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GENDER AND PERCEPTION OF DYSPNEA

THE ROLE OF THE VARIATION IN THE FORCED EXPIRATORY VOLUME IN ONE SECOND

CARLOS A. NIGRO, MARIA EUGENIA ALAIS, EDGARDO E. RHODIUS

Laboratorio Pulmonar, Hospital Alemán, Buenos Aires, Argentina

Abstract During bronchoconstriction women perceive more breathlessness than men. The aims of study were 1) to evaluate if quality of dyspnea in bronchoconstriction was different in women and men 2) to assess if gender difference in the perception of dyspnea could be related to the level of bronchoconstriction. 457 subjects (257 women) inhaled methacholine to a 20% decrease in FEV_1, or 32 mg/ml. Dyspnea was evaluated using the modified Borg scale and a list of expressions of dyspnea. Borg scores were recorded immediately before the challenge test baseline and at the maximum FEV_1 decrease. The prevalence of descriptors of dyspnea reported by women and men was similar. Dyspnea was related to the level of FEV_1 (ΔFEV_1: OR 1.05, 95%CI 1.01-1.09, p 0.0095), females (OR 2.90, 95%CI 1.33-6.33, p 0.0072), younger subjects (OR 0.93, 95%CI 0.89-0.97, p 0.0013) and body mass index (BMI) (OR 1.11, 95%CI 1.01-1.23, p 0.023). As the FEV_1 fell less than 20% from baseline, only the ΔFEV_1 was significantly associated with dyspnea (ΔFEV_1:OR 1.15, 95%CI 1.07-1.24, p 0.0002). Instead, if the FEV_1 fell higher $\geq$ 20%, the presence of dyspnea was related to the degree of bronchoconstriction (ΔFEV_1: OR 1.04, 95%CI 1.01-1.09, p 0.0187), females (OR 3.02, 95%CI 1.36-6.72, p 0.0067), younger subjects (OR 0.92, 95%CI 0.88-0.96, p 0.0007) and BMI (OR 1.12, 95%CI 1.01-1.23, p 0.023). The quality of dyspnea during the bronchoconstriction was similar in women and men; women showed a higher perception of dyspnea than men only when the FEV_1 fell more than 20% from baseline.

Key words: asthma, breathlessness, bronchoconstriction, bronchial hypereactivity, dyspnea, perception of airway narrowing

Resumen ***Género y percepción de disnea: el rol de la variación del volumen espiratorio forzado en un segundo.*** Durante la broncoconstricción las mujeres perciben más disnea que los hombres. Los objetivos del estudio fueron evaluar: 1) si la calidad de la disnea durante la broncoconstricción fue diferente en mujeres y hombres, 2) si la diferencia entre sexos en la percepción de disnea podría relacionarse al nivel de broncoconstricción. 457 sujetos (257 mujeres) inhalaron metacolina hasta un descenso del $FEV_1 \geq$ 20% o 32 mg/ml. La disnea fue evaluada mediante escala de Borg y una lista de expresiones de disnea. El Borg fue registrado en forma basal y con el máximo descenso del FEV_1. La frecuencia de descriptores de disnea informados por mujeres y hombres fue similar. La disnea estuvo relacionada al grado de broncoconstricción (ΔFEV_1: OR 1.05, 95%CI 1.01-1.09, p 0.0095), sexo femenino (OR 2.90, 95%CI 1.33-6.33, p 0.0072), edad (OR 0.93, 95%CI 0.89-0.97, p0.0013) e índice de masa corporal (IMC) (OR 1.11, 95%CI 1.01-1.23, p 0.023). Cuando el FEV_1 cayó menos del 20%, solo el ΔFEV_1 se asoció con disnea (ΔFEV_1: OR 1.15, 95%CI 1.07-1.24, p 0.0002). En tanto que si el FEV_1 cayó $\geq$ del 20%, la disnea estuvo relacionada al grado de broncoconstricción (ΔFEV_1: OR 1.04, 95%CI 1.01-1.09, p 0.0187), sexo femenino (OR 3.02, 95%CI 1.36-6.72, p 0.0067), edad (OR 0.92, 95%CI 0.88-0.96, p 0.0007) e IMC (OR 1.12, 95%CI 1.01-1.23, p 0.023). La calidad de la disnea durante la broncoconstricción fue similar en hombres y mujeres; las mujeres tuvieron mayor percepción de disnea que los hombres solo cuando el FEV_1 descendió más del 20%.

