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Influence of water content of inspired air during and after exercise on induced bronchoconstriction

L-P. Boulet, H. Turcotte

Influence of water content of inspired air during and after exercise on induced bronchoconstriction. L-P. Boulet, H. Turcotte.

ABSTRACT: This study looked at the influence of inspired air water content on exercise-induced bronchospasm (EIB).

On separate days, 12 mild asthmatics (4M, 8F), aged 18–39 yrs (mean: 27 yrs), performed four six minute steady-state exercises on ergometer at 80% of their maximum workload. Exercises were randomized to the following inspired air conditions: dry air (0% relative humidity (RH)) during exercise followed by dry (DD) or humid air (100% RH) (DH) after exercise, humid air during exercise followed by dry (HD) or humid air (HH). Room temperature was kept constant (22±1°C) at all visits. Forced expiratory volume in one second (FEV_1) was measured before and every 5 min for 25 min after exercise.

Ventilation ($\dot{V}E$) was not significantly different whether the exercise was done under dry or humid air. There was a residual bronchodilatation at the end of exercises performed in humid air, while at this time FEV_1 was already lower than baseline when exercise was done in dry air conditions. The maximal fall in FEV_1(%) following exercise was significantly greater after those performed in dry air: DD (29±5.6%) and DH (30±5.8%) than in humid air: HD (12±4.9%) and HH (20±4.9%) ($p<0.05$). The time-course of recovery from bronchoconstriction was significantly improved when inhaling dry air after exercise. However, the difference found in the maximal % fall in FEV_1 after exercise when recovery was in dry compared to humid air did not achieve statistical significance.

In conclusion, EIB is influenced by the changes in water content during and after exercise. Bronchoconstriction following exercise is minimal if exercise is done in humid air and recovery in dry air, and maximal if the exercise is performed in dry air and recovery in humid air.

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Most asthmatics develop a bronchoconstriction after exercise. This has been attributed to heat and water exchange required to condition the inspired air during exercise-induced hyperventilation [1, 2]. More recently, McFadden *et al.* [3] showed that inspired air conditions during recovery after exercise could also influence the degree of exercise-induced bronchospasm (EIB). They showed that bronchoconstriction induced by exercise while breathing cold dry air was worse when warm humid air was inhaled during the recovery period, compared to when cold dry air was inhaled during recovery. They suggested that this resulted from a rapid rewarming of the airways, with reactive hyperaemia and possibly oedema.

The observations of Mihalyka *et al.* [4] were in keeping with the latter observations. They showed that inspired air water content during the recovery from isocapnic hyperventilation (IH) was a major determinant of the magnitude of IH-induced bronchoconstriction: after hyperventilation in warm dry air, recovery in warm humid air induced a greater response than a recovery in warm dry air. They suggested that the condensation of water during recovery in humid air could have induced an airway hypoosmolarity, thus adding another stimulus to airway narrowing. This last study, however, explored neither the effects of inspired air conditions during recovery of an IH in humid air, nor the effect of exercise. Although isocapnic hyperventilation is usually a good model of exercise-induced asthma, other factors may influence this response.

Furthermore, Smith *et al.* [5] were unable to reproduce the observations of McFadden *et al.* [3]. They did not find an enhancement of EIB with rapid rewarming.

This study was done to determine the influence of acute changes in water content of inspired air during and immediately after exercise on the magnitude of EIB.

