

## Perception of dyspnea in children with asthma

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### 1. ABSTRACT

The subjective experience of discomfort in breathing, termed dyspnea (or breathlessness), is a symptom with multifactorial causes of highly complex and largely undefined psycho-physiologic mechanism(s). There are at least three discrete qualities of dyspnea likely corresponding to different types of respiratory stress and separate underlying mechanisms. Perception of dyspnea can be measured by diverse means; however, none of these scales has been standardized in children. In general, the same degree of bronchoconstriction causes various levels of perception of dyspnea in different patients. There are large discrepancies among patients in subjective rating of the severity of dyspnea and objective measurement of lung function. Since reporting symptoms is an integral part of therapeutic management of asthma, poor perception of dyspnea may lead to delayed diagnosis and undertreatment of the disease.

### 2. INTRODUCTION

Dyspnea is a Greek word meaning labored or difficult breathing, and is usually described by patients as shortness of breath or air hunger. Dyspnea is a symptom, i.e. a subjective sensation and thus a thorough and exact definition is not straightforward. A strict, although not very intuitive, definition has been proposed by the American Thoracic Society; it describes dyspnea as "a subjective experience of breathing discomfort that consists of qualitatively distinct breathing sensations that vary in intensity" (1). Dyspnea is a complex symptom that can be considered a warning sign to a critical threat to homeostasis. It can be viewed as a kind of protective mechanism that leads to adaptive responses intended to minimize the work of breathing, such as resting or taking the necessary medicines (1). Breathlessness is considered a synonym of dyspnea and both terms will

be used interchangeably in this text. Since dyspnea is a perception of an abnormal state by an individual (i.e., a symptom) the clinician must distinguish it from the various signs that characterize respiratory distress, such as tachypnea, intercostal retractions and use of accessory muscles.

Dyspnea is a common symptom in numerous cardiopulmonary diseases. However, what is perceived as dyspnea by an individual is affected not only from the severity of the underlying medical condition, but also from psychological factors (2). In addition, it may occur in healthy individuals, e.g. during intense emotional states and heavy labor or exercise (3,4).

Inaccurate perception of dyspnea with discrepancies between patients' subjective ratings of their lung function impairment and objective measurements, is a well described problem in both children and adults with asthma (5-7). Treatment of asthma is largely based on reported symptoms and therefore, the reported perception of dyspnea constitutes a cardinal feature of asthma management. Inadequate perception of dyspnea is a major threat for asthmatic patients, and contributes significantly to morbidity and mortality of the disease since it could lead to its under- or overtreatment. Moreover, and despite a variety of methods which have been developed in order to estimate the perception of dyspnea, the incorporation of a real life method in everyday clinical practice still remains elusive.

### 3. DYSPNEA IN CHILDREN

#### 3.1. Pathophysiology of dyspnea

Dyspnea is a very complex psycho-physiologic sensation. Specific dyspnea receptors have not been

found as yet and, since a clear beginning of the nervous sensory transduction pathway is missing, it is not easy to unravel the neurophysiology of dyspnea and depict it as a well-defined model, such as the ones that exist for vision, hearing, or pain.

However, the general principle of peripheral sensory information from the respiratory system, traveling through an intact afferent pathway and triggering regions of the cerebral cortex to produce the perception of dyspnea, does seem to exist. Many different sensory afferent sources have already been described in the literature (8-10). The variety of sensory mechanisms may be further reason for the differences in the perception of dyspnea among individuals.

Recent research with neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), has suggested that dyspnea activates distinct areas in the cortico-limbic system of the brain. These specific areas are also responsible for the perception and response to homeostatic threats such as thirst, hunger, and especially pain (11-14). The instructive information offered by the above techniques has made it quite reasonable to suggest that the procession of both pain and dyspnea is under the control of a common emotion-related homeostatic brain network. This network probably has a crucial role in translating threatening stimuli and activating advantageous behaviors which promote survival. However, the interpretation of these neuroimaging studies, many of which have been conducted in healthy volunteers, is not straightforward and any inferences should be accepted with caution (1). Furthermore, the generalization of conclusions may not be justified, since dyspnea is not the result of a unique condition, and distinct responses may be elicited depending on the underlying condition.

Three discrete qualities of uncomfortable breathing sensation have been defined, at least in adults: "work/effort", "air hunger" and "chest tightness". Although they often coexist, data support that the underlying mechanisms and afferent pathways are different, and dyspnea is experienced in different ways depending on the underlying physiological conditions (15).

