

Evolution Over Time in Over Perceivers of Dyspnea in Asthma

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OBJECTIVE: In previous studies we identified a subgroup of patients whose perception of breathlessness was exaggerated during acute bronchoconstriction and who were termed "over perceivers" or "hyperperceivers." In this study we aimed to determine whether such over perception is sporadic or stable over time. We also examined whether there is an association between over perception of dyspnea and hyperventilation syndrome.

PATIENTS AND METHODS: The subjects were 22 stable asthmatics (11 men, 11 women) who had been over perceivers of dyspnea in a study 9 years earlier. After a medical history was taken, a patient performed forced spirometry and a severity classification was made according to the criteria of the Global Initiative for Asthma (GINA). A bronchial histamine challenge was then administered to measure dose-related perception of dyspnea on a Borg scale, according to a procedure that was similar to the one used 9 years earlier by the same investigator. The patients were also asked for a subjective assessment of the severity of their asthma (scale, 0-10) and to respond to items on the Nijmegen hyperventilation questionnaire and the trait form of the State-Trait Anxiety Inventory.

RESULTS: The overall perception of severity of disease, level of anxiety, and perception of dyspnea at rest were lower after 9 years ($P < .001$). No change was observed in bronchial hyperresponsiveness (dose of inhaled histamine required to provoke a 20% decline in forced expiratory volume in the first second [FEV₁]-PD₂₀) or objective parameters of severity (FEV₁ and GINA classification). Fourteen asthmatics (64%) were still over perceivers and the other patients had changed: 6 were normal perceivers and 2 were "poor perceivers." Only subjective perception of disease severity improved for the patients who were still over perceivers; the other patients, on the other hand, showed improvements in subjective assessments, objective ones (except PD₂₀), and anxiety. Finally, those who remained over perceivers had higher scores for anxiety (24 vs 15; $P < .05$) and hyperventilation (18 vs 13; $P =$ not significant).

CONCLUSIONS: Most over perceivers of dyspnea remain so over the years and this trait is related to anxiety. We have been unable to demonstrate an association with hyperventilation syndrome.

Key words: *Dyspnea. Asthma. Perception. Over perception. Hyperventilation.*

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Evolución temporal de la percepción exagerada de disnea en los pacientes con asma

OBJETIVO: En investigaciones previas para estudiar la percepción de disnea de los asmáticos durante la broncoconstricción aguda, encontramos un subgrupo de pacientes que presentaban una percepción exagerada (hiperperceptores). En el presente trabajo hemos querido comprobar si esta alteración perceptiva es un fenómeno esporádico o mantenido en el tiempo. Asimismo nos planteamos conocer si existe una asociación entre la hiperpercepción de la disnea y el síndrome de hiperventilación.

PACIENTES Y MÉTODOS: Se incluyó en el estudio a 22 asmáticos estables que en un estudio realizado 9 años antes se habían mostrado hiperperceptores de disnea (11 varones y 11 mujeres). Tras una espirometría forzada y una entrevista clínica, se les clasificó en su categoría de gravedad de asma -GINA (Global Initiative for Asthma)-. A continuación se les sometió a una prueba de provocación bronquial con histamina para medir la disnea percibida con cada dosis en una escala de Borg (procedimiento similar al empleado 9 años antes por el mismo investigador). Además se les pidió una valoración subjetiva de la gravedad de su asma (escala de 0-10) y que rellenaran el cuestionario Nijmegen de hiperventilación y el STAI-R (State-Trait Anxiety Inventory) de ansiedad.

