

Impact of Exercise-Induced Bronchoconstriction on Athletic Performance and Airway Health in Rugby Union Players

Authors

Bonello Spiteri Danica MD MRCP MSc (SEM) ⁽¹⁾ (Leeds General Infirmary, Leeds)
Dickinson John PhD ⁽²⁾, Greenwell John MBBS MRCP MFSEM MSc⁽³⁾, Ingle Lee PhD⁽⁴⁾

(1) Leeds General Infirmary, Leeds, UK

(2) Endurance Research Group, School of Sport and Exercise Science, University of Kent, Chatham Maritime, UK

(3) Leeds Carnegie, Leeds, UK

(4) Department of Sport, Health & Exercise Science, University of Hull, Hull, UK

Conflicts of Interest: None declared

Running Title: Exercise-induced bronchoconstriction in rugby players

Word Count: 2,968 (excluding title page, abstract, and references)

Abstract

Background: There is emerging evidence that the prevalence of exercise-induced bronchospasm (EIB) is significantly under-reported in many sports. There is little known about the potential performance improvement that may exist when sports players are detected and treated for EIB.

Methods: Semi-professional rugby union players with no previous history of asthma volunteered to participate in the study. Each player performed the rugby football union (RFU) fitness test and completed a eucapnic voluntary hyperpnoea (EVH) challenge at baseline and 12 weeks later. A player with a positive EVH result was prescribed beclomethasone inhaler (200 µg; two puffs per day) for 12 weeks. Players with a negative EVH test were randomly allocated to either a placebo inhaler group or acted as controls.

Results: Twenty nine rugby union players (mean ± SD; age 22.1 ± 4.2 years; body mass 100.1 ± 6.9 kg; stature 1.84 ± 0.07 m) were recruited. Seven players (24% of total) had a positive EVH challenge with a mean decrease in FEV₁ of -13.6 ± 3.5 % from baseline. There was no significant group difference ($P=0.359$) in performance improvement of the RFU fitness test between the EVH positive group (mean Δ: -22.3 seconds; 8.0 ± 2.8% improvement), placebo group (mean Δ: -16.5 seconds; 6.7 ± 1.6% improvement), and controls (mean Δ: -12.2 seconds; 5.7 ± 3.5% improvement).

Conclusion: Prevalence of EIB in semi-professional rugby union players was 24%. A 12-week prescription of beclomethasone (200 µg) showed similar improvements in RFU fitness test performance in players diagnosed with EIB compared to players with healthy airway responsiveness.

Keywords: screening; asthma, exercise-induced bronchoconstriction; athletic performance

Introduction

Exercise-induced bronchoconstriction (EIB) is closely related to asthma and is defined as a transient narrowing of the airways limiting expiration that usually follows a bout of exercise, and is reversible spontaneously or through inhalation of β_2 -agonists (Anderson, 1997). Emerging evidence has demonstrated that susceptible athletes do not recognise they have EIB (Lund et al., 2009; Rundell et al., 2001; Dickinson et al., 2005; 2011). Without the intervention of screening programmes, athletes may remain undiagnosed and may continue to suffer from EIB potentially compromising performance and health (Holzer and Brukner 2004; Dickinson et al 2011). The risk of acute bronchoconstriction in athletes can be reduced through early detection of EIB and suitable treatment (Carlson et al., 2008). Diagnosis of EIB should incorporate a medical consultation and an indirect airway challenge. The inclusion of an indirect airway challenge is crucial as diagnosing EIB through symptoms alone can result in a higher prevalence of false positives (Rundell et al., 2002; Ansley et al. 2012). The eucapnic voluntary hyperpnoea (EVH) indirect airway challenge has a high level of sensitivity and specificity for the identification of EIB (Holzer et al., 2003), and is a suitable airway challenge in athletic populations (Dickinson et al., 2006).

