Arch Bronconeumol. 2011;**47(2)**:73-78

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Original Article

Psychological Profile of Patients with Bronchial Asthma and Functional Dyspnea: A Comparison with a Non-Asthmatic Population and Impact on the Disease

Carlos Martínez-Rivera,[a,e,*] M. del Carmen Vennera,[b,e] Conchita Cañete,[c] Santiago Bardagí,[d] César Picado[b,e]

[a]*Servicio de Neumología, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, Barcelona, Spain*
[b]*Servicio de Neumología, Hospital Clínic, IDIBAPS, Universitat de Barcelona, Spain*
[c]*Servicio de Neumología, Hospital General de L'Hospitalet de Llobregat, L'Hospitalet de Llobregat, Barcelona, Spain*
[d]*Servicio de Neumología, Hospital General de Mataró, Mataró, Barcelona, Spain*
[e]*Centro de Investigaciones Biomédicas en Red Enfermedades Respiratorias (CIBERES)*

ARTICLE INFO

Article history:
Received July 21, 2010
Accepted October 3, 2010

Keywords:
Asthma
Dysfunctional breathing
Anxiety
Asthma control

ABSTRACT

Background: Few studies analyze the relationship between anxiety and alexithymia with dysfunctional breathing (DB) and its impact on quality of life and asthma control. The aim of this study was to assess the prevalence of DB in asthma, its impact on quality of life and asthma control, and its relationship with anxiety and alexithymia.
Patients and methods: We performed a cross-sectional study of 264 asthmatic patients and 111 control subjects. Both groups completed the following questionnaires: quality of life (AQLQ), alexithymia (TAS-20), anxiety (STAI) and DB (Nijmegen). We evaluated each asthma patient for asthma severity, dyspnoea, exacerbation and control of the disease (ACT test).
Results: 38% of asthmatics and 5.5% of non-asthmatics had DB. Asthma subjects had more anxiety and were more alexithymic. Asthmatics with DB had significantly more anxiety, more alexithymia, poorer asthma control, more exacerbations and poorer quality of life than asthmatics without DB. Asthmatics with an ACT < 19, a score >3 in the emotion subscale of the AQLQ, who were being treated for anxiety and scored >19 on the alexithymia subscale that assesses difficulty in identifying emotions, showed ORs for DB of 2.6 (1.1-5.9), 6.8 (2.9-15.8), 4.4 (1.9-9.8) and 3.3 (1.5-7), respectively. A predictive DB model was constructed for asthma patients.
Conclusions: We have demonstrated the close relationship between anxiety, alexithymia and DB in asthmatics, as well as the significant impact of DB on the control and quality of life of asthma patients.

Perfil psicológico de los pacientes con asma bronquial y disnea funcional: comparación con población no asmática e impacto sobre la enfermedad

Palabras clave:
Asma
Disnea funcional
Ansiedad
Control del asma

RESUMEN

IIntroducción: Pocos estudios analizan la relación de la ansiedad o la alexitimia con la disnea funcional (DF) y su impacto en calidad de vida y control del asma. El objetivo de este estudio fue evaluar la prevalencia de la DF en el asma, su repercusión sobre la calidad de vida y el control del asma y su relación con la ansiedad y la alexitimia.
Pacientes y métodos: Se realizó un estudio transversal de 264 pacientes asmáticos y 111 controles. Ambos grupos cumplimentaron los siguientes cuestionarios: calidad de vida (AQLQ), alexitimia (TAS-20), ansiedad (STAI) y DF (Nijmegen). En asmáticos se evalúo: gravedad del asma, grado de disnea, exacerbaciones y control de la enfermedad (test ACT).
Resultados: Un 38% de asmáticos y un 5,5% de no asmáticos tenían DF. Los asmáticos tenían más ansiedad y eran más alexitímicos. Los asmáticos con DF tenían de manera significativa más ansiedad, más alexitimia,

*Corresponding author.
E-mail address: 29002cmr@comb.cat (C. Martínez-Rivera).

peor control del asma, más exacerbaciones y peor calidad de vida que asmáticos sin DF. Los asmáticos con ACT < 19, una puntuación > 3 en la subescala de emoción del AQLQ, que estaban siendo tratados para ansiedad y que puntuaban > 19 en la subescala de alexitimia que evalúa dificultad para identificar emociones mostraban OR para DF de 2,6 (1,1-5,9), 6,8 (2,9-15,8), 4,4 (1,9-9,8) y 3,3 (1,5-7), respectivamente. Se construyó modelo predictivo de DF en asmáticos.

