Eur Respir J, 1996, 9, 1363–1367
DOI: 10.1183/09031936.96.09071363
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European Respiratory Journal
ISSN 0903 - 1936

The influence of breathhold on peak expiratory flow in normal and asthmatic children

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The influence of breathhold on peak expiratory flow in normal and asthmatic children. I. Matsumoto, S. Walker, P.D. Sly. ©ERS Journals Ltd 1996.

ABSTRACT: We have previously demonstrated a 10% reduction in peak expiratory flow (PEF) in healthy adults following a breathhold at total lung capacity (TLC). This fall was attributed to dissipation of airway wall viscoelasticity, increasing airway wall compliance (C_{aw}).

To investigate this phenomenon in children and to determine whether the effect of breathhold would be greater in asthmatics than in normal children, 15 asthmatics and 14 normal children (aged 10–15 yrs) performed maximal post expirations (MFE) with and without a 5 s breathhold at TLC. The entire study was repeated following the inhalation of salbutamol (800 μg) to relax the airway smooth muscle (and to increase C_{aw}).

Breathhold at TLC resulted in a significant decrease in PEF both in the asthmatics (group mean fall 5.8%; $p<0.01$) and normal children (group mean fall 10.3%; $p<0.05$). Salbutamol diminished this fall, becoming nonsignificant in the normal children. Similar patterns were also seen in forced expiratory volume in one second (FEV_1) and in maximal expiratory flow at 50% vital capacity (V'_{50}).

These data are consistent with the proposal that breathhold at total lung capacity dissipated viscoelastic energy (increasing airway compliance) and decreased maximal expiratory flows both in normal and asthmatic children. They also demonstrate the need to standardize the forced vital capacity manoeuvre to decrease the variability in the flows recorded during the subsequent forced expiration.

Eur Respir J., 1996, 9, 1363–1367.

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Keywords: Airway mechanics
airway tone
forced expiration
pulmonary function tests
standardization
viscoelastic properties

Received: October 12 1995
Accepted after revision March 21 1996

Supported by a grant from the National Health and Medical Research Council of Australia.

The importance of the mechanical properties of the airways in the determination of the maximal flow (V'_{max}) that a given airway can carry is well-established [1–3]. DAWSON and ELLIOT [4] described the V'_{max} using wave speed (V'_{ws}) theory, which stated that the V'_{max}, in a nonrigid airway, was determined by the airway wall compliance (C_{aw}) and the airway cross-sectional area at the choke point of that airway. Recently, PEDERSEN *et al.* [5] argued that the peak expiratory flow (PEF) is likely to match V'_{ws} if forced expiratory flow profile has a well-defined peak. KANO *et al.* [6] have previously demonstrated a 10% reduction in PEF in healthy adults following a breathhold at total lung capacity (TLC). They suggested that this change could be attributed to a dissipation of airway wall viscoelasticity (stress-relaxation) increasing airway calibre and increasing C_{aw}. Whilst the increased airway calibre would be expected to increase the maximal flow sustainable, this was more than offset by the increased collapsibility of the airway during the subsequent forced expiration.

The previous studies [6] were undertaken in healthy adults. Few, if any, studies have compared the resting airway tone (or C_{aw}) in children and adults. However, airway tone has been described to be increased in some asthmatic subjects [7]. To investigate the influence of breathhold at TLC on PEF in children, we studied 15 asthmatics and 14 healthy children. To confirm that reductions in airway tone (resulting in increases in C_{aw}) were responsible for the reduction in PEF following a breathhold at TLC, the studies were repeated following inhalation of salbutamol.

Methods

Subjects

Fifteen asthmatic children and 14 healthy controls (aged 10–15 yrs) were studied. Anthropomorphic data are presented in table 1. Bronchodilators (but not corticosteroids) were discontinued for 6 h before the study.