Palabras clave: asma, disnea, broncoconstricción, hiperreactividad bronquial, percepción de la broncoconstricción

Asthmatic patients vary greatly in the perception of their symptoms of bronchial obstruction[1-4]. Discrepancies in perception may be due to differences in the disease severity, in methods assessing the dyspnea, or in cultural characteristics of the study population[5]. The influence of sex in the perception of dyspnea during induced bronchoconstriction has been evaluated in several reports that used explanatory multiple regression models[6-10]. After adjusting for potential confounders, most of the studies showed that women had a higher perception of breathlessness than men[6-9]. These observations are in accordance with some reports that found females used more rescue medications for asthma[11], reported more symptoms and had poorer quality of life than men at the

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Dirección postal: Carlos A. Nigro, Avda. Pedro Goyena 620 - 3° B - 1424 Buenos Aires, Argentina
Fax: (54-11) 4827-7000, interno 2722 e-mail: cnigro@intramed.net

same level of airflow obstruction[12, 13]. Gender differences in airway behaviour and in the clinical manifestations of airway disease occur throughout the human life span and are related to biological as well as sociocultural factors[14]. The term dysanapsis has been used to describe this disproportionate but physiologically normal growth between the airways and the lung parenchyma. Mead et al[15] estimated that the airways of men were approximately 17% larger in diameter than the airways of women, and speculated that the adult sex difference in airway size develops relatively late in the growth phase. The relation RV/TLC, an indicator of hyperinflation is higher in females than males and increases with age[16]. Because these biological gender differences, we postulated that the perception of dyspnea reported during a bronchospasm would be different in women and men. To investigate this question, we studied the dyspnea in women and men in whom bronchoconstriction was induced by inhalation of methacholine.

Materials and Methods

We consecutively studied all subjects who attended the pulmonary laboratory from January 2002 to January 2005 to undergo a methacholine challenge test due to clinical suspicion of bronchial asthma. No comprehensive clinical details about individual patients were obtained. A routine medication questionnaire disclosed that 280 had been prescribed inhaled steroids and/or inhaled β_2-agonists and 59 had been prescribed oral theophylline or leukotriene receptor antagonist for the relief of symptoms. The inclusion criteria were: 1) Baseline $FEV_1 \geq 60\%$ of predicted value taken from Morris and associates[17], 2) Age > 12 years and 3) Informed consent. Exclusions included: 1) Deterioration in respiratory symptoms requiring any alteration in the subject's usual medication within 3 wk prior to the study, 2) Medical contraindications to methacholine challenge testing (heart disease, hypertension, thyroid disease, urinary obstruction, pregnancy, or lactation) and 3) Absence of any previous experience of sensory testing. The total number of subjects initially evaluated was 519 out of whom only 457 fulfilled inclusion and exclusion criteria (257 women and 200 men). The Hospital Alemán's institutional review board approved the study protocol.

