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EXERCISE INDUCED ASTHMA (EIA), EXERCISE INDUCED BRONCHOSPASM (EIB), AIRWAY HYPER-RESPONSIVENESS (AHR) AND EXERCISE INDUCED BRONCHIAL LABILITY (EIBL): ARE THEY SAME?

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ABSTRACT

The relationship between asthma and physical activity is very interesting and complex. The terms like exercise, asthma, airway dynamics, bronchospasm, bronchoconstriction, hyper-responsiveness, hyper-reactive, bronchial lability are being very frequently used in medical literature. These terms are very confusing sometimes due to their interchanging use. This review article was attempted to define and describe the phrases which contains these terms, with special attention towards their pathophysiology for better understanding. It was found that although sounds very similar, the terms like "Exercise induced asthma", "Exercise induced bronchospasm", "Airway hyper-responsiveness" and ''Exercise induced bronchial lability" are very different in their pathophysiology, and should be used very appropriately.

Keywords: exercise, asthma, hyper-responsiveness, lability

INTRODUCTION

Since many years, physical exercise has been used to understand the airway dynamics in asthma patients, thus developed as an important tool to diagnose the asthma and, whereas at another side it is as being used as a patient management tool for preventive, therapeutic as well as prognostic purpose. This composite relation between exercise and asthma lead to the frequent use of various terms which contain the exercise and airway dynamics in its core. Following is the detailed description of each phenomenon:

Exercise induced asthma

There are many asthmatic patients, who do not have daily symptoms, but they suffer only after exercise; this is called exercise induced asthma (EIA). EIA is characterized by symptoms of coughing, wheezing, shortness of breath, and chest tightness during / after exercise, and associated with demonstrable airway obstruction as a drop in pulmonary function parameters[1]. Its definitive diagnosis requires symptoms associated with objective demonstration of a drop in flow rates, typically ≥15% for forced expiratory volume in one second (FEV_1) and ≥15–20% for peak expiratory flow rate (PEFR) after a physical exercise[2].

EIA can be seen in subjects at any level of exercise ranges from school children running or playing to elite Olympic-level athletes. This large range is due to differing physical activity protocols and depends on the type of activity, its intensity, duration, environmental conditions, severity of the disease and variations in preventative therapy regimens[3]. Certain sports activities such as long distance running, jumping, or cycling are considered more problematic in contrast, swimming is considered the relatively safe. The most challenging activity for asthmatics is relatively short and intense spell that may cause a

significant rise of heart rate and/or maximal oxygen uptake[5]. High intensity exercise is mostly related to the induction of asthma attacks[6].

Exercise–induced bronchospasm (EIB) is almost a very similar phenomenon, but it may also be seen in normal healthy individuals, without known to be an asthmatic[7]. The diagnosis after objective exercise challenge methods in conjunction with similar clinical history is must. Objective testing should begin with spirometry at rest, in true EIB the results should be within normal limits. Abnormal resting value is seen in asthma and other chronic lung conditions. There is no reason why asthma and exercise-induced bronchoconstriction should not co-exist, but the distinction is important because without successful treatment of underlying asthma, treatment of an exercise component will likely be unsuccessful.

The pathologic mechanisms that explain EIA or EIB are based on at least two contrasting theories: the airway rewarming theory described by McFadden et al[8] and the hyper-osmolarity theory described by Anderson et al[9]. The cooling of airway was demonstrated by recording temperature in the esophagus, and later by direct recording within the airways. It was found that at identical levels of respiratory heat loss (RHL) all exercise produces equal bronchospasm and there was a significant linear relationship between the quantum of RHL and alterations in lung mechanics. Mc Fadden *et al*[10] and Gilbert *et al*[11] explained that the airways cool during exercise or hyperventilation and rewarm once the exercise or hyperventilation stops. The rewarming of these cooled airways causes reactive hyperemia which directly affects bronchial caliber and obstructs the airflow. However, some researchers found that responses to exercise at various levels are not significantly different despite the large RHL differences[12]. This led to proposal of a hypothesis that respiratory water loss and not only heat loss is also the triggering event[13,14]. It was proposed that hyperventilation induced hyperosmolarity of the airway membrane (due to water loss) as another operating mechanism. Bar-Yishay[15] studied that children who made to swim while breathing dry air, developed more bronchoconstriction than swimming breathing humid air from pool surface, still they developed significantly less airway obstruction than after running with breathing dry air. Studies also showed that asthma closely resembling EIA could be provoked by inhaling hypotonic or hypertonic salt solutions[16].

The possibility that chemical mediators are involved in the intermediary pathway seems more likely, although much of the evidence in favor is highly circumstantial. Neutrophil chemotactic factor and mast cell-derived mediator which rise in blood during exercise in patients developing EIA and that rise could be prevented by pretreatment with Sodium Chromoglycate.[17] One of the characteristic features of EIA is being refractory to a subsequent challenge for some time after the initial attack. Therefore it was thought the depletion of the presumed stores of mediators which were liberated by the trigger and cause bronchospasm and sufficient time is required to resynthesize these stores[18]. Stearns et al suggested that refractoriness was due to the secretion of endogenous catecholamines[19]. Recently, Tahan et al hypothesized that the development of exercise-induced bronchoconstriction in asthmatic children may be in relation to a reduced endogenous lipoxin activity. Lipoxin mimetic and related compounds could provide novel therapeutic approaches to the treatment of exercise-induced bronchoconstriction in asthma[20].