Table 1. – Subject characteristics

No.	Age yrs	Sex	FEV_1 *l* (% pred)	FVC *l* (% pred)	PC_{20} $mg \cdot ml^{-1}$
1	33	F	1.87 (63.6)	2.75 (79.3)	0.06
2	24	F	3.34 (109.5)	3.74 (103.3)	4.1
3	28	M	3.29 (121.0)	3.96 (80.8)	0.61
4	23	F	2.60 (82.8)	3.29 (88.0)	0.97
5	22	F	2.01 (65.0)	2.91 (79.5)	1.2
6	32	M	3.09 (81.7)	5.39 (115.4)	1.6
7	24	F	3.01 (103.4)	3.52 (102.6)	3.3
8	18	F	4.03 (119.9)	4.28 (115.4)	8.4
9	27	F	2.79 (87.2)	3.75 (94.0)	4.6
10	39	M	4.10 (100.0)	5.37 (105.3)	3.3
11	19	M	3.23 (78.4)	4.71 (99.4)	2.6
12	34	F	2.55 (84.7)	3.49 (98.3)	0.73
Mean	26.9	8F, 4M	2.99 (91.4)	3.93 (96.8)	1.57
±SEM	±1.9		±.20 (±5.6)	±.25 (±37)	(1.08, 2.29)

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; PC_{20}: provocation concentration of methacholine producing a 20% fall in FEV_1.

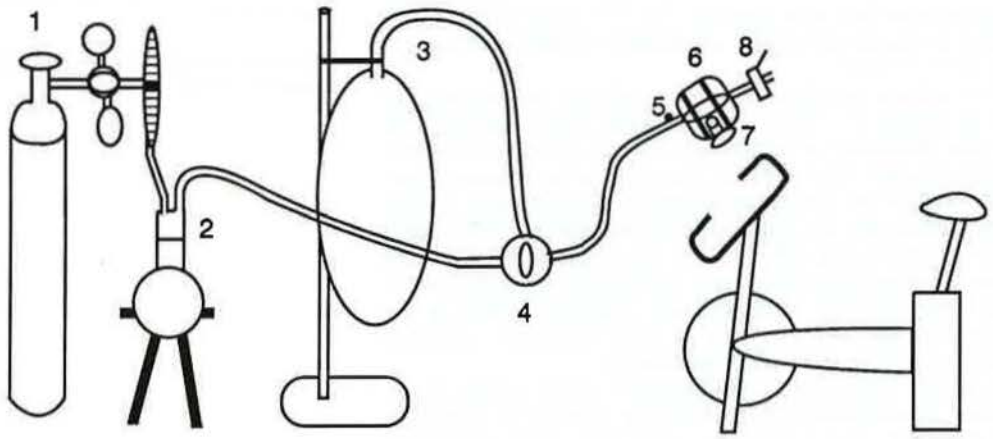

Fig. 1. – Experimental set-up. Medical air (1) is humidified through an ultrasonic nebulizer (2) and dry air stored in a meteorological balloon (3). Either dry or humidified air is delivered to the respiratory valve (6) and mouthpience (7) *via* a two-way valve (4). Temperature and humidity are recorded throughout the study with a probe (5) at the entry of the respiratory valve. Ventilation is measured by a pneumotachograph (8) on the expiratory circuit.

Methods

Subjects

We studied 12 mild asthmatics (4M, 8F), nonsmokers, aged 18 to 39 yrs (mean: 26.9 yrs) with exercise-induced asthma (table 1). Baseline provocation concentration producing a 20% fall in forced expiratory volume in one second (PC_{20}) ranged from 0.06–8.4 $mg \cdot ml^{-1}$. Asthma was stable and controlled by a β_2-agonist on demand, added to inhaled beclomethasone in two (400 and 1,000 $\mu g \cdot day^{-1}$) and budesonide (800 $\mu g \cdot day^{-1}$) in one subject. None took cromoglycate, theophylline or oral corticosteroids. The study was approved by our local Ethics Committee and signed informed consent was obtained from the subjects.