All subjects were asked to abstain from drinks containing caffeine and from oral theophylline and leukotriene receptor antagonist for 48 hours before the challenge, and from all inhaled medications for 24 hours prior to the methacholine test. Spirometry was measured by a flow sensing spirometer connected to a computer for data analysis (Med Graphics 1085DL-Medical Graphics Co, St Paul, MN, USA). Each patient underwent an abbreviated methacholine challenge test. Baseline FEV_1 was taken as the best of three technically satisfactory measurements performed immediately before the challenge. After baseline spirometry had been made sequential, concentrations of buffered methacholine chloride were administered at 5-min intervals. When the baseline spirometry showed airflow obstruction ($FEV_1/FVC < 0.75$), the starting concentration of methacholine was 0.125 mg/ml. In all other instances, the initial concentration of methacholine was 0.5 mg/ml. We skipped one concentration of methacholine if the fall in FEV_1 respect to the baseline value was lower than 5%. Each dose of methacholine was inhaled by tidal breathing for 2 min using a mouthpiece with noseclips. Solutions were delivered in 3 ml aliquots via a nebulizer DeVilbiss 646 (DeVilbiss Co, Somerset, PA, USA) calibrated to deliver 0.13-0.16 ml/min. and driven by compressed air. Spirometry was measured 30 and 90 s after each dose, and values from the flow-volume loop with the highest post dose FEV_1 were used for analysis. The test was terminated when the FEV_1 decreased by ≥ 20% of the highest baseline value or when the greater dose of methacholine had been administered. Bronchial responsiveness, expressed as the concentration of methacholine producing a 20% fall in FEV_1 from the highest baseline FEV_1 (PC_{20}) was calculated[18].

Dyspnea was defined as the presence of one or more of the descriptors listed in Table 1. The list of terms for dyspnea in the Spanish language included in this study was compiled by reviewing the literature and consulting patients. The literal translation of most of the main descriptors previously published for the English language was included[19-21]. The 8-item list of dyspnea descriptors was given to the subjects by the investigator. Subjects were instructed to read the entire list of 8 phrases before making their choices. Patients were asked to choose one or more of the phrases that best described their "breathing discomfort" at that time. Each subject was aware of the option of choosing none of the phrases. Following this, subjects were instructed to grade the intensity of their breathlessness by assigning a numerical value using a modified Borg scale[22] and its end points were anchored so that 0 and 10 were used to indicate "no breathlessness" and "the most breathlessness that the subject had experienced, respectively. All subjects were asked to ignore other methacholine related

TABLE 1.– *Descriptors of dyspnea in English/Spanish*

My chest feels tight. My chest is constricted	Siento mi pecho cerrado o apretado
My breath does not go in all the way. Breathing in more difficult	Mi respiración no entra bien. Tengo dificultad para entrar el aire
My breathing requires more work. My breathing requires effort	Mi respiración requiere más esfuerzo. Mi respiración requiere esfuerzo
My breath does not go out all the way. Breathing out more difficult	Mi respiración no sale bien. Tengo dificultad para sacar el aire
My breathing is heavy	Mi respiración es pesada
I feel that I am smothering	Siento que me estoy asfixiando
I feel that I am suffocating	Siento que me estoy sofocando o agitando
Shortness of breath	Falta de aire

symptoms such as cough, salivation, flushing or irritation of the nose or throat. Borg scores were recorded immediately before the challenge test baseline and at the maximum decrease of FEV_1[8].

Comparisons of predicted FEV_1, forced vital capacity (FVC), FEV_1/FVC and age were performed using unpaired Student's t test. Comparisons between or within groups for variables such as maximal Borg scores and the reduction in FEV_1 as a percentage of the baseline value (ΔFEV_1) were made using Mann-Whitney U- test. The frequency of symptoms reported by men and women during bronchoconstriction was compared using the Chi-Square test. All tests were performed two-sided, and a p value of < 0.05 was considered to be significant. Multiple logistic regression analysis was performed to determine the relationship between the Borg (depend variable 0 = no, 1 = yes) and the following independent variables: age, sex (1 = female, 0 = male), baseline predicted FEV_1, baseline predicted FVC, relation FEV_1/FVC, body mass index (BMI), ΔFEV_1 and PC_{20} (0 = ≥ 2 MG/ML, 1 = < 2 MG/ML). In order to evaluate if the gender difference in the perception of dyspnea was associated with the level of FEV_1, we divided the subjects in two groups according to the ΔFEV_1 (ΔFEV_1 < 20% and ≥ 20%) and multiple logistic regression analysis was applied. In this case the PC_{20} was not included in the model because it could not be calculated in ΔFEV_1 < 20% group.

