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Inhalational challenge using hypertonic saline in asthmatic subjects: a comparison with responses to hyperpnoea, methacholine and water

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Inhalational challenge using hypertonic saline in asthmatic subjects: a comparison with responses to hyperpnoea, methacholine and water. C.M. Smith, S.D. Anderson.

ABSTRACT: Non-isotonic aerosols are being used increasingly for bronchial provocation testing in patients with asthma. We investigated changes in forced expiratory volume in one second (FEV_1) in response to inhaling ultrasonically nebulized 4.5% saline in 10 normal subjects and 68 subjects with asthma. A comparison of the sensitivity to this challenge was made with sensitivity to challenge with methacholine, water, exercise and eucapnic voluntary hyperventilation (EVH). In normal subjects the FEV_1 was reduced by 6±2% (mean±SD) after inhalation of 33 ml of aerosol. Eighty four percent of the asthmatic subjects exhibited a fall in FEV_1 of >20% after inhaling 4.5% saline. The provoking dose (geometric mean ±95 % confidence limits) of saline to induce a 20% fall (PD_{20}) was 2.05 ml (1.34–4.48). The sensitivity to inhaled 4.5% saline was significantly related (p<0.001) with responsiveness to methacholine, exercise and EVH, but not to water. Those patients recording a PD_{20} to 4.5% saline had a PD_{20} to methacholine less than 2 µmol which is a response consistent with moderate to severe bronchial hyperresponsiveness.

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There is now considerable interest in the use of non-isotonic aerosols, not only for research purposes but also for clinical use in diagnosis and assessment of the severity of asthma [1–3]. Although it has been known for some years that non-isotonic aerosols provoke bronchoconstriction in patients with asthma, the majority of studies using non-isotonic aerosols have examined the effects of ultrasonically nebulized water. Following the introduction of ultrasonic nebulizers as humidifying devices in the 1960's, there were a number of studies reporting that their use could be associated with increased airway resistance and decreased arterial oxygen tension in subjects with asthma [4] and chronic obstructive airways disease [4–7].

The characteristics of the airway response to ultrasonically nebulized water in subjects with asthma has been well-described [1, 8–10] and the sensitivity and specificity of the response to water has been reported in relatively large groups of subjects with asthma [2, 10, 11]. Similar data has not been reported for responses to hyperosmolar aerosols. The aim of this set of studies was to examine the sensitivity and specificity of the response to inhaling hyperosmolar aerosols, and to determine how responsiveness to hyperosmolarity compares with responsiveness to other forms of bronchial provocation tests commonly used in the pulmonary function laboratory.

Subjects

Normal subjects

The control subjects were ten healthy nonsmoking subjects, 9 females and 1 male, aged 20–32 yrs. All had a normal forced expiratory volume in one second (FEV_1) at rest (mean % predicted ±SD; 117±10) [12]. No subject had a history of wheeze or chronic cough, and none had ever required the use of a beta-adrenoceptor agonist. Only one subject had a family history of atopy or wheeze. A summary of the morphometric details is given in table 1.

Subjects with asthma

The studies were performed in 50 adults, 26 males and 24 females, aged18–57 yrs, and 18 children (8 males and 10 females) aged between 6–16 yrs, all of whom had a clinical diagnosis of asthma. A summary of their morphometric details is given in table 1, and current medications in table 2.

With the exception of one subject, aerosol medications were withheld for at least 4 h before challenge. The timing between medication and challenge was constant for each study day. The remaining subject, with steroid dependent asthma, required two hourly bronchodilators to maintain his FEV_1 at 70% of his predicted normal value. This subject continued his normal medication regimen, but withheld bronchodilator therapy for 2–2.5 h before all challenges. Oral theophylline was withheld for at least 12 h in all subjects, and oral steroids were taken as prescribed.

Table 1. – FEV_1 before challenge, expressed as a percentage of the predicted normal, and the reduction in FEV_1 and PEFR after challenge, expressed as a percentage of the pre-challenge value

	Normal subjects	Patients with asthma	
		Adults	Children
Age yrs	22±4	27±8	13±3
Baseline FEV_1 % predicted	117±10	89±18	92±18
Maximum % fall in FEV_1	6±2	29±13	29±20
Maximim % fall in PEFR	15±7	32±16	27±19

FEV_1: forced expiratory volume in one second; PEFR: peak expiratory flow rate. Mean±SD.