The proposed mechanism for the development of EIB is a dehydration of the airway surface liquid caused by the inhalation of large volumes of 'unconditioned' air requiring humidification by the lower airways. The dehydration of the ASL causes an osmotic effect that leads to an inflammatory response causing bronchoconstriction (Anderson and Kippelen 2008). It is possible that if the inflammatory process is not controlled it may lead to damage of the epithelium and resultant airway remodelling. Hence sports that have high minute ventilation demands and take place in cold, dry environments are at risk of

airway damage and EIB development. It is crucial therefore that EIB is detected as early as possible in order to control airway inflammation and minimise the potential for airway remodelling. Rugby union is a sport that requires bouts of high minute ventilation and can take place in cold and dry environments. Therefore players can put themselves at increased risk of EIB and EIB development through training and game play. The dry environments encountered either at cold temperatures or at altitude accompanied by high ventilatory requirements could increase the risk of an acute episode of EIB in susceptible rugby players (Helenius et al., 1998). Despite a number of studies reporting a high prevalence of EIB in athletes whose sports take place in cold environments (Helenius et al. 1998; Rundell et al. 2001), there is limited data available investigating the prevalence of EIB in rugby union players.

Once diagnosis of EIB has been made the most appropriate prevention strategy has been shown to incorporate regular use of inhaled corticosteroids (O'Byrne et al., 2001; Pauwels et al., 2003; Boushey et al., 2005). However, it is unclear whether detection of athletes with previously undiagnosed EIB and appropriately treating them with inhaled corticosteroid therapy results in an improvement in health and performance (Holzer et al., 2007). At present there are no studies that have investigated the longer-term impact on health and performance of treating athletes with an initial diagnosis of EIB. Accordingly the aim of our study is two-fold: 1) to investigate the prevalence of EIB in rugby union players; 2) investigate the impact of corticosteroid therapy on airway function of susceptible rugby union players and how this impacts on a rugby-specific performance test.

Methods

Participants

Forty semi-professional male rugby players from the same club in Northern England were approached to participate in the study. All participants agreeing to participate in the study provided written informed consent and ethical approval was provided by Leeds Metropolitan University. All tests were performed during pre-season training. Inclusion and exclusion criteria for the study are outlined in Table 1.

Table 1 Inclusion and exclusion criteria for study participation

Inclusion criteria	Exclusion criteria
Member of the same rugby union club	Recent chest infection (less than four weeks prior to testing)
Male	A current diagnosis of asthma and/or EIB and using inhaler therapy.
Age: 18-30 years	FEV ₁ of <70% predicted value at baseline spirometry.
	Participants with injuries which will prevent them from completing maximal fitness testing

The Rugby Football Union (RFU) fitness test

The RFU fitness test ⁽¹⁵⁷⁾ was conducted by all participants (Figure 1). The test was familiar and was conducted regularly as part of routine training and fitness assessments. The RFU fitness test is similar to the 20m multi-stage fitness test ⁽¹⁵⁸⁾, involving a number of timed repeated sprints. There are two different RFU fitness tests dependent on whether

the player is a forward or back, and participants completed the test according to their playing position.

