

# Anxiety in adolescents with severe asthma and response to treatment

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**Summary.** Asthma is a complex and multifactorial disorder. Actually, anxiety may affect asthma, mainly concerning frequent exacerbations, pharmacoeconomic costs, and uncontrolled asthma. On the basis of this background, we tested the hypothesis that anxiety could affect severe asthma outcomes in asthmatic adolescents. Therefore, a longitudinal real-world study included 40 consecutive adolescents (22 males, 18 females, mean age  $14.18 \pm 1.97$  years) with severe asthma and visited for the first time at a third-level pediatric clinic. The current study showed that anxiety is common in adolescents with severe asthma as about 60% of them was anxious. In addition, anxiety was associated with frequent use of bronchodilators on demand. This outcome may conceivably depend on the anxiety trait. Interestingly, depression was present only in anxious adolescents: this outcome underlines the close link between emotional disorders. Therefore, emotional aspect should be considered in the adolescent asthma management in clinical practice. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** asthma, adolescents, anxiety, asthma control, treatment

## Introduction

Asthma is a complex and multifactorial disorder. Actually, anxiety may affect asthma, mainly concerning frequent exacerbations, pharmacoeconomic costs, and uncontrolled asthma (1, 2). In this regard, relationship between asthma control and anxiety/depression has been recently evaluated in a Spanish population over a 6-month period of standardized treatment (3). Significant association has been documented between anxiety/depression and uncontrolled asthma; interestingly, specialist-managed treatment improved anxiety/depression, asthma control, and lung function. A real-life study also demonstrated that anxiety and depression are a common and relevant comorbidity in asthmatic outpatients and are associated with uncontrolled asthma and lower ACT scores (4). Moreover, emotional disorders may affect also children and adolescents, so new interventional strategies should be developed to empower children and adolescents to improve their

asthma self-management. In particular, the adolescence represents a challenge in asthma management.

On the basis of this background, we tested the hypothesis that anxiety could affect severe asthma outcomes in asthmatic adolescents.

## Methods

A longitudinal real-world study included 40 consecutive adolescents (22 males, 18 females, mean age  $14.18 \pm 1.97$  years) with severe asthma and visited for the first time at a third-level pediatric clinic. The inclusion criteria were adolescent age (12-17), asthma diagnosis, and severe asthma grade according to the Global Initiative for Asthma (GINA) document (5). The procedure was approved by the Ethics Committee and the parents signed an informed consent. Anxiety and depression were evaluated by the Hospital Anxiety Depression Scale (HADS) questionnaire. The HADS

gives clinically meaningful results as a psychological screening in clinical group comparisons (6). In the interpretation of the questionnaire, a score  $>7$  (in the two subscales) has been found to define anxious or depressive symptoms (7).

Adolescents were treated according to the GINA guidelines and re-evaluated after 12 months. The visits entailed a careful history, current inhaled corticosteroids (ICS) dosage, use of short acting Beta2-agonist (SABA) on demand, clinical examination, perception of breathing and nasal patency assessed by the visual analogue scale (VAS), nasal total symptom score, lung function testing, body mass index (BMI), and asthma control test (ACT) questionnaires. Asthma severity and control were assessed by GINA criteria.

Data were reported as median with inter-quartile range or as absolute and relative (percentages) numbers. All comparisons were made by Chi-square test and Fisher exact test; Statistica software 9.0 (StatSoft Corp., Tulsa, OK, USA) was used.

## Results

Patients were stratified in two groups according to the presence of anxiety symptoms at baseline: 17 non-anxious asthmatics and 23 anxious asthmatics. After 12-month treatment, the asthma severity significantly improved in both groups: only two adolescents unchanged, notably both were anxious at baseline (Table 1). Consistently, asthma control significantly improved in both groups. ICS dose significantly diminished in both groups. The perception of breathing and nasal patency measured by VAS significantly increased, i.e. improved, in both groups. ACT score significantly increased in patient with anxiety, but not in non-anxious group. SABA users significantly diminished only in non-anxious adolescents. Depression co-morbidity was present only in anxious adolescents.

## Discussion

The current study showed that anxiety is common in adolescents with severe asthma as about 60% of them was anxious. In addition, anxiety was associated

with frequent use of SABA on demand. This outcome may conceivably depend on the anxiety trait. Interestingly, depression was present only in anxious adolescents: this outcome underlines the close link between emotional disorders.

On the other hand, anxiety did not significantly affect the response to treatment both concerning the severity and the control grade. This outcome could be related to the severity of asthma: in fact, aggressive strategy are adopted in these patients so its responsiveness may be poorly influenced by emotional factors.

This study confirms the results obtained in adult asthmatics. Indeed, adolescents, well managed by pediatricians at a third-level clinic, achieved an improved asthma control and severity when guidelines are followed.

The present study was open designed, but lung function and clinical validated parameters were measured over time. In particular, HADS questionnaire has been previously validated for use with adolescents aged 12-17 years (8). The HADS showed satisfactory psychometric properties as a screening instrument in assessing anxious and depressive states as two correlated but distinct factors in adolescents.

