



A STUDY OF ASSOCIATION OF EXERCISE INDUCED ASTHMA AND FAMILY HISTORY OF ASTHMA.

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ABSTRACT

Introduction: Asthma is a chronic condition caused by narrowing of small airways. It can be triggered by exercise and is called Exercise induced asthma (EIA). EIA causes a decline in FEV1, a Pulmonary Function Test (PFTs) parameter. The aim was to study the association of EIA and family history or previous history of asthma. **Materials And Methods:** A cross sectional comparative study was done over 3 months including the student group of a rural Medical College and Hospital. The study included 90 asymptomatic subjects - 30 normals (control group), 30 with family history but no previous history of asthma, 30 with previous history of asthma. Detailed history, anthropometry and PFT (before, immediately after and following recovery from exercise) were performed. All acquired data was statistically analyzed. **Observations And Results:** The basic characteristics of the 3 groups were comparable. PFT parameters at baseline, after exercise and recovery -, FEV1/FVC, FEF 25-75, FEF 50, FEF 75 of individuals with family history / previous history of asthma were significantly decreased as compared to controls. FEV1 of cases was much lesser as compared to controls and showed a trend towards significance. **Conclusion:** EIA is a well established and often under diagnosed condition. PFT testing with a decreased FEV1, FEV1 / FVC, FEF 25-75 is fairly diagnostic of the condition with a background family history / previous history of asthma. This implicates the scope towards the exercise training with knowledge of the underlying pathophysiology to plan preventive measures to care for those subjects with EIA.

KEYWORDS : Exercise induced asthma, family history, previous history, exercise, PFT, FEV1.

INTRODUCTION:

Asthma is a chronic condition with symptoms of cough, wheezing, chest tightness or pain, and/or difficulty breathing in relation to specific triggering agents/events. The small airways in asthmatics narrow during these episodes; the narrowing is partial or complete. The airways in asthma patients react to a variety of stimuli, including viral illnesses, exercise, inhalant or food allergens or environmental conditions. It is the most common chronic disease in children, affecting a significant percentage in the younger age¹. Exercise being one of the triggering events affects different people differently. People without a history of asthma also tend to develop asthma upon performing some form of exercise. Narrowing of the airways can be triggered by exercise². This is called Exercise induced asthma (EIA). EIA is a temporary increase in airway resistance after intensive sport. Increased training load and the environmental factors are responsible for EIA. The incidence of EIA is high among athletes, especially athletes who do outdoor sport activities. Cold air is more harmful to the respiratory tract compared to hot and humid air, thereby the prevalence of EIA is higher in winter³.

The airway obstruction can objectively be measured as a decline in Forced Expiratory Volume in one second (FEV1), a Pulmonary Function Test (PFTs) parameter. PFTs are an essential tool in the investigation and monitoring of patients with respiratory diseases. They provide information concerning the large and small airways, the pulmonary parenchyma and the size and integrity of the pulmonary capillary bed. A sitting position is usually preferred in cases of syncope or injury that may arise in the standing position, although PFTs can be performed in the standing position. Normal or predicted range of values is obtained from large population studies of healthy subjects. Values are taken for people matched for sex, height, age and where appropriate, ethnicity⁴.

Symptoms of EIA usually occur within 5 to 10 minutes of the cool-down period after vigorous exercise and also during exercise. These symptoms tend to disappear after 20 to 45 minutes. Certain types of exercise like running and skating are more likely to cause EIA than others, probably because they produce lesser airway cooling and drying. Short bursts of activity tend to be better tolerated than prolonged exercise⁵. Affecting a significant percentage of the younger population, it is one of the most common chronic inflammatory conditions. The immunohistopathologic features of asthma are; Neutrophils (sudden onset asthma, occupational asthma and patients who smoke), Eosinophils, Lymphocytes, Mast cell activation and epithelial cell injury. There is an extensive inflammatory cell infiltration. Airway inflammation leads to airway hyperresponsiveness, airflow limitation, respiratory symptoms and

disease chronicity⁶. Martin, has found an association of the allergens exposed during exercise triggering an allergic reaction and has suggested this as a probable factor for EIA. However, this finding has been inconclusive^{7,8}.