Results

One hundred and seventy patients showed a fall in the baseline FEV_1 lower than 20% (37%) and two hundred and eighty seven (63%) had a decrease in baseline FEV_1 equal or higher than 20%. At the beginning of the methacholine challenge, no patients had dyspnea. The median change in the Borg score was 4 (25-75th percentile 0-6) and the median reduction in FEV_1 as a percentage of baseline value was 23% (25-75th percentile 15-33). Fifty patients (27 women) had baseline mild airway obstruction (FEV_1 between 60 to 80% of predicted and FEV_1/FVC < 0.75). The baseline predicted FEV_1 was similar in women than men (mean FEV_1: 70.4 ± 6.1% vs. 72.5 ± 5%, p 0.19). The female and male patients' characteristic and score Borg changes during methacholine challenges are shown in Table 2. The age and ΔFEV_1 were lightly greater in women than men (43.2 ± 17.7 *vs.* 37.2 ± 16.8 years, p 0.0003; 23.6%, 25-75th percentile 16 - 35 *vs.* 20.5%, 25-75th percentile 13.4-32, p 0.04) and the BMI was higher

TABLE 2.– *Female and male patient characteristic and score Borg changes during methacholine challenges*

	Female	Male	p
Number	257	200	
Age (yrs) #	43.2 ± 17.7	37.2 ± 16.8	< 0.0003
BMI (Kg/m^2) #	24.2 ± 4.6	25.4 ± 4	< 0.002
FVC (% pred.) #	97.1 ± 12.5	94.7 ± 14.2	0.06
FEV_1 (% pred.) #	91.7 ± 13.5	89.5 ± 13.8	0.09
FEV_1/FVC #	78.9 ± 7.6	77.3 ± 8.5	0.53
PC_{20} Mch. (mg/ml)*	3.5 (1.6 – 5.8)	3.5 (2.2 – 6.2)	0.59
ΔFEV_1 (% of baseline)*	23.6 (16 – 35)	20.5 (13.4 – 32)	0.04
Maximal Borg*	5 (0 – 6)	4 (0 – 6)	0.18

*Data are expressed as # the mean ± SD or * median (25% -75% percentiles). ΔFEV_1 (% of baseline): reduction in FEV_1 as a percentage of the baseline value.*

TABLE 3.– *Quality of dyspnea during methacholine challenges*

Descriptors of dyspnea	Female (%)	Male (%)	p
My chest feels tight / My chest is constricted	88.7	85.5	NS
My breath does not go in all the way / Breathing in more difficult	86.4	83.9	NS
My breathing requires more work / My breathing requires effort	90.9	83.9	NS
My breath does not go out all the way / Breathing out more difficult	74.6	75	NS
My breathing is heavy	76.3	82.2	NS
I feel that I am smothering	84.2	82.2	NS
I feel that I am suffocating	76.8	77.4	NS
Breathless	82.5	79	NS