Table 2. – A summary of medications used by the 50 adults and 18 children with asthma

Medications	Number (%) Adults	Number (%) Children
Beta-adrenoceptor agonist		
a) regularly	31 (62)	12 (67)
b) as required	9 (18)	5 (28)
Glucocorticosteroids		
a) inhaled	21 (42)	8 (44)
b) oral	3 (6)	1 (6)
Theophylline	14 (28)	6 (33)
Disodium cromoglycate	12 (24)	8 (44)
None	10 (20)	1 (6)

Test procedures

All subjects were challenged with aerosols of 4.5% saline which were generated by an ultrasonic nebulizer. To determine the reproducibility of the response to hyperosmolar saline, 8 subjects were challenged on two occasions, 1–37 days apart.

We were also interested in the relationship between responsiveness to 4.5% saline and responsiveness to other forms of bronchial challenge. We therefore compared the response to 4.5% saline with the response to methacholine (n=25), eucapnic voluntary hyperventilation (n=22), exercise (n=9) and water (n=16). All challenges were performed within 5 weeks of the challenge with 4.5% saline aerosol.

Methods

Challenge with 4.5% saline aerosol

Two slightly different protocols were used:

i) For 41 of the 50 subjects studied, the challenge was administered according to the protocol described by Smith and Anderson [13]. The aerosol was generated by an ultrasonic nebulizer (Mistogen EN143A, Timeter Pennsylvania, USA) and was passed through tubing to a two-way valve (Hans-Rudolph No. 2700, Kansas City, Mo, USA), through which the subjects were asked to breathe quietly. A nose-clip was used to ensure that the subjects were breathing through the mouthpiece.

Subjects breathed 40 *l* of room air through the valve. The FEV_1 measured after this procedure was taken as the baseline value. The subjects were then challenged with increasing volumes of 4.5% saline aerosol. The first dose delivered was either 5 *l* or 10 *l*. The subsequent doses were then doubled until 250–305 *l* of aerosol had been inhaled. If the FEV_1 fell by more than 10% in any one challenge period, the same dose was given again rather than being doubled.

ii) Having used this protocol in over 50 subjects, we observed that the volume of 4.5% saline delivered to the valve was a function of time, rather than of ventilation. Thus, those with a low rate of ventilation, who took longer to inhale the aerosol, received more than those with a high rate of ventilation. The protocol was therefore modified slightly and the remaining 9 subjects were challenged by timing the dose delivered. The subjects breathed room air through the valve for 2 min. The FEV_1 measured after breathing the room air through the valve was taken as the baseline value. The subjects then inhaled the aerosol for 2 min, and for periods of between 2 and 4 min until the fall in FEV_1 was greater than 20% or until the aerosol had been inhaled for a total of 8 min. For both protocols the total dose of aerosol delivered to the inspiratory port of the valve was determined by weighing (Sartorius 1216MP, Gottingen, W. Germany) the nebulizer canister and tubing to the valve before and after the challenge. Thus, the relationship between the % fall in FEV_1 and the volume of 4.5% saline delivered could be plotted.

Either a Cavitron spirometer (Cavitron, California, USA) or a Minato autospirometer (AS-500 Minato, Osaka, Japan) was used to measure spirometry. The FEV_1 was measured before challenge, 60 s after inhaling room air, and 60 s after each volume of 4.5% saline aerosol had been delivered. Measurements were made in duplicate and where the values differed by more than 200 ml, a third measurement was taken. The highest of two or three measurements was recorded.

Challenge with methacholine

The methacholine challenges were adminstered using a protocol similar to that described by YAN *et al.* [14] for histamine. Methacholine solutions (0.625%, 2.5% and 5.0% w/v) were delivered *via* a de Vilbiss No. 40 hand-held nebulizer (de Vilbiss Co, Pennsylvania, USA). On the basis of previous reports on the output of these nebulizers, these concentrations correspond to 0.096, 0.384 and 0.768 μmol. The cumulative doses administered were 0.096, 0.385, 1.54, 3.84 and 7.8 μmol.

Spirometry was measured 90 s after each dose, in duplicate or triplicate as previously described.