Study design

Expiratory flows were measured with a PFT II Vitalograph spirometer. During and after exercise, the subjects breathed through a mouthpiece connected to a Otis-McKerrow respiratory valve (Collins cat. no 021023) (fig. 1). The inspiratory line was connected to a two-way valve allowing the delivery of either dry or humid air and a rapid change from one to the other without dry air or humid air contamination. Dry air (Canox) was humidified through a $Mist O_2 gen$ ultrasonic nebulizer containing a normal saline solution and adjusted to give saturated inspired air; no aerosol was inhaled directly. The osmolarity of the inspired air was measured at the mouthpiece on four occasions (mean: 320.5±19.0 mosm) and compared to the osmolarity of the normal saline

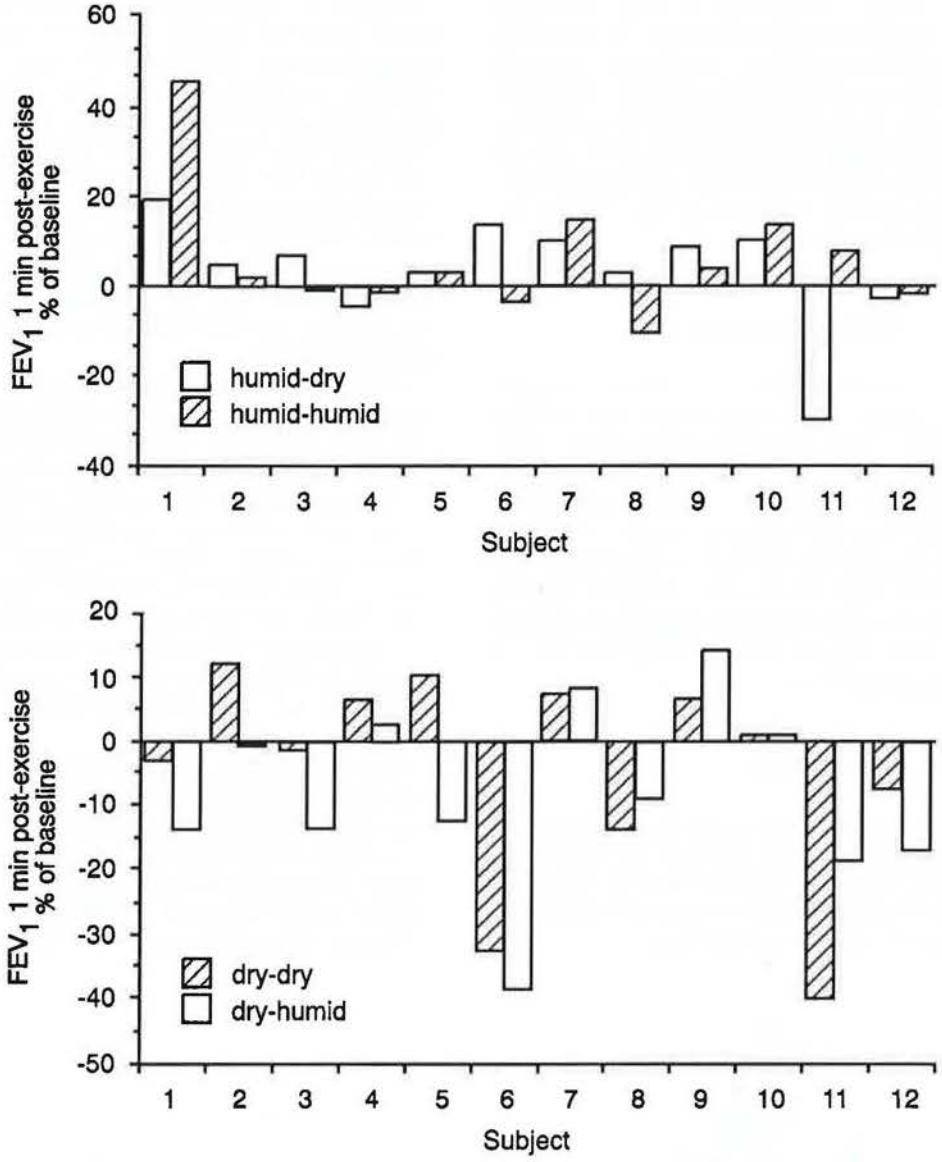

Fig. 2. – One minute following the end of exercise, most subjects who had performed the exercise in humid air were still in their bronchodilatation phase, while most of those who had performed the exercise in dry air were bronchoconstricted. FEV_1: forced expiratory volume in one second.