in men than women (25.4 ± 4 *vs.* 24.2 ± 4.6, $p < 0.002$). The maximal Borg score was similar in females and males (5, 25-75th percentile 0-6 *vs.* 4, 25-75th percentile 0-6, p 0.18). At maximal bronchoconstriction, 314 out of 457 subjects (69%) reported the presence of one or more descriptors of dyspnea whereas 143 (31%) reported none (71 females and 72 males). The frequency of descriptors of dyspnea selected by women and men during the methacholine challenge was similar (Table 3). After adjusting for possible confounding variables all patients showed that dyspnea was related to the level of decline in FEV_1 (ΔFEV_1: OR 1.05, 95%CI 1.01-1.09, p 0.0095), females (OR 2.90, 95%CI 1.33-6.33, p 0.0072), younger subjects (OR 0.93, 95%CI 0.89-0.97, p 0.0013) and BMI (OR 1.11, 95%CI 1.01-1.23, p 0.023) (Table 4). Similarly, after excluding patients with airflow obstruction, dyspnea was associated with the same variables that the entire population (ΔFEV_1: OR 1.05, 95%CI 1.01-1.09, p 0.0095; females: OR 2.1, 95%CI 1.16-3.9, p 0.015; age: OR 0.95, 95%CI 0.92-0.98, p 0.0023, BMI: OR 1.09, 95%CI 1.01-1.17, p 0.019). Table 5 shows the characteristics of groups according to the ΔFEV_1. When bronchoconstriction was mild ($\Delta FEV_1 < 20\%$) only the ΔFEV_1 was significantly associated with dyspnea (ΔFEV_1: OR 1.15, 95%CI 1.07-1.24, p 0.0002) (Table 6). On the other hand, when bronchoconstriction was more severe ($\Delta FEV_1 \geq 20\%$), the presence of dyspnea was related to the degree of bronchoconstriction (ΔFEV_1: OR 1.04, 95%CI 1.01-1.09, p 0.0187), females (OR 3.02, 95%CI 1.36-6.72, p 0.0067), younger subjects (OR 0.92, 95%CI 0.88-0.96, p 0.0007) and BMI (OR 1.12, 95%CI 1.01-1.23, p 0.023) (Table 7).

TABLE 4.– *Multiple logistic regression analysis in all patients relating the Borg to the ΔFEV_1, age, baseline spirometry, BMI, sex and PC_{20}*

Variable	Coefficient	Std Err	OR	95%CI	p
ΔFEV_1 (% of baseline)	0.051	0.019	1.05	1.01 - 1.09	0.0095
Age	-0.069	0.021	0.93	0.89 - 0.97	0.0013
FEV_1/FVC	-0.181	0.136	0.83	0.64 - 1.09	0.1816
FEV_1 (% pred.)	0.127	0.123	1.13	0.89 - 1.45	0.3021
FVC (% pred.)	-0.111	0.118	0.89	0.70 - 1.13	0.3451
BMI	0.109	0.048	1.11	1.01 - 1.23	0.0230
Sex	1.067	0.397	2.90	1.33 - 6.33	0.0072
PC_{20}	-0.036	0.358	0.96	0.478 - 1.95	0.9196

OR: odds ratio. 95%CI: 95% confidence interval. ΔFEV_1 (% of baseline): reduction in FEV_1 as a percentage of the baseline value; Std Err: Standard Error.

TABLE 5.– *Characteristics of the analyzed subgroups*

	$\Delta FEV_1 < 20\%$	$\Delta FEV_1 \geq 20\%$	p
Number	170 (37.2%)	287 (62.8%)	< 0.0001
Age (yrs)#	44.5 ± 17	38.3 ± 17.5	< 0.0002
Female/male	87/83	170/117	
BMI (Kg/m²)#	25.1 ± 4.2	24.5 ± 4.5	0.16
FVC (% pred.)#	97.3 ± 14.5	95.4 ± 12.5	0.14
FEV_1 (% pred.)#	95 ± 13.8	88.2 ± 13	< 0.0001
FEV_1/FVC#	80.8 ± 7.2	77.5 ± 8.3	< 0.0001
ΔFEV_1 (% of baseline)*	12.3 (7.9 - 15.7)	29.5 (23.6 - 41.3)	< 0.0001
Maximal Borg*	0 (0 - 5)	5 (3 - 7)	< 0,0001
Borg = 0	96 (56%)	47 (16%)	< 0.0001

*Data are expressed as # the mean ± SD or * median (25% -75% percentiles). ΔFEV_1 (% of baseline): reduction in FEV_1 as a percentage of the baseline value.*

TABLE 6.– *Multiple logistic regression analysis in patients with* $\Delta FEV_1 < 20$ *relating the Borg to the* ΔFEV_1*, age, baseline spirometry, BMI and sex*

