

Letter to the editor

Lower thresholds for bronchial challenge testing

Airway hyper-responsiveness (AHR) is a hallmark of the asthmatic disease process. Recently, indirect bronchial challenge testing with adenosine monophosphate (AMP) has been shown to be more closely related to the underlying inflammatory process in asthma, when compared with the direct stimulus of methacholine (1). The use of bronchial challenge as an adjunct to decision-making in persistent asthma has been investigated by Sont et al. (2). Their data suggested that the titration of inhaled corticosteroid (ICS) dose against AHR to methacholine was associated with reduced exacerbations, dissociated from pulmonary function and symptoms.

Currently, bronchial challenge testing requires expensive equipment and specialist training for operators, which has tended to restrict its use to the laboratory setting. Anderson et al. have developed a novel bronchial challenge using mannitol which requires only the use of a simple hand held dry powder inhaler (3). This challenge test is quick, relatively cheap, requires minimal training and shows potential for use out of the laboratory setting. Currie has showed recently a strong correlation between the dose of mannitol required to provoke a 15% decrease in FEV_1 (PD_{15}) and the concentration of AMP required to provoke a 20% fall in FEV_1 (PC_{20}) (4). Moreover, Leuppi et al. found the mannitol PD_{15} was predictive of exacerbations during tapered step down of ICS therapy (5).

American Thoracic Society guidelines suggest that patients with an FEV_1 of < 60% predicted should not undergo bronchial challenge testing because of the safety issue of provoking a 20% fall in FEV_1 (6). This precludes the use of challenge testing as a monitoring tool in the management of more severe asthmatics. This poses the question as to whether lower threshold values can be used for mannitol challenge. In this respect, the cut off for eucapnic voluntary hyperventilation is an 8% fall in FEV_1 (7) while mannitol PD_{10} has been shown to correlate well with eucapnic voluntary hyperventilation (8). We have, therefore, performed a further *post hoc*

evaluation of the data from Currie et al. to assess the use of mannitol PD_{10} .

Comparison of the mannitol PD_{10} with the AMP PC_{20} resulted in a Pearson correlation coefficient of 0.70 ($P = 0.004$) as depicted in Fig. 1. Converse comparison of AMP PC_{10} compared with mannitol PD_{20} gives a Pearson correlation coefficient of 0.37 ($P = 0.17$). Reproducibility of the data comparing values at initial screening and whilst on placebo during the study as shown by Altman-Bland plot is depicted in

Fig. 2, which revealed only one value beyond the 95% confidence limits.

Long-term asthma management has shifted from a secondary to a primary care setting. Current guidelines based on conventional outcomes such as pulmonary function, symptoms and reliever use may potentially miss and lead to under-treatment of airway inflammation. This was illustrated by Green et al. who showed that adjusting ICS dose against sputum eosinophilia resulted in a fivefold reduction in

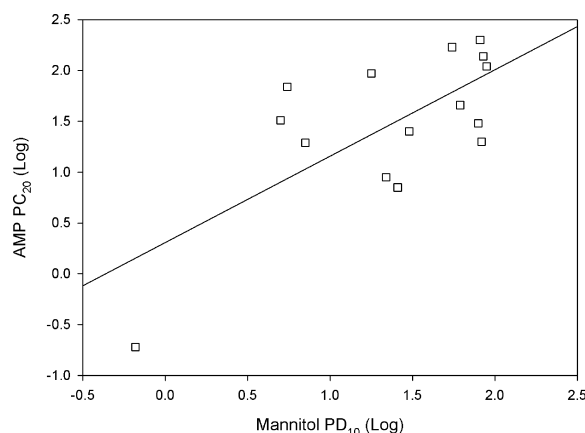


Figure 1. Correlation between adenosine monophosphate (AMP) PC_{20} and mannitol PD_{10} .

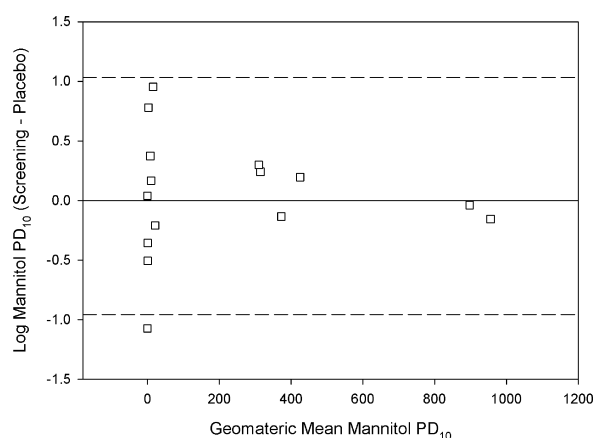


Figure 2. Altman-Bland plot showing the repeatability between mannitol PD_{10} on successive challenge tests. The solid line indicates the point of no difference. The dashed line represents 95% CI.

severe exacerbations over 1 year, when compared with conventional outcome measures (9). Interestingly methacholine PC₂₀ but not lung function was also increased in the sputum intervention group, suggesting that AHR may be a useful inflammatory surrogate.

Mannitol challenge appears to be a suitable surrogate to noninvasively evaluate airway inflammation that is cheap, simple to administer and reliable enough

to be utilized in primary care. We have shown that mannitol PD₁₀ correlates well with AMP PC₂₀, which has previously been shown to reflect airway inflammatory changes. A mannitol challenge test measuring PD₁₀ would be even safer, quicker and cheaper than one based on PD₁₅ or PD₂₀ and could perhaps be used in the more severe patient groups. Further, large-scale primary care-based studies are now indicated to evaluate the use of mannitol chal-

lenge with respect to titrating ICS dose, and its consequent effect on long-term exacerbations, when compared with conventional outcome measures such as lung function, symptoms and reliever use.

*Tom Fardon, Graeme Currie, Daniel Lee,
Brian Lipworth
Asthma and Allergy Research Group
University of Dundee*

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