solution (292.5±0.6 mosm). This trivial increase in salt concentration should not contribute to the fall in forced expiratory volume in one second (FEV_1) observed in humid air [6–8]. Dry air was inhaled from a 50 *l* meteorological balloon filled and continuously replenished during exercise and recovery to supply enough air for the whole study. Ventilation was measured on the expiratory branch with a Fleisch No. 3 pneumotachograph. Relative humidity of the inspired air was measured with an Omega RH-201 hygrometer, at the entry of the respiratory valve, during exercise and recovery periods. Temperature was also measured at the inspiratory port.

The subjects came to the laboratory on five different days within the period of one month. Before the tests, β_2-agonists were withheld for 8 h. At each visit, baseline FEV_1 had to be greater or equal to 60% of predicted or the test was postponed. On the first visit, subjects had a physical examination and an evaluation of the stability of their asthma. To determine the maximum workload, a progressive incremental exercise test was performed on ergometer according to the method described by JONES [9]. Airway responsiveness to methacholine was measured according to method described by COCKCROFT *et al.* [10]. On the four other days, at the same time of the day, a six minute steady-state exercise was performed on ergometer at 80% of the maximum workload of each subject as determined on day 1. Room temperature and humidity were kept constant (22±1°C and 40±10%, respectively) at all visits. Before each test, subjects remained at room temperature and humidity for 30 min and baseline FEV_1 was measured. Before each exercise, FEV_1 was obtained after breathing in the circuit for 5 min. FEV_1 was measured immediately and 1, 3, 5,

7, 9, 11, 13, 15, 20 and 25 min after exercise. For these measurements, subjects inspired through the breathing circuit, expired in the spirometer's mouthpiece and then immediately returned to the breathing circuit. Exercises were randomized to the following inspired air conditions: dry air (0% RH) during exercise followed by dry air (DD) or humid air (DH) (100% RH) during recovery, humid air during exercise followed by dry (HD) or humid air (HH) after exercise.

Statistical analysis

Baseline FEV_1 on the four study days were compared by analysis of variance. For each subject, pre-exercise and baseline FEV_1 were compared using paired t-test. The % fall in FEV_1 from 1 to 25 min after exercise were compared by analysis of variance. A Student-Newman-Keuls test (SNK) was performed to identify difference between groups. Results are expressed as mean±SEM. The global means of the four curves were compared using the GLM procedure of a SAS statistical package with group and subject as class and the polynomial model FEV_1 = time time^2 class group [11].

Results

Baseline FEV_1 was ≥60% predicted in all subjects and was not significantly different between the study days (HH: 2.99±0.19 *l*, 91±5.0%; HD: 3.14±0.19 *l*, 96±4.9%; DD: 3.08±0.20 *l*, 94±5.4%; DH: 3.14±0.19 *l*, 96±4.8%; p>0.05, analysis of variance (ANOVA)).

Inspired air temperature was stable (±1°C) during the study; humidity rapidly reached 0 or 100% and then remained stable. Baseline FEV_1 was not significantly different on the four study days. The mean fall in pre-exercise FEV_1 from baseline was 2.3±1.6% (HH: 3.4±1.9%, HD: 3.8±1.3%, DD: 1.2±1.8%, DH: 0.9±1.2%). The fall in FEV_1 measured after 5 min breathing dry or humid air immediately before exercise was not significantly different between the groups inhaling dry or humid air (p=0.11, paired t-test). Minute ventilation (V_E) during exercise was not significantly different whether the exercise was done with dry or humid air (52.0±3.0 *vs* 50.0±6.6 $l \cdot min^{-1}$).

Immediately after exercise, subjects who exercised in humid air showed residual bronchodilatation, while at this time those who exercised in dry air conditions had already started to bronchoconstrict (fig. 2).