This study also underlined the relevant prevalence of anxiety in adolescents with severe asthma: about 60% of the sample. This impressive outcome is however conflicting with the relatively low prevalence, about 24%, of anxiety in adolescents suffering from cystic fibrosis (9). Another study reported that children and adolescents with cystic fibrosis had more severe anxious symptoms than healthy controls (10). A very recent study reported an anxiety prevalence of 50% in adolescents with cystic fibrosis, but the sample was very restricted: only 12 subjects (11). This inconsistency might depend on different perception of respiratory symptoms in the two disorders; this issue deserves further investigation. On the contrary, in a group of adolescents and young adults (12-35 years) with asthma, anxiety and depression were associated with impaired quality of life and asthma control. Therefore, the current findings confirm the previous observation in asthmatic adolescents.

Another relevant finding was the large percentage, all but one, of adolescent users of SABA on demand despite the documented asthma improvement

**Table 1.** Clinical data of adolescents suffering from severe asthma and with or without anxiety at baseline and after 12-month follow- (FU)

Clinical parameters	Non-anxious asthmatics			Anxious asthmatics			P value (comparison between 12 mo FU values)
	At baseline	At 12 mo FU	P value	At baseline	At 12 mo FU	P value (comparison between baseline values)	
Age (yrs)	13.94 (1.68)			14.35 (2,187)			
BMI [kg/m <sup>2</sup> ]	21.7 (3.328)	21.17 (3.688)	0.71	22,04 (4,532)	22,94 (4,348)	0.52	0.80
FVC (% of predicted)	107.1 (11.66)	108.8 (15.51)	0.75	105,0 (11,98)	104,8 (11,40)	0.56	0.46
FEV <sub>1</sub> (% of predicted)	97.47 (14.44)	102.9 (15.37)	0.38	98,22 (12,96)	100,9 (12,53)	0.50	0.86
FEV <sub>1</sub> /FVC	90.59 (9.76)	94.33 (5.612)	0.30	93,26 (11,16)	95,50 (8,148)	0.48	0.44
FEF <sub>25-75</sub> (% of predicted)	81.35 (24.81)	89.22 (20.45)	0.42	87,83 (24,74)	91,22 (24,15)	0.66	0.42
ACT score	20.53 (3.573)	22.18 (2.157)	0.11	19,52 (2,826)	22,00 (2,393)	<b>0.003</b>	0.33
ICS mg	1000 (820-1000)	500 (250-500)	<b>&lt;0.0001</b>	1000 (820-1000)	500 (250-570)	<b>&lt;0.0001</b>	0.97
T5SS	5 (2-7)	4 (2-6)	0.62	5,00 (2,00-7,00)	5,00 (4,00-7,00)	0.89	0.77
VAS breathing	5 (2-7)	7 (6-8)	<b>0.0006</b>	3,00 (2,00-7,00)	8,00 (7,00-9,00)	<b>&lt;0.0001</b>	0.40
VAS nasal patency	6 (5-9)	10 (8-10)	<b>0.003</b>	8,00 (5,00-9,00)	9,00 (8,00-10,00)	<b>&lt;0.0001</b>	0.92
<i>Asthma severity</i>							
Mild	0	4 (23.53%)	<b>&lt;0.0001</b> <sup>#</sup>	0	2 (8.7%)	<b>&lt;0.0001</b> <sup>*</sup>	-
Moderate	0	13 (76.47%)		0	19 (82.61%)		
Severe	17 (100%)	0		23 (100%)	2 (8.7%)		
<i>Asthma control</i>							
Not controlled	3 (17.65%)	0	<b>0.0006</b> <sup>#</sup>	6 (26.09%)	0	<b>&lt;0.0001</b> <sup>*</sup>	0.78 <sup>*</sup>
Partially controlled	10 (58.82%)	2 (11.76%)		13 (56.52%)	4 (17.39%)		
Controlled	4 (23.53%)	15 (88.24%)		4 (17.39%)	19 (82.61%)		
SABA	100%	66.67%	<b>0.0323</b> <sup>#</sup>	95%	95%	1.00 <sup>*</sup>	1.00 <sup>*</sup>
Depression (HADS-D)	(0%)	(0%)		9 (39.13%)	10 (43.48%)	0.76	<b>0.005</b> <sup>*</sup>
							<b>0.002</b> <sup>#</sup>

All data are presented as N (%). All comparisons were made by Chi-square test, unless otherwise specified (<sup>#</sup>, Fisher exact test).

who continued to use it. These outcomes underline the relevance of emotional issue in adolescents with severe asthma as recently pointed out (12). In particular, the overuse(abuse) of SABA deserves particular attention from two point of views. First, use of SABA is considered a main measure to classify asthma control. Inadequate SABA use leads consequently to definition of asthma control in that adolescent and consequently inconsistent step-up of therapy. Second, excessive use of SABA implicates a downregulation of b2-adrenoceptor, so SABA become less effective in the time of need.

On the other hand, the current study has two main limitations: the small cohort and the lack of a formal anxiety diagnosis. However, severe asthma affects about 5% of asthmatics (13), therefore the present sample needed to screen about one thousand asthmatic adolescents. In addition, HADS is a reliable test able to identify anxious symptoms.

In conclusion, the present study documented that anxiety in adolescents with severe asthma could not affect the response to the treatment, but anxiety was associated with depression and large use of bronchodilators on demand. Therefore, emotional aspect should be considered in the adolescent asthma management in clinical practice.

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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