*Perception of work/effort* is probably due to the combined effect of respiratory muscles' afferent stimuli and perceived cortical motor command or 'corollary discharge' in sensory cortical areas. Subjects report sensations localized to respiratory muscles when the work of breathing is increased and patients describe it as "my breathing requires effort" or "my breathing requires more work" (16-18). During exercise in healthy persons, alveolar ventilation matches metabolic demand through a complex physiological adaptation. As the exercise increases in intensity, individuals become aware that

limb muscles are working harder and that breathing requires more work or effort. The sensation of increased work/effort of breathing is not usually unpleasant and it is not a reason for stopping, provided that the achieved ventilation is consistent with the responses expected for the level of exercise. However, if cardiopulmonary problems are present, the breathing discomfort is much greater and it frequently limits exercise (20).

The term *air hunger* denotes the perception of an urge to breathe or of not getting enough air. It resembles the sensation experienced at the end of a long breath and originates from insufficient pulmonary ventilation (21). It is usually described as "I cannot get enough air" or "I am starved for air" (15). Originally, air hunger was described as the respiratory discomfort of inspiratory difficulty" and "unsatisfied inspiration" caused by having the thorax and the abdomen bound by broad adhesive tape during exercise and thought to characterize restrictive lung disorders (22). However, it may also be a quality of dyspnea in patients with asthma, COPD, or dysfunctional breathing and a common feature of dyspnea bouts in patients with panic disorders (23-25). Air hunger probably represents an imbalance between the automatic drive to breathe and afferent responses from mechanoreceptors of the respiratory system or, to put it more plainly, it results from a mismatch between drive and ventilation. Air hunger is not correlated with voluntary drive (i.e., cortical motor activity) and it is clearly distinct from work/effort, since voluntary hyperpnea produces strong work sensation but not true air hunger (26).

*Chest tightness* is more specific to bronchoconstriction and is the earliest symptom of asthma. This probably reflects the fact that many asthmatics, contrary to general belief among doctors, have greater difficulty breathing in rather than exhaling (27). However, as the disease progresses increased work and air hunger may be sensed by patients. Interestingly, mechanical ventilation does not relieve tightness but eliminates the sense of excessive respiratory work (28). There is also some evidence that in asthmatic patients perception of increased work/effort does not respond as rapidly as chest tightness to albuterol treatment (29), suggesting that work/effort may be primarily related to strenuous respiratory muscle exertion needed to overcome airflow resistance, whereas tightness is primarily related to stimulation of airway receptors. These findings, put together, suggest that tightness occurs from pulmonary afferents rather than being a work load-related sensation (1).

The description of dyspnea in asthmatic children is in agreement with the above qualitative categorization. Children with moderate to severe persistent asthma were shown to be consistent in their choice of the descriptors applied to their breathing discomfort. Furthermore, the descriptors they selected were the same as those used by asthmatic adults in previous studies. The terms most

consistently chosen by children to describe their dyspnea were “My chest feels tight”, “I cannot get enough air in”, and “I feel out of breath”. The first of these descriptors denotes a tightness quality of dyspnea whereas the second and third descriptors relate to a work/effort dyspnea (30).

### 3.2. Scales in use for the assessment of perception of dyspnea in asthmatic children

Many types of scales have been developed in an effort to provide quantitative assessments for the perception of dyspnea, standardization of symptoms, and reproducible follow-up of patients. In general, the most commonly used is the Borg scale and its modifications (31,32).

The majority of these scales have been extensively used and studied in adults. However, their applicability in pediatric populations is more problematic and, in order to be used in children, simplicity is a precondition. Furthermore, such scales can be used only on the assumption that the child's ability to organize objects in order – something that it is generally achieved around the age of 7 years – has reached an operational stage (33,34). Moreover, none of the many dyspnea scales has been sufficiently validated for use in children (35). For all of the above reasons, interpretation of research results involving the scoring of dyspnea in children should be approached with caution. A brief description of the most commonly used scales is as follows.

