

Undiagnosed Exercise-Induced Bronchoconstriction and Treatment in Iraqi Male Intermediate School Students

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ABSTRACT

Exercise -induced bronchoconstriction (EIB) is a transient increase airway resistance that occurs following a brief period of vigorous physical activity. The occurrence and severity of Exercise-Induced Bronchospasm depend on the level of ventilation reached during exercise and the water content of the inspired air. Sever EIB still occur in patients with normal baseline spirometry, leading to a reduction in quality of life. Peak Expiratory Flow Rate (PEFR) was measured twice before and after exercise. Four hundred boy students aged between 12-16 years participated in this study in a boy intermediate school. Six minutes free running on their own speed as a good indirect challenge to induce airway narrowing. Any subject regarded as asthmatic when show a reduction in PEFR ≥ 15 , this give an incidence rate of occult EIB 5% of all students. Seventeen students with EIB were participating in the study of EIB treatment. Zafirlukast give 82.3% protection rate, Salbutamol treatment protects 88.2% of student with EIB. Only 64.7% of EIB boys respond to Sodium Cromoglycate. A regular measurement of PEFR in schools appears to be a good indicator for EIB. While Sulbutamol inhalation 15min. before exercise inhibits EIB attacks in asthmatic boys.

1. INTRODUCTION

EIB is a phenomenon of airway narrowing that occurs during or after exercise or any physical exertion. This condition has been occurred in range of sporting activities but most common in children and participants in cold environment. 30% of these patients with EIB may develop adult asthma ⁽¹⁻⁵⁾. The term EIB and EIA (Exercise-Induced Asthma) have been used interchangeably ^(1, 4, 5). EIB occurs in subjects with or without asthma, it is especially problematic in children ⁽⁴⁾. 30% of these patients with EIB may develop adult asthma. In recent years EIB is a condition that developed a much higher profile in both medical, sports field and with the public generally.

A significant number of elite athletes are still suffering of the effect of EIB without discovered by their coaches, by themselves or their doctors being aware. The symptoms occur with EIB are wheeze, shortness of breath, chest tightness and cough ^(1, 2, 4, 5, 6).

The mechanism of EIB is not established certainly yet. The most acceptable theory is that airway dehydration caused by increased rapid ventilation resulting in loss of heat and water content of airway mucosa, which cause intracellular hyperosmolarity leading to release of inflammatory mediators from the mast cells. These mediators will cause airway smooth muscles spasm, oedema of the mucosa, thick mucus hypersecretion, all these factors lead to dyspnoea. The mediators include prostoglandins, histamine that contribute to the onset and severity of EIB. Mast cell and eosinophil are abnormally high in people with currently active asthma ^(1, 4, 5).

Diagnosis of EIB: the simplest system suitable for field work include a watch and inexpensive, available, portable Peak Expiratory Flow meter ^(4,7,8). Sport specific field testing is ideal when resources allow ^(1, 3). The examiner should measure the peak expiratory flow rate (PEFR) before at rest and after 6 min of continuous free running at 3,6 and 9 min ^(2,4,7). Any decrease greater than or equal to 15% in PEFR or FEV₁ (forced expiratory volume in the first second) is of significance.

Diagnosis of EIB is established by changes in lung function provoked by exercise. The airway response expressed as percent fall in PEFR or FEV₁, the reduction in PEFR post exercise was recorded as following: ^(9, 10)

$$PEFR\ reduction\% = \frac{Preexercise\ PEFR - Postexercise\ PEFR}{Preexercise\ PEFR} \times 100$$

Any student who shows a reduction greater than or equal to 15% regarded as asthmatic^(3, 5, 6, 11, 12). Exercise is a good indirect challenge; free running for 6 minutes will cause airway smooth muscles contraction^(4, 7, 11, 13).

Beta adrenergic stimulants are regarded often the simplest convenient and inexpensive treatment for the patient with EIB. Short acting inhaling β_2 agonist (SABA) includes albuterol, terbutaline. These medicines are considered first line therapy for preventing EIB attacks^(2, 5, 14, 15). SABA taken as inhalation 15 minutes before exercise and lasts 4-6 hour^(4, 8, 16).

