Depression and pulmonary function in outpatients with asthma

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Summary The purpose of this study was to examine the relation between depression, anxiety and pulmonary function in asthmatics. Thirty-eight adult asthmatic patients underwent psychometric evaluation with the DSSI/sAD questionnaire, filled in an asthma questionnaire and underwent spirometry. The majority of patients suffered from mild-persistent asthma. Twenty-six reported symptoms of anxiety and 25 reported symptoms of depression. A statistically significant reduction in FEV1 and FEV1/FVC values was observed in asthmatic patients with symptoms of depression. The mean value of FEV1 was 81.84(±20.83) in patients without symptoms and 63.73(±17.99) in patients with symptoms of depression. The mean values of FEV1/FVC were 0.85(±0.11) and 0.75(±0.10), respectively. These findings indicate a high frequency of depression and anxiety in adult asthmatic patients. A biological linkage between depression and impaired pulmonary function is proposed.

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Introduction

Anxiety and depression are closely related to asthma. Estimates of psychopathology in severe asthmatics range from 30% to 63%. Children with asthma have higher rates of depression than children with certain other chronic medical conditions. Exposure to stress and strong emotions can make asthma worse, while having asthma can give patient an increased vulnerability towards the development of anxiety disorders. Whether these high rates of depression and anxiety observed in asthmatics are due to the consequence of the disease only or there is also a genetic link between asthma and psychiatric disorders is controversial. On the other hand, psychiatric symptoms in asthmatic patients have been shown to be a risk factor for increased asthma morbidity and mortality.

The present study investigated the relation between asthma and anxiety, asthma and depression and particularly the possible impact of these psychiatric disorders on the pulmonary function tests.
Samples and methods

Subjects

We selected 40 asthmatic patients (14 women; age range: 17–65 year old.). Patients were consecutively recruited during a 3-month period among patients that visited the University outpatient pulmonology clinic and asthma diagnosis was made according to Global Initiative for Asthma (GINA) guidelines. Asthma was diagnosed by the Lung Function Laboratory of the Physiology Department of the University of Thessaly. Most patients had already a clinical asthma diagnosis made by a G.P. or a Pulmologist and they visited University Laboratory for the confirmation of the diagnosis and further investigation. Others attended the University outpatient pulmonology clinic. The diagnosis of asthma was based on clinical findings, spirometry, and provocation tests, as necessary (reversibility in FEV1 and/or airway hyperresponsiveness to histamine). We only included lifetime non-smoking patients, with no previous history of near fatal asthma attack or hospitalization for asthma. Subjects did not experience respiratory infections or spontaneous asthmatic relapses during the 4 weeks preceding study. Two patients refused to undergo the psychological evaluation. The finally 38 enrolled patients were receiving anti-asthmatic therapy on a regular basis or as needed. All these patients were on inhaled medication only. Degree of asthma severity was assessed according GINA guidelines.8 A brief asthma questionnaire based upon a scale proposed by Woolcock and Jenkins9 was used. Assessment of asthma severity was based on symptoms and use of anti-asthmatic drugs. For length of asthmatic history, we divided asthmatics into three groups: subjects with newly diagnosed asthma (duration of the disease \( \leq 1 \) year), subjects with long asthmatic history and with prolonged history of asthma (duration of the disease \( > 1 \) and \( \leq 10 \) and \( > 10 \) years, respectively).

Before entering the study, each patient attended a screening interview by a psychiatrist (N.A) to rule out any form of present or past mental disorder according to the Greek version of ICD- 10.10 No subjects reported history of cognitive impairment, low instructional level, recent negative life events, and past or present endocrine or metabolic disorder, obesity or recent weight loss, drug or alcohol addiction. Presence of atopy was not a prerequisite for selection. Atopy was assessed by skin prick tests to a standard battery of eight common inhalant allergens.

Pulmonary function assessment

Pulmonary function was measured by a flow-sensing spirometer connected to a computer for data analysis. Forced expiratory volume in the 1st second (FEV1), forced vital capacity (FVC) and the ratio FEV1/FVC were calculated. FEV1/FVC is an index of airway obstruction.