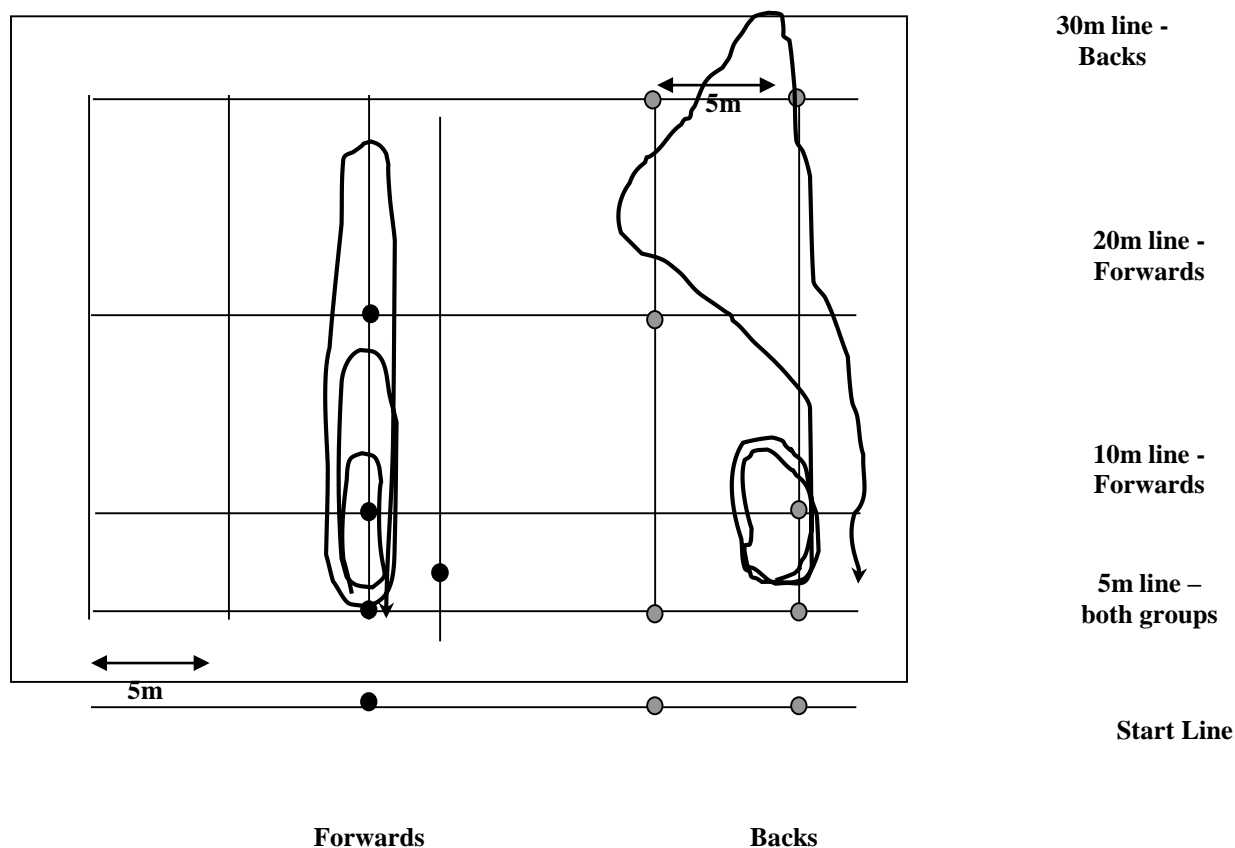


Figure 1: The RFU fitness test for forwards (left panel) and backs (right panel)

EVH challenge

All participants performed an EVH challenge within the same week as the fitness test ⁽⁸¹⁾. Maximal flow volume loops were recorded using a digital spirometer (ML3500 Micro Medical Spirometer, Cardinal Health, UK). The European Community for Coal and Steel (ECCS) reference values were used to predict maximal lung flow-volumes ⁽¹⁶⁰⁾. All maximal flow-volume manoeuvres were performed in accordance with the European

Respiratory Society criteria (Miller et al 2005). Prior to the EVH challenge participants completed three maximal-flow volume manoeuvres. The best FEV₁ was recorded and taken as baseline lung function. Other measurements collected included forced vital capacity (FVC), peak expiratory flow (PEF), and mid-expiratory flow rate at 50% of FVC (FEF₅₀).

The EVH challenge was carried out in accordance with methods outlined by Anderson *et al.* (2001) ⁽⁸⁴⁾. During the EVH challenge each participant was asked to achieve target minute ventilation (\dot{V}_E) of 85% of the maximal voluntary ventilation (MVV) for six minutes. Target \dot{V}_E was calculated by multiplying the baseline FEV₁ by 30 (Anderson et al. 2001). The gas inhaled during the EVH challenge consisted of 74% nitrogen, 21% oxygen, and 5% carbon dioxide. At the point of air entering the mouth the gas temperature was 18°C and humidity <2%. During the EVH challenge verbal encouragement and visual feedback was provided. Upon completion of the EVH challenge, two maximal flow volume loops were recorded at 3, 5, 7, 10 and 15 minutes. At each time point the flow volume loop with the best FEV₁ was recorded and used to calculate the decrease from the baseline FEV₁ at each time point. If FEV₁ was >10% from baseline at two consecutive time points this was deemed a positive EVH challenge. If participants presented with two consecutive time points where FEV₁ fell \geq 10% from baseline they were offered 200 µg of inhaled salbutamol and a repeat flow volume loop was measured 10 minutes after inhalation. All participants were asked to remain in the laboratory until their FEV₁ was within 10% of the baseline measure.