Sodium Cromoglycate (SCG) is effective in eliminating EIB. It is available as capsule for inhalation with spinhaler and nebulizer solution. It is effective in blocking symptoms of EIB in 70-80% of patient with minimal side effects^(1, 2, 5, 12). These agents inhibit the degranulation of mast cells. This drug can be given 15 minutes to 1 hour before exercise, lasts for 4 hours, like Sodium Cromoglycate (SCG) and Nedocromil.

Leukotriene Receptor Agonists, such as Motilukast (Singulair), Zafirlukast (Accolate). Zafirlukast is a selective and competitive receptor antagonist of leukotriene D4 and E4. Zafirlukast inhibits Bronchospasm caused by different challenge, Zafirlukast also attenuate the increase in broncheal hyperresponsiveness. These medicines last up to 24h. this drug should be taken every day help the airway open. It is the second choice prophylactic treatment for EIB^(1, 4, 11, 13). Other drugs can be used like Long Acting β_2 Agonists (LABA) like Formetrol⁽¹³⁾, Fenoterol⁽¹⁷⁾, Corticosteroid and Vitamin C.

The aim of this study is to determine the incidence rate of Exercise- Induced Bronchoconstriction among intermediate boy school students (aged between 12-16 years) and to identify EIB therapeutic treatment.

2. SUBJECTS AND METHODS.

Over 16 visits to intermediate boy school in Baghdad, Iraq. Four hundred boy students aged between 12-16 years participate in this study; the exercise was part of their routine physical education class. The PEFR values was recorded before and after exercise in all 400 students, the activity includes a form of continuous free running in the field for 6 minutes on their own speed, after a short period of warm up activity started with stretching and jogging⁽⁹⁾.

PEFR was measured by using standard Wright Peak Flow Meter (Clemet Clarke International Ltd. Harlow England). It is a portable, inexpensive, simple system and suitable for field exercise test. The best of two readings was taken. The readings were taken before exercise at rest and after exercise at 3, 6, and 9 minutes. PEFR is the highest flow rate reached shortly after the beginning of forced expiration, it reflects the expiratory obstruction^(18, 19, 20).

For ethical reason, agreement taken from students and their parents, also asthmatic person, any one that took any anti-asthmatic treatment, any one complaining of respiratory infection or allergies were excluded from the study. Any student shows a reduction in PEFR ≥ 15 were regarded as asthmatic.

All information and values were taken in a period extend from 20th November 2018 to March 2019 in all visits, the range of temperature and relative humidity were recorded and they were 12 to 17° C and 40 to 60% respectively. Zafirlukast tablet (Accolate Tablet 20mg) was given for 17 asthmatic students twice daily for four days before the test and the last tablet was given two hours before exercise on empty stomach then Six minutes of exercise, PEFR values were recorded pre-exercise at rest and post-exercise at 3, 6 and 9 min. after treatment. Cromolyn available as a solution for nebulizer and dry powder inhaler formulation (Intal). Cromolyn had given 30-60 minutes before exercise as 2 puffs for 17 asthmatic boys (with EIB). PEFR values measured pre-exercise at rest and post-exercise at 3, 6 and 9 min after Cromolyn inhalation.

Salbutamol treatment (Ventolin inhaler) given as a 2 puffs to 17 students with EIB, 15 min before exercise, then 6 min of continuous free running, PEFR values were recorded before exercise at rest and after exercise at 3, 6 and 9 min post-treatment.

3. RESULTS

Four hundred boys aged between 12-16 years were involved in this study for testing the prevalence rate of unrecognized EIB in normal population. Only 20 boys had a reduction in PEFR readings post exercise $\geq 15\%$. PEFR readings taken before exercise at rest and after exercise at 3, 6, and 9 minutes. The results show that the prevalence rate equal to 5% among boys student aged between 12-16 years (Table1, Fig. 1).

Table 1: the total number of normal and EIB subjects.

