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EFFECT PARAMETERS FOR THE ASSESSMENT OF AIRWAY RESPONSIVENESS TO METHACHOLINE: COMPARISON OF SPIROMETRY AND BODY PLETHYSMOGRAPHY

F. Nensa[1], N. Kotschy-Lang[2], H.-J. Smith[3] and R. Merget[1]

[1]Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University, Bochum (IPA), Bochum;
[2]Berufsgenossenschaftliche Klinik für Berufskrankheiten, 08223 Falkenstein; 3CareFusion Germany 234 GmbH, Höchberg, Germany

Introduction: While methacholine (MCH) testing is commonly used in the clinical diagnosis of asthma, the detection of airway narrowing often relies on either spirometry or bodyplethysmography, however comparative studies are rare. **Methods:** MCH testing was performed in 74 subjects. The asthma group consisted of 37 patients with a medical record of occupational and/or allergic asthma. The control group consisted of 37 patients with no clinical symptoms of asthma, which matched the asthma group in terms of age, gender, BMI and baseline forced expiratory volume in one second (FEV_1). The patients were included into the comparative study by the following criteria: no acute respiratory infection or exacerbation within the preceding 6 weeks; no severe diseases; normal baseline specific airway resistance (sR_{tot}) (0.7?0.2 control; 0.9?0.2 asthma [kPa*s]); normal baseline FEV_1 (3.3?0.8 control; 3.4?0.7 asthma [L]); FEV_1/FVC >70%; no previous treatment with oral or inhaled steroids within 14 days; no short acting bronchodilators within 24 hours. A paradox increase in FEV_1 >5% from baseline during the challenge was regarded as a sign of unstable breathing control and tests were excluded from the study. All patients were over 18 years of age (47?14 asthma; 48?13 control; [years]) and informed written consent was obtained from each subject. MCH was used in a concentration of 3.3 mg/ml at the first provocation step and in a concentration of 16.5 mg/ml at steps 2 to 5. MCH was aerosolized by a MedicAid nebulizer and an APS dosimeter (CareFusion, Höchberg, Germany). The cumulative inhaled MCH doses of 0.003 mg, 0.014 mg, 0.059 mg, 0.239 mg and 0.959 mg were obtained by taking 1 breath (steps 1 and 2), 3 breaths (step 3) and 10 breaths (step 4). At step 5 patients took multiple breaths until a total inspiration time of 16.36 seconds was reached. SR_{tot} was recorded by bodyplethysmography (MasterScreen, CareFusion). Spirometry was performed after sR_{tot} tidal breathing analysis. A FEV_1 decrease of ? 20% from baseline and a 100% increase of sR_{tot} to ? 2 kPa*s was defined as end-of-test-criterion and $PD_{20}FEV_1$ and $PD_{+100}sR_{tot}$ were calculated by interpolation. Performance of lung function parameters was compared using receiver-operating-characteristic (ROC) analysis taking the MCH dose as the varying discrimination threshold. **Results:** Twenty (54%, spirometry) and 27 (73%; bodyplethysmography) subjects of the asthma group showed a positive reaction after the highest MCH dose, but only 3 (8%, spirometry) and 6 (16%, bodyplethysmography) of the controls showed such a reaction. ROC analysis resulted in an area under the ROC-curve (AUC) of 0.74 for FEV_1 vs. an AUC of 0.82 for sR_{tot}. The corresponding Youden-Indices (J) were 0.46 for FEV_1 and 0.57 for sR_{tot}, respectively. The Youden-Index in sR_{tot} was not only higher, but sensitivity and specificity (73% / 84%) were also rather well-balanced, in contrast

to *FEV$_1$* (54% / 92%). **Conclusions:** In cumulative MCH challenges we found sR_{tot} to be the overall most useful parameter for the detection of bronchial hyperresponsiveness. Bodyplethysmography yielded a more balanced sensitivity-specificity ratio with higher sensitivity, but comparable specificity.