Challenge with eucapnic voluntary hyperventilation

The circuit used in these studies was similar to that described by PHILLIPS *et al.* [15]. Dry compressed gas, at room temperature, was delivered by a special demand valve to a target balloon. The demand valve could be set to deliver gas at 30–150 $l \cdot min^{-1}$. A calibrated rotameter was placed in the circuit between the target balloon and the subject to monitor the rate of flow. The subjects breathed through a two-way valve (Hans-Rudolph No. 2700). To obtain the required rate of ventilation the subject was instructed to keep the target balloon filled to a constant volume. The rate of ventilation actually achieved was measured by passing the gas to a 350 *l* chain compensated gasometer and recording the ventilation on a chart recorder (Watanabe Miniwriter, Japan). The inspired gas contained a mixture of 4.9% CO_2, 21% O_2 and the balance N_2. This percentage of CO_2 produces near-normal end-tidal CO_2 at ventilation rates of 30–105 $l \cdot min^{-1}$ [15].

The procedure used for challenge was similar to that described by O'BYRNE *et al.* [16]. The subjects were instructed to ventilate at the targeted rate for periods of 3 min. For the first three minutes the subjects inhaled air at resting ventilation through a demand valve from a tank of compressed air. For each subsequent 3 min challenge period, the subjects were asked to breathe from the tank containing 4.9% CO_2, first at 30–40 $l \cdot min^{-1}$, then at 60–80 $l \cdot min^{-1}$, and finally at their maximum voluntary ventilation (MVV). The challenge ended if the reduction in FEV_1 was greater than 20%. If the reduction in FEV_1 was still less than 20% after 3 min of MVV, a final challenge was performed at MVV for 6 min.

The FEV_1 was measured at the end of each challenge period at 0.5, 1.5 and 3.0 min, and then at 2 min intervals until the values had reached a plateau, or had begun to increase.

Challenge with exercise

The exercise challenges were performed on a cycle ergometer for between 6–8 min, at 75% of the predicted maximum workload. The inspired air was heated to between 29.5°C and 47°C, and the inspired water content was between 4–10 mg $H_2O \cdot l^{-1}$. Subjects continued to breathe the heated air for 2 min following challenge. Spirometry was measured before exercise, and after exercise at 2, 5, 7 and 10 min, and then at 5 min intervals until the values had reached a plateau, or had begun to rise.

Air from the room was heated by blowing it through stainless steel coils immersed in a bath (Frigomix, Braun, Melsungen, W. Germany) maintained at 90–95°C. The temperature of the inspired air was measured with a thermistor (No. 401, Yellow Springs Instruments, Ohio, USA) 8 cm upstream from the inspiratory port of the valve. The temperature of the inspired air increased as the rate of ventilation increased. This was presumably because the residence time of the air in the connecting tubing was decreased.

Challenge with water

The challenges with ultrasonically nebulized water were performed in an identical manner to the challenges with hyperosmolar saline, the only difference being that distilled water was placed in the nebulizer canister, instead of hyperosmolar saline.

Analysis of data

For challenge with 4.5% saline, methacholine and water, stimulus-response plots were drawn relating the cumulative dose delivered, on a logarithmic scale, to the % fall in FEV_1. The dose that provoked a 20% fall in FEV_1 (PD_{20}) was obtained from these plots by linear interpolation, and was used as an index of sensitivity to the aerosols [17]. The PD_{20} for 4.5% saline, methacholine and water are referred to as PD_{20}(S), PD_{20}(M) and PD_{20} (H_2O), respectively. For challenge with eucapnic voluntary hyperventilation, stimulus-response plots were drawn relating the cumulative ventilation to the % fall in FEV_1. The cumulative ventilation that provoked a 20% fall in FEV_1 (PVE_{20}) was determined from these plots by linear interpolation. For exercise, the sensitivity to the test was determined by calculating the maximum % fall in FEV_1 following the exercise challenge.