Subjects	Boys
Normal Subjects	380
EIB Subjects	20
Total	400

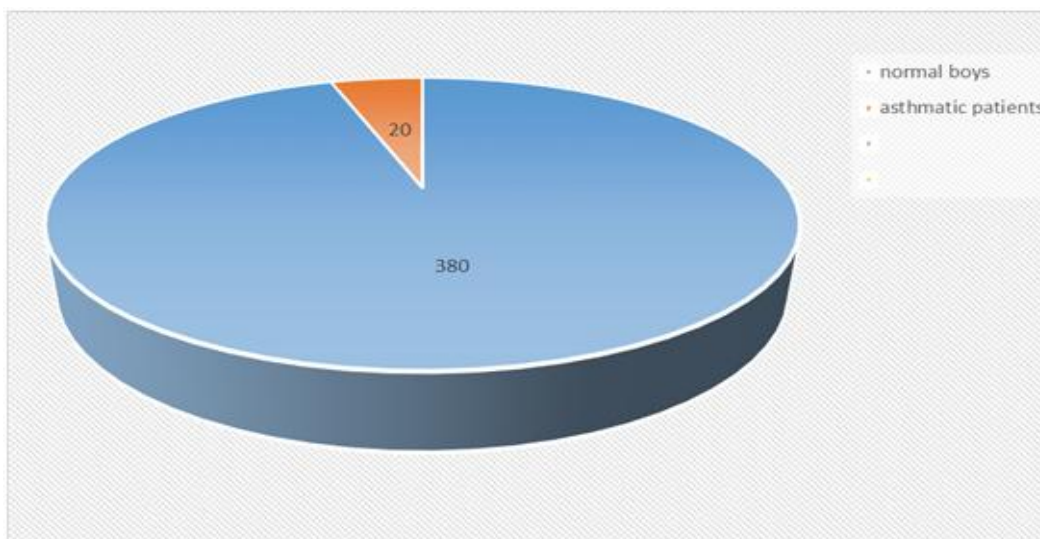


Figure 1: incidence of EIB among 400 male students aged 12-16 years.

The main standard deviation and the range of the age, body weight, height and resting PEFR were summarized in (Table 2).

Table 2: summarized the mean, slandered deviation and the range of age, body weight, height and resting peak expiratory flow rate of asthmatic boys.

Parameter	Boys
	17 students
1. Age (year)	
Mean	13.94
S.D.	1.51
Range	12-16
2. Body weight (kg)	
Mean	39.49
S.D.	3.49
Range	34-45
3. Height (cm)	
Mean	159.38
S.D.	10.5
Range	135-170
4. Resting PEFR (liter/min)	
Mean	370.6
S.D. range	58.9
	283-495

Results of Zafirlukast treatment, fourteen students out of 17 asthmatic boys (with EIB) were responded to Zafirlukast (82.3%). Significant changes in PEFR values in post- exercise after treatment measured at 3, 6, and 9min compared with PEFR values. Results of Zafirlukast treatment, fourteen students out of 17 asthmatic boys (with EIB) were responded to Zafirlukast (82.3%). Significant changes in PEFR values in post- exercise after treatment measured at 3, 6, and 9min compared with PEFR values pre-exercise at rest (Fig. 2).