*Borg Scale* in its original form consists of a vertical scale ranging from 6 to 20, with corresponding verbal expressions of progressively increasing intensity of dyspnea. Six means “no exertion at all” and 20 means “maximal dyspnea” (36). It is not very suitable for use in children because of its complexity, which derives from the high number of items, all of which require specific verbal expressions. The Borg Category-Ratio Perceived Exertion Scale (CR-10) usually referred to as modified Borg Scale is better adjusted to the particularities of young age because it consists of fewer items (37). However, even the modified Borg scale takes into account that the intensity of dyspnea may increase exponentially with increasing workload, fatigue, and exhaustion and therefore contains nonlinear items. Non-linearity is a concept not easily intelligible to children and prior coaching is necessary in order to overcome this drawback (38).

*Visual Analogue Scale (VAS)* consists of a 10 cm straight line, on which 0 at the left end indicates no symptoms, and 10 at the right end is for most severe symptoms. Its main advantage is that a vertical line is easily understood by younger children. Patients place a mark on this line indicating their ease of breathing and the scoring is performed by measuring the distance from

the beginning of the scale to the point indicated by the subject (39, 40).

The *Dalhousie University Dyspnea Scale* (41) contains 3 series of pictures, of 7 items each, in ordinal arrangement. Each series depicts chest tightness, throat closure, and breathing effort, thus encompassing the full range of the perception of breathlessness. There is an additional pictorial scale for use during exercise that depicts leg exertion. Dalhousie scale provides an easy means of assessing the sensation of breathlessness in children aged 8 years or older without regard to language. However, its results may be less consistent in the younger children (42).

The *15-count breathlessness score* is based on the subjects' taking a deep breath and then counting out loud to 15; the number of breaths taken to complete the count is the score. This objective evaluation of breathlessness was validated in children as young as 7 years old and it is easy to perform, regardless of their mother tongue, provided that the child is able to count fluently (43). The “how-much-puff score” uses the same principle as the above method. It is a computerized scale that incorporates the concept of blowing up a balloon representing the degree of breathlessness which is experienced, asking the question “How much puff have you got?” This gives a six point scale, with a small balloon (score 1) representing little puff, or maximal breathlessness, and a large balloon (score 6) representing lots of puff, or minimal breathlessness (44).

The different concept and design of each scale define its advantages and disadvantages. The choice of scale is probably less important than it is the individual's variability in dyspnea perception (34). In any case, one should bear in mind that it is not the scales but the descriptions of the sensation of dyspnea that are related with the underlying condition or mechanism through which breathlessness is induced (45-47). The descriptive terms used by patients may even reflect the degree of threat imposed by the sensation of dyspnea (48).

### 3.3. Relation of dyspnea perception and lung function in asthmatic children

Baker *et al* (6), in an effort to investigate the relation between dyspnea perception and bronchoconstriction, used VAS scale during metacholine challenge tests in asthmatic children. They found a wide intersubject variability in subjective perception of changes in FEV<sub>1</sub> and that although 94% of patients demonstrated increased AHR, approximately 50% of them were unable to realize either airway obstruction or bronchodilation after the challenge, and feel dyspnea or relief, respectively. This inadequate perception was not correlated with age, gender, baseline lung function, airway reactivity, or self-reported asthma symptoms. Because challenge tests are not a component of routine

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pediatric asthma management, the authors suggested that it is important to perform the commonly used pre- and post-bronchodilator studies, along with the VAS scale, since, according to their results, improvement of < 20% in VAS scores post-bronchodilation could identify patients with poor perception of dyspnea; these patients may be at risk for severe or even fatal exacerbations of asthma.

In a similar study involving children with moderate to severe asthma, Motomura *et al* (49) used acetylcholine chloride challenge and the modified Borg scale and showed that children with severe airway hyper-reactivity (AHR) begin to perceive their dyspnea only after the bronchoconstriction becomes relatively severe, in contrast with those who have mild AHR. Quite interestingly, the same study showed that children with high FeNO also have levels poor perception of dyspnea. Given the well-known relation between airway eosinophilia and FeNO (50), as well as the efficacy of inhaled corticosteroids in reducing eosinophilic inflammation, the authors postulated that eosinophilic inflammation may mediate the relative insensitivity to dyspnea (51-53) and that improved control of asthma with steroids may result in a better perception of dyspnea and more timely intervention during acute exacerbations.