Values for PD_{20} were log-transformed for the purposes of statistical analysis, and the data for PD_{20} is presented as the geometric mean and 95% confidence limits of the mean. In the 8 subjects who performed two challenges with 4.5% saline, the reproducibility of the response was compared using the paired t-test and Pearson's correlation coefficient and the coefficient of variation was also calculated. The difference between the two PD_{20}(S) values was also plotted against the average of the two PD_{20}(S) values, as suggested by ALTMAN and BLAND [18]. This plot is useful for displaying the magnitude of the difference in the two values, and whether there is any relationship between the magnitude of the PD_{20}(S) and the magnitude of the difference. The following relationships were also determined:

1. The provoking dose (ml) of 4.5% saline required to induce a 20% fall in FEV_1 (PD_{20}(S)) and the provoking dose (µmol) of methacholine required to produce a 20% fall in FEV_1 (PD_{20}(M));
2. PD_{20}(S) and the provoking cumulative ventilation (litres) required to induce a 20% fall in FEV_1 (PV_{20}(EVH));
3. PD_{20}(S) and maximum % fall in FEV_1 following exercise;
4. PD_{20}(S) and the provoking dose (ml) of water required to produce a 20% fall in FEV_1 ($PD_{20}(H_2O)$).

Both the Pearson's correlation coefficient, and the Spearman's rank order correlation coefficient were calculated. The Pearson's correlation coefficient was calculated using the subjects who had at least a 20% fall in FEV_1 in response to both challenges being compared. However, the Spearman's correlation coefficient was calculated with all subjects included. To calculate the rank order of sensitivity to challenge with 4.5% saline, methacholine, eucapnic hyperventilation or water, the subjects were ranked from lowest PD_{20} to highest PD_{20}. Where the response could not be ranked using the PD_{20}, the ranking was then based on the maximum % fall in FEV_1 recorded during challenge. For exercise, the subjects were ranked from the greatest to the least % fall in FEV_1 following challenge.

Results

Normal subjects

The mean maximum % fall (±SD) in FEV_1 after challenge with 4. 5% saline was 6±2%. This reduction, though small, was significant ($p<0.001$). The mean maximum % fall in peak expiratory flow rate (PEFR) was 15±7%. There was a significant correlation between the % fall in FEV_1 and the % fall in PEFR ($r=0.78$; $p<0.005$), but the reduction in PEFR was significantly greater than that for FEV_1 ($p<0.001$). The subjects experienced a moist and sometimes productive cough both during and following challenge, but this was not systematically documented.

Subjects with asthma

The distribution of PD_{20}(S) values for 4.5% saline in the asthmatic subjects is shown in (fig. 1). Solid symbols represent the values from the adults, and open symbols represent the values from the children. Of the 50 adults studied, 44 (88%) responded with at least a 20% reduction in FEV_1, and of the 18 children studied, 13 (72%) responded with at least a 20% reduction in FEV_1. Although the proportion of children who responded with at least a 20% fall in FEV_1 was less when compared with the adults, there was no difference in the distribution of the PD_{20} between adults and children in those subjects who did respond. For the adults, the geometric mean and 95% confidence intervals were 2.21 ml (1.52–3.20), and for the children were 2.45 ml (1.34–4.48). These values were not statistically significantly different by unpaired t–test.

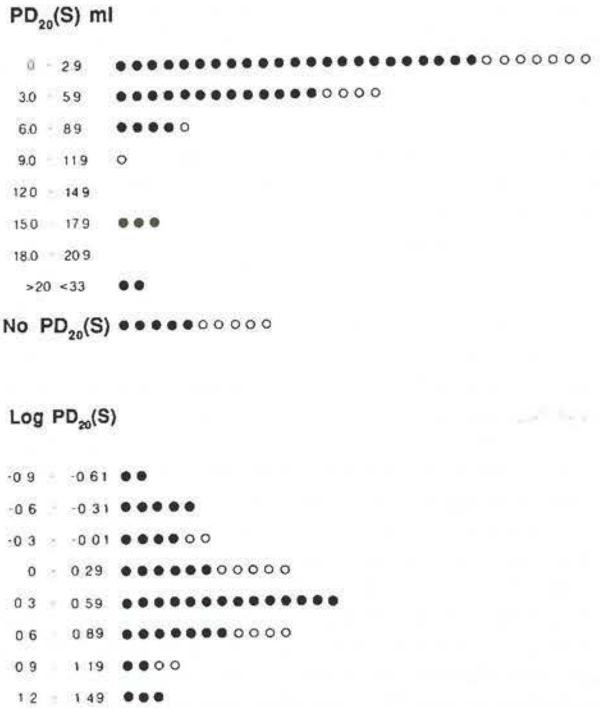

Fig. 1. – Individual values for the provoking dose of 4.5% saline required to induce a 20% fall in forced expiratory volume in one second (PD_{20}(S)) in 50 asthmatic adults and 18 asthmatic children. Values are expressed in number of ml delivered to the inspiratory port of the breathing valve. The values for PD_{20}(S) ml have been log-transformed in the bottom panel and demonstrate the normal distribution of the response in both the adults and children. ●: adults; ○: children.