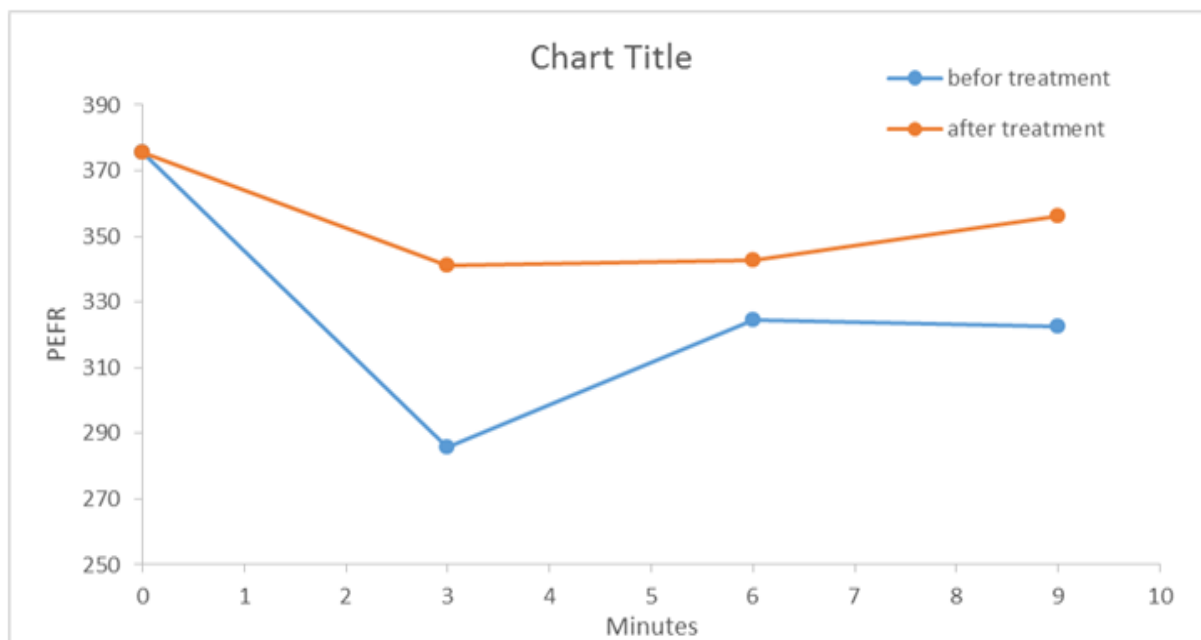


Figure 2: the PEFR before and after Zafirlukast treatment.

Result of Sodium Cromoglycate (SCG). Intal inhalation is given as 2 puffs 1 hour before exercise to 17 asthmatic students (with EIB). Only 11 boys respond to the SCG treatment (64.7%). They show a significant difference in PEFR values post exercise after using SCG recorded at 3,6 and 9 minutes compared with PEFR values pre-exercise at rest before treatment (Fig. 3).

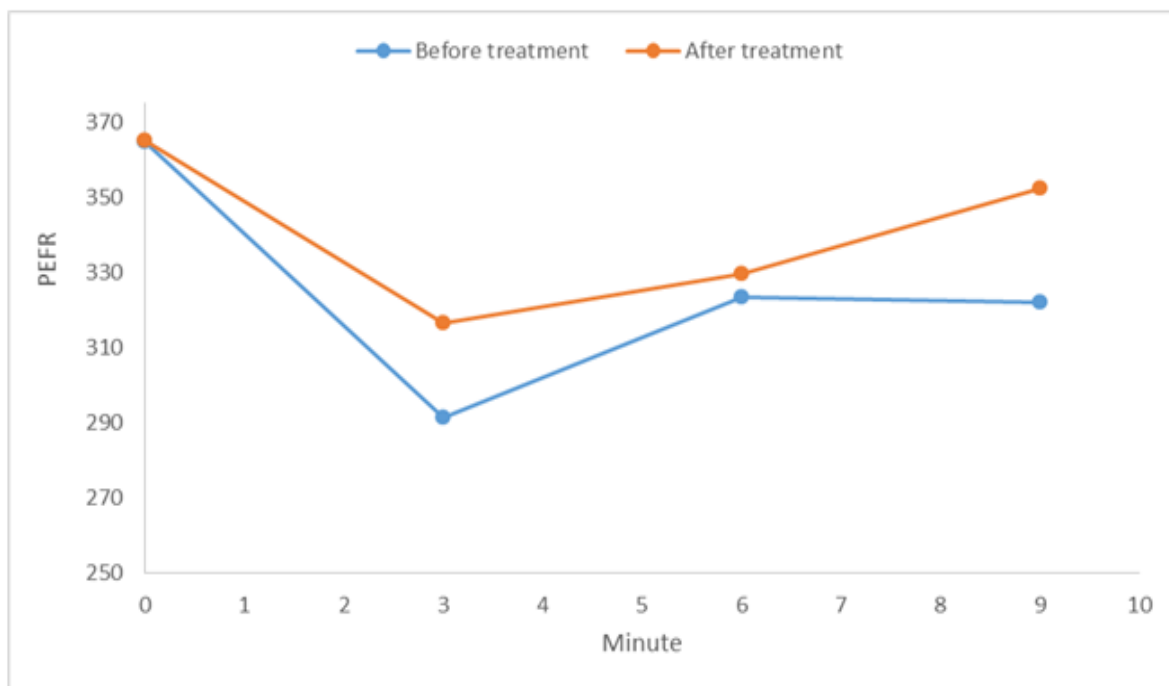


Figure 3: the PEFR readings before and after SCG treatment in boys.