The importance of this study is to deduce a management program for individuals based on their reaction to exercise. Subjects without history of asthma that have a positive reaction to the test exercise may be advised to take up exercise as a regular habit so as to slowly lessen the tendency to develop EIA. As time passes, the intensity of the exercise should be increased to habituate the body to the newer stimulus.

These unclear issues regarding the development of EIA potentiate the need to study the effect of exercise in asymptomatic individuals. This study intends to reveal a relationship between family history of asthma and exercise induced asthma, if any.

MATERIALS AND METHODS:

The aim of the study was to assess and compare Pulmonary function Tests (PFTs) before and after the exercise and also to study the association of exercise induced asthma (EIA) and family history or previous history of asthma. A cross sectional comparative study design including 90 asymptomatic (without symptoms indicating asthma) subjects was adapted. Controls were 30 normal subjects (Group - 1) with neither family history nor previous history of asthma. Cases were 30 subjects with family history (Group - 2) but no previous history of asthma and 30 subjects with previous history (Group - 3) of asthma. All subjects were age, sex and basic characteristics matched. Subjects were asymptomatic (without symptoms indicating asthma) and in the age group 18-25 years. Symptomatic (with symptoms indicating asthma) subjects. All those with recent surgeries, acute diseases like tuberculosis / cough / respiratory infections, any history of vessel aneurysm, those intolerant / incapacitated to exercise were excluded from the study. Study duration was for 3 months.

Methodology:

The study was conducted at the Department of Physiology MVJ Medical College and Research Hospital, Hoskote, Bangalore, INDIA. Study subjects who meet the inclusion criteria were chosen from MVJ Medical College and Research Hospital, Hoskote, Bangalore. Subjects who consent, and who satisfy the above inclusion criteria underwent a detailed general physical examination with anthropometry. A detailed history focusing on duration of the disease, medications, if any, and their frequency, previous history of asthma and family history (at least one first- degree relative) of asthma were collected. PFT was

performed before exercise. The subjects were made to exercise for 6-10 mins such that the heart rate reaches at least 80-90% of the target peak heart rate. PFT was performed immediately (5-10 mins) after exercise and once again following a recovery phase of 25-30 mins. An informed, written consent to participate in the study was taken from the study subjects. Subjects' participation was voluntary and provided with details about the procedures involved and were free to withdraw from study if they wish any time without prejudice. The data was maintained confidentially. There was no financial burden on the study subjects. The study protocol was approved by the Institutional Ethical committee.

Rationale For Sample Size Estimation: Existing literature⁵ reveals that % patients suffering with EIA in those with family history and normals were 58.53% and 26.8% respectively. In order to obtain a statistically significant difference in the % EIA, at a power of 80% and an alpha error of 5%, it is estimated that nearly 30 subjects in each group need to be studied.

Procedures Involved:

Anthropometry: Anthropometric measurements were recorded with the subjects in light clothing without shoes. Neck circumference (cms), chest circumference (cms), height and weight were measured in standing. Height was measured with a horizontal wall mounted height meter to the last complete 0.1 cm and weight with a digital weighing scale to the last complete 0.1 kg. BMI (in kg/m²) was calculated for each subject.

Pulmonary function tests (PFTs): PFT was performed with the Helios 401 instrument at the Dept of Physiology for all study subjects. A well documented standard protocol with instructions was followed during the PFT testing. PFT parameters recorded included forced vital capacity (FVC), forced expiratory volume in 1st second (FEV₁), FEV₁/FVC, forced expiratory flow 25-75% (FEF 25-75), peak expiratory flow rate (PEFR), forced inspiratory volume capacity (FIVC), forced expiratory flow 25% (FEF 25), forced expiratory flow 50% (FEF 50), forced expiratory flow 75% (FEF 75).

Helios 401: RMS Helios Series of Spirometers are available in PC Based and Stand alone Versions capable of diagnosing, differentiating and measuring various pulmonary diseases. The Helios series comes with a highly advanced and user-friendly Software offering 34 Parameter readings, Pre-Post Bronchodilation Results, Percentage Improvement and Lung Age Calculations. The interpretation of the test results, trends and pediatric incentives are also available in the software. RMS is the leading manufacturer of PC Based Spirometer and Portable Spirometers.

Exercise⁶: Exercises included walking / jogging / squatting / bicycling. The subjects were made to exercise for 6-10 mins such that the heart rate reaches at least 80-90% of the target peak heart rate.