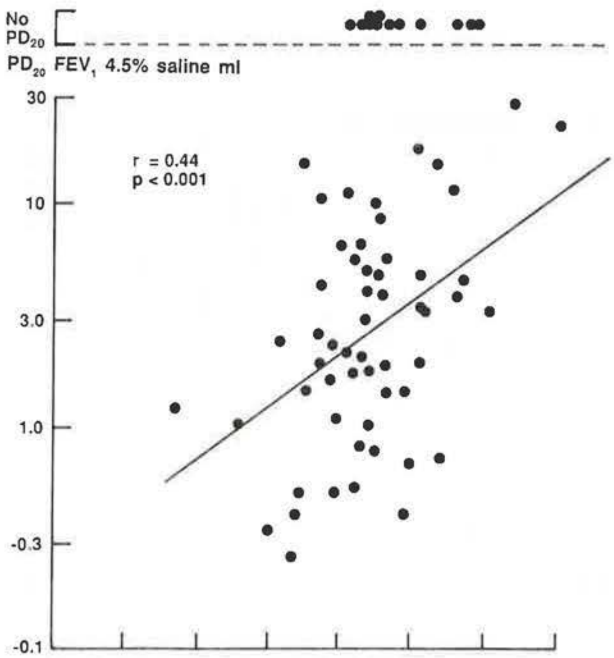

Fig. 2. – Individual values for PD_{20} FEV_1 obtained on 4.5% saline in relation to the pre-challenge FEV_1 expressed as a percentage of the predicted normal value.

The distribution of PD_{20} was skewed, with 75% of the subjects responding with a 20% fall in FEV_1 after 6.0 ml or less had been delivered to the inspiratory port of the valve, and 84% after less than 15 ml. This suggests that the distribution of PD_{20} values for 4.5% saline is log-normal in the asthmatic population. Figure 1 (lower panel) also shows the distribution after transformation to a logarithmic scale.

Unlike the responses recorded in the normal subjects there was no significant difference between the values for maximum % fall in FEV_1 (30±15%) and PEFR (30±17%) for the subjects with asthma. There was a correlation between baseline FEV_1 and PD_{20} 4.5% saline (r=0.44; p<0.001) (fig. 2). This relationship was weak, however, and in those subjects with a normal FEV_1 at rest (*i.e.* >80% of predicted) it would not be possible to predict sensitivity to 4.5% saline based on resting FEV_1.

The response to challenge with 4.5% saline was reproducible within 37 days. The geometric mean PD_{20}(S) and 95% confidence limits on the first challenge was 2.69 ml (1.06–6.85), and on the second was 3.36 ml (1.52–7.43). The coefficient of variation was 14% and the correlation coefficient for these values was 0.92 (p<0.001). The PD_{20} was reproducible to within 2 ml, regardless of the magnitude of the PD_{20} and there was no systematic difference between the two values measured after challenge using the analysis of Altman and Bland [18].

Responsiveness to 4.5% saline was significantly correlated (p<0.001) with responsiveness to methacholine, eucapnic voluntary hyperventilation and exercise, but was not significantly correlated with responsiveness to water. A summary of the results is given in figures 3–6.

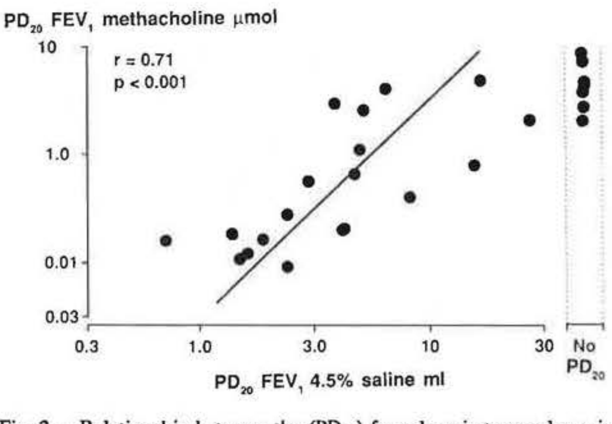

Fig. 3. – Relationship between the (PD_{20}) forced expiratory volume in one second (FEV_1) for 4.5% saline (ml) and the PD_{20} for methacholine (µmol) in 25 subjects with asthma. The regression line is shown for those subjects who responded to both challenges with at least a 20% fall in FEV_1.