Nuijsink *et al* (54) used the modified Borg scale to study the perception of bronchoconstriction during methacholine bronchoprovocation challenge in children with moderately severe atopic asthma. They demonstrated that the more severe the airway hyper-reactivity, the less likely it was for patients to perceive bronchoconstriction. They also showed that children having low baseline FEV<sub>1</sub> values tended to use less beta-agonist bronchodilator as a "rescue medication". A subgroup of children repeated the test 3 months later and the repeatability of the results was good. In general, the Borg scale showed good correlation with the severity of bronchoconstriction; the authors suggested that the measurement of symptom perception should be taken into account in individual management plans for children with asthma. Although the study has received criticism both for its design and interpretation of results (55), it undoubtedly shows that children with more severe asthma tend to underestimate their symptoms, which predisposes them to severe attacks.

In a cross-sectional study (56), among children with intermittent or mild persistent asthma who performed spirometry, Tosca *et al* assessed the perception of breathlessness in relation to lung function values, using VAS. The major difference between the design of this study and that of the previous ones was that it compared 2 groups of asthmatic children without inducing bronchoconstriction by pharmacologic means; the first group had bronchoconstriction (FEV<sub>1</sub><80%) whereas the second did not (FEV<sub>1</sub>>80%). Data analysis

showed that VAS was significantly but weakly correlated with FEV<sub>1</sub> ( $r = 0.1.91$ ) and FEF<sub>25-75</sub> ( $r = 0.1.23$ ). The relation was stronger in the group of patients with bronchial obstruction in both FEV<sub>1</sub> ( $r = 0.4.7$ ) and FEF<sub>25-75</sub> ( $r = 0.4.2$ ). Authors also demonstrated that a VAS value of 6 could be considered as a reliable cut-off for discriminating children with bronchial obstruction (AUC 0.8.3). They suggested that, especially in children with bronchial obstruction, VAS may be useful as a quick tool, either at home or at doctor's office, in providing a clinically useful approximation of lung function, thus suggesting the necessary measures.

The same research group investigated the usefulness of VAS in assessing breathlessness perception in response to bronchodilation testing in children with asthma (39). They recruited 50 children with overt bronchial obstruction (FEV<sub>1</sub><80%) and matched them with 100 asthmatic children without bronchial obstruction (FEV<sub>1</sub>≥80%). VAS was recorded immediately before and after bronchodilation test. The VAS scores of children either with or without bronchial obstruction improved significantly after bronchodilation. However, in children with bronchial obstruction the reported VAS increase was much higher (>2 units) than children without bronchial obstruction who demonstrated a lower increase (approximately 1 unit). Therefore, according to the authors, VAS assessment of bronchodilation testing may discriminate subjects with overt bronchial obstruction if the VAS breathlessness measurement increases at least 2 units after BD.

Male *et al* (44) tried to determine whether poor perception of breathlessness could be a factor in children presenting to hospital with a severe attack. They retrospectively studied 27 children admitted to hospital with asthma exacerbation. All children had recordings of oxygen saturation, clinical score, FEV<sub>1</sub>, and breathlessness score with the "How Much Puff" scale at admission and at 5, 10, 24, 48, and 72 hours after admission. The authors used the presence of significant hypoxia (SaO<sub>2</sub><92%) at admission as an indicator of a severe asthma attack. Hypoxic children had a trend towards less breathlessness at admission. They also experienced a smaller decrease in dyspnea score for a similar improvement in FEV<sub>1</sub>, in comparison with children presenting without hypoxia. Authors' findings argued that differences in perception of breathlessness do occur among asthmatic children and this may be one of the factors that affect the severity upon presentation to the Hospital.

Melani *et al* (7) used retrospective data from children, adolescent, and adult patients (median age 13 yrs, range 5-56 yrs) who had undergone exercise challenge test exercise-induced bronchoconstriction, and at the same time had quantified their dyspnea with modified Borg scale. They demonstrated that the

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perception of dyspnea could occur independently from bronchoconstriction. This was evident from patients with negative challenge who reported dyspnea. Breathlessness was related to bronchoconstriction in asthmatic patients, but also occurred in non-asthmatic patients who reported exceptional breathlessness without any decrease in FEV<sub>1</sub>. Furthermore, in subjects with positive challenge there was inconsistency in the synchronization of dyspnea and bronchoconstriction, with dyspnea preceding bronchoconstriction and reverting more quickly to baseline. The degree of dyspnea perception was also found to increase with age. They reported, as a general conclusion, that in case of dyspnea, at least when recorded in the laboratory after exercise testing, there was a strong relation with exercise-related symptoms and, as far as bronchoconstriction is concerned, such relation was also present, albeit quite weak.

