, Moss J, Manganiello V, Remaley AT and Levine SJ. Serum apolipoprotein A-I and large high-density lipoprotein particles are positively correlated with FEV1 in atopic asthma. Am J Respir Crit Care Med 2015; 191: 990-1000.
[24] Chae EJ, Kim TB, Cho YS, Park CS, Seo JB, Kim N and Moon HB. Airway measurement for airway remodeling defined by post-bronchodilator FEV1/FVC in asthma: investigation using inspiration-expiration computed tomography. Allergy Asthma Immunol Res 2011; 3: 111-117.