Psychometric evaluation

Each patient underwent psychometric evaluation with the Bedford and Fould’s (DSSI/sAD) inventory.11,12 It consists of 14 questions, seven measuring anxiety and seven depression. The sAD scale is statistically a highly acceptable measure of general psychological disturbance.13 It is an indicator of the intensity of anxiety and depression. The total score for each subscale is the sum of its item scores (0– 21). The cut-off score for each subscale is 3. A score below 3 \(( \leq 3 \)\) means no psychiatric symptomatology, a score between 3 and 6 indicates some sort of borderline symptomatology, while people that score above 6 should be regarded as psychiatric patients. Approximately 95% of healthy individuals give scores below the cut-off score, and should be regarded as free from psychic symptoms; 2.2% give score between 3 and 6 and they are regarded as having some sort of borderline symptomatology, while 1.4% score above six \(( > 6 \)\) and could be regarded as having significant psychopathology. Thus a cumulative 5.1% of healthy persons score above the 4+ threshold. On the contrary, percentages exceeding the 4+ threshold on state of anxiety and depression among psychiatric patients are 71.3% and 69%, respectively.11 High compliance has been reported in both non-psychiatric patient and non-patient groups. British adult norms are used as a reference in this study, as the existing studies of validity and psychometric structures of sAD are based upon British patients.11,13 However, results from other countries, including Greece, highlighted the need for local norms in transcultural research.13

Variables and data analysis

FEV1 values were expressed as percent of predicted values. In order to include persons with even minor manifestations of depression and anxiety, separate categorical variables for anxiety and depression that included the patients scoring below the cut-off score \(( \leq 3 \)\) and above 3 were defined. Independent samples \( T \)-test was used to assess differences in
pulmonary parameters between these groups. Comparisons of proportions were evaluated by means of $\chi^2$. A $P$ value less than 0.05 was considered significant. Statistics was processed by SPSS for Windows, 7.5 version (Standard Version, 1996, SPSS Inc., Chicago, IL, USA).

**Results**

The subjects’ characteristics are shown in Table 1. The mean age of the patients was 47 year. Female were 14 individuals. Twenty-five out of 38 patients were atopic. The mean duration of asthmatic disease was 6.5 years with a range of 0.5–40 years. The mean values of FEV$_1$ and FEV$_1$/FVC were 71.8 and 0.81, respectively. According to asthma symptoms and also taking into account the use of drugs, 28 out of 38 patients were presented with either intermittent or mild-persistent asthma (less than 500 mg of BDP or equivalent). Seven patients were classified as having moderate-persistent asthma and two as severe-persistent (8). Twenty-six patients (68.5%) reported symptoms of anxiety and 25(65.8%) patients reported symptoms of depression (score $>3$ in DSSI/sAD inventory) (Tables 2 and 3). Mean value for anxiety scale was 7.9(SD:5.1) and for depression 5.6(SD:4.5). Twelve (31.5%) and 18(47.3%) patients could be regarded as having significant psychopathology since their score was above 6 in the scales of depression and anxiety, respectively, compared with the 1.4% reported in healthy individuals. Asthmatic patients had a statistically significant higher score in psychometric evaluation in comparison with normals (Table 2).

Symptoms of depression were found to be associated with a statistically significant reduction in the values of FEV$_1$ and FEV$_1$/FVC, when patients with no symptoms (score $\leq 3$) were compared with patients with some kind of depressive symptoms (either mild or severe psychopathology-score $>3$). The mean value of FEV$_1$ was $81.84(\pm20.83)$ in patients without symptoms and $63.73(\pm17.99)$ in patients with symptoms of depression. The mean values of FEV$_1$/FVC were $0.85(\pm0.11)$ and $0.75(\pm0.10)$, respectively. On the contrary, patients with symptoms of anxiety had no statistical differences in the pulmonary measures compared with patients without any symptoms (mean value of FEV$_1$ was $84.75(\pm0.91$) in patients without symptoms and $71.63(\pm9.94$ in patients with symptoms of anxiety, $P$:NS).

**Discussion**

Psychological disturbances are positively related to the severity of asthma. The same happens in other chronic conditions. Frequent admissions to hospital, inability to work and limitations in other activities often lead to behavioral problems indicative of psychiatric morbidity. Although there is not a unique pattern attributable solely to asthma, sometimes the scores in psychometric evaluation are proven to be higher than in other severe chronic conditions, such as diabetes mellitus. Rates of anxiety and depression in this study were compatible with prior clinical studies, reporting increased rates of anxiety and depressive disorders in persons with asthma. Yellowlees et al., studied adult patients with asthma and found psychiatric morbidity in 58% of the sample with anxiety disorders being the most common diagnosis. High levels of anxiety and marked emotional imbalance characterize asthmatic patients. Certain personality profiles are detected in adult asthmatics. Affective and anxiety disorders are more common in children with asthma. Lower rates, however, have been demonstrated in epidemiological samples. These differences could be attributed to selection bias in clinical studies, where sicker patients are more likely to volunteer to participate in research. Greek populations exhibit higher scores in sAD scales by contrast with the initial British norms. Lyketsos et al., translated the sAD into Greek and collected data on 220 healthy women with means of anxiety of 3.2 and depression of 2.2, significantly higher than Greek men. However, the scores in the present study still remain considerably high. Indeed, percentages above the threshold were quite close to those obtained from British psychiatric patients and comparable to data from psychosomatic groups in