Study protocol

Pulmonary function was measured in a whole body plethysmograph (SensorMedics Autobox 6200) using standard techniques which met American Thoracic Society (ATS) criteria. Subjects sat in the box with their neck in a neutral position, supporting their cheeks with their hands and wearing a noseclip. Maximal forced expiratory (MFE) manoeuvres were performed by instructing

Table 1. – Characteristics of the study group

	Asthmatic group (n=15)	Control group (n=14)
Sex M/F	10/5	7/7
Age yrs	12±2	12±2
Body weight kg	49±9	45±11
Body height cm	160±10	158±14
FVC % pred	103±16	92±12
PEF % pred	91±18	93±14
FEV_1 % pred	91±20	93±12
V'_{50} % pred	78±31**	105±30
RV/TLC %	31±9**	23±4

Values are presented as mean±SD. M: male; F: female; FVC: forced vital capacity; PEF: peak expiratory flow; FEV_1: forced expiratory volume in one second; V'_{50}: maximal expiratory flow at 50% vital capacity; RV/TLC: residual volume as percentage of total lung capacity; % pred: percentage of predicted value. **: $p<0.01$ *vs* control group.

subjects to inspire to TLC from end-tidal expiration as rapidly as possible, followed immediately by a maximal exhalation to residual volume (RV). After repeating this standard MFE manoeuvre in triplicate (meeting ATS criteria for reproducibility), subjects performed identical MFE manoeuvres (also in triplicate), but with a 5 s breathhold at TLC. In all MFE, the inspiratory manoeuvre was carried out in the same manner to avoid any differences in inspiratory volume history. RV and TLC were then measured using standard techniques. The entire study was repeated following the inhalation of salbutamol (800 μg), delivered by metered-dose inhales with aerosol holding chamber. For each set of measurements, the manoeuvre which had the largest value of PEF was used. Measurements of forced expiratory volume in one second (FEV_1), and maximal flow at 50% of vital capacity (V'_{50}) were also compared before and after breathhold.

Statistical analysis

Paired t-tests were used to determine significant changes in forced expiratory flows, before and after breathhold, and following salbutamol. To take into account variations in size between children, statistical analyses were performed on data expressed as percentage predicted [8]. Statistical significance was accepted at the 5% level. Throughout this paper, results are quoted as group mean±SD.

Results

Baseline lung function in both groups were within the normal range (table 1). In the asthmatic group, the RV/TLC ratio was significantly higher than in the control group ($p<0.05$). Age, body weight, height and other lung function variables did not differ significantly between the two groups.

PEF (% pred) decreased significantly following a 5 s breathhold at TLC in the asthmatic group (from 91±18 to 85±15% pred; $p<0.01$) (table 2), and in the control group (from 93±14 to 83±16% pred; $p<0.05$) (table 3). When expressed in absolute terms, these falls were 5.8±7.1% and 10.3±12.9%, respectively. There were no tendencies for the effect of breathhold to differ with gender either in the asthmatic (table 2) or the control groups (table 3). Pretreatment with salbutamol diminished the fall in PEF following breathhold in both groups; the post-salbutamol fall in PEF with breathhold was not significant in the control group (table 3). In contrast, in asthmatic children, there was still a significant fall in PEF following breathhold after salbutamol inhalation (table 2).

Similar patterns were seen in FEV_1 and V'_{50} following breathhold. In the asthmatic group, FEV_1 (% pred) fell from 91±20 to 89±20% pred ($p=0.018$) following breathhold (table 4). Falls in FEV_1 of similar magnitude (93±12 to 90±13% pred; $p=0.033$) were seen in the control group (table 5). After salbutamol inhalation, the group mean FEV_1 in the asthmatic group increased to 99±19% pred ($p=0.0001$); there was no significant increase in the control group. Breathhold led to a decrease in FEV_1 to 96±18% pred ($p=0.039$) in the asthmatic group (table 4). Again, the fall in FEV_1 with breathhold following salbutamol pretreatment was smaller in the control group and