Airway hyper-responsive or hyper-reactivity:

Airway hyper-reactivity or hyper-responsiveness (AHR) is used to describe the exaggerated response to any trivial stimuli, commonly seen in patients with asthma. This reactivity may be seen with cold air, pollen, mold, animal exposure, upper respiratory infections and laboratory testing (e.g. histamine or methacholine). In patients with asthma, airway inflammation is the primary underlying disease process, even when patients are

asymptomatic and this inflammation is associated with AHR.

Both genetic predispositions (associated with atopy) and environmental factors could be involved in its pathogenesis[21,21]. AHR is a composite physiological disorder, determined by a heterogeneous mechanism in asthma[23] as well as in other chronic obstructive pulmonary diseases (COPD)[24] e.g. chronic bronchitis and peripheral airway diseases. It is associated with inflammatory disorders in the airways in all these disease entities. In asthma, the mucosal inflammation comprises epithelial desquamation, thickening of the sub-epithelial reticular layer, micro-vascular congestion, plasma exudates and edema and sub-mucosal infiltration with mast cells, activated lymphocytes and eosinophils[25, 26]. In COPDs the inflammatory disorders differ between the various subtypes of the disease[26, 27]. Activated T-lymphocytes and macrophages seem to be the predominant infiltrating cells, without concomitant basement membrane thickening[28, 29]. Several of the above mentioned inflammatory abnormalities were correlated with the results of inhalation challenge tests. Therefore, the degree of AHR indirectly reflects the severity of the disease process in the airways in asthma and COPDs. Exercise is one of the trigger stimuli like others, which interact with hyper-responsive airway to precipitate the asthmatic attack.

Exercise induced bronchial Lability

Bronchial lability is an important feature of asthmatic patient which demonstrate in response to various apparently unrelated factors, such as allergy, infection, emotion, exercise and drugs[30]. This is a different entity than just airway or bronchial responsiveness. There are many bronchial challenges devised or understood which could test the bronchial lability. Exercise has been used as a stimulus to test bronchial lability because it can be produced in a controlled and reasonably repeatable reaction which mimics clinical asthma in a number of aspects[31]. The response of the airway or bronchi to a short bout of exercise is biphasic: initial airway dilation followed by a constriction. The cause of the initial bronchodilation during exercise may be related to an increase in sympathetic activity[33].

The bronchial lability is expressed in terms of rise in peak flow rate during exercise and fall in peak flow rate after exercise, each given as a proportion of the pre-exercise, resting peak flow rate and also in term of the total bronchial lability or exercise lability index (ELI) which is the sum of the percent rise and fall. The ELI is thus, the measure of total change in airway caliber i.e. bronchodilation and bronchoconstriction[32].

(ELI = Highest PEFR during exercise – Lowest PEFR after exercise / Initial PEFR x 100); ELI > 22 is being considered abnormal[34].

Exercise testing is also being used for another two important reasons – awareness that resting cardiopulmonary measurements do not provide a dependable estimation of functional capacity and impact of physical exertion in the clinical decision making process. Several modalities of exercise testing are being used in clinical practice. The following are the most popular clinical exercise tests, in order of increasing complexity[35]: Six Minute Walk Test (6MWT), Shuttle Walk Test, Exercise Induced Bronchial Lability (EIB), Cardiac Stress Test and Cardio-pulmonary Exercise Test (CPET).

Silverman and Anderson[32] showed that 70% of asthmatic children had a significant fall in peak expiratory flow rate after treadmill running. They suggested that this increased lability was a feature of asthmatics and that it was not closely related to the clinical condition in individual patients. Konig *et al*[36] demonstrated that there was a significant increase in bronchial lability among the wheezy bronchitis group compared with the controls. In the mildly asthmatics children who had wheezy bronchitis as infants, majority had an abnormal post exercise fall of FEV1 and abnormal total bronchial lability[35]. Balfour *et al*[37] found that exercise induced bronchial lability was a sensitive indicator of clinical asthma, which disappeared

when the patient was symptom free. Thus bronchial lability is an intrinsic characteristic of an individuals' broncho-pulmonary system.

CONCLUSION

Exercise-induced asthma, occurs when the airways narrow as a result of exercise. The exercise does not cause asthma, but is an asthma trigger. So, the preferred term for this condition is exercise-induced bronchoconstriction or bronchospasm. Bronchospasm can occur in healthy individual with normal airway, however, asthma and exercise-induced bronchoconstriction frequently co-exist. Airway hyper-reactivity or hyper-responsiveness is a state characterized by easily triggered bronchospasm. The hyper-responsiveness is an important feature of asthma but also occurs frequently in people suffering from COPD. Bronchial lability is an inherited characteristic of airway, which must combine with a triggering mechanism to result in clinical asthma. Thus the terms like EIA, EIB, AHR and EIBL are very different in their pathophysiology and should be used with caution during writing of research paper, academic teaching-learning activities, clinical practice and finally in management.

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