Participants were diagnosed with EIB if:

- They had a fall in FEV₁ $\geq 10\%$ from baseline at two consecutive time points following the EVH challenge.
- The participant had an initial low-normal FEV₁ (70-80% of predicted value at baseline spirometry with persistent respiratory symptoms. Following the EVH challenge there was a minimal decrease in the percentage of the FEV₁, yet following use of a salbutamol inhaler there was an improvement of $>12\%$ from the baseline FEV₁.
- Each decision about a participant being diagnosed with EIB was taken in consultation with the club's team doctor.

A participant was deemed to be EVH negative if the FEV₁ did not demonstrate a drop of $\geq 10\%$ on two consecutive time points.

Randomisation of participants

All players diagnosed with EIB were prescribed beclomethasone inhaler 200 μ g (two puffs per day). The negative EVH group was randomly selected to either receive a placebo inhaler to be used twice daily or they formed part of the control group that received no treatment. Both groups were shown how to use the inhaler by the club doctor. All participants completed their regular pre-season exercise training regimens. After twelve weeks, all players underwent re-assessment of the RFU fitness test under identical conditions. The EVH challenge was repeated in players with a positive diagnosis for EIB.

Data Analysis

Continuous variables are presented as mean and standard deviation (SD); categorical variables are reported as percentages. A one-way analysis of variance (ANOVA) was

used to identify baseline differences between groups. A repeated measures ANOVA with Bonferroni post hoc adjustment was used to identify differences over time (baseline to 12 weeks). An arbitrary level of 5% statistical significance (two-tailed) was assumed. SPSS software v17.0 (IBM, NY, USA) was used to analyse the data.

Results

29 semi-professional rugby union players (mean \pm SD; age 22.1 \pm 4.1 years; stature 1.84 \pm 0.07 m, body mass 100.1 \pm 12.3 kg) agreed to participate in the study. There were no baseline differences in age, stature, and body mass between players with positive and negative EVH results (Table 2). The baseline RFU fitness test was completed by 24 participants; however, due to injury and/or illness, only 16 participants completed both the baseline and 12 week post intervention RFU fitness tests.

Table 2: Player characteristics separated by positive and negative EVH results at baseline

Characteristic	EVH positive (n=7)	EVH negative (n=22)	
Age (years)	22.6 \pm 3.8	22.0 \pm 4.4	
Height (m)	1.87 \pm 6.3	1.83 \pm 7.0	
Weight (kg)	101.9 \pm 11.2	99.6 \pm 12.8	
FEV ₁ (l)	4.5 \pm 0.7	5.0 \pm 0.7	0.76
Percent of predicted FEV ₁	94.3 \pm 11.1	109.0 \pm 11.0	0.01
FVC (l)	5.8 \pm 0.9	6.0 \pm 0.9	0.670
PEF (l/min)	601.9 \pm 69.8	640.7 \pm 88.3	0.299
FEF50 (l/min)	4.3 \pm 0.8	5.8 \pm 1.4	0.12
Max FEV ₁ decrease post EVH challenge	-11.6 \pm 4.6	-6.0 \pm 3.6	0.002

All 29 players completed the EVH challenge. None of the 29 participants had a previous diagnosis of asthma or EIB. Seven players (24%) were diagnosed with EIB. Of these, five

had a positive EVH challenge and two presented with significant reversibility following inhalation of salbutamol. Three other participants demonstrated a fall in FEV₁ of >10%, but only at one time point. There was no significant difference in the baseline maximal flow volume measures between players with positive and negative EVH challenges. However, the baseline percentage of predicted FEV₁ was significantly higher in the players with negative results ($P=0.01$). Seven participants (24%) were diagnosed with EIB. The maximal decrease in FEV₁ was significantly ($P=0.002$) higher in the EVH positive group (Table 2). There was no significant relationship between the percentage of MVV achieved and the maximum FEV₁ fall post EVH challenge ($P=0.74$) (Figure 2). Figure 3 illustrates the individual percentage decrease in FEV₁ in players with positive and negative responses.

