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Title: Comparison of validity of methacholine and mannitol bronchial challenges in asthma diagnosis

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Body: Background: Detection of BHR with methacholine or mannitol have been highly sensitive tests to identify asthma diagnosis. Purpose: The purpose of this study was to demonstrate the diagnostic validity of the two bronchial challenges and their correlation with symptoms, atopy and inflammatory markers. Methods: Eighty-eight patients, 47 women and 41 men, aged 14-75 years who presented with asthma related symptoms and were not on any anti-asthma medication, were challenged with mannitol and methacholine. Medical history, physical examination, skin prick tests, Asthma Control Test (ACT) and FeNO levels were also assessed. The clinical diagnosis of asthma was based on bronchodilator reversibility test. Results: Sixty seven patients were diagnosed with asthma and 21 without asthma. Both methacholine ($p<0,014$) and mannitol ($p<0.000$) challenges were significant in diagnosing asthma. The sensitivity/specificity was 62,68%/85,71% for methacholine, 64,17%/95,23% for mannitol and 64,70%/93,75% for both methods together, whereas the positive/negative predictive value was 93,33%/41.86%, 97,72%/45,45% and 97,05%/45,45%, respectively. There was a negative correlation between PC20 of methacholine and the FeNO level $p<0,001$, and positive with the PD15 of mannitol $p<0,001$ and the pre-test FEV1% pred $p<0,005$, whereas PD15 of mannitol was negatively correlated with the FeNO level $p<0,001$. Furthermore, dyspnoea was the only asthmatic symptom associated with FeNO level $p<0,035$ and the positivity of mannitol $p<0,014$ and methacholine $p<0,04$. Conclusions: Both provocation methods were equivalent in diagnosing asthma, although sensitivity/specificity values appeared to be slightly higher in mannitol challenge.