Discussion

These studies indicate that hyperosmolarity is a stimulus that provokes airway narrowing in subjects with symptoms of severe to moderate asthma. Seventy five

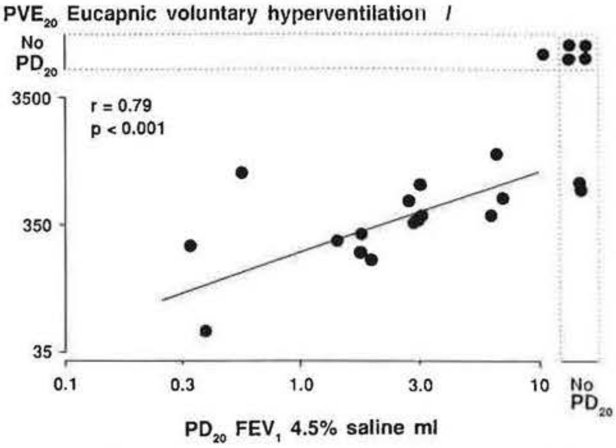

Fig. 4. – Relationship between the PD_{20} forced expiratory volume in one second (FEV_1) for 4.5% saline (ml) and eucapnic voluntary hyperventilation (cumulative volume of ventilation) in 22 subjects with asthma. The regression line is shown for those subjects who responded to both challenges with at least a 20% fall in FEV_1.

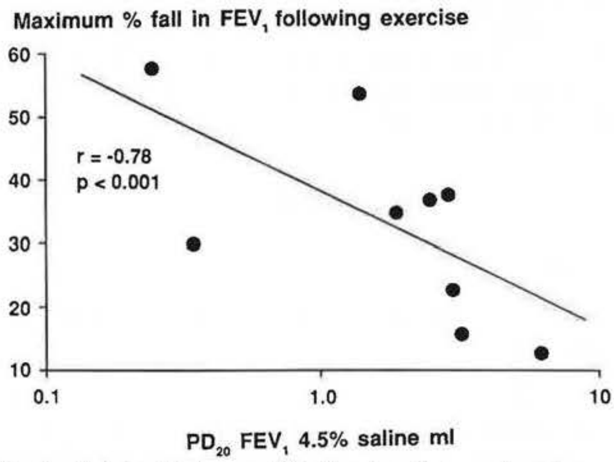

Fig. 5. – Relationship between PD_{20} forced expiratory volume in one second (FEV_1) for 4.5% saline (ml) and the maximum % fall in FEV_1 provoked by cycling exercise in 9 adult subjects with asthma. The regression line is shown.

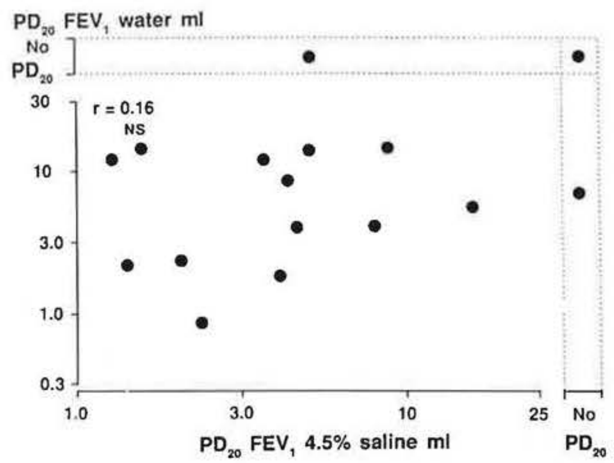

Fig. 6. – Relationship between the PD_{20} forced expiratory volume in one second (FEV_1) for 4.5% saline (ml) and the PD_{20} for water (ml) in 16 subjects with asthma.