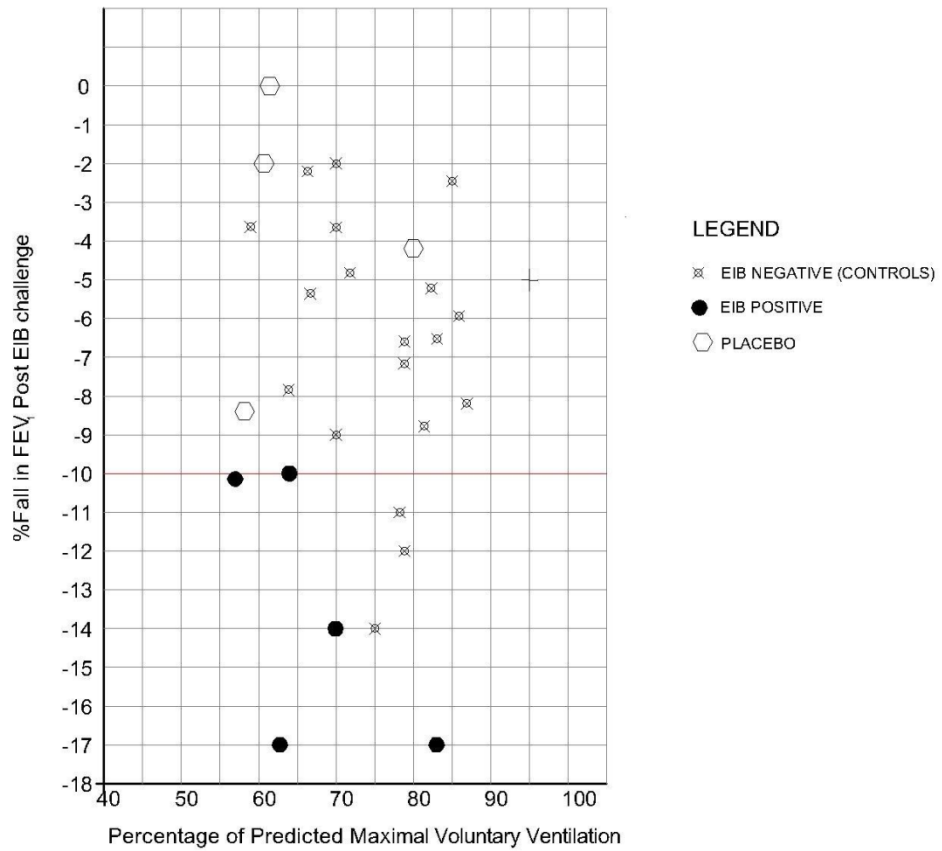


Figure 2: Percentage of MVV achieved during the EVH challenge and the percentage decrease in FEV₁ from baseline following the EVH challenge.