Conclusiones: Se demuestra la relación estrecha entre ansiedad, alexitimia y DF en asmáticos, así como importantes repercusiones que tiene la DF sobre el control y calidad de vida del asmático.

Introduction

It is well-known that treatment with the best antiasthmatic drugs is not able to stabilize the disease in around 5 to 10% of patients. This group of patients has what is known as severe incontrollable asthma, refractory asthma or difficult-to-control asthma.[1,2] It is known that difficult-to-control asthma is made up of a heterogeneous group of patients, whose poor response to antiasthmatic treatment can be due to multiple causes that may have either isolated or combined presentation in one same patient. Several algorithms have been designed in order to establish the origin of the poor therapeutic response. In the first place, it is recommended to try to distinguish between real and false refractory asthma. False refractory asthma is considered not due to factors of the disease itself. Among false asthmas are those caused by organic diseases of the upper airways (stenosis, amyloidosis, tumors, malformations, etc.) and those caused by functional alterations (vocal cord dysfunction). On other occasions, difficult-to-control asthma is actually another irreversible obstructive disease of the airways that, logically, either does not respond or responds very little to anti-asthmatic treatment (bronchiolitis obliterans, chronic obstructive pulmonary disease). Finally, it should be ruled out that the poor response is not being caused by associated comorbidities, such as left cardiac insufficiency or gastro-esophageal reflux. Among the comorbidities that should be investigated in an asthmatic who is refractory to treatment is functional dyspnea, or dysfunctional breathing (DB). DB is an anomalous respiratory pattern which the patient describes as lack of air that is alleviated by sighing, frequently associated with restlessness and general malaise.[3] This term, proposed by some authors,[4] is comparable with the concept of hyperventilation syndrome (HS).[5] It is considered that the prevalence of DB is 5-10% in the general population. This entity has been reported to be related to anxiety disorders[6]; its pathogenesis is not well known, and emotional alterations can play an important role.[7]

There is not much literature available about the asthma-hyperventilation syndrome connection; what there is, however, reports a high prevalence of dysfunctional breathing bronchial asthma patients: between 29-42%.[8-10] Furthermore, the studies done up until now have not evaluated the influence of DB on the quality of life of these patients or on their asthma control, nor have they thoroughly evaluated to what point a state, or psychological traits like anxiety or alexithymia, play a role in the development of DB.

Suspected DB should be evaluated by means of a specific test, called the Nijmegen test. Patients with DB present some traits that make the specialist suspect that at least part of the symptoms the patient describes are not due to asthma, or are only partially so. The way to describe the dyspnea as a difficulty to "fill the lungs", "the need to sigh in order to alleviate the dyspnea", "the presence of notable hyperventilation" and behavior that reveals an anxious personality can alert the doctor attending the patient to the existence of DB, which could be a significant influence in the apparent lack of response to antiasthmatic treatment.

The objective of this paper has been to develop an in-depth study of the prevalence of dysfunctional breathing in asthmatics, evaluating its impact on quality of life, exacerbations, control of the disease and symptoms, all in a hospital setting. We have also studied the relationship between anxiety and alexithymia with the presence of dysfunctional breathing. Later, with the variables studied we have attempted to construct a predictive model for dysfunctional breathing in patients with bronchial asthma. Finally, we evaluated whether the doctor attending a patient during a standard clinical interview in an asthma patient consultation could suspect the presence of a "functional" component, and we compared this diagnostic suspicion with a test designed to detect dysfunctional breathing (Nijmegen questionnaire).

Patients and Methods

Subjects

We carried out a transversal study including 264 patients diagnosed with bronchial asthma and 111 control patients selected from among family members of patients and health-care professionals. Patients came from the outpatient consultations of four Barcelona-area hospitals: Hospital General in Mataró, Hospital General in L'Hospitalet de Llobregat, Hospital Clínic in Barcelona, and Hospital Germans Trias i Pujol in Badalona. The patients had been consecutively identified in said consultations and had been previously diagnosed with asthma, with the requisite of having a typical history and positive bronchodilator test or, if not, a positive methacholine test. The inclusion criteria also required that the patients be between the ages of 18 and 80, with a disease evolution time of more than 6 months and stable clinical situation over the previous month.