Variable	Coefficient	Std Err	OR	95%CI	p
ΔFEV_1 (% of baseline)	0.143	0.038	1.15	1.07 - 1.24	0.0002
Age	-0.020	0.019	0.97	0.94 - 1.01	0.2995
FEV_1/FVC	0.135	0.125	1.14	0.89 - 1.46	0.2784
FEV_1 (% pred.)	-0.169	0.105	0.84	0.68 - 1.03	0.1088
FVC (% pred.)	0.139	0.100	1.14	0.94 - 1.40	0.1667
BMI	0.043	0.047	1.04	0.95 - 1.14	0.3622
Sex	0.447	0.402	1.56	0.71 - 3.44	0.2657

OR: odds ratio. 95%CI: 95% confidence interval. ΔFEV_1 *(% of baseline): reduction in* FEV_1 *as a percentage of the baseline value.*

TABLE 7.– *Multiple logistic regression analysis in patients with* $\Delta FEV_1 \geq 20$ *relating the Borg to the ΔFEV1, age, baseline spirometry, BMI and sex*

Variable	Coefficient	Std Err	OR	95%CI	p
ΔFEV_1 (% of baseline)	0.047	0.020	1.04	1.01 - 1.09	0.0187
Age	-0.075	0.022	0.92	0.88 - 0.96	0.0007
FEV_1/FVC	-0.185	0.139	0.83	0.63 - 1.09	0.1835
FEV_1 (% pred.)	0.133	0.126	1.14	0.89 - 1.46	0.2917
FVC (% pred.)	-0.112	0.121	0.89	0.70 - 1.12	0.3554
BMI	0.114	0.049	1.12	1.01- 1.23	0.0203
Sex	1.106	0.407	3.02	1.35 - 6.72	0.0067

OR: odds ratio. 95%CI: 95% confidence interval. ΔFEV_1 *(% of baseline): reduction in* FEV_1 *as a percentage of the baseline value.*

Discussion

The main findings of study were that 1) acute bronchoconstriction produce the same quality of dyspnea in women and men, and 2) women had more probability to report dyspnea than men when the FEV_1 descended more than 20%. Although the gender differences previously published in the airways caliber and lung size, we could not demonstrate that the prevalence of the different descriptors of dyspnea reported at the maximum bronchoconstriction was different in women and men (Table 4). On the other hand, as the FEV_1 decreased less than 20% (median 12%), the perception of dyspnea was similar in both genders. Instead, when the FEV_1 reduced ≥ 20% (median 29%) from baseline, women reported more frequently dyspnea than men (Tables 6 and 7). The association between gender and perception of dyspnea could be related to the close relationship between the sensation of breathlessness and respiratory effort. Lougheed et al[23] showed that the inspiratory effort quantified by tidal change of oesophageal pressure as a percentage of maximal inspiratory pressure (ΔPes / %PImax) progressively increased during induced bronchoconstriction by 17± 3 cm H_2O or 31 ± 6 % of maximal inspiratory pressure (PImax). Likewise, they observed that ΔPes /%PImax was the strongest single correlate of breathlessness ($r = 0.84$, $p < 0.001$). Although we did not measure respiratory effort, we speculate that at the same level of bronchoconstriction, women possibly perform more inspiratory effort (ΔPes/%PImax) than men because their PImax is about 30% lower than in males[24]. Thus, women would have more probability to perceive the sensation of breathlessness than men. Possibly, at low levels of bronchoconstriction, the inspiratory effort in both genders is not enough to stimulate respiratory tract receptors and provoke an increase in the central motor command output with the consequent sense of breathlessness[24, 25]. As FEV_1 falls more and the mechanical load on the system increases, women would have more probabilities to perceive dyspnea because their Pes/PImax (i.e., an estimation of central motor command output) is higher than men's at the same level of bronchoconstriction. Weiner et al[26] studied the influence of gender and inspiratory muscle training on the perception of dyspnea (POD) in patients with mild asthma. For the same level of predicted FEV_1, the Borg score sum and the mean daily β_2-agonist consumption in women were significantly higher than in men (Borg: 13.1 vs. 10.1, $p < 0.01$; β_2-agonist consumption: 3.2 vs. 2, $p < 0.05$). Besides, the increase in the PImax after inspiratory muscle training in asthmatic women was associated with a statistically significant decrease in their dyspnea perception to a similar level as in male subjects.