RESULTADOS: Globalmente, transcurridos 9 años, se han reducido ($p < 0,001$) la percepción de gravedad del asma, la ansiedad y la disnea basal. No se observaron cambios en el grado de hiperrespuesta bronquial (PD₂₀: concentración de histamina capaz de provocar un descenso del volumen espiratorio forzado en el primer segundo del 20%) ni en parámetros objetivos de gravedad (volumen espiratorio forzado en el primer segundo y GINA). Catorce asmáticos seguían siendo hiperperceptores (64%) y en el resto había cambiado la percepción de la disnea: 6 normoperceptores y 2 hipoperceptores. En el grupo que seguía siendo hiperperceptor sólo mejoró significativamente la percepción subjetiva de gravedad; en cambio, en el grupo restante mejoraron la enfermedad subjetiva y objetivamente (excepto la PD₂₀) y la ansiedad. Por último, los que continuaban siendo hiperperceptores puntuaron más alto en los cuestionarios de ansiedad (24 frente a 15; $p < 0,05$) e hiperventilación (18 frente a 13; $p =$ no significativa).

CONCLUSIONES: La mayoría de hiperperceptores de disnea se mantienen así con el paso de los años, lo cual está relacionado con la ansiedad (no hemos podido demostrar su asociación con el síndrome de hiperventilación).

Palabras clave: *Disnea. Asma. Percepción. Hiperpercepción. Hiperventilación.*

Introduction

The study of asthmatic breathlessness has generated great interest since the pioneering study of Rubinfeld and Pain¹ in 1976. Those authors pointed out that there was variation in how patients with the same degree of bronchial obstruction report “breathing discomfort.” Although our understanding has advanced a great deal since then, there is still much to elucidate. One of the most important concerns, in our judgment, is to know whether asthmatics maintain the same altered perception as the years go by if no interventions that target changing that perception have been applied. Such longitudinal studies are difficult to carry out but the information they can provide would help to improve our understanding of the perception of dyspnea and the importance of planning treatment options that take altered perception into consideration.

Perhaps the least studied of the changes in perception of dyspnea in asthmatics is exaggerated, hyper-, or “over” perception. The opposite extreme—hypo- or “poor” perception—has been studied because it has been tied to fatal or near-fatal asthma,² given that patients with this anomaly fail to follow treatment and thereby put their lives in danger.³ However, asthmatics who are over perceivers of dyspnea are a subgroup of patients who are seen often in consultation and who generate a high level of demand for health care and medical services.⁴ Moreover, over perception of dyspnea has been related to emotional disturbances, particularly anxiety,⁴ and therefore may also be related to hyperventilation syndrome although such a relationship has not been demonstrated.

Our pulmonary function laboratory has been studying some of these aspects of dyspnea in asthma for some time,^{4,6} and in the present study we aimed to analyze both of the aforementioned conditions. On the one hand, our main purpose was to determine whether perception disorders (specifically exaggerated perception of dyspnea) are phenomena that appear sporadically or are maintained over time. Our second objective was to confirm whether there is an association between over perception of dyspnea and hyperventilation syndrome, that is to say, if both are found in the same patients.

Patients and Methods

The patients enrolled in this study came from a sample of asthmatics who were seen to be over perceivers of dyspnea during a bronchial provocation test in a study 9 years earlier in our hospital.⁴ The 37 over perceivers identified in that study had asthma in varying degrees of severity. Those who still attended our clinic for monitoring of their asthma were recruited. After we informed them of the general objectives of the study, we asked them to give signed consent to participation in a new study of dyspnea perception. Six patients declined to participate and 9 were lost to follow-up. Thus, 22 patients (11 men, 11 women) with a mean age of 44 years were included. The patients had been clinically stable

for at least the past 4 weeks and had no associated disease able to cause dyspnea (heart disease, neuromuscular diseases, other lung diseases). The following protocol was applied to all patients:

1. In a detailed clinical interview that included forced spirometry, following the guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)⁷ the patients were classified by severity of asthma according to the criteria of the Global Initiative for Asthma (GINA)⁸ and the Spanish guidelines for the management of asthma (GEMA).⁹

2. The patients were asked to quantify their breathlessness at rest on a modified Borg scale¹⁰ and to assess the severity of their asthma on a numerical scale from 0 to 10 (0, minimum severity; 10, maximum severity).

3. Next the patients underwent a nonspecific bronchial provocation test with histamine phosphate to measure dyspnea experienced after each dose of the drug on the modified Borg scale. This test was carried out by the same investigator who had administered it 9 years earlier⁴ following the same procedure (developed by Cockcroft et al¹¹).