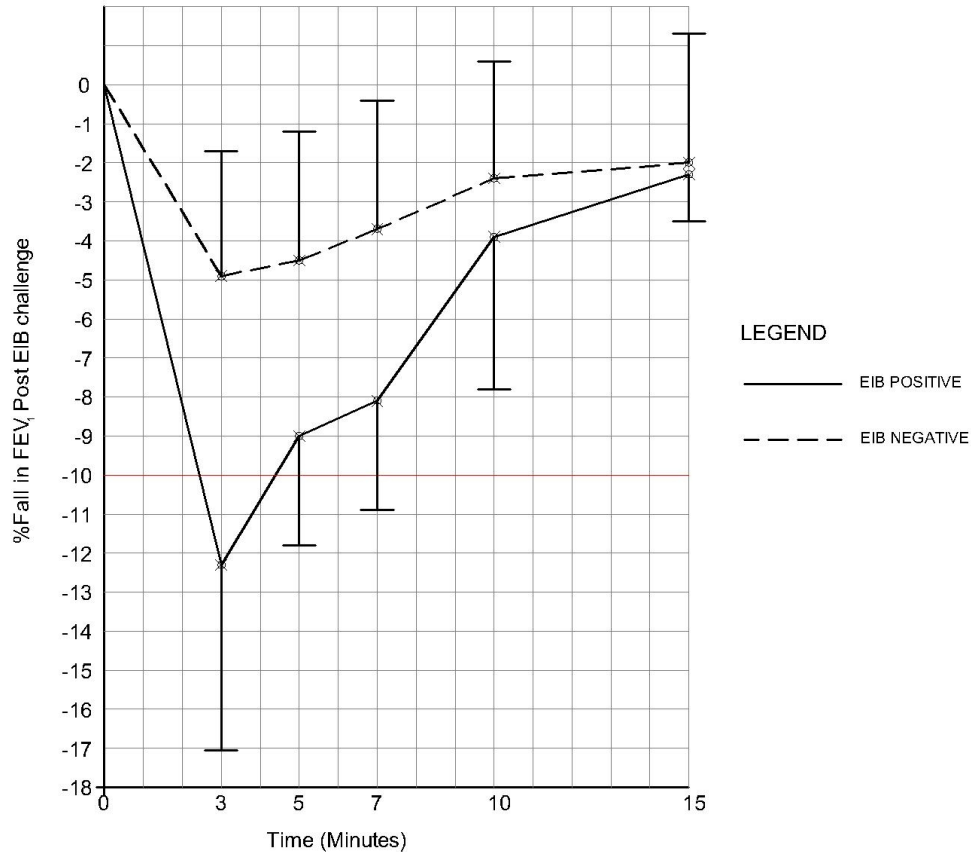


Figure 3: Changes in FEV₁ in rugby union players with positive and negative responses to the EVH challenge

RFU Fitness Test

Sixteen out of twenty-four players completed the baseline and 12 week follow up RFU fitness test. All three groups, EIB positive, placebo and control improved their fitness test scores after 12 weeks of training ($P=0.014$). When taken on an individual basis, all participants improved their RFU fitness test performance times over the 12 week period. There was no significant group difference ($P=0.359$) in performance improvement of the RFU fitness test between the EVH positive group (mean Δ : -22.3 seconds; $8.0 \pm 2.8\%$ improvement), controls (mean Δ : -12.2 seconds; $5.7 \pm 3.5\%$ improvement), and the

placebo group (mean Δ : 16.5 seconds; $6.7 \pm 1.6\%$ improvement) (Figure 4). A second EVH test was repeated after 12 weeks in players with an initial diagnosis of EIB. A decrease in FEV₁ of >10% continued to remain in all players following the treatment period.