Table 2. – Peak expiratory flow (PEF) for the asthmatic group

Subject No.	Sex	Baseline PEF $L\cdot s^{-1}$	Baseline PEF % pred	Post-breathhold PEF $L\cdot s^{-1}$	Post-breathhold PEF % pred	Salbutamol Baseline PEF $L\cdot s^{-1}$	Salbutamol Baseline PEF % pred	Salbutamol Post-breathhold PEF $L\cdot s^{-1}$	Salbutamol Post-breathhold PEF % pred	Medications
1	M	6.9	83	6.3	76	7.1	86	6.7	80	B
2	M	5.1	82	4.9	79	5.8	93	5.1	82	B
3	M	4.6	71	4.1	64	6.1	96	6.5	101	B,C
4	M	5.6	74	5.8	77	6.0	79	5.6	74	B,C
5	M	5.5	86	5.0	78	5.7	90	5.2	81	B
6	M	5.8	75	5.8	76	7.2	93	6.9	89	B
7	M	4.6	77	4.9	77	4.5	76	4.3	72	B
8	M	6.8	91	6.7	89	7.1	94	6.9	91	B,C
9	M	8.3	143	7.3	125	8.5	145	7.8	133	B,C
10	F	5.5	113	5.1	104	5.4	112	5.8	119	B
11	M	4.3	102	4.1	98	4.3	104	4.0	96	B
12	F	4.6	84	4.5	82	4.9	91	4.4	81	B
13	F	4.5	82	4.4	79	4.5	82	4.5	81	B
14	F	5.7	98	4.6	78	5.9	101	5.1	85	B,C
15	F	6.5	108	5.5	91	4.8	79	5.1	85	B,C,T
Mean		5.6	91	5.2**	85**	5.9	95	5.6#	90#	
SD			1.1	18	1.0	15	1.2	17	1.1	16

M: male; F: female; B: inhaled β-adrenergic; C: inhaled corticosteroid; T: oral theophylline; % pred: percentage of predicted value. **: $p<0.01$ *vs* baseline PEF without breathhold; #: $p<0.05$ *vs* post-salbutamol PEF without breathhold.

Table 3. – Peak expiratory flow (PEF) for the control group

Subject No.	Sex	Baseline PEF		Post-breathhold PEF		Salbutamol Baseline PEF		Salbutamol Post-breathhold PEF		Medications
		L·s^{-1}	% pred	L·s^{-1}	% pred	L·s^{-1}	% pred	L·s^{-1}	% pred	
1	F	4.9	101	3.0	61	4.3	90	4.1	85	-
2	M	6.7	92	6.5	88	6.5	89	6.0	82	-
3	F	4.8	93	5.0	97	4.7	91	4.9	95	-
4	M	8.4	97	6.9	80	8.0	92	7.5	86	-
5	F	5.0	79	5.7	89	5.7	90	5.8	91	-
6	M	4.7	78	4.4	73	5.0	84	4.9	81	-
7	M	7.7	97	6.6	84	7.1	89	6.8	86	-
8	F	7.1	126	6.9	122	7.1	125	7.0	123	-
9	F	6.6	107	4.7	77	6.1	100	4.3	69	-
10	F	2.9	65	2.6	59	2.8	65	3.1	70	-
11	M	5.9	86	5.2	76	5.7	84	5.3	77	-
12	F	6.4	87	5.6	77	6.2	85	5.9	81	-
13	F	5.1	100	5.3	105	5.2	103	5.1	101	-
14	F	4.3	93	3.7	81	3.8	82	4.1	89	-
Mean		5.7	93	5.2*	83*	5.6	91	5.3	87	
SD		1.4	14	1.3	16	1.4	13	1.2	13	

M: male; F: female; % pred: percentage of predicted value. *: $p<0.05$ *vs* baseline PEF without breathhold.

Table 4. – FEV_1 for the asthmatic group

Subject No.	Sex	Baseline FEV_1		Post-breathhold FEV_1		Salbutamol Baseline FEV_1		Salbutamol Post-breathhold FEV_1	
		L	% pred	L	% pred	L	% pred	L	% pred
1	M	3.4	84	3.2	80	3.7	91	3.6	88
2	M	2.5	91	2.4	88	2.9	106	2.6	95
3	M	2.3	78	2.3	77	2.2	76	2.4	81
4	M	2.6	72	2.7	76	2.9	80	2.9	80
5	M	2.5	87	2.4	84	2.8	97	2.7	94
6	M	2.3	63	2.1	57	3.0	81	3.1	82
7	M	2.2	82	2.1	80	2.4	90	2.3	88
8	M	3.5	96	3.5	96	3.8	107	3.8	106
9	M	3.9	151	3.9	154	4.1	159	4.0	154
10	F	2.3	106	2.2	100	2.5	114	2.5	113
11	M	2.1	101	2.1	100	2.2	108	1.9	92
12	F	1.9	79	1.8	75	2.1	87	1.9	80
13	F	2.2	87	2.1	85	2.4	96	2.4	93
14	F	2.4	91	2.3	87	2.7	100	2.4	90
15	F	2.8	99	2.7	95	2.8	96	2.9	101
Mean		2.6	91	2.5*	89*	2.8	99	2.8#	96#
SD		0.6	20	0.6	20	0.6	19	0.6	18