Methods

At the outpatient consultation, demographic data were compiled and asthma severity was classified as either intermittent, persistent mild, persistent moderate or persistent severe, according to the criteria of the Spanish Asthma Management Guidelines (Guía Española para el Manejo del Asma -GEMA).[11] The degree of dyspnea was evaluated from 0 to 4 according to the *Medical Research Council* (MRC) scale. We registered the number of hospitalizations over the previous year, as well as the number of non-programmed visits, both outpatient as well as hospital, and patients were asked about any current or previous diagnosis or treatment for anxiety or depression.

The subjects later completed the following questionnaires: Nijmegen Questionnaire (dysfunctional breathing),[12] Asthma Control Test (ACT), Asthma Quality of Life Questionnaire (AQLQ-Sydney),[13,14] Toronto Alexithymia Scale (TAS-20)[15] and State-Trait Anxiety Inventory (STAI) that evaluates anxiety as a transitory state and as a latent trait.[16] Once the questionnaires were completed, forced spirometries were performed in accordance with SEPAR guidelines. Finally, we compiled the subjective impression of the doctor who evaluated whether the patient presented symptoms of having a psychological or functional component to their dyspnea. This possibility was described in three categories: "without presence of dysfunctional breathing", "probable presence" or "definite presence".

Table 1
Comparison of the asthma population and control subjects in % of sex, anxiety, anxiety treatment, diagnoses of dysfunctional breathing and variables such as age, Nijmegen score, STAI trait/state and TAS-20 score

	Control group (n = 111)	Asthma group (n = 264)	p
Age (years)	42 ± 16	48.8 ± 16	0.001
Nijmegen	10.9 ± 7	20 ± 11.6	< 0.000
STAI trait	17.01 ± 9	23.9 ± 12	< 0.000
STAI state	16.03 ± 11	23.4 ± 15	< 0.000
TAS-20	40.1 ± 10	43.8 ± 14	0.004
% anxiety diagnosis	5.5	35	< 0.000
% anxiety treatment	7.3	32.8	< 0.000
% women	6.2	71.4	0.038
% dysfunctional breathing	5.5	38	< 0.000

The values are expressed as mean ± standard deviation for quantitative variables and as percentage for qualitative variables.
% anxiety diagnosis: percentage of patients diagnosed with anxiety; % anxiety treatment: percentage of patients that state having been treated for anxiety.

Table 2
Multivariate logistic regressions showing that the OR for having DB is independent of sex and age

	p sig.	OR	95% CI for OR	
			Inferior	Superior
Asthma	0.000	7.798	3.247	18.727
Female	0.000	3.153	1.665	5.968
Age	0.001	1.028	1.011	1.045

Table 3
Comparison between general variables and those related to asthma management/control among asthma patients with and without DB

	Dysfunctional breathing (n = 99)	No dysfunctional breathing (n = 165)	p
Age	51.9 ± 13	46.8 ± 16	0.009
% of women	84.8	63.7	0.000
Years diagnosed	18.1 ± 13	18.6 ± 14	0.824
Dyspnea (MRC)	1.7 ± 1	0.72 ± 0.8	0.000
Asthma control (ACT)	14.5 ± 5	20.6 ± 4	0.000
FEV1%	77.9 ± 21	83.1 ± 21	0.063
N hospitalizations	0.22 ± 0.6	0.21 ± 0.5	0.824
N exacerbations	1.13 ± 1.7	0.43 ± 0.9	0.000

Values are expressed as mean ± standard deviation for the quantitative variables and as percentage for the qualitative variables.

The study was carried out following the Declaration de Helsinki and after having been approved by the ethics committees of the hospitals involved. Informed consent was given by all patients.