percent of the asthmatic subjects responded with at least a 20% fall in FEV_1 after 6.0 ml or less had been delivered to the inspiratory port of the two-way valve. Of this dose, we have estimated that approximately 41% is actually inhaled [19], and of this 15–35% would be predicted to deposit within the airways below the pharynx [20, 21]. Thus, if 6 ml were delivered to the valve, approximately 0.6 ml would be predicted to deposit within the tracheobronchial tree, below the pharynx. When it is considered that the volume of fluid lining the first 5–10 generations of the respiratory tract is estimated to be 0.2–0.8 ml, there is considerable potential even for this small volume of aerosol to alter osmolarity within these more proximal airways [22].

In the normal subjects there was a small but significant decrease in expiratory flow rates which was not overcome by inhaling to total lung capacity before repeating the spirometry manoeuvre. The changes induced by the hyperosmolar aerosols appear to affect mostly the effort-dependent portion of the flow-volume curve since the PEFR was significantly more reduced than the FEV_1, and measurement of FEV_1 appears to distinguish better between normal subjects and those with bronchial hyperresponsiveness than does measurement of PEFR.

Several studies have reported that sensitivity to ultrasonically nebulized water in asthmatic subjects is considerably less in children than in adults [23, 24]. In our study the percentage of children who responded to 4.5% saline (72%) was slightly lower than the percentage of adults who responded (88%). However, the fact that the distribution of the PD_{20} in the children and the adults was similar suggests that the difference was probably due to the relatively small number of children we studied.

We found that sensitivity to 4.5% saline was correlated with sensitivity to methacholine, eucapnic voluntary hyperventilation and exercise. We were interested to find that of the 18 subjects who responded to both 4.5% saline and methacholine, 14 had a PD_{20} to methacholine that was less than 2 µmol; a value generally associated with symptoms of severe to moderate asthma [17]. The PD_{20}(M) in the remaining 4 subjects was 2–5 µmol; values associated with mild symptoms of asthma. Those subjects who did not respond to hyperosmolar saline had a PD_{20}(M) of 2–9 µmols; again values associated with either mild or past asthma. Thus, challenge with hyperosmolar saline is likely to identify patients with severe and moderate bronchial hyperresponsiveness to methacholine, but not mild airway hyperresponsiveness to methacholine.

The finding that there was no relationship between responsiveness to hyperosmolar saline and water is unusual, in that the response to most forms of bronchial provocation tests are correlated to a significant degree. However, Magyar *et al.* [25] have also reported that there is no significant relationship between responsiveness to hyperosmolar potassium chloride and water in asthmatic subjects. Similarly, sensitivity to water has been found to correlate poorly with sensitivity to carbachol [11], methacholine [23, 24], and histamine [11]. The reasons for the lack of correlation between the response to water and the responses to 4.5% saline and other pharmacological challenges are not known. However, they may relate to differences in the nature of mediators released or synthesized in response to these challenges. Challenges with non-isotonic aerosols may also influence the rate or direction of ion fluxes, and thus stimulate afferent nerves within the epithelium and submucosa. Such fluxes are likely to be different for 4.5% saline and water, and may contribute to the differences in responsiveness.

Conclusions and recommendations

During these studies we made two observations that have led us to modify our protocol for challenge with ultrasonically nebulized aerosols. Firstly, the output of the nebulizer was found to be constant with time (mean±SD, 1.2±0.2 ml·min⁻¹). In those subjects for whom the dose was metered by ventilation, this meant that subjects with a slow rate of ventilation received more aerosol than subjects with a fast rate of ventilation, even though the total ventilation was the same. Secondly, the duration of the challenge was typically 45 min in unresponsive subjects. However, 91% of the subjects who ultimately recorded a 20% fall in FEV_1 had done so after a total of up to 15 ml of nebulizer solution had been delivered to the valve. The time taken to deliver 15 ml of solution as aerosol and make the necessary spirometry measurements is between 20–25 min. The sensitivity of the test was only marginally improved by inhaling up to 33 ml of aerosol, despite the fact that the duration of the challenge was almost doubled by including this final volume. We have, therefore, modified the protocol in subsequent studies in order to deliver a standard dose to subjects and to shorten the duration of challenge. The doses are now metered by time, as follows: 30 s, 1, 2, 4 and 8 min, with spirometry measured 60 s after each challenge period. We have found that this form of the challenge typically takes less than 10 min to complete, but even in the less responsive or unresponsive subjects, the maximum duration for challenge is 25 min. In this form, the challenge is suitable for routine use in the laboratory as well as for research purposes.