4. Finally, the patients were asked to fill in Spanish versions of 2 self-administered questionnaires: the trait portion of the State-Trait Anxiety Inventory¹² to assess anxiety and the Nijmegen questionnaire on hyperventilation.^{13,14}

The bronchoconstrictor response was expressed by PD₂₀—the concentration of histamine needed to produce a 20% decrease in forced expiratory volume in the first second (FEV₁), according to the guidelines of the European Respiratory Society.¹⁵ To analyze individual perception of bronchoconstriction we assessed the Borg scale score for perception of dyspnea when FEV₁ had fallen 20% (PS₂₀)¹⁶ as well as the change in dyspnea perception on the Borg scale (difference between the PS₂₀ and the baseline Borg score).⁴

The scores recorded for each patient were compared with those available from the similar study carried out 9 years earlier in the same laboratory by the same investigator. We assessed whether a change in the subjective measures, evaluated by the same patient on a similar scale, had changed over the years and categorized severity of asthma (GINA/GEMA criteria, bronchial obstruction, visits to the emergency department, and hospitalizations for asthma in the preceding year). We also analyzed whether the degree of anxiety, measured by the same questionnaire, had changed and, finally, if the manner of perceiving dyspnea during acute bronchial obstruction was different. The same criteria used in the original study to classify patients as poor perceivers, normal perceivers, or over perceivers of dyspnea, that is to say, the change Borg scale assessment of dyspnea—the difference between initial Borg score and PS₂₀.

The Nijmegen questionnaire was not used in the study 9 years earlier, and therefore change in hyperventilation over time could not be analyzed. The correlations between the Nijmegen score, anxiety, and over perception of dyspnea were analyzed in the present study.

Statistical Analysis

The data for all variables were entered into a database managed by the statistical package SPSS version 11 for Windows. Analysis of variance or a χ^2 test was used as appropriate in order to test for between-group differences in each of the variables analyzed.

Results

Data was analyzed for 22 subjects (11 men, 11 women) for whom we had information on perception of dyspnea from the current study and the one 9 years earlier. The patients had asthma of varying degrees of severity. Patient characteristics at the time of the present

TABLE 1
General Patient Characteristics: Current Study and 9 Years Earlier*

	Study 9 Years Earlier (n=22)	Current Study (n=22)	P
Age, years	35 (17)	44 (17)	.0001
Active smokers	7	9	.368
Anxiety, STAI-T	26 (10)	21 (10)	.012
Severity of disease, GINA			.087
Intermittent	5	10	
Mild persistent	9	5	
Moderate persistent	6	6	
Severe persistent	2	1	
Baseline dyspnea, Borg scale	1.1 (1)	0.5 (1)	.025
Subjective severity of asthma	5 (2)	2.8 (2)	.0001
FEV ₁ , % of predicted	90 (20)	96 (17)	.175
Change in Borg score for dyspnea, from initial assessment to PS ₂₀	4.5 (1)	4.2 (2)	.477
PS ₂₀	5.6 (1)	4.8 (2)	.135
PD ₂₀ , mg/mL	1.6 (1.5)	2 (1)	.469
Emergencies in the past year	9	1	.016
Hospitalizations in the past year	4	0	.042

*Results are expressed as means (SD) or as an absolute number of patients. STAI-T indicates the trait form of the State-Trait Anxiety Inventory; GINA, Global Initiative for Asthma; FEV₁, forced expiratory volume in the first second; PD₂₀, concentration of histamine able to cause a 20% fall in FEV₁; PS₂₀, dyspnea perception score (Borg scale) when FEV₁ falls 20%.

