Measuring Exertional Dyspnoea in Health and Disease

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AIMS

- To understand current concepts on the physiological origins of exertional dyspnoea in common chronic obstructive and restrictive lung diseases:
- To present a physiological rationale for dyspnoea amelioration based on current neuro-physiological constructs.
- To briefly review methods to measure multidimensional dyspnoea across its sensory intensity, affective and impact domains, giving appropriate examples.

SUMMARY

Activity-related dyspnoea is the most common symptom of patients with chronic lung diseases and underpins perceived poor health status. Our understanding of the nature and source of dyspnoea continues to grow but successful amelioration of this distressing symptom can remain elusive, especially in those with advanced lung diseases.

According to the 2012 ATS definition, dyspnoea is: “A subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity”. A central recommendation of the ATS group was that dyspnoea should be measured across three major domains: sensory-perceptual experience (intensity, quality), affective distress and symptom impact or burden on daily living.

Physiology of dyspnoea

Norman Jones, the great Canadian physiologist, summarized his thoughts on the origins of dyspnoea as follows: “Breathlessness can be seen to result from the imbalance between the demand for breathing and the ability to achieve the demand”. Indeed, in most clinical situations where patients report severe dyspnoea, ventilatory demand-capacity imbalance is present. Thus, in patients with chronic lung conditions, ventilatory demand reaches or exceeds maximal ventilatory capacity (MVC) during physical exertion. In other words, for a given work rate the ratio of ventilation (VE) to MVC is abnormally high compared with healthy controls. Similarly, the ratio of respiratory muscle effort (measured by esophageal manometry) to maximal possible respiratory effort is increased at a given work rate or VE in patients with lung disease versus healthy controls.

Dyspnoea and increased respiratory neural drive (RND)

Increased RND (compared with normal) is a common final pathway in dyspnoea causation in patients with chronic lung diseases during activity. The motor output of respiratory centers in the medulla and cortex cannot currently be measured directly. However, ventilatory output (tidal volume *breathing frequency) provides an indirect measure of RND in patients with milder lung disease. Ventilatory output measured in this way underestimates RND in advanced lung disease because of the attendant mechanical constraints. Tidal measurements of esophageal pressure and diaphragmatic electromyography (both expressed relative to maximum) also provide indirect measures of motor
command output, and are uniformly amplified in patients with lung disease compared to healthy individuals. The magnitude of RND during exercise is mainly determined by the CO2 output (VCO2) reflecting the metabolic requirement of the task. An additional determinant in patients with lung diseases is the extent of wasted ventilation [dead space (VD)] and the regulated arterial CO2 set-point. In most chronic lung diseases [COPD, interstitial lung disease (ILD), pulmonary arterial hypertension], the VD component of the tidal breath is abnormally high reflecting relatively reduced pulmonary blood perfusion of alveolar units with preserved or increased ventilation. This inefficiency of CO2 elimination by the diseased lungs results in increased chemostimulation of medullary centers and consequent increased RND. It is thought (based on animal studies) that sensory information about increased RND arising from the medulla (and motor cortex) is directly conveyed to the somatosensory cortex where it is perceived as increased sense of respiratory muscle effort.

**Abnormal respiratory mechanics and dyspnoea**

In healthy individuals during spontaneous breathing, tidal volume (VT) is positioned in the linear portion of the respiratory system’s pressure-volume (PV) relaxation curve. Even at high exercise intensities the expanding VT remains within this linear portion of the PV curve where the force-velocity and length-tension properties of the respiratory muscles are optimized. By contrast, in COPD the PV curve is compressed from below because of lung hyperinflation but maintains its sigmoid shape. Because of the resultant reduced inspiratory capacity (IC) – indicating proximity of VT to total lung capacity (TLC) – the muscles of the respiratory system become overloaded and functionally weakened. In this scenario of “high-end mechanics”, critical mechanical limits on VT expansion are in place despite near maximal RND. Similarly, in patients with lung fibrosis the sigmoidal PV curve is compressed, this time from above (reduced TLC), and VT expansion is again restricted because of the reduced IC. The growing disparity between increasing RND and VT after it has reached a plateau has been termed neuromechanical dissociation (NMD). We have postulated that NMD contributes to perceived “unsatisfied inspiration” – a distressing qualitative dimension of dyspnoea common in both obstructive and restrictive lung diseases, which is rarely (if ever!) reported in healthy individuals.