Statistical Analysis

The results are expressed as means (SD) for quantitative variables and as percentage for the qualitative variables. The comparisons between quantitative variables were calculated with the Student's t- test. The comparisons between qualitative variables were done with the χ^2 test. For the ordinal qualitative variables, the analysis of variance (ANOVA) was used. After classifying the asthmatics as patients with or without dysfunctional breathing according to the Nijmegen questionnaire, we analyzed the independent or explicative variables as binary variables depending on the average, and they were analyzed in a logistic regression model to determine their capacity for predicting dysfunctional breathing. Later, we calculated odds ratios (OR) and 95% confidence intervals of the independent variables. The data were analyzed with SPSS, version 15 software for Windows (SPSS Inc, Chicago IL, USA). P values ≤ 0.05 were considered statistically significant.

Results

We observed that 38% (99 out of 264) of the asthma group had DB compared to 5.5% (6 out of 111) of the non-asthma subjects. In comparing the two populations, the following results were obtained: the asthma patients presented higher scores on the Nijmegen questionnaire, more anxiety according to the STAI state and trait, more alexithymia and a higher percentage of anxiety diagnoses and treatment. These differences between patients and control subjects were statistically significant in all cases (table 1). In order to rule out a significant influence of either age or sex on the different DB percentages obtained between the two groups, a logistic regression was carried out, calculating OR for developing DB in the asthma patient group compared with the non-asthma group. Sex and age were entered step by step. In the first place, we observed that the OR for having DB in the asthma group was 9.35 (CI 95%: 3.9-22.1). When adjusted for age and sex, it was 7.80 (95% CI: 3.2-18.7), maintaining statistical significance (table 2).

Later, the group of asthma patients was divided into two groups, those with and those without DB according to the Nijmegen score. Those patients scoring ≥ 23 were considered to have DB. The comparative analysis of the two groups showed that the patients with DB differed statistically from those who did not have DB as they were older and had more dyspnea according to MRC, poorer control of asthma according to the ACT score, and a greater number of exacerbations, all of which were significant. The percentage of women among the DB patients was also significantly higher. No significant differences were observed in the years since asthma diagnosis up until the time of the study, nor in FEV1%, nor in the number of hospitalizations in the year previous to the study (table 3).

The evaluation also showed that patients with lower levels of education and more serious asthma scored higher on the Nijmegen questionnaire ([Figure 1] and [Figure 2]).

In comparing the psychological variables and the data obtained with the quality-of-life questionnaires, we observed that all the scores for the AQLQ Sydney quality-of-life questionnaire were statistically poorer in the asthma patients with DB. Likewise, the anxiety questionnaires, like the STAI trait and state, also indicated significantly more anxiety among the asthmatics. This observation was associated with the fact that a greater percentage of patients with DB, when compared with those who did not present DB, had been diagnosed with anxiety and were receiving or had received anxiety treatment with a significantly higher frequency. Last of all,

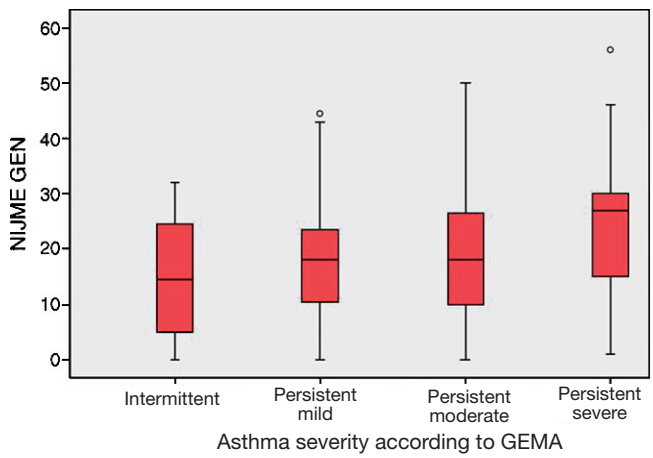

Figure 1. Relationship of asthma severity according to GEMA and the Nijmegen score. ANOVA: F: 3.18; p = 0.014.