TABLE 2
Changes Over Time in Patients Who Remain Over Perceivers of Dyspnea*

	Study 9 Years Earlier (n=14)	Current Study (n=14)	P
Active smokers	5	7	.133
Anxiety, STAI-T	25 (11)	24 (11)	.525
Severity of disease, GINA			.183
Intermittent	0	6	
Mild persistent	5	4	
Moderate persistent	6	4	
Severe persistent	3	0	
Baseline dyspnea, Borg scale	0.92 (1)	0.67 (1)	.089
Subjective severity of asthma	4.7 (2)	3.4 (2)	.010
FEV ₁ , % of predicted	95 (17)	96 (11)	.956
Change in Borg score for dyspnea, from initial assessment to PS ₂₀	4.9 (1)	5.7 (1)	.115
PS ₂₀	5.9 (1)	6 (1)	.270
PD ₂₀ , mg/mL	1.9 (1.5)	1.9 (2)	.980
Emergencies in the past year	3	1	.272
Hospitalizations in the past year	0	0	1

*Results are expressed as means (SD) or as an absolute number of patients. STAI-T indicates the trait form of the State-Trait Anxiety Inventory; GINA, Global Initiative for Asthma; FEV₁, forced expiratory volume in the first second; PD₂₀, concentration of histamine able to cause a 20% fall in FEV₁ del 20%; PS₂₀, dyspnea perception score (Borg scale) when FEV₁ falls 20%.

study and the previous one are shown in Table 1. Severity indicated by GINA category had not changed for 9 patients (42%), had improved for 9 (42%), and had worsened for 4 (18%), but the differences were not statistically significant. Overall, the results indicated no change in either objective signs of asthma severity (GINA, FEV₁, PD₂₀) or findings indicative of over perception of dyspnea with bronchial obstruction (PS₂₀, and the change in Borg score from the initial rating of dyspnea to PS₂₀). what had declined over the years were subjective assessments of severity (Borg score for subjectively evaluated severity), baseline dyspnea assessed on the Borg scale, number of times the patient visited an emergency service and/or was hospitalized for asthma exacerbations and anxiety.

As explained in the preceding section, the patients were reclassified by perception of dyspnea during a new bronchial challenge test. Currently, 14 asthmatics (6 men, 8 women) were over perceivers (change in Borg score for dyspnea, 5.7 [SD, 1.05]), 6 (4 men, 2 women) were normal perceivers (change in Borg score for dyspnea, 1.9 [0.08]), and 2 (1 man, 1 woman) were poor perceivers (change in Borg, 0.45 [0.6]). There were no statistically significant differences related to sex for change in perception of dyspnea (P=.621). Analyzing information on the course of perception in the subgroup of 14 patients who continued to be over perceivers of dyspnea with acute bronchoconstriction (Table 2), we saw that they had not in fact undergone significant changes except for subjective perception of severity of asthma—they now considered their asthma to be less severe. Most patients (8) experienced no changes, while

TABLE 3
Changes Over Time in Patients Who Ceased to Be Over Perceivers of Dyspnea*

	Study 9 Years Earlier (n=8)	Current Study (n=8)	P
Active smokers	2	2	.536
Anxiety, STAI-T	27 (8)	15 (7)	.005
Severity of disease, GINA			.041
Intermittent	0	4	
Mild persistent	3	1	
Moderate persistent	3	2	
Severe persistent	2	1	
Baseline dyspnea, Borg scale	1.96 (1)	0.40 (1)	.040
Subjective severity of asthma	5.6 (2)	1.8 (1.4)	.0001
FEV ₁ , % of predicted	81 (23)	97 (26)	.053
Change in Borg score for dyspnea, from initial assessment to PS ₂₀	3.7 (0.7)	1.5 (0.7)	.001
PS ₂₀	5.2 (1.8)	2.1 (1.8)	.003
PD ₂₀ , mg/mL	1.09 (1.6)	2.1 (1.8)	.303
Emergencies in the past year	6	0	.028
Hospitalizations in the past year	4	0	.033

*Results are expressed as means (SD) or as an absolute number of patients. STAI-T indicates the trait form of the State-Trait Anxiety Inventory; GINA, Global Initiative for Asthma; FEV₁, forced expiratory volume in the first second; PD₂₀, concentration of histamine able to cause a 20% fall in FEV₁; PS₂₀, dyspnea perception score (Borg scale) when FEV₁ falls 20%.