Salbutamol inhalation was given as 2 puffs 15 minutes before exercise to 17 asthmatic students (with EIB). Only 15 boys show significant readings after exercise at 3, 6 and 9 minutes post treatment (88.2%). All responded students to Salbutamol give a reduction in PEFR value after exercise less than 5% compared with pre-exercise values before treatment (Fig. 4).

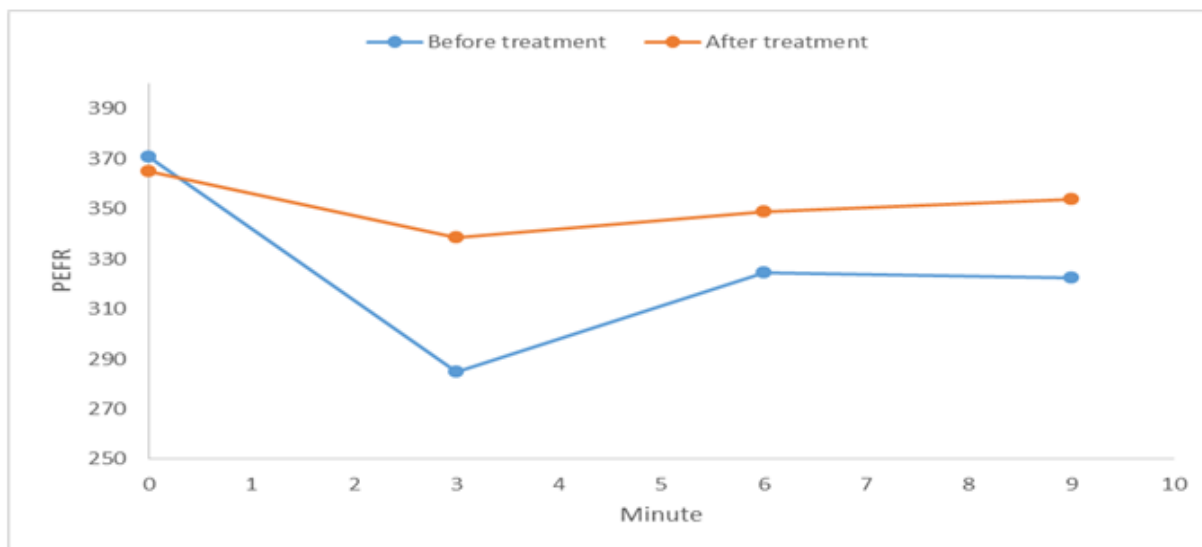


Figure 4: the PEFR before and after salbutamol treatment in boys.

The result of the EIB treatment with Zafirlukast, SCG and salbutamol were summarized in table (3). This table shows the mean and S.D of PEFR before exercise and after cessation of exercise at 3, 6 and, 9 minutes after treatment, Salbutamol has a higher protection rate in boy students while SCG has the lowest rate.

Table 3: the mean and standard deviation of PEFR of boys before and after using each treatment and the reduction percentage of PEFR at the 3, 6, 9 minutes after exercise.

Drug	Pre-exercise resting reading	Post exercise readings(minute)		
		3	6	9
1-zafirlust				
Before	370.6±58.9	285.6±34.8	324.5±52.4	322.6±58.6
After	364.7±57.6	341.1±66.6	342.6±63.6	356.2±59.9
R%	Before treatment	22.9%		
	After treatment	6.5%		
2-SCG				
Before	364.8±62.4	291.5±39.4	323.3±54.8	322.6±58.5
After		316.4±43.9		352.4±45.9
	365.2±57.2		329.5±46.8	
R%	Before treatment	20%		
	After treatment	13.4%		
3-salbutamol				
Before	370.6±58.9	285.3±34.6	324.5±34.6	322.6±58.6
After	564.8±59.8	338.4±60.2	348.8±57.7	353.9±59.7
R%	Before treatment	23%		
	After treatment	7.6%		