The neurophysiological construct described above provides a practical basis for an approach to the alleviation of dyspnoea in individual patients with chronic lung diseases. Thus, treatment is primarily directed towards reducing RND (e.g., reducing VCO2 or metabolic acidosis), improving mechanics (e.g., increasing IC) or modifying the affective aspect of dyspnoea (e.g., counseling, sedation).

**Measuring multidimensional dyspnoea**

**Sensory intensity**

Intensity of dyspnoea can be measured by validated instruments, such as visual analogue scales (VAS) and the Borg category scales with ratio properties, during a standardized physical task (i.e., six-minute walk distance tests, shuttle walk tests, incremental or constant work rate treadmill or cycle exercise tests). This approach allows us to evaluate the sensory intensity responses to a quantifiable stimulus (e.g., increasing work rate, oxygen uptake, or ventilation). These perceptual responses should preferably be compared with reference values from a healthy population studied under similar experimental conditions.

For the purpose of evaluating the efficacy of an intervention (e.g., supplemental oxygen, exercise training, bronchodilators, etc.) in reducing dyspnoea intensity, constant work rate (~60-80% maximum) endurance studies are preferable to incremental tests. The demonstration that following the intervention dyspnoea intensity is reduced (by 1 Borg unit) at a submaximal standardized time or ventilation, thereby allowing greater exercise tolerance, indicates that the intervention is effective. Thus, after the intervention the patient is capable of undertaking a demanding physical task with less respiratory discomfort and for a longer duration than before. This approach to dyspnoea intensity
measurement during standardized physical tasks allows an assessment of the mechanisms of dyspnoea in the individual which can be targeted for treatment.

Quality of dyspnoea

Qualitative dimensions of dyspnoea are more difficult to measure during activity. One approach is to present patients with a selection of pertinent descriptor choices after exercise completion and to rank the descriptors that most faithfully represent their particular experience of dyspnoea. For example, healthy individuals invariably select descriptors that allude to increased work or effort of breathing, whereas patients with obstructive or restrictive lung conditions additionally select descriptors of “inspiratory difficulty” and “unsatisfied inspiration.”

Affective components of dyspnoea

It is believed that intensity and affective components of dyspnoea have distinct neurobiologic origins: intensity reflects increased RND and central corollary discharge, and the affective responses represent increased activation of limbic and para-limbic centers of the brain. Exercise training may have differential effects on these two components. For example, affective responses (fear, anxiety, frustration, distress) to exercise can be improved following pulmonary rehabilitation in the absence of reduction in standardized Borg intensity ratings during exercise. In practice, the affective aspect of dyspnoea is difficult to measure and current approaches remain experimental.

Measuring the impact of dyspnoea

A number of “magnitude of task” questionnaires have been validated for the purpose of assessing the impact of this symptom on the ability to perform daily activities. These widely used questionnaires include the Medical Research Council (MRC) dyspnoea scale, an oxygen cost diagram (OCD), Baseline Dyspnoea Index (BDI), the dyspnoea component of the Chronic Respiratory Questionnaire (CRQ) and the activity component of the St. George’s Respiratory Questionnaire (SGRQ). All scales are reproducible and have construct validity and are adequately responsive to various therapeutic interventions. They provide valuable information about the functional status of the individual patient as it relates to dyspnoea. The Transition Dyspnoea Index (TDI) has been used extensively in clinical trials: the minimal clinically important difference is 1 unit. The MRC scale, while useful in stratifying severity of dyspnoea and activity restriction, is less sensitive even in response to effective interventions such as exercise training.

Glossary

DH, dynamic lung hyperinflation
EELV, end-expiratory lung volume
EILV, end-inspiratory lung volume
EMGdi, diaphragmatic electromyography
ERV, expiratory reserve volume
F, breathing frequency
IC, inspiratory capacity
ILD, interstitial lung disease
IRV, inspiratory reserve volume
P0.1, negative airway pressure during the first 100 msec of an occluded inspiration (neuromuscular drive)
PaCO2, partial pressure of arterial carbon dioxide
PaO2, partial pressure of arterial oxygen
Pes, esophageal pressure
Pimax, maximum inspiratory pressure
RA, room air
RV, residual volume
SaO2, arterial oxygen saturation
TLC, total lung capacity
VAS, visual analogue scale
VC, vital capacity
VCO2, carbon dioxide output
VE, minute ventilation
VT, tidal volume

REFERENCES