3 improved with respect to severity of asthma and 3 worsened. When we analyzed the results for the 8 asthmatics who were no longer over perceivers, however, we saw that their disease severity status had improved from both objective and subjective points of view and that anxiety had also decreased (Table 3); the only objective parameter that had not changed was the degree of bronchial hyperresponsiveness. The GINA classification improved for most of these patients (6), worsened for 1, and stayed the same for 1.

However, comparisons between individuals who continued to be over perceivers and those who no longer were (Table 4) showed that severity of asthma was similar for the 2 subgroups and that the main difference between them was in level of anxiety. The patients who continued over perceiving dyspnea had more anxiety and tended to higher hyperventilation scores, although the difference in the latter scores was not statistically significant. Analysis of bivariate correlation between anxiety and hyperventilation scores showed a significant relation (Spearman correlation coefficient, 0.894; $P=.0001$). No significant correlation was observed between the Nijmegen questionnaire score and the change in Borg score to assess dyspnea (Spearman correlation coefficient, 0.238) or classification as an over perceiver or not (Spearman correlation coefficient, 0.313).

We also investigated whether there were differences in the initial descriptors from the initial study 9 years earlier for patients who continued to be over perceivers and those who changed their manner of perceiving dyspnea (Table 5). This analysis showed that anxiety was similar in the 2 subgroups but that the latter had more severe asthma (worse GINA category, more visits to the emergency department and more hospitalizations). There was also a slight difference in perception of dyspnea between the 2 subgroups; although all were over perceivers, the patients who would eventually change their manner of perception had a significantly smaller change in Borg score than the ones who would remain over perceivers (3.7 [0.7] vs 4.9 [1]; $P=.031$).

Discussion

The current study shows the evolution over nearly 10 years of a series of asthmatics who are over perceivers of dyspnea monitored in our outpatient clinic for respiratory diseases. The patients had not received psychological treatment to try to control their anxiety or modify their perception of breathlessness. Although this study is not large, it is the only study of its kind and therefore contributes data unavailable until now. The severity of asthma of most patients remains similar and most over perceivers of dyspnea remain so. However, we found that they perceive their asthma to be less severe, report having less dyspnea at rest and experience fewer exacerbations; to summarize, their disease is better controlled and they have lower anxiety scores. Although various studies have detected

TABLE 4
Differences Between Patients Who Remain Over Perceivers of Dyspnea and Patients Who Changed Their Perception, at the Final Assessment*

	Over Perceivers (n=14)	Change in Perception (n=8)	P
Age, years	41 (18)	48 (16)	.340
Sex, men/women	6/8	5/3	.330
Active smokers	7	2	.273
Anxiety, STAI-T	24 (10)	15 (7)	.049
Hyperventilation, Nijmegen score	18.4 (9)	13.6 (6)	.221
Severity of disease, GINA			.749
Intermittent	6	4	
Mild persistent	4	1	
Moderate persistent	4	2	
Severe persistent	0	1	
Baseline dyspnea, Borg scale	0.67 (1)	0.40 (1)	.610
Subjective severity of asthma	3.4 (2)	1.8 (1.4)	.172
FEV ₁ , % of predicted	96 (11)	97 (26)	.850
Change in Borg score for dyspnea, from initial assessment to PS ₂₀	5.7 (1)	1.5 (0.7)	.0001
PS ₂₀	6 (1)	2.1 (1.8)	.0001
PD ₂₀ , mg/mL	1.9 (2)	2.1 (1.8)	.878
Emergencies in the past year	1	0	.463
Hospitalizations in the past year	0	0	1

*Results are expressed as means (SD) or as an absolute number of patients. STAI-T indicates the trait form of the State-Trait Anxiety Inventory; GINA, Global Initiative for Asthma; FEV₁, forced expiratory volume in the first second; PD₂₀, concentration of histamine able to cause a 20% fall in FEV₁; PS₂₀, dyspnea perception score (Borg scale) when FEV₁ falls 20%.