It is important to note that we have reported the volume of aerosol delivered to the inspiratory port of the valve. This is because the delivery circuit significantly modifies the output of the nebulizer and the characteristics of the aerosol. We have determined that our Mistogen EN143A nebulizer has a maximum output of 3.5 $ml \cdot min^{-1}$, and that the aerosol produced is heterodispersed with a mass median aerodynamic diameter (MMAD) of 5.6 µm. With the delivery circuit attached, the maximum output is reduced to1.2 $ml \cdot min^{-1}$, and the aerosol becomes monodispersed, with a smaller MMAD of 3.6 µm. Presumably the larger droplets impact on the delivery circuit and the valves of the mouthpiece. Since the delivery circuit is likely to be different in each laboratory, we would recommend that the output reported is that which is measured with the breathing circuit and patient attached, rather than that measured at the outlet of the nebulizer canister. This is easily determined by weighing the nebulizer and the connecting tubing to the valve before and after the challenge.

It is possible that the rate of change of osmolarity is an important determinant of the response to hyperosmolar aerosols. If this is the case, then using a nebulizer with a higher output, or a more concentrated solution of saline may further shorten the time of challenge required. However, we have noted that increasing the concentration of saline above 4.5% is sometimes associated with nausea. The rate of change of osmolarity can also be increased by increasing the output of the nebulizer but this too may be associated with nausea and coughing in some patients.

We have used a 20% fall in FEV_1 as the cut-off point for a positive response. However, this criterion may be too stringent, since the maximum % fall in FEV_1 observed in the normal subjects was 10%. It is therefore possible that a 15% fall in FEV_1 should be used as the cut-off point for defining a positive response. However, even if we had defined a positive response as at least a 15% fall in FEV_1, the sensitivity of the test would not have been different in the children, and would have only marginally increased in the adults from 88 to 92%.

In conclusion, challenge with ultrasonically nebulized hyperosmolar 4.5% saline is a test which is likely to detect severe and moderate bronchial hyperresponsiveness, but is unlikely to detect hyperresponsiveness in subjects with symptoms of mild asthma. It is likely to give the same outcome in terms of diagnosis and assessment of asthma as challenge with either exercise or eucapnic voluntary hyperventilation and, because the test requires less effort on the part of the patient, it may be the preferable form of challenge.

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Provocation utilisant la solution saline hypertonique à 4.5% par inhalation chez des patients asthmatiques. Comparaison avec les réponses à l'hyperpnée, la méthacholine et l'eau. C.M. Smith, S.D. Anderson.

RÉSUMÉ: Des aérosols non-isotoniques sont utilisés de manière croissante pour les tests de provocation bronchique chez les malades asthmatiques. Nous avons investigué les modifications du ventilation expiratoire maximal seconde (VEMS) en réponse à une inhalation de solution saline à 4.5%, nébulisée par ultrasons chez 10 sujets normaux et chez 68 sujets asthmatiques. Une comparaison entre la sensibilité à cette provocation et à celle obtenue par la méthacholine, l'eau, l'effort et l'hyper ventilation volontaire eucapnique (EVH) a été conduite. Chez les sujets normaux, le VEMS est diminué de 6% (moyenne±1 SD) après inhalation de 33 ml d'aérosol. 84% des sujets asthmatiques ont une chute de VEMS supérieure à 20% après inhalation de solution saline à 4.5%. La dose provoquant une chute de 20% (PD_{20}) du VEMS est de 2.05 ml (1.34–4.48): moyenne géométrique+limite de confiance de 95%). La sensibilité à la solution saline à 4.5% par inhalation est en relation significative ($p<0.001$) avec la réactivité à la méthacholine, à l'effort, à EVH mais pas à l'eau. Chez des patients qui enregistrent une chute de 20% du VEMS aprés inhalation de solution saline à 4.5%, la PD_{20} à la méthacholine est inférieure à 2 µmol, réponse correspondant à une hyperréactivité bronchique modérée à sévère.

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