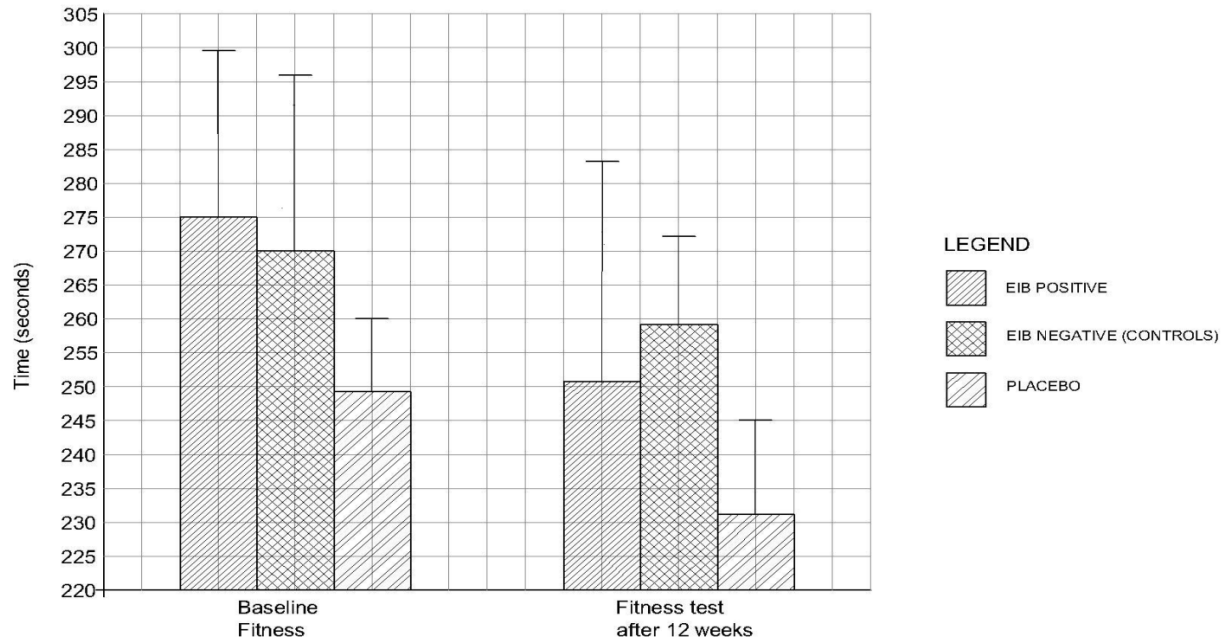


Figure 4: Comparison of the mean time taken to complete the RFU fitness test at baseline and after the 12-week intervention for players with a positive EVH test, placebo group, and controls

Discussion

This is the first study to screen a team of rugby union players for EIB and track changes in performance in those detected with EIB with no previous diagnosis. Our study shows that the prevalence of EIB in rugby union players with no previous history of asthma is 24%. Following 12-week inhalation of prescribed beclomethasone (200µg) the EIB group showed significant improvement in the RFU fitness test. Although the EIB positive group significantly improved their RFU fitness performance from baseline they did not improve at a significantly greater rate than the placebo group or controls. The EIB group demonstrated the greatest fitness improvement over the intervention and our findings are similar to previous data from asthmatics recruited to a six-week treatment programme with inhaled corticosteroids ⁽⁷⁴⁾

The high airway resistance that occurs during EIB increases the expiratory flow limitation during exercise ⁽¹⁶¹⁾ predisposing athletes to hypoxaemia during exercise. Haverkamp (2005) found a significant decrease in arterial oxygen saturation during exercise caused by an increased difference in alveolar to arterial PO₂ pressure and an insufficient ventilatory response resulting in reduced exercise performance.⁽⁷²⁾ Six weeks of inhaled corticosteroids increased arterial blood oxygen saturation during exercise and exercise performance in asthmatics (Haverkamp, 2005). It is hypothesised that had we not treated the EIB group they may have had impaired adaptation in fitness over the 12 weeks of

training. Due to ethical issues surrounding not treating an athlete for EIB once a diagnosis has been made we are unable to test this hypothesis in our study.

The EVH challenge identified 24% of rugby union players with underlying EIB. This is similar to previous findings by Dickinson *et al.* (2011) where 32% of rugby players were found to have undiagnosed EIB ⁽¹²⁾. There is the potential for EIB to develop in an athlete following over exposure during training and competition to high ventilatory demands, dry air, or poor air quality. It may take several years for EIB to develop in susceptible individuals. Our group of rugby players were relatively young (22.6 years). It may be if we had an older group of rugby players the number of EIB positive athletes we detected may have been greater and similar to the report by Dickinson *et al.* (2011) (12).