TABLE 5
Differences Between Patients Who Remain Over Perceivers of Dyspnea and Patients Who Changed Their Perception, at the Initial Assessment*

	Over Perceivers (n=14)	Change in Perception (n=8)	P
Age, years	32 (18)	40 (16)	.307
Active smokers	5	2	.273
Anxiety, STAI-T	25 (11)	27 (8)	.657
Severity of disease, GINA			.009
Intermittent	0	0	
Mild persistent	5	3	
Moderate persistent	6	3	
Severe persistent	3	2	
Baseline dyspnea, Borg scale	0.92 (1)	1.96 (1)	.273
Subjective severity of asthma	4.7 (2)	5.6 (2)	.438
FEV ₁ , % of predicted	95 (17)	81 (23)	.123
Change in Borg score for dyspnea, from initial assessment to PS ₂₀	4.9 (1)	3.7 (0.7)	.031
PS ₂₀	5.9 (1)	5.2 (1.8)	.317
PD ₂₀ , mg/mL	1.9 (1.5)	1.09 (1.6)	.215
Emergencies in the past year	3	6	.012
Hospitalizations in the past year	0	4	.002

*Results are expressed as means (SD) or as an absolute number of patients. STAI-T indicates the trait form of the State-Trait Anxiety Inventory; GINA, Global Initiative for Asthma; FEV₁, expiratory volume in the first second; PD₂₀, concentration of histamine able to cause a 20% fall in FEV₁; PS₂₀, dyspnea perception score, Borg scale when FEV₁ falls 20%.

relationships between anxiety and over perception,^{4,17} and the over perceivers in our study are less anxious than 9 years ago, their manner of perceiving breathlessness has continued to be exaggerated in a bronchial challenge test in the lung function laboratory; this is to say, their condition of being over perceivers has generally been maintained over time.

However, not all patients continue to be over perceivers. The asthma of those who no longer perceive breathlessness in an exaggerated manner was now less severe, as shown not only by subjective assessment but also by objective parameters. They also came to have less anxiety. In fact, these patients had more severe asthma, but it improved with time. In a parallel manner, their anxiety and over perception of asthma improved. Additionally, the change in dyspnea assessment on the Borg scale from baseline to PS₂₀, which we find gives very accurate information about the dyspnea of these patients, whether they have asthma⁴ or chronic obstructive pulmonary disease,¹⁸ was significantly less in the study 9 years earlier for the patients who had ceased to be over perceivers than for those whose manner of perception remained stable as time passed.

We failed to demonstrate a relationship between hyperventilation syndrome and over perception of breathlessness. The patients who were over perceivers tended to have slightly higher scores on the hyperventilation questionnaire but the difference was not significant. As perception of dyspnea is correlated with anxiety and anxiety is correlated with hyperventilation,^{14,19} we think that these disorders coexist in the same patients, although further study would be needed to demonstrate the relationship reliably.

Some studies have found an association between perception of dyspnea and gender.¹⁷ In our study, women predominated in the group who remained over perceivers, but the difference was not statistically significant. It is possible that, as with hyperventilation syndrome, this tendency would have reached statistical significance in a larger group of patients.

It was striking that none of the patients had appreciable changes in PD₂₀. Even though their disease was better controlled, this parameter remained stable. This study was not designed to analyze long-term improvement in bronchial hyperreactivity arising as a result of treatment plans currently applied in asthma; however, it seems important to point out that we were unable to effect any change in this parameter among our patients after nearly a decade of follow-up and treatment of their disease at our clinic.

From our point of view, the practical conclusion that can be drawn from the results of this study is that if in spite of the usual therapeutic measures for controlling asthma a patient continues to have a significant level of anxiety, therapy targeting anxiety should be provided. It

seems clear that there is a group of patients who have severe asthma who cease to be over perceivers and anxious about controlling their disease. However, others remain over perceivers as a result of anxiety and the overall therapeutic approach should aim to treat both their anxiety and their asthma because, as we have demonstrated, anxiety does not tend to resolve with time for them but rather persists.

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