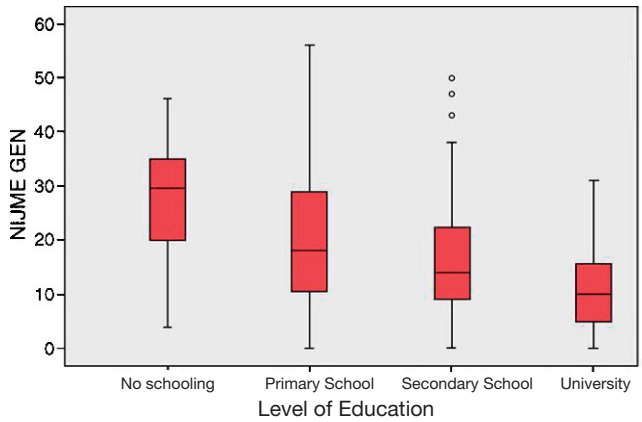

Figure 2. Relationship between level of education and the Nijmegen score. ANOVA: F: 6.21; p = 0.000.

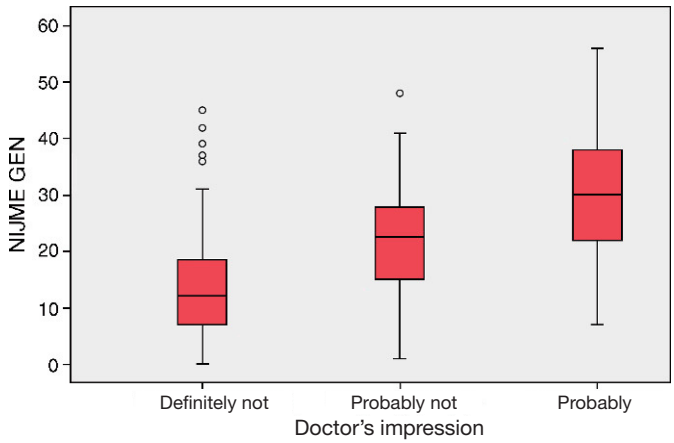

Figure 3. Relationship between the specialist's impression of the functional component and the Nijmegen score. ANOVA: F: 58.6; p < 0.05.

the TAS-20 alexithymia questionnaire showed significantly higher scores on the general scale and in the different subscales in patients with DB compared with those who had not been diagnosed with DB (table 4).

We later carried out a univariate logistic regression analysis for each of the variables described, which showed significance in the Student's t- test. Odds ratios (OR) were calculated for each of the variables regarding the presence or not of DB, confirming that each were individually associated with DB (data not shown). Afterwards, a multivariate regression analysis study showed that only four of these variables are independently and significantly associated with DB. Thus, having an ACT ≤ 19, scoring on the emotion subscale of the AQLQ Sydney > 3, receiving anxiety treatment or scoring > 19 in the alexithymia subscale that evaluates problems for reading the body sensations associated with emotions means a relative risk or OR for having DB of 2.6 (1.1-5.9), 6.8 (2.9-15.8), 4.4 (1.9-9.8) and 3.3 (1.5-7), respectively.

This predictive model for dysfunctional breathing obtained a sensitivity of 70% and a specificity of 90%.

Lastly, we analyzed the degree of coincidence between the subjective impression of the pulmonologist as to whether the patients were affected by DB or not, compared with the Nijmegen questionnaire score. A statistically significant relationship was observed between the subjective impression and the objective measurement for DB, evaluated using ANOVA (F: 58.6; p < 0.05) (fig. 3).

Table 4
Comparison between asthmatics with and without DB, data related to previous anxiety diagnosis and /or treatment and the scores obtained from the quality of life (AQLQ Sydney), anxiety trait/state (STAI-T and STAI-S) and alexithymia (TAS-20) questionnaires

	Dysfunctional breathing (n = 99)	No dysfunctional breathing (n = 165)	p
% anxiety diagnosis	70.7	30.1	0.000
% anxiety treatment	55.1	18.6	0.000
STAI state	29.96 ± 14	16.65 ± 10	0.000
STAI trait	32.68 ± 11	18.83 ± 10	0.000
TAS-20 general	52.43 ± 13	40.69 ± −9	0.000
AQLQ-general	5.32 ± 2.6	1.94 ± 1.9	0.000
AQLQ-mood	5.96 ± 2.8	2.17 ± 1.9	0.000
AQLQ-breathlessness	4.86 ± 2.8	1.61 ± 2	0.000
AQLQ-social	4.95 ± 3	1.82 ± 2.4	0.000
AQLQ-preoccupation	5.34 ± 2.8	1.88 ± 2.1	0.000

The values are expressed as mean ± standard deviation for quantitative variables and as percentage for qualitative variables.
% anxiety diagnosis: percentage of patients diagnosed with anxiety; % anxiety treatment: percentage of patients that report have been treated for anxiety.

