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## Anxiety/depression and impaired asthma control in adolescents. Is an increased basal cholinergic tone a possible link?

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### KEY WORDS

*Adolescents; anxiety; asthma control; bronchial asthma; increased cholinergic tone; depression; hypersensitivity.*

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### To the Editor

We read with interest the excellent article of Licari et al. (1) reporting that anxiety and depression are regulated with the perception of asthma control in adolescents. Since asthma control grade is significantly correlated with emotional scoring, the authors show that optimal asthma management improves both asthma control and anxiety/depression. However, they did not provide comments on the causal and temporal association be-

tween anxiety and asthma outcomes. From a general point of view, it is not clear if a poor asthma control worsens patient's psychological status or vice-versa. Otherwise, both hypotheses are possible. A fundamental premise is that asthmatic adolescents may experience a period of physical and psychosocial changes that affect their health and well-being. Overall, adolescents with asthma are at increased risk for asthma morbidity, asthma death and even suicidal behaviour. Increased rates of depression and anxiety, in adolescents and their caregivers, can lead to non-ad-

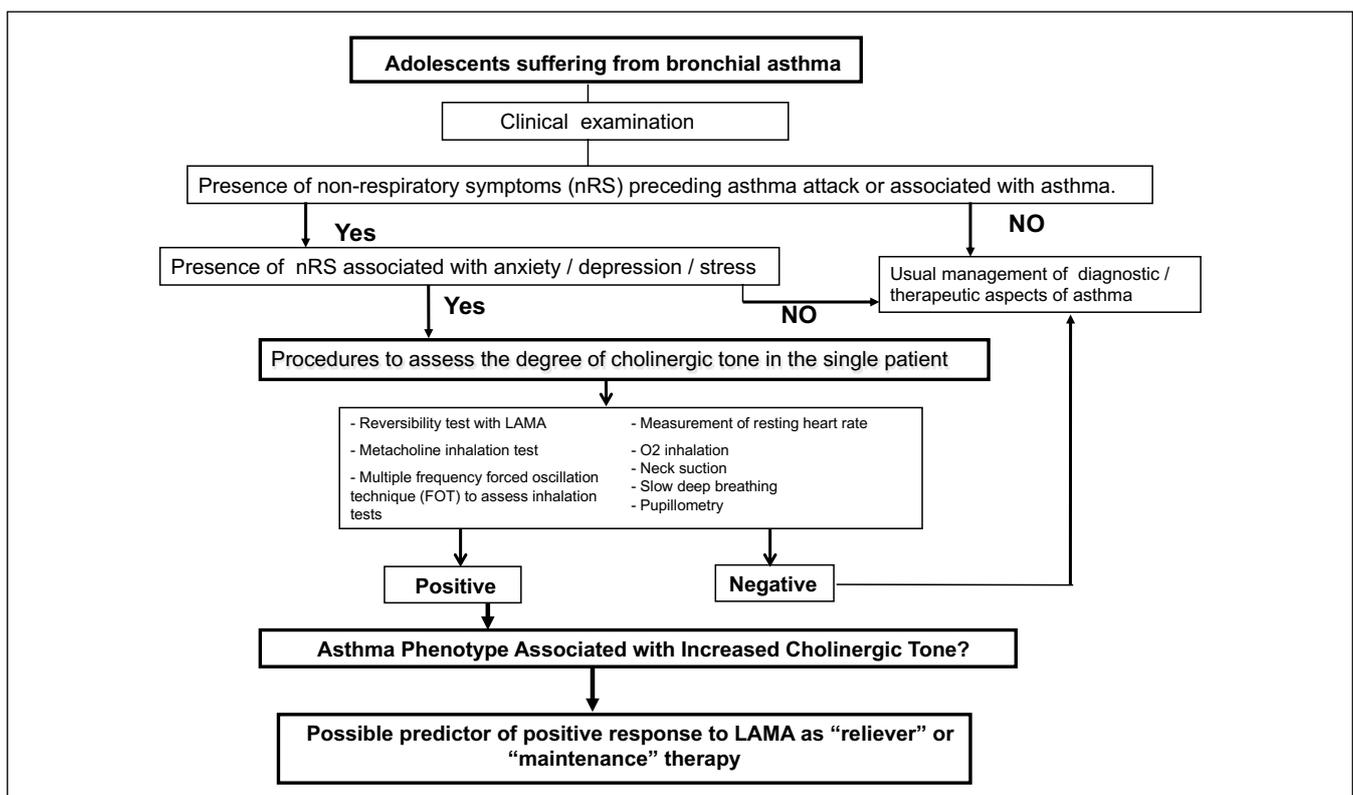
herence to their medical regimens, poor symptom control and poor treatment outcomes. Asthma during adolescence impairs health-related quality of life, especially in case of uncontrolled symptoms (2). It has been demonstrated that parental stress and air pollution were synergistically associated with increased childhood asthma, indicating a common biological effect of parental stress and air pollution during both prenatal and postnatal periods. Therefore, we would like to suggest some potential mechanisms to explain the correlation between stress/anxiety and asthma in adolescents. We have previously shown that about 63% of asthmatic patients reported the usual appearance of at least one non-respiratory symptom (n-RS) before an asthma attack (3). Anxiety and, to a lesser extent, depression, represented the most common n-RSs in our study, suggesting that both anxiety and depression may have a possible role in the development and trigger of an asthma attack. Several studies have shown that psychological stress may enhance bronchial hyperreactivity through different mechanisms, such as mast cell activation, mediator release, inflammation, impairment of respiratory tolerance. Moreover, Ritz. et al. (4) reported a significant correlation between psycho-social stress and stimulation of the cholinergic system, resulting in an increased airway resistance. Visual stimulations