The maximal % fall in FEV_1 following exercises performed in dry air was significantly greater than when exercising in humid air (mean maximal fall in FEV_1±SEM): HD: 12.3±4.9%, HH: 19.8±4.9%, DD: 28.6±5.6% and DH: 30.0±5.8%; SNK (p<0.05). No significant difference was found in the maximal % fall in FEV_1 when recovery was in dry compared to humid air: HH and HD (p>0.05), DH and DD (p>0.05).

The time-course of post-exercise FEV_1 for the four inspired air conditions is illustrated in figure 3. Significant differences between the four study days were found only when comparing FEV_1 at the same time post-challenge. Bronchoconstriction was minimal on HD day; it was of larger magnitude on HH day, but significantly different from HD only at 9 min. On DD day,

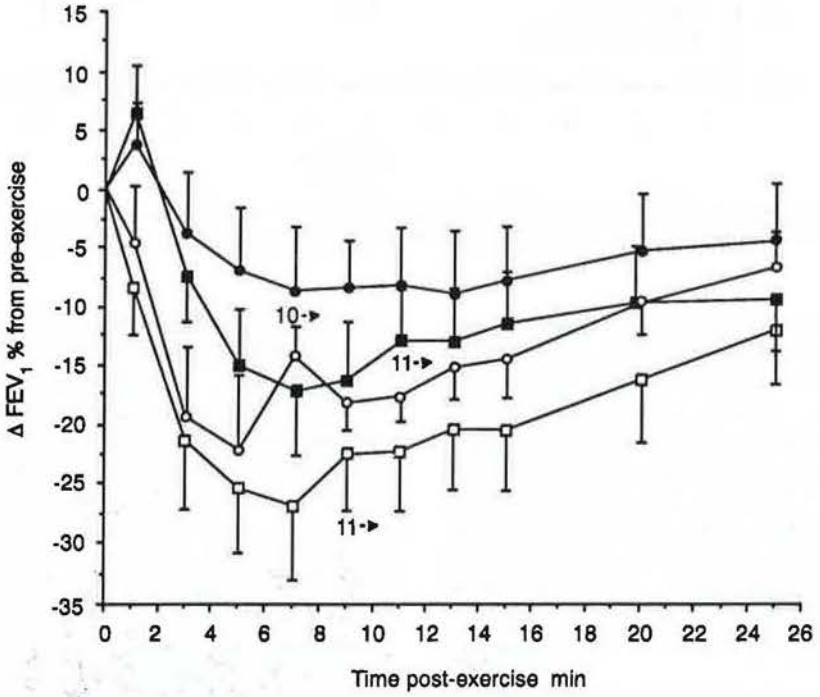

Fig. 3. – Time-course of the fall in FEV_1 and recovery for the four inspired air conditions. Exercises performed in dry air induced more bronchoconstriction than those performed in humid air. The fall in FEV_1 was less when the recovery occurred in dry air, whether the exercise was done in dry or humid air. (10->, 11->: from this point, mean of only 10 or 11 subjects). FEV_1: forced expiratory volume in one second. —□— : dry humid (DH); —○— : dry dry (DD); —■— : humid humid (HH); —●— : humid dry (HD).