M: male; F: female; % pred: percentage of predicted value. *: $p<0.05$ *vs* baseline FEV_1 without breathhold; #: $p<0.05$ *vs* post-salbutamol FEV_1 without breathhold.

Table 5. – FEV_1 for the control group

Subject No.	Sex	Baseline FEV_1		Post-breathhold FEV_1		Salbutamol Baseline FEV_1		Salbutamol Post-breathhold FEV_1	
		L	% pred	L	% pred	L	% pred	L	% pred
1	F	2.2	96	1.8	77	2.2	94	2.0	87
2	M	3.6	104	3.6	104	3.8	108	3.8	108
3	F	2.5	108	2.6	113	2.6	116	2.6	114
4	M	4.5	103	4.3	97	4.1	92	3.7	85
5	F	2.8	93	2.6	87	3.0	101	3.0	101
6	M	2.4	88	2.3	85	2.5	93	2.6	98
7	M	3.8	99	3.6	93	4.0	104	3.7	96
8	F	3.1	118	3.0	113	3.1	118	2.9	112
9	F	2.7	95	2.7	95	2.9	101	2.7	96
10	F	1.5	80	1.4	74	1.3	72	1.3	72
11	M	2.6	82	2.5	79	2.7	84	2.6	82
12	M	2.6	74	2.5	72	2.7	78	2.7	78
13	M	2.0	90	2.0	91	2.0	89	2.1	93
14	F	1.6	78	1.6	78	1.6	81	1.7	83
Mean		2.7	93	2.6*	90*	2.8	95	2.7	93
SD		0.8	12	0.8	13	0.8	14	0.7	12

M: male; F: female; % pred: percentage of predicted value. *: $p<0.05$ *vs* baseline FEV_1 without breathhold.

did not reach statistical significance (95±14 to 93±12% pred; p=0.096) (table 5). The changes in V'_{50} following breathhold in both groups were more variable than the changes in PEF or in FEV_1 and did not reach statistical significance in either group. The group mean values for V'_{50} before and after breathhold were 2.78±0.95 and 2.65±1.01 $L \cdot s^{-1}$ for the asthmatic group and 3.79±1.17 and 3.51±1.14 $L \cdot s^{-1}$ for the control group. Following salbutamol inhalation, these values were 3.31±0.77 and 3.17±0.81 $L \cdot s^{-1}$ for the asthmatic group and 4.0±1.02 and 3.73±1.03 $L \cdot s^{-1}$ for the control group.

Discussion

The results of the present study demonstrate that a 5 s breathhold at TLC results in a 5.8% fall in PEF in asthmatic children and a 10.3% fall in PEF in normal children (when expressed in absolute terms). When expressed as % predicted, these falls become 6.3% and 9.6%, respectively. These falls in PEF were of similar magnitude to those previously observed in adults [6]. Following salbutamol inhalation, the falls in PEF were diminished in both groups, becoming nonsignificant in the normal group. Similar patterns of results were seen in FEV_1 and in V'_{50}, achieving statistical significance for FEV_1. KANO *et al*. [6] explained the fall in PEF in adults by speculating that breathhold leads to stress relaxation of the tissues in the airway wall, with a resulting increase in C_{aw}. They argued against this effect being due to stress relaxation of the pulmonary parenchyma. The results of the present study are consistent with this idea. Under baseline conditions, there were no qualitative differences between the asthmatic and control groups. The falls in PEF, FEV_1 and V'_{50} following breathhold at TLC were of similar magnitude in both groups. This could be interpreted as suggesting that the viscoelastic properties were similar between the asthmatic and control groups. However, we have no way of determining whether the breathhold at TLC has dissipated all, or just some of, the viscoelastic energy stored in the airway wall.