Discussion

This study shows that DB is very frequent in asthma patients (38%) compared with a non-asthmatic control population (5.5%). The asthmatics are also more frequently affected with anxiety and alexithymia than the non-asthmatic population. The asthma patients with DB presented anxiety and alexithymia more frequently than the asthmatics without DB. DB is more frequent in patients of older age with severe asthma, poorer control of their asthma, frequent exacerbations and a lower level of education. Patients with DB present traits that, when detected in the medical interview, allow the attending specialist to suspect its presence with a high degree of reliability.

The high frequency of DB observed in this study is similar to that found in other previous publications by different groups, which have shown prevalences of DB between 29 and 42% in asthma patients, diagnosed using the Nijmegen test.[8-10] A previous Spanish study showed very similar data: 36% of the asthma patients showed Nijmegen scores of ≥ 23.[10] Along the same lines, in a rural setting in England, Thomas et al. found a prevalence of DB in the general population to be around 8%, while in asthma sufferers the percentage of DB reached 29%.[9,17] In comparison with our study, which took place in a hospital setting, the patients evaluated by Thomas et al. were evaluated in a primary care setting. In the English study, the control group was recruited from the general population, unlike ours which was recruited from hospital personnel and patient family members. Despite this fact, the frequency of DB in the non-asthma population showed very similar values. Aside from the Thomas et al. study, we have found no other articles evaluating the prevalence of DB in the general population using the Nijmegen questionnaire. Therefore, it is difficult to compare the findings of this present study in healthy subjects with those of other groups.

The origin of a greater presence of DB in asthma when compared to a non-asthma control population is unknown. It could be because asthma disease, characterized by the intermittent presence of dyspnea, causes a disorder in the perception of respiratory difficulty that facilitates the presence of this sensation regardless of the existence of changes in airway permeability. It could be, as suggested by some authors, that the inflammation and remodeling of the airways causes changes in the perception of the difficulty to breath, brought about by alterations in nerve sensory pathways.[18] The present study and others have found an association between DB part, the result of a state of anxiety present in a chronic disease, in which dyspnea is the main symptom that worries patients most. Along this line, a previous paper by Martínez-Moragón showed that asthma patients with DB live asthma symptoms with more anxiety.[10] Several

studies have reported that asthma is associated with higher psychiatric morbidity, repeating the finding that anxiety is more frequent in asthma sufferers than in the general population.[6,7,19-21] There is even a study that points out the possibility that anxiety or depression during childhood could predict the development of adult asthma.[22] Likewise, other studies have shown that anxiety and hyperventilation syndrome are two frequently-associated pathologies.[23,24] Therefore, the anxiety component could be a relevant factor in the genesis of DB in patients with asthma.

One of the characteristics of DB is that it is frequently accompanied by quick, superficial breathing (hyperventilation). As hyperventilation causes an increase in the osmolarity of the airways, which at the same time is able to produce bronchospasm, it cannot be ruled out that part of the sensations that asthma patients experience with the hyperventilation that accompanies anxiety is due at least in part to the possible effects of quick, superficial breathing on the epithelial and inflammatory cells.[2] Several studies on repeated hyperventilation in animal experimentation and in humans show greater bronchial hyperreactivity, higher cellularity in the airway and an increase in the levels of leukotrienes and derivatives of prostaglandins, all proinflammatory mediators.[2-4,18] Greater exudation of the airways and thickening of the bronchial walls are also observed, as are signs of bronchial rmodelling.[1]

The presence of DB is associated with poorer disease control, which also occurs with the presence of anxiety. In a recent article, Di Marco demonstrated that having anxiety represented a high risk (OR 3.76) for having a poor control of asthma.[25] It therefore cannot be ruled out that at least part of the poor control detected in patients with DB is due to its association with anxiety.

