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Exercise-induced bronchoconstriction: a survey of diagnostic practice in secondary care across the United Kingdom

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To the Editor,

Exercise-induced bronchoconstriction (EIB) is highly prevalent in children and adults with asthma, and elite athletes. There is strong evidence to support that bronchial provocation tests that act indirectly are essential to obtain an accurate diagnosis of the condition.¹ Despite these recommendations, people with respiratory symptoms on exertion are regularly diagnosed with EIB based on symptoms alone and treated in primary care.² In secondary care, debate remains regarding the optimal diagnostic protocol.³ Further, it is unclear which diagnostic tests are commonly utilized and, importantly, the extent to which practitioners adhere to bronchial provocation guidelines in secondary care.

In this survey of diagnostic practice in secondary care, we aim to identify current indirect bronchial provocation challenges in use across the United Kingdom for the diagnosis of EIB and, where applicable, assess adherence to exercise bronchial provocation guidelines.

Methods

We conducted a survey of EIB diagnostic practices in hospitals with respiratory physiology laboratories, identified through the Association for Respiratory Technology and Physiology (ARTP). Forty-three hospitals were identified and approached via e-mail and/or phone. Details of the first-line indirect bronchial provocation test and standard operating procedures (SOP) for exercise challenge tests were requested. SOPs were subsequently examined for adherence to five criteria specified in the American Thoracic Society exercise bronchial provocation guidelines,^{1,4} as detailed in Table 1. Data regarding EIB diagnosis thresholds for exercise provocation testing were also obtained.

Results

Forty of 43 centers responded; 29 (73%) of these stated that they offered one or more indirect bronchial provocation tests for the diagnosis of EIB. As a first line diagnostic test, 48% of respondents conducted mannitol challenges, 45% exercise provocation challenges, 3% cardiopulmonary exercise testing and 3% histamine challenge testing.

Exercise bronchial provocation SOPs were provided by nine centers (21%) and their adherence to ATS guidelines assessed. All nine SOPs referred to measuring exercise intensity via heart rate at an appropriate intensity and all but one (89%) followed the guidance on exercise duration (figure 1). Spirometry timings did not follow ATS criteria in 67% of SOPs (figure 1). Importantly, only two of the SOPs (22%) included guidance on appropriate environmental conditions (figure 1). No center provided details sufficient

to indicate full adherence to medication restrictions were routinely implemented in the SOPs; the authors were therefore unable ascertain with any certainty whether medication restrictions were considered. The criterion for EIB diagnosis varied between centers; 56% specified a fall in FEV₁ of $\geq 10\%$, with the remaining SOPs stating a $\geq 15\%$ fall in FEV₁ as the threshold for diagnosis following exercise provocation.

Discussion

Due to the poor sensitivity and specificity of respiratory symptoms to diagnose EIB,⁵ an indirect bronchial provocation challenge is recommended.¹ Strong evidence suggests that the prevalence of EIB will vary with the type of challenge and the conditions under which the challenge is performed.^{1,3} Thus, strict adherence to provocation guidelines is essential if results are to be valid and comparable across centers. Here, we report that mannitol and bronchial provocation with exercise are utilized in the vast majority of UK hospitals for the diagnosis of EIB; both of which are considered appropriate for the diagnosis of the condition.¹ Interestingly, eucapnic voluntary hyperpnoea, which is often referred to as the 'gold standard' for the diagnosis of the condition in athletes, was not utilized by any of the participating centers. Adherence to mannitol provocation guidelines was not considered further, due to the nature of this bronchial provocation challenge being typically well standardized.

The lack of standardization for exercise challenge testing however is of concern. Many variables including exercise intensity, duration, humidity, temperature and time since medication will affect the airway response to exercise in individuals with EIB.⁶ Of these factors, our data suggest that medication restrictions were often not detailed and environmental conditions (i.e., temperature and humidity of inspired air) were rarely considered in the SOPs. As the inhalation of dry air is the main contributing factor in the pathophysiology of EIB,⁷ lack of consideration of this variable will undoubtedly result in missed diagnoses. Recommendations to overcome this problem include the use of an environmental chamber, which can reduce and control the temperature and humidity of inspired air. However this method is often limited to research facilities or sport science departments. Or, more practical for a hospital setting, the inhalation of medical grade air which is dry.⁴ Crucially, our data indicated that these recommendations are scarcely adhered to in clinical practice. As data were retrieved directly from the SOPs provided, we do not foresee any problems with recall bias in the study, however we acknowledge a risk of non-response bias in the sample.

The problem of poor standardization of exercise challenge testing goes beyond clinical practice and may affect the diagnostic guidelines themselves. Indeed, previous research suggest that environmental

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conditions are rarely reported or considered in diagnostic studies for EIB,⁸ even those used to inform clinical guidelines. For example, NICE guidelines on asthma diagnosis, monitoring and management state that exercise challenge tests should not be used for the diagnosis of asthma in persons aged 17 and over;⁹ a recommendation based on findings from five studies. It is therefore highly likely that inferences from poorly performed exercise provocation challenges are informing clinical guidelines.

To conclude, our data show that poor adherence to exercise bronchial provocation guidelines is commonplace in secondary care. The consequence is potentially widespread under-detection of EIB. More effort must be made to educate practitioners in the importance of controlling environmental conditions and ensure strict adherence to exercise provocation guidelines. Where adherence to the environmental criteria are not feasible, a surrogate indirect bronchial provocation challenge (e.g., mannitol, eucapnic voluntary hyperpnoea) should be performed.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Author contributions

AJS (guarantor), SMD and SJF planned the research study. SMD collected the data. AJS, SMD SJF analyzed results. AJS drafted the manuscript. AJS, SMD and SJF approved the final version of the manuscript.

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Table 1. Exercise bronchial provocation specifications from exercise challenge testing guidelines^{1,4}

| Guideline domain | Guideline Specification |
|--|--|
| Medication restriction | Short-acting bronchodilators, 8h; long acting bronchodilators, 48h; cromolyn sodium, 8h; nedocromil, 48h; anti-histamines, 3d; leukotriene modifiers, 24 h. |
| Exercise intensity | Monitored via heart rate (HR) or ventilation (VE). Target HR >80% of predicted max (220 – age in years). VE 40-60% of predicted max maximum voluntary ventilation (FEV ₁ x 35). |
| Exercise duration | Total duration 6-8 minutes with 4-6 minutes at exercise intensity described above. |
| Environmental conditions (inspired air) | A nose clip should be worn and inhaled water content <10mg/l or <25°C with <50% relative humidity. Alternatively, dry air delivered from medical grade compressed gas source. |
| Post-challenge spirometry timings | Spirometry performed pre-test and at 5, 10, 15, 20 and 30 minutes post-exercise. |

FEV₁, Forced Expiratory Volume in 1 second.

Figure 1. Adherence to exercise bronchial provocation guideline specifications^{1,4}