Van Gent *et al* (57), in a cross sectional study used modified Borg and VAS scales to measure dyspnea in 2 groups of “diagnosed” and “undiagnosed” asthmatic children. Subjects in the first group were already diagnosed with asthma, whereas in the second group asthma –not diagnosed until that time–was actually diagnosed during the recruitment phase of the study. All children underwent hypertonic saline testing for bronchial hyperresponsiveness. The authors found that children with “undiagnosed” asthma had worse perception of dyspnea than children with “diagnosed” asthma and concluded that the blunted sensation of dyspnea in some asthmatic children may result in delayed diagnosis of the disease and put them in jeopardy of a threatening asthma attack.

Horak *et al* (58) investigated 90 children with asthma attending their outpatient clinic. They did not perform challenge tests but compared the children's spirometric indices with the VAS score. The study further attempted to characterize the relation between lung function measurements and the parents' perception of their child's dyspnea. A significant but weak correlation between VAS and spirometric indices ( $r=-0.3.3$  and  $r=-0.3.7$  for FEV<sub>1</sub> and FEF<sub>50</sub>, respectively) was found in patients <10 years of age but not among the older ones. No correlation was found between the parent's scoring and their children's lung function status.

Panditi *et al* (5) measured the perception of dyspnea in asthmatic children during exercise challenge testing on treadmill, using the VAS and Likert scales (the latter is a five point ordinal categorical scale). They further compared parents' independent perception of their children's dyspnea due to exercise induced asthma (EIA) with the dyspnea perception of their children. The study specifically aimed to assess the validity of reported severity of dyspnea by asthmatic children and that by their parents. The authors concluded that there

was only a weak relation of the children's reported dyspnea measurements following the exercise test with the change in FEV<sub>1</sub> before and after the challenge. No relation was found with the rest of spirometric indices (PEF, FEF<sub>50</sub>, or FEF<sub>25-75</sub>). Children's perception of EIA was not affected by any of the checked potential confounders namely, age, gender, asthma severity, medication, and habitual exercise. Parents' perception of their child's EIA was measured in the laboratory by the two different scales, and was not related to any of the lung function measurements. Approximately half of the children had a repeat challenge a few weeks later in which the discrepancies from the first visit were so great that no relation could be established between the changes in VAS and the spirometric indices between visits. An additional interesting finding of this study was that children's retrospective reports of EIA over the previous week, which is the commonly used information in everyday clinical management, had no relation to the laboratory measurements.

In general, children, especially those with undiagnosed asthma, may become tolerant to a certain degree of bronchoconstriction because of adaptation related to frequent bronchoconstriction (59). The asthmatic inflammatory process may reduce perception by damaging sensory receptors associated with dyspnea in the airways (60). Patients may reduce their oxygen demands and experience less dyspnea by learning to stay still and calm instead of being anxious and fidgety (61). In certain cases there is no detectable anxiety-provoking stimulus in their surroundings but instead they receive positive emotions, then despite being aware of their dyspnea, they tend to get used to labored breathing and decrease the amount of perceived breathlessness (62). This is a neglect or indifference of symptoms rather than the so-called blunting (61,63) of symptoms.

## 4. CONCLUSIONS

Dyspnea is a complex symptom and the underlying psycho-physiologic mechanism is largely undefined. Its perception varies among individuals and this may have important consequences on issues regarding diagnostic approach and management of patients.

A number of studies have investigated the perception of dyspnea in children with asthma and have tried to clarify the relation between this subjective feeling of difficulty in breathing and actual bronchoconstriction. In general, the results support that this relation is weak and variable. Poor perception of dyspnea may be a risk factor for severe asthma exacerbations. Patients who do not perceive dyspnea may not be motivated to adherence with their daily treatment with inhaled corticosteroids. Children who underestimate their symptoms tend to seek medical help only at a late stage of their exacerbations.

Moreover, poor perception contributes to the considerable number of children without proper diagnosis despite suffering from asthma. In this case, the absence of prophylactic treatment combined with poor alertness may result in the first clear presentation of their disease with a severe and possibly life threatening acute attack. Parents and caregivers appear to be even less accurate in detecting their child's symptoms. Since dyspnea is the main symptom of asthma, and disease management is based largely on the description of symptoms between clinic visits, unreliable symptom report may mislead decision-making for long-term treatment of asthma. Thus, therapeutic decisions should not be taken solely on patients' perception and description of dyspnea.

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