We found that the maximal flow volume measures at baseline did not distinguish between players with positive and negative results. FEV₁ is commonly used to help diagnose intrinsic asthma, as it measures the expiratory flow at high and mid-lung volumes. The baseline FEV₁ was within the normal range for all participants (>80% of the predicted FEV₁), hence identification of undiagnosed EIB through analysis of the resting FEV₁ (pre-exercise) was not possible. This is supported by previous findings (Dickinson *et al.* 2005, 2011) ^(12,87). The exception to this is the % predicted FEV₁ obtained at baseline. Players with a positive diagnosis of EIB had significantly lower ($P=0.011$) % predicted FEV₁ values compared to healthy controls at baseline. This result is similar to studies conducted on large cohorts of elite athletes that report EIB athletes to have significant lower % of predicted FEV₁ measures (Dickinson 2005; 2011). It is difficult to distinguish players with a positive EVH test by analysis of the % predicted FEV₁ as values are still within the normal range (>80% predicted value). Beck and colleagues (1994) demonstrated that

baseline spirometry in an athletic population was >20% higher than the predicted values for the general population. Future studies should determine an adjusted 'normal range' for high performance athletes (which may require further sub-specialisation for sporting mode i.e. power vs endurance sports).

In our study, the players diagnosed with EIB were treated with inhaled corticosteroids as per the British Thoracic Society Guidelines ⁽¹⁰⁸⁾, with inhaled beclomethasone, as this was found to improve EIB ⁽⁷⁴⁾. The option of providing the EIB positive participants with solely β_2 -agonists was not feasible, as although β_2 -agonists can inhibit mast cell mediator release, this response is susceptible to desensitisation, a process that can be inhibited by corticosteroids. Corticosteroids can increase the transcription of the β_2 -receptor gene in the lung and the nasal mucosa. This effect of corticosteroids lessens the reduction in transcription of the β_2 -receptors, which would occur as a result of long term β_2 -agonist administration ⁽¹⁶³⁾. However, when players with positive results for EIB underwent a repeated EVH challenge after 12 weeks of treatment, all participants still demonstrated a decrease in FEV₁ >10%. Thus, other treatment options including fluticasone ⁽¹³⁸⁾ or leukotrienes may require further consideration, although the latter is not considered a first-line treatment for EIB ⁽¹⁴⁷⁾.

There does not appear to be a relationship between respiratory symptoms and the presence/absence of EIB. Rundell and co-workers (2001) showed that in athletes experiencing a decrease of $\geq 10\%$ in FEV₁ post exercise challenge, respiratory symptoms were reported by 39% of athletes. Conversely, in athletes with EIB, respiratory symptoms

were reported by 41%. We found a similar trend in our study; 76% of the rugby players without EIB experienced respiratory symptoms, whilst 71% of the players with EIB denied any respiratory symptoms. This finding adds weight to previous studies which indicates that the analysis of signs and symptoms is not reliable method of diagnosing or rejecting EIB ⁽⁷⁶⁾. Thus diagnosis of EIB must include an objective test of airway function alongside a medical consultation.

Limitations

Our study cohort presented with mild bronchoconstriction following the EVH challenge (decrease in FEV₁ from baseline between 10-25%). We may have seen larger performance gains by using a group of athletes with moderate to severe EIB. In addition, the field-based assessment (RFU fitness test) whilst being ecologically valid and familiar to the rugby players, was less well controlled than a laboratory testing environment. The EVH challenge is a highly sensitive and specific test for the diagnosis of underlying EIB ⁽⁸²⁾. However the humidity of the air (2%) is much lower than any athlete is likely to inhale during most sporting situations. Occasionally, this may lead to over-cautious diagnosis of EIB where the impact of inhaled medication may be less significant.

Conclusion:

Prevalence of EIB in semi-professional rugby union players was 24%. A 12-week prescription of beclomethasone (200µg) showed similar improvements in RFU fitness test performance in players diagnosed with EIB compared to players with healthy airway responsiveness.

What is already known?

- Screening athletes with an indirect airway challenge such as EVH testing may result in diagnosis of EIB in previously undiagnosed athletes

What this study adds?

- The prevalence of EIB in UK-based rugby union players was 24%
- Diagnosing EIB in rugby union players with no previous history and treating them with inhaled corticosteroids for 12 weeks allows them to make similar performance gains as players with healthy airway responsiveness.