(i.e. scenes from educational surgery) can rapidly induce (after 1-2 minutes) vagal-mediated responses associated with airway resistance increase. Therefore, we suggest that attention should be focused on the potential role of the parasympathetic system as a trigger of bronchial obstruction in asthmatic adolescents reporting the usual onset of cholinergic-related n-RSs (i.e. stress and/or anxiety) before an asthma attack. Indirectly, the results of our study (5) confirm a significant role of the cholinergic pathway in the enrolled asthmatic subject.

The vagal hyperactivity induced by anxiety and stress in asthmatics also represents the basis of important considerations by a therapeutic point of view, such as the use of anticholinergic agents. Considering this background, we suggest the need of an adequate phenotyping of asthmatic adolescents who could exhibit an increased basal cholinergic tone (6,7). The effect of oxygen and methacholine inhalation, neck suction, slow deep breathing assessed by multiple frequency forced oscillation technique (FOT), as well as measurement of resting heart rate and pupillometry, represent the most effective methods for evaluating the level of vagal tone (8) (**figure 1**).

According to our previous study (5), a simple question exploring the presence of vagal-related n-RSs during the collection of an-

**Figure 1** - Suggested flow-chart for a better phenotyping of asthmatic adolescents suffering from anxiety/depression.



amnesic data could help to identify asthmatics with imbalance between sympathetic and parasympathetic systems who could benefit of further diagnostic evaluation of vagal tone. Since the degree of cholinergic tone is likely to be different among asthmatics, we believe it is not possible to rule out that the effectiveness of anticholinergic agents such as tiotropium could be greater in patients with an increased degree of cholinergic tone (9). This possible increased responsiveness to tiotropium may be usefully exploited also in the event of poor efficacy or occurrence of adverse events with the use of long-acting  $\beta_2$  agonists (LABAs) (**figure 1**).

In conclusion, the currently available literature indicates that anxiety and related psychological disorders should be considered as mechanisms that might trigger the airway inflammation, the onset of asthma attacks, and the severity of respiratory symptoms. We concur with Licari et al (1) and others (10) that

adequate educational programs should be planned for those asthmatic patients suffering from psychological disorders (both in adults and minors). We believe that this approach requires a peculiar attention in adolescents, in order to obtain a better control of respiratory symptoms in the short term, a delay in asthma progression, and a reduced airway remodeling in the long term.

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### Conflict of interests

The authors declare that they have no conflict of interests.

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