A Comparison of 2 Methods of Continuous Aerosol Administration During Methacholine Challenge Testing

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BACKGROUND: Exposure to the bronchoconstricting agent methacholine is a potential hazard to technical staff during methacholine challenge testing, which remains a useful and frequently performed test. There are several methods of performing the test. One of the 2 methods listed in the American Thoracic Society’s guidelines is the 2-min tidal-breathing method. The methacholine can be inhaled using one of several methods. The loosely-fitting-mask method is likely to produce more contamination of the local environment than a filtered exhalation system. METHODS: We tested 2 variations of the tidal-breathing method of measuring the methacholine provocational concentration (PC_{20}, the dose that produces a 20% decrease in forced expiratory volume in the first second). One involved use of the open-mask technique and the other a T-piece-and-filter system that precluded the release of methacholine-containing droplets into the environment. We performed duplicate methacholine challenge tests with 10 subjects who had a wide range of PC_{20}. The tests were done in random order, and each subject performed one test using the mask and one using the T-piece/filter system. RESULTS: With the mask system the geometric mean PC_{20} was 4.7 mg/mL, versus 5.1 mg/mL with the T-piece-filter system ($p = 0.36$). These values are very close and would not be substantially different clinically. CONCLUSION: The 2 methods are equivalent, and the low cost of the products used in the T-piece/filter method makes it suitable for reducing technician exposure to methacholine, using potentially completely disposable components. Key words: methacholine challenge test, technician exposure, T-piece, filter. [Respir Care 2006;51(1):46–48. © 2006 Daedalus Enterprises]
lines recommend that the test be performed in a well-ventilated location or that other methods, such as T-piece and filter, be employed to reduce technician exposure. We tested whether the use of a valveless T-piece and an exhalation filter changed the results of methacholine challenge tests, when compared with the open-mask method.

**Methods**

**Subjects**

Subjects were adults (5 male, 5 female) between the ages of 28 and 63 years (mean ± SD 49.9 ± 11.33 y). None had pulmonary disease other than asthma, which was well controlled. No subject used bronchodilators for at least 48 hours prior to the test, and none were taking an anti-muscarinic agent. All had a forced expiratory volume in the first second > 75% of predicted. The subjects had a wide range of responsiveness to methacholine. The subjects had initial methacholine provocational concentrations (PC_{20}, the dose that produces a 20% decrease in forced expiratory volume in the first second) between 0.55 and 29.1 mg/mL. Approval was obtained from the biomedical research ethics board of the University of Saskatchewan, and patients gave informed written consent.

**Study Design**

We performed duplicate methacholine challenge tests with 10 subjects, using a 2-min tidal-breathing method. The 2 tests were performed in random order, at the same time of day, not less than 2 days and not more than 7 days apart, using 2 different methods of methacholine (Provocholine, Methapharm, Brantford, Ontario, Canada) administration. The methodology was similar to that described by Cockcroft et al., but slightly different equipment was used. The apparatus is shown in Figure 1. We used the same (previously calibrated) nebulizer (Bennett/Twin Nebulizer, Nellcor Puritan Bennett, Pleasanton, California) for each pair of tests. The nebulizer had an output of 130 mg/min. For the tests with the face mask, the nebulizer was attached to the mask by a 90° plastic curve (18-mm inner diameter). The face mask was held approximately 1 cm from the face, not in direct contact with it. The apparatus for the test with the exhalation filter is shown in Figure 1B. The nebulizer was attached to a plastic T-piece (Salter Labs, Arvin, California), which had a mouthpiece (Salter Labs, Arvin, California) attached to one of the horizontal arms and a filter (Barrierbac S, Mallinckrodt DAR [Tyco], St Hubert, Québec, Canada) attached to the other. Nose clips were used for all spirometry and during all methacholine administrations. For each exposure, the subject inhaled the nebulizate for 2 min and performed truncated FEV_{1} maneuvers at 30 s and 90 s after completion of exposure. The forced expiratory volume in the first second was recorded. Exposures were performed at 5-min intervals. The PC_{20} was calculated according to the method described by Cockcroft et al.

**Statistical Analysis**

The methacholine PC_{20} values were log-transformed and analyzed with a computerized regression analysis, and also compared with a paired t test (Statistix for Windows, Analytical Software, Tallahassee, Florida). The study had > 90% power to detect a change in PC_{20} of one half of a doubling concentration.
**Results**

The results are shown graphically in Figure 2. The geometric mean PC20 was 4.7 mg/mL (95% confidence interval = 1.8–12.9 mg/mL) with the mask and 5.1 mg/mL (95% confidence interval = 1.9–13.2 mg/mL) with the T-piece (p = 0.36). Regression analysis showed a slope of 1.02, an intercept of 0.042, and a regression coefficient of 0.99. This indicated that the regression line for the 2 methods is exceedingly close to the line of identity.

**Discussion**

These 2 methods of performing this routine diagnostic test give similar results. The values for all the subjects changed by less than one half of a doubling concentration, one doubling concentration change being considered the minimum clinically important difference in an individual. It is reasonable to assume from these data that the 2 methods are interchangeable with respect to patient safety and accuracy of measurement of methacholine PC20.

There are 2 major differences between the 2 methods. The first is the avoidance of the contamination of the immediate environment with a nebulized bronchoconstrictive agent. Three of the 4 technicians who perform these tests in our laboratory had begun to complain of effects associated with methacholine exposure. Two of those technicians are known asthmatics. Improving the ventilation of the room where methacholine tests are performed would involve considerable expense, so we looked to other methods of reducing exposure. The methacholine challenge test has proved safe, even with subjects whose airflow is substantially reduced, and we know of no literature that would indicate that technical staff are at substantial risk. However, we feel that reducing environmental contamination with a bronchoconstricting agent is felt to be desirable.

The second advantage of the T-piece method relates to cost. The method of Juniper et al involves the use of a Wright nebulizer and a Hans Rudolph inspiratory-expiratory valve. Though both of those are excellent pieces of apparatus, they are relatively expensive to purchase and must be regularly cleaned and disinfected. Our method uses a disposable mouthpiece, T-piece, and filter. There are no valves included as part of the delivery system. The nebulizer used is not expensive and so new equipment can be used each time, thereby eliminating the risk of contamination from patient contact, without the delay and cost of cleaning and disinfection.

**Conclusions**

We feel that our T-piece method has advantages, even if used in a well-ventilated location, and adoption of this method in routine testing in our laboratory has been associated with a cessation of complaints of symptoms attributed to methacholine.

**REFERENCES**