3. DISCUSSION

To determine the incidence of EIB in population a reduction in PEFR ≥ 15 regarded as asthmatic^(3, 5, 6, 11, 12). The severity of EIB cannot be predicted from the resting level of lung function, for this reason exercise chosen as a good challenge to produce bronchospasm⁽³⁾. Six minutes of continuous free running at their own speed to induce bronchoconstriction^(3, 4, 7, 11, 13). Krafczyk *et al*⁽²¹⁾ found that more than 10% of general population and up to 90% of persons previously diagnosed with asthma have EIB. Katten *et al*⁽²²⁾ found that an exercise challenge test demonstrated EIB in 105 asthmatic children (99%) so asthmatic patients should be excluded from these studies.

Incidence rate of EIB can occur in association with exercise in up to 15% of general population, including 100% of people with asthma, 35-40% of these with Allergic Rhinitis, and some who have an evidence of Allergy^(9,23,24). In this study the incidence rate of male students equal to 5%. Karen holzer⁽³⁾ found that the prevalence rate of EIB 6-12% within the general population nearly similar to this study (5%). Drake et al 2008⁽²⁵⁾ found that asthma is a common but complex respiratory disease caused by the interaction of genetic and environmental factors. Asthma show significant racial and ethnic disparities in the prevalence and mortality rate.

Stolof *et al*⁽²⁶⁾ found 5% of the general population with EIB. It is equal to the prevalence rate of EIB in this study. S. Chan 2008 found that the prevalence of EIB in the general population is only 5-20% compared to 90% in asthmatic patients⁽²⁷⁾. Proper management of EIB should allow the patient to participate in any physical activity without symptoms of asthma. Three safe drugs are useful in inhibiting EIB attack. Beta adrenergic aerosols (Ventolin Inhaler), SCG (Intal), leukotriene agonist (Zafirlukast).

Zafirlukast is leukotriene receptor agonists, the brand name is Accolate. The PEFR readings after exercise post-treatment compared with values before exercise at rest. Fourteen students show significant changes in PEFR (82.3%). The action of Zafirlukast reduces inflammation and thus helps to control the symptoms of bronchial asthma and improve lung function. Zafirlukast blocks the induced bronchoconstriction action of leukotriene^(1,2,6,11,12,15,16,28).

Mast cell membrane stabilizers such as Sodium Cromoglycate (Cromolyn) used widely for the prevention of EIB. They block masts cell degranulation^(1,7). Cromolyn inhibits bronchoconstriction^(4,5,7), Cromolyn is generally second line treatment in prevention of EIB attacks because of the duration of effect and efficacy is less than beta agonists⁽⁷⁾. Cromolyn action lasts for 4 hours⁽⁴⁾. Most investigators reported that Sodium Cromoglycate (SCG) was effective in 60-70% of patients with EIB^(29,30). While Sinha *et al*⁽²⁾ found that Cromolyn was effective in 70-85% of patient and have minimal side effect. These results go nearly with this study (64.7%). Report showed that a protection rate of 80% for EIB patients by SCG regardless of the side of airway obstruction⁽²⁹⁾. Cromoglycin is an effective therapy and the lack inhalers limits its use.

Salbutamol is considered to be a first choice among athletes with EIB. Rapid onset of action of Salbutamol, means that patients can take Salbutamol inhaler close to the time of exercise (15 minutes)^(1,2). Inhaled beta agonist is first line medication in the management of EIB both as prophylaxis and treatment^(1, 2, 5,11,17).

Inhalation of β_2 -agonists immediately before physical activity will stimulate β_2 -receptors on mast cells and inhibiting the release of contractile mediators, inducing relaxation of airway smooth muscles⁽⁵⁾. SABA offered greater protection than other medicines.

CONCLUSIONS

1. The prevalence rate of EIB in Iraq intermediate male students was found 5%.
2. Salbutamol (albuterol) is the drug of choice if given 15 minutes before exercise. The response rate of Salbutamol treatment is 88.2%.
3. Zafirlukast treatment showed a protection rate 82.3%.
4. SCG treatment shows a protection rate 64.7%.

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