Statistical Analysis:

All the quantitative data such as age, height, weight, neck circumference, chest circumference, BMI, PFT parameters were summarized through descriptive statistics in terms of mean, median and standard deviation. In order to test for differences in means between the study groups, students T test / appropriate non parametric test (if the data do not follow normal distribution) were employed. Significance level of $p < 0.05$ was considered.

OBSERVATIONS AND RESULTS

This is a cross sectional comparative study involving a student group from a Medical College and Tertiary Healthcare Hospital in a rural setup. The study included 90 asymptomatic (without symptoms indicating asthma) subjects. Of all subjects, 30 were normal subjects (control group) with neither family history nor previous history of asthma formed Group - 1. 30 subjects with family history but no previous history of asthma formed Group - 2. 30 subjects with previous history of asthma formed Group - 3.

The basic characteristics with respect to age, and Anthropometry including weight, height, BMI, neck circumference, chest circumference, waist circumference and hip circumference did not show any significant difference between the 3 groups. ($p > 0.05$) [TABLE 1].

The PFT parameters at baseline, FEV₁/FVC, FEF 25-75, FEF 50, FEF 75 of Group - 2 (with FH of BA) and Group - 3 (with Previous history

of BA) was significantly decreased as compared to Group - 1 (controls). ($p < 0.05$) [TABLE 2].

The PFT parameter at baseline, FEV₁ of Group - 2 (with FH of BA) and Group - 3 (with Previous history of BA) was much lesser as compared to Group - 1 (controls) and showed a trend towards significance. ($p = 0.096$) [TABLE 2].

The PFT parameters at baseline, FVC, PEFR, FIVC, FEF 25 of Group - 2 (with FH of BA) and Group - 3 (with Previous history of BA) was not significantly different compared to Group - 1 (controls). ($p > 0.05$) [TABLE 2].

The PFT parameters immediately after exercise, FEV₁, FVC, FEF 25-75, FEF 75 of Group - 2 (with FH of BA) and Group - 3 (with Previous history of BA) was significantly decreased as compared to Group - 1 (controls). ($p < 0.05$) [TABLE 3].

The PFT parameters following recovery after exercise, FEV₁/FVC, FEF 25-75, FEF 25, FEF 75 of Group - 2 (with FH of BA) and Group - 3 (with Previous history of BA) was significantly decreased as compared to Group - 1 (controls). ($p < 0.05$) [TABLE 4].

Group		Age (yrs)	Wt (kg)	Ht (mt)	BMI	Neck Cir (cms)	Chest Cir (cms)	WC (cms)	HC (cms)
Group 1 (Controls)	Mean	19.1	65.00	1.68	23.0	34.69	89.00	79.04	99.08
	SD	0.92	12.94	0.08	3.48	3.56	8.73	10.98	7.15
Group 2 (FH BA +)	Mean	19.4	59.00	12.9	20.7	33.07	88.21	76.14	99.50
	SD	1.16	11.48	42.3	7.01	3.05	7.79	9.75	11.94
Group 3 (Pre BA +)	Mean	19.3	64.73	1.65	23.7	34.20	91.80	80.60	102.4
	SD	1.21	15.27	0.09	5.29	4.83	10.59	12.04	14.26
p value		0.46	0.152	0.17	0.16	0.158	0.780	0.414	0.889

* p value < 0.05 (Significant at 5% level of significance)

Group		FVC	FEV ₁	FEV ₁ /FVC	FEF 25-75	PEFR	FIVC	FEF 25	FEF 50	FEF 75
Group 1 (Controls)	Mean	3.02	2.82	93.6	3.63	5.06	2.84	4.86	3.99	2.38
	SD	0.84	0.74	4.76	1.00	1.57	0.76	1.46	1.21	0.82
Group 2 (FH BA +)	Mean	2.59	2.36	91.8	3.11	4.43	2.43	4.21	3.56	1.94
	SD	0.70	0.61	9.00	1.12	1.24	0.70	1.23	1.39	0.86
Group 3 (Pre BA +)	Mean	2.86	2.32	80.1	2.67	4.88	2.84	4.32	2.93	1.57
	SD	0.58	0.90	25.1	1.12	1.12	0.61	1.15	1.17	0.81
p value		0.58	0.09	0.01	0.01	0.74	0.99	0.30	0.02	0.011