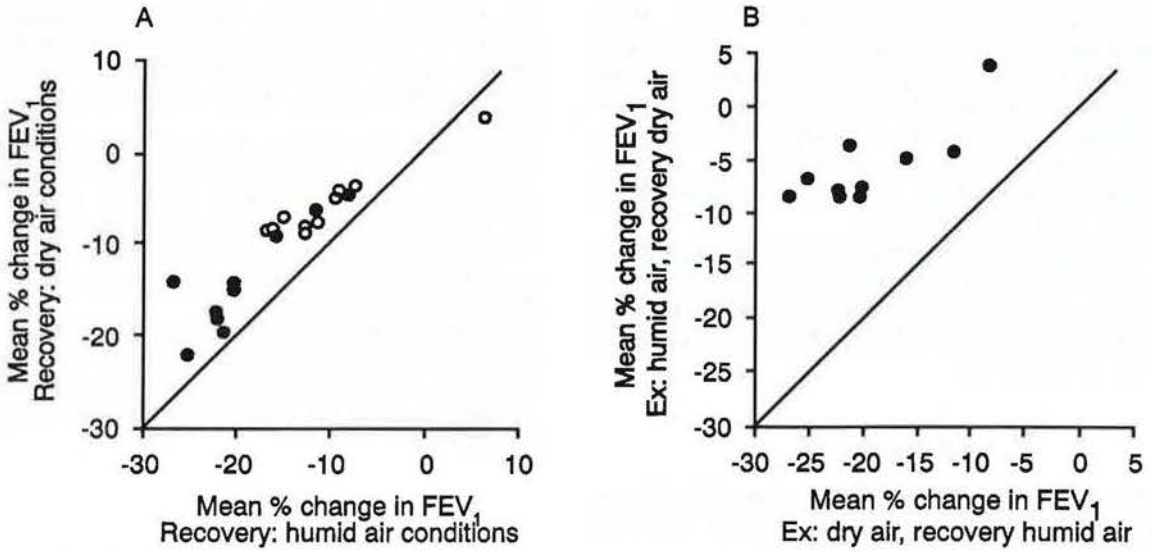

Fig. 4. – A) From 1–25 min post-exercise, recovery was better in dry air conditions, whether the exericse was done in dry or humid air. O: exercise in humid air; ●: exercise in dry air. B) The worst condition was to exercise in dry air and to recover in humid air, while the best was to exercise in humid air and recover in dry air. FEV_1: forced expiratory volume in one second; Ex: exercise.

bronchoconstriction was greater than on day HH, but the difference was significantly different only at 3 min. The maximal fall in FEV_1 was observed after DH air conditions. This was significantly different from DD day only at 7 min (SNK: $p<0.05$).

The global means of the four curves were, however, significantly different (HH: -10.46, HD: -5.64, DD: -14.12 and DH: -19.47, SNK: $p<0.05$), suggesting a difference between each of the four groups for the time-course of recovery. Recovery from bronchoconstriction was improved when inhaling dry air, whether the exercise was done in dry or humid air (fig. 4A). The worst condition was to exercise in dry air and recover in humid air, while the best was to exercise in humid air and recover in dry air (fig. 4B).

Discussion

This study shows that in asthmatics, changes in water content of inspired air during exercise and recovery from exercise modify the magnitude of exercise-induced bronchospasm. Bronchoconstriction was maximal if the effort was performed breathing dry air and recovery breathing humid air. Moreover, although the difference was not significant at each time point of the curves, the time-course of recovery was altered by the conditions of the air breathed during recovery, the recovery being slower in humid air.

McFadden *et al.* [3] have suggested that vasoconstriction of the bronchial circulation is induced by exercise in cold air and that the vasoconstriction is followed by a post-exercise hyperaemia. A rapid rewarming of the airways, amplified if warm air is inhaled during the recovery, could then contribute to EIB. There is, however, evidence that vasodilatation occurs during airway cooling and drying, suggesting that these other factors may also be involved [12, 13].

Stimulus for EIB is perhaps more related to hyperosmolarity of airway secretions due to water loss than to heat loss [14–17]. Inhalation of hyperosmolar saline can induce a bronchoconstriction which correlates well with the degree of response to exercise [6]. The present study shows that airway obstruction is worse when exercise is conducted in dry air. This may be due to an increased airway hyperosmolarity following exercise-induced hyperventilation. The total water loss may increase when inhaling dry air during exercise. This may explain why subjects had already begun to bronchoconstrict immediately after the end of exercise, while most of those inhaling humid air during the exercise were still in their bronchodilatation phase.