The identification of factors that influence the perception of bronchoconstriction is clinically important. Patients with low perception of dyspnea are at an increased risk of future hospitalization, a near-fatal asthma attack, or even death from an asthma attack[27]. We have showed that men have a lower perception of bronchoconstriction than women at higher levels of bronchoconstriction. Therefore, we could hypothesize that the male gender is a risk factor that may potentially increase morbidity and mortality by asthma. Several studies are in line with this hypothesis. Desideri et al[28] and Romano et al[29] showed that death rates for asthma were significantly higher in males than females. Campbell et al[30] showed that in near fatal asthma cases, patients tended to be younger, were more likely to be males, and less likely to have concurrent medical condition. Similarly, in comparison with those admitted with acute asthma, patients with severe life threatening asthma were more likely to be men[31]. However, other publications have showed the predominance of women in severe episodes or mortality by asthma[32-37]. Finally, in order to avoid a potential dangerous lack of perception in the male group of asthmatic patients, education programmes which should include self monitoring of peak expiratory flow, regular medical review and written action plans could reduce hospitalizations, emergency room visits or unscheduled doctor visits and could improve quality of life[38, 39].

This study had several limitations: 1) The main predictive variable of breathlessness during a challenge test is the inspiratory capacity, which represents the level of hyperinflation. Since the ΔFEV_1 was similar in women and men and there is a close relationship between the percentage of fall FEV_1 and inspiratory capacity[23] then it is probable that the degree of hyperinflation in both groups had not been substantially different. 2) We did not measure oxygen saturation (SO_2), end tidal CO_2 ($ETCO_2$) and breathing pattern during the bronchoconstriction with methacholine. These parameters could have modified the perception of breathlessness in women and men during the challenge test. Despite this, these variables do not change significantly during bronchoconstriction induced by methacholine[23]. 3) The methacholine challenge has its limitations as it does not reflect the real life situation of episodes of spontaneous bronchoconstriction. However, several publications have showed that the perception of spontaneously bronchoconstriction is higher in women than men[11-13, 40]. 4) We did not know the smoking history and the proportion of patients with COPD in our sample study. It is probable that we have included subjects with COPD in our patient population. However, we think this has not influenced our results. In fact, Ekici et al[7] demonstrated that men with asthma, chronic bronchitis and bronchiectasis showed a lower perception of breathlessness than women. On the other hand, Brand et al[9] evaluated the perception of airway obstruction during histamine-induced bronchoconstriction in a heterogeneous population that included patients with and without smoking history and asthmatics subjects. The relation of possible confounding variables to an increase in Borg score was assessed in a multiple logistic regression. An increase in Borg score after histamine challenge was related to younger age, level of bronchial hyperreactivity, positive skin test and female sex. Similarly, de Torres et al[41] compared gender differences in the clinical expression of Chronic Obstructive Pulmonary Disease (COPD) patients. Even though women had the same FEV_1, better oxygenation, better $PaCO_2$, and fewer comorbidities than men, they had a higher degree of dyspnea (Modified Medical Research Council scale > 2, 28% vs. 6%, p 0.05). Finally, we used a list of sentences for dyspnea that were a literal translation of most of the main descriptors published for the English language. It could have introduced a bias that modifies the perception of dyspnea. However, in the Spanish language[42], most of the sentences describing breathlessness were the literal translation of most of the main dyspnea descriptors used in the English language. Besides, the reproducibility of Spanish and English dyspnea descriptors in patients with chronic lung disease was similar[20, 21, 42].

In conclusion, the quality of dyspnea in bronchoconstriction was similar in women and men, but the likelihood to perceive dyspnea with moderate to severe airway obstruction was higher in female than male. At lesser degrees of bronchoconstriction, both males and females had a similar perception of breathlessness.

Conflicts of interests: We declare there were no conflicts of interest related to this investigation.

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