* p value < 0.05 (Significant at 5% level of significance)

Group		FVC	FEV ₁	FEV ₁ /FVC	FEF 25-75	PEFR	FIVC	FEF 25	FEF 50	FEF 75
Group 1 (Control s)	Mean	2.95	2.78	94.9	4.03	5.05	2.84	4.82	4.33	2.84
	SD	0.82	0.73	5.40	1.33	1.53	0.68	1.45	1.46	1.14
Group 2 (FH BA +)	Mean	2.44	2.31	94.7	3.10	4.21	2.38	4.03	3.43	2.10
	SD	0.55	0.52	5.89	1.14	1.34	0.58	1.19	1.28	0.97
Group 3 (Pre BA +)	Mean	2.70	2.50	92.3	3.11	4.92	2.60	4.63	3.47	1.91
	SD	0.66	0.70	7.85	1.38	1.87	0.72	1.87	1.61	0.83
p value		0.04	0.038	0.91	0.03	0.09	0.03	0.08	0.05	0.04

* p value < 0.05 (Significant at 5% level of significance)

TABLE – 4: Pulmonary Function Test Parameters - Following Recovery after Exercise

Group		FVC	FEV 1	FEV 1 / FVC	FEF 25- 75	PEF R	FIV C	FEF 25	FEF 50	FEF 75
Group 1 (Controls)	Mean	3.00	2.80	93.71	3.74	4.83	2.91	4.63	4.09	2.55
	SD	0.85	0.74	5.53	1.14	1.45	0.74	1.35	1.32	0.95
Group 2 (FH BA +)	Mean	2.55	2.37	92.81	3.24	4.52	2.43	4.37	3.64	2.00
	SD	0.57	0.57	7.48	1.35	1.96	0.58	1.89	1.64	0.82
Group 3 (Pre BA +)	Mean	2.67	2.37	88.05	2.68	4.01	2.62	3.78	2.89	1.75
	SD	0.61	0.66	9.45	1.09	1.06	0.60	0.99	1.14	0.87
p value		0.26 6	0.11 7	0.030 *	0.01 5 *	0.11 4	0.26 5	0.07 9	0.01 6 *	0.02 5 *

* p value < 0.05 (Significant at 5% level of significance)

DISCUSSION:

This cross sectional comparative study was designed to compare Pulmonary function Tests (PFTs) before and after the exercise and the association of exercise induced asthma and family history or previous history of asthma. The study included 90 asymptomatic (without symptoms indicating asthma) subjects. Of all subjects, 30 were normal subjects (control group) with neither family history nor previous history of asthma formed Group – 1. 30 subjects with family history but no previous history of asthma formed Group – 2. 30 subjects with previous history of asthma formed Group – 3.

The basic characteristics with respect to age and anthropometry including weight, height, BMI, neck circumference, chest circumference, waist circumference and hip circumference did not show any significant difference between the 3 groups. This implies that the 3 groups in the study were comparable with respect to the age and anthropometric measurements and thus the results further obtained were not influenced by these variables⁸.

Standard guidelines for performing and interpreting PFTs were followed as being published by the international regulatory agencies^{9, 10, 11}. Subjects were screened for active respiratory infections and were precluded for the conduct of PFTs to avoid any risk of cross contamination¹². A sitting position was typically used at the time of testing to prevent the risk of falling and injury in the event of a syncopal episode, although PFTs can be performed in the standing position. Patients were advised not to smoke for at least one hour before testing, not to eat a large meal two hours before testing and not to wear tight fitting clothing as under these circumstances results may be adversely effected¹².

The PFT parameters at baseline, FEV1/FVC, FEF 25-75, FEF 50, FEF 75 of Group – 2 (with FH of BA) and Group – 3 (with Previous history of BA) was significantly decreased as compared to Group -1 (controls). Calculation of the ratio, FEV1/FVC allows the identification of obstructive or restrictive ventilatory defects. A reduced FEV1/FVC along with a reduced FEV1 signifies an obstructive defect like asthma. Similarly a reduction in FEF25-75, FEF 50, FEF 75 indicates small airways obstruction which can also occur in patients with asthma with a normal PEFR¹³. These findings were evidenced in the study with the study cases in Group – 2 and Group – 3 having a reduced FEV1/FVC, FEF 25-75 as compared to controls. Further more the authors observed that the reduced FEV1 in Group – 2 and Group – 3 showed a trend towards significance and also that the observed PEFR showed no significant difference amongst the groups. These results are very similar to those observed in earlier studies³.