Our results, showing a worsening of EIB when recovery is in humid air, are in keeping with the report from Mihalyka *et al.* [4] and suggest that water gradient is a major determinant of the airway response to exercise. Mihalyka *et al.* suggested that condensation of water on a cool airway may lower osmolarity and that this hypoosmolarity of airway fluid may act as an additional stimulus to airway narrowing. An increase in mucus secretion could also be part of the explanation.

Since bronchoconstriction was minimal when subjects inhaled dry air after exercising in humid air, the increase in EIB when humid air is inhaled after an exercise in dry air does not seem to be due to the humidity "gradient" *per se* or to the acute change in airway osmolarity. This is in keeping with the data of McFadden *et al.* suggesting that factors that increase the speed of rewarming or reduce the heat and water loss during recovery from exercise increase EIB.

Humidification of the airways during exercise protects against the effects of dry air inhaled in the recovery period. The mechanism involved in this protective effect may simply be a reduction in water loss from the airways.

These observations have clinical implications as changes in inhaled air humidity conditions during and

after exercise may influence the degree of EIB. If an asthmatic performs an exercise outdoors when the air is cold and dry then recovers indoors in hot and humid air, EIB may be worse than if he recovers outdoors. Clinical observations, such as those reporting that exercise-induced asthma is often less severe in a dry and cool rather than in a warmer and more humid environment are in keeping with our results [18].

In conclusion, EIB is influenced by the changes in water content during and after exercise. Bronchoconstriction following exercise is greater if the exercise is performed in dry air and this effect is worsened by recovery in humid air.

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Influence du contenu aqueux de l'air inspiré pendant et après l'effort sur la bronchoconstriction induite. L-P. Boulet, H. Turcotte.

RÉSUMÉ: Cette étude a examiné l'influence du contenu hydrique de l'air inspiré sur le bronchospasme induit par l'effort.

A des jours séparés, 12 asthmatiques légers (4H, 8F), âgés de 18 à 39 ans (moyenne: 27), ont subi des efforts en état stable de six minutes, à 4 reprises, sur bicyclette ergométrique, à 80% de leur charge maximale. Les exercices ont été exécutés de façon randomisée dans les conditions suivantes de l'air inspiré: air sec [humidité relative (RH) de 0%] du cours de l'effort, suivi d'air sec (DD) ou humide (RH 100%) (DH) après l'effort, d'air humide pendant l'effort, suivi d'air sec (HD) ou d'air humide (HH). La température de la chambre a été maintenue constante à 22° à toutes les visites. Le VEMS a été mesuré avant et toutes les 5 minutes pendant 25 minutes après l'effort.

La ventilation ($\dot{V}_E$) n'est pas significativement différente, que l'exercice soit fait sous air sec ou humide. L'on a noté une bronchodilatation résiduelle à la fin des efforts pratiqués en air humide, alors qu'à ce moment le VEMS était déjà inférieur à la valeur basale quand l'exercice était exécuté dans des conditions d'air sec. La chute maximale du VEMS en % après l'effort est significativement plus grande après les efforts dans l'air sec: DD (29±5.6%) et DH (30±5.8%) que dans l'air humide (HD (12±4.9%) et HH (20±4.9%) ($p<0.05$). Le décours de la récupération après bronchoconstriction est amélioré de façon significative par l'inhalation d'air sec après l'effort. Toutefois, la différence trouvée dans la chute maximale du VEMS en % après l'effort, lorsque la récupération a lieu en air sec par comparaison à l'air humide, n'atteint pas le niveau de signification statistique.

En conclusion, le bronchospasme induit par l'effort est influencé par les modifications du contenu en eau de l'air inspiré pendant et après l'effort. La bronchoconstriction après l'effort est minimale quand l'effort est exécuté dans l'air humide et la récupération assurée sous air sec. Par contre, elle est maximale quand l'effort est exécuté dans l'air sec et la récupération dans l'air humide.

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