At this point, we wanted to highlight data a factor that was not compiled in this study: how therapeutic incompliance could be another factor to keep in mind when analyzing the poor control of these asthma patients. In the present study we also observed that asthmatics with DB scored higher for alexithymia than non-DB patients. Alexithymia is a trait characterized by having an impaired capacity to correctly identify the body symptoms associated with emotions. The presence of alexithymia can influence the capacity of the patients to interpret the severity of their symptoms. This makes it more difficult to detect the signs of alarm for the worsening of the disease, which at the same time motivates the exacerbation progression and results more frequently in severe situations that require hospital care. In fact, the first article has been published that relates poor asthma control as measured by ACT with a high score for alexithymia, although the number of asthma patents evaluated was too small (25 patients) to draw definitive conclusions.[26]

The origin of the association between DB and alexithymia detected in this study is difficult to interpret. On one hand, DB seems to be a sensory misperception phenomenon, while alexithymia is characterized by the presence of emotional hypoperception. In the case that the association detected in our study between DB and alexithymia were real and not causal, we do not know the reasons that could explain the relationship between the two dysfunctions.

In this study, as in others previously published, the diagnosis of DB/hyperventilation was established using the Nijmegen questionnaire. Some of the questions of the test are about respiratory symptoms, which could allege a lack of specificity in the diagnosis of DB in asthma patients. Nevertheless, there is no gold standard for the diagnosis of DB, and other tests used for diagnosis have not demonstrated having sensitivity or specificity higher than the Nijmegen test.[7] One fact that seems to back the use of the test is the fact that, in therapeutic intervention studies on dysfunctional breathing in asthma, good correlation has been observed between changes in the test score and in quality-of-life after treatment.[27]

The present study compared the sensitivity of the test with the clinical skill of the specialist to detect DB in the interview. Our study has demonstrated that the specialists that treat asthma patients can, in many cases, deduce whether an asthmatic presents DB associated with their respiratory disease based on the data collected at the office visit.

Table 5
Multiple logistic regression with 4 variables dichotomized by the average that maintain the OR for DB referred in the table, independently and significantly

	p sig.	OR	95% CI for OR	
			Lower	Upper
ACT	0.023	2.613	1.140	5.988
Anx. treatment	0.000	4.397	1.967	9.826
AQLQ-S, mood	0.000	6.862	2.976	15.822
SEN_emotions20	0.003	3.261	1.506	7.060

ACT: Asthma control test; Anx. treatment: patients that have required treatment for anxiety; AQLQ-S, mood: subscale for state of mood in AQLQ; SEN_emotions20: TAS-20 subscale evaluating problems in reading body sensations associated with emotions.

This study provides a predictive model for dysfunctional breathing in asthma patients. With four clinical variables, the risk for developing DB can be predicted with acceptable sensitivity and specificity. This can be helpful in managing these asthmatics, and is a way to put the findings of our paper into practical use. According to the model constructed, given a patient who was previously diagnosed with anxiety, poor asthma control (ACT < 19), with a score < 19 in the mood subscale of the AQLQ or with an ill perception of the symptoms caused by emotions, there is a great chance that the asthma patient also has DB (table 5).

Given that this study has taken place in a specialized medicine hospital setting, the application of the results obtained cannot be extrapolated to the entire asthma population, most of which is treated in the area of primary care. It is well known that the severity of the disease of patients treated at a hospital is greater than that of patients treated at family medical centers. This and other possible differences impede extending the findings of this study to all asthma patients.

In conclusion, we have demonstrated the close relationship between anxiety and dysfunctional breathing in asthma sufferers, as well as the important impact that dysfunctional breathing has in the control and quality of life of our asthmatics. In addition, we propose a predictive model for DB in asthma patients. Given that the poorer control in these subjects can favor inadequate treatments that add undesired side effects, it seems logical to contemplate a differential management in these patients, which may entail breathing re-education techniques as well as adding a psychological focus to the treatment. There are various studies that evaluate treatment in these patients, many of which evaluate breathing re-education techniques. Our study suggests that psychological intervention for anxiety in asthma patients with dysfunctional breathing could be a treatment to consider in these patients.

Funding

This study has been completed with aid from a Sociedad Española de Neumología y Cirugía Torácica (SEPAR) grant.

Conflict of Interest

The authors declare having no conflict of interest.

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