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Subjects’ characteristics ($n=38$).</th>
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<tbody>
<tr>
<td>Patients with intermittent/mild-persistent asthma ($n$)</td>
<td>28</td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>14/24</td>
</tr>
<tr>
<td>Atopy yes/no</td>
<td>25/13</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>Mean 47</td>
</tr>
<tr>
<td></td>
<td>Range (17–65)</td>
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<tr>
<td>Duration of disease (yr)</td>
<td>Mean 6.5</td>
</tr>
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<td></td>
<td>Range (0.5–40)</td>
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<tr>
<td>FEV$_1$ (% pred)</td>
<td>Mean 71.8</td>
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<td></td>
<td>Range (44–119)</td>
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Greece, including patients with hypertension, irritable bowel syndrome, psoriasis and inpatients with bronchial asthma. In the latter, the inpatients’ sAD mean of 13.4 on admission grossly exceeded control and norms scores.

Depression and anxiety have been shown to be risk factors for increased asthma morbidity and mortality. Moderate to severe asthma, pessimistic attitude towards prognosis, high levels of denial and non-compliance lead to steroid dependency and deaths from asthma. Most studies refer to severe asthma. In this study, patients were presented with mild asthma. Nevertheless, they scored significantly high in the scales of anxiety and depression reminding of more severely ill somatic patients. If few crises during the year cause far less embarrassment compared to severe and difficult-to-control asthma, the scores observed in the psychiatric tests could hardly be attributed to the chronic disease alone. Moreover, there is some evidence that even mild asthma is associated with anxiety and depression. This may be consistent with common underlying mechanisms. Defects in the function of the autonomic nervous system such as a-adrenergic and cholinergic hyperresponsiveness and b-adrenergic hyporesponsiveness even distal from the airways has been demonstrated in asthmatic patients, as well as in depression. Moreover, in depression, studies of central mediators in the brain also demonstrate parasympathetic hyper-responsiveness and b-adrenergic responsiveness. Although a similar imbalance to the autonomic nervous in the central nervous system is yet to be found in asthmatics, these data raise the question of common biological pathways. It is supported that depression and asthma may each have similar relative transmitter imbalance that additively worsen the severity of either or both in a given patient. Wamboldt et al., suggested a possible genetic risk for both depression and asthma. However, this also may represent the contribution of medication and resultant side effects. In this study, patients were on inhaled medication and no constitutional effects were expected. The environmental link between psychopathology and asthma seems to be less strong in these cases in favor of a biological-genetic one, which could make asthmatics more liable to psychiatric disorders.

In this study, a statistically significant difference was observed in FEV1 and FEV1/FVC values between asthmatic patients with symptoms of depression (score > 3 in DSSI/sAD) and patients with no symptoms of depression (score ≤3 in DSSI/sAD).

<table>
<thead>
<tr>
<th>Patients with no symptoms (n = 13)</th>
<th>Patients with symptoms of depression (n = 25)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>Mean ± SD</td>
<td>81.84 ± 20.83</td>
</tr>
<tr>
<td>FVC</td>
<td>Mean ± SD</td>
<td>96.30 ± 25.02</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>Mean ± SD</td>
<td>0.85 ± 0.11</td>
</tr>
</tbody>
</table>

*P-test.
asthmatic patients through exposure to emotional stimuli.\textsuperscript{24} Gustaffson et al.,\textsuperscript{25} found a negative correlation between peak expiratory flow (PEF) in children and disturbed family cohesion in non-steroid dependent cases. In another study of ours, asthmatic attacks were more frequent in children with mild asthma, whose parents had high scores of anxiety and depression in sAD scales. This finding was attributed rather to a biological link than the disease of the children.\textsuperscript{26} There is also some suggestion in the literature that treating the anxiety or depression of the asthmatic may actually improve the control of asthma.\textsuperscript{5,27} Subjects given biofeedback training for facial relaxation exhibited higher pulmonary scores and more positive attitudes towards asthma.\textsuperscript{28}

This study focuses on the issue that the presence of depressive symptoms in adult asthmatics may indicate worse objective pulmonary measures. If so, this could also mean that a most aggressive therapy and psychological support are necessary in these patients. The findings of this study lend support to the hypothesis that there are further implications between depression and asthma and that common biological pathways may exist. However, this was a preliminary study. Further studies confirming our findings are necessary. These could probably include the use of psychiatric drugs and their possible impact on the course of asthma. The results of this study emphasized the relations between psychiatric parameters and pulmonary measures and support the provision of intervention services to asthmatics.

\textbf{References}