The resting tone of airway smooth muscle is likely to be a major contributor to the viscoelastic properties of the airway wall. Previous studies have demonstrated a variable bronchoconstriction or bronchodilatation following a deep inspiration in asthmatic but not control subjects [9–11]. These data have been explained in terms of differences in the relative hysteresis of airways and parenchyma: in normal subjects, airway hysteresis is reported to be greater than parenchymal hysteresis, whereas the pattern varies with asthmatic subjects with the likelihood of greater parenchymal hysteresis increasing with disease severity [10]. These data are interpreted as suggesting that asthmatics have impaired airway hysteresis [10], presumably due to increased airway tone or stiffer airways. The increase in FEV_1 seen following bronchodilator in the asthmatic group but not in the control group in the present study, is consistent with this idea, *i.e.* increased airway tone (secondary to smooth muscle contraction) in the asthmatics.

By relaxing airway smooth muscle, salbutamol will have decreased airway tone and increased C_{aw}. This could result in a decrease in forced expiratory flows, as has been reported in some children with cystic fibrosis [12]. In fact, there was a tendency for PEF to be lower in the control group following salbutamol inhalation (table 3). In the asthmatic group, this effect is hidden by the bronchodilator effects of decreased airway smooth muscle contraction. A breathhold at TLC following salbutamol pretreatment still led to a significant fall in PEF and in FEV_1 in the asthmatic group. These data are consistent with residual airway tone following bronchodilator in the asthmatics. In contrast, the falls in forced expiratory flows with breathhold following salbutamol pretreatment in the control group were smaller and no longer statistically significant, suggesting that salbutamol abolished most of the airway tone in this group.

D'ANGELO and co-workers [13, 14] have reported that the time course of the preceding inspiration influences the flows obtained during the subsequent forced expiratory manoeuvre, both in normal adults [13] and in adults with chronic obstructive pulmonary disease [14]. They demonstrated that PEF and FEV_1 were increased with manoeuvres that included a rapid inspiration, and attributed their results to "stretching of viscoelastic elements during inspiration resulting in an increase in the effective elastic recoil during the subsequent FVC manoeuvre". However, scrutiny of their methods reveals that the major differences in forced expiratory flows were likely to be due to a 4–6 s breathhold at TLC. The force driving expiration during a FVC manoeuvre is a combination of the elastic recoil of the respiratory system and the force provided by the expiratory muscles. As demonstrated by KANO *et al*. [6], the force provided by the expiratory muscles during the FVC manoeuvre far exceeds that required to achieve maximal flow, provided a reasonable effort is produced. Under these circumstances, it is hard to imagine that an increase in "effective elastic recoil" is going to contribute much to the forced expiratory flows. In the present study, the inspiratory manoeuvre was standardized (maximal inspiratory effort producing a rapid inspiration), eliminating any potential influence from our results.

The practical implications of the results of the present study are an increase in variability of forced expiratory flows unless the FVC manoeuvres are adequately standardized. In absolute terms, the falls in PEF following breathhold averaged approximately 10% in the control group and 6% in the asthmatic group. However, the range of falls in PEF extended from -12 to 39% in the control group and -7 to 20% in the asthmatic group. The falls in FEV_1 were somewhat smaller, being 4% (-4 to 20%) and 3% (-5 to 9%) in the control and asthmatic groups, respectively. Using a pneumotachograph spirometer, one can inhale through the spirometer and exhale without a breathhold. However, this is not possible with some other designs. While the reproducibility and repeatability of this phenomenon has not been studied, the results of the present study clearly demonstrate that the presence or absence of a breathhold at TLC will influence the flows obtained during the subsequent FVC manoeuvre. Therefore, fully reporting the methodology used, including whether subjects were specifically instructed not to breathhold at TLC, will be necessary to adequately interpret the data, particularly following a therapeutic or investigational intervention.

In summary, the results of the present study are consistent with our previous conclusion that a breathhold at

total lung capacity dissipates viscoelastic energy in the airway wall, resulting in an increased airway compliance and a decreased maximal flow. This effect is seen both in normal and asthmatic children. Pretreatment with salbutamol diminishes this effect, supporting the proposed mechanism.

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