The PFT parameters immediately after exercise, showed a significantly decreased FEV1, FVC, FEF 25-75, FEF 75 in Group – 2 (with FH of BA) and Group – 3 (with Previous history of BA) as compared to Group -1 (controls). Also the PFT parameters following recovery after exercise, showed significantly decreased FEV1 / FVC, FEF 25-75, FEF 25, FEF 75 of Group – 2 (with FH of BA) and Group – 3 (with Previous history of BA) as compared to Group -1 (controls). Exercise-induced asthma (EIA) is defined as lower airway obstruction and symptoms of cough, wheezing or dyspnea induced by exercise in patients with underlying history of asthma. The same clinical presentation in individuals without asthma is defined as exercise-induced bronchoconstriction (EIB). However, these definitions are limited by the heterogeneity in asthma expression¹³. The terms exercise-induced asthma (EIA) or exercise-induced

bronchoconstriction (EIB) are used to describe transient bronchoconstriction occurring during or immediately after vigorous exercise in some subjects. For the diagnosis of EIA it is necessary to demonstrate a decrease in FEV1 from baseline following physical exercise¹⁴.

There are two key theories explaining EIA: thermal and osmotic. Differential diagnosis of EIA should include chronic cardio-pulmonary diseases, vocal cord dysfunction, hyperventilation syndrome and poor physical fitness or overtraining. According to the ATS guidelines from 1999 for the diagnosis of EIA a standardized exercise test with stable environmental conditions should be employed¹⁵. EIA is not sport specific in terms of the type, duration and intensity¹⁶. An interesting earlier study has tried to bring together the different hypotheses to explain the probable underlying mechanism of EIA. Here it was concluded that neither abnormal airway cooling nor rapid rewarming of the airways is a prerequisite for EIA and that the thermal hypothesis does not explain many of the facts about EIA, particularly under hot dry conditions. It was agreed that airway cooling and rapid rewarming of the airways occur when cold air is inhaled during exercise, but these events are not necessary for EIA to occur. Subsequent suggestion that hyperpnea with cold dry air be considered not only for its capacity to cool the airways but also for its potential to involve smaller airways in the humidifying process and, as a result, becoming dehydrated and hyperosmolar. It was considered that the mechanism for EIA to be due to the dehydrating and osmotic effects of respiratory water loss that lead to mediator release. It was proposed that regulatory volume increase, after cell shrinkage, is the key event leading to the release of mediators. Potentially, all cells can be subjected to cell volume loss and these include the epithelial cells, the mast cells, the eosinophils, the macrophages, and the sensory nerve cells. The airways get narrowed by contraction of bronchial smooth muscle in response to the mediators and the effect will be amplified in the presence of airway edema⁸.

This study clearly establishes an abnormal PFT with a reduced FEV1, FEV1/FVC, FEF 25-75 in Group – 2 (with FH of BA) and Group – 3 (with Previous history of BA) at baseline prior to exercise and also following standard exercise. It thereby points to the association of exercise induced asthma and family history or previous history of asthma as hypothesized by the authors. The widespread incidence of EIA, particularly in those with asthma and also in those with no overt respiratory condition, suggests that the pathogenesis of EIA is not fully elucidated. It is probably caused by exercise-induced hyperventilation and corresponding changes in airway physiology¹⁷.

Rather than seeking medical diagnosis and management, individuals with asthma or EIA may decide not to participate in exercise, leaving them at higher risk for other conditions, such as obesity, which may impact their overall health and lifestyle habits¹⁸.

CONCLUSION:

Exercise induced asthma (EIA) is a well established and often under diagnosed condition. PFT testing with a decreased FEV1, FEV1 / FVC, FEF 25-75 is fairly diagnostic of the condition with a background family history / previous history of asthma. Subjects with EIA should be encouraged to participate fully in physical exercise. Healthcare providers should remain vigilant to identify untreated EIA and ensure that appropriate advice and treatment options are fully discussed with the affected. This implication inducts the scope for further study towards the exercise training and rehabilitation sessions tailored with a balanced expertise of the underlying pathophysiology and available options / preventive measures to care for those subjects with EIA.

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