SYMPOSIUM ARTICLE
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Evaluation and management of dyspnoea

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Dyspnoea is one of the commonest symptoms experienced by patients with cancer - both as a feature of the disease and also as a consequence of its treatments. In a recent Canadian series of nearly 1000 cancer out-patients, 46% reported dyspnoea (1). The Medical Research Council (MRC) of the UK has found that of lung cancer patients entering its trials, dyspnoea was a presenting complaint in 87% of small cell cancer and in 86% of non-small cell cancer patients. In advanced cancer, 33% of patients entering a Japanese hospice reported dyspnoea but that rose to 66% near to death (2).

CAUSATION

Dyspnoea is the end result of many discrete but overlapping potential pathways of pathophysiological change that can occur in patients with cancer. These are modified and may be amplified by :

- Co-morbidities (especially COPD, other chronic lung diseases and heart disease);
- De-conditioning associated with immobility and cancer cachexia;
- Effects of ageing;

In any single patient, several of these factors could be involved, to produce a symptom level and an effect on functioning and quality of life. Thus, the assessment and management of dyspnoea requires a good understanding of the underlying mechanisms. However, the clinical features displayed by patients with dyspnoea are often non-specific and this often makes it difficult -even with laboratory testing and medical imaging - to differentiate between different pathophysiological causes.

There are three basic dimensions of the sensation of dyspnoea: (1) Air hunger - the unpleasant sensation of the need to breathe harder, but being unable to actually increase ventilation; (2) Effort of breathing - the physical discomfort and tiredness associated with prolonged hard breathing; (3) Chest tightness - the feeling of constriction in the chest wall and the inability to breathe in or out.

There are several validated questionnaires, which have been developed to capture these dimensions of dyspnoea and their impact on functioning and quality of life (3).

In broad terms, the main causes of dyspnoea are :

- Increased chemical or neurological drive to breathe
- Increased work of breathing
- Decreased neuromuscular power to ventilate.

Often in cancer patients, especially those with cachexia, there is a combination of these factors. Identifying which of these mechanisms are at work in an individual patient can be helpful for planning rational treatment.

The major neurochemical drives, which control normal breathing and can influence dyspnoea, are the response to hypercapnia and to hypoxia. Usually the hypercapnic drive is stronger and is mainly responsible for the sensation of air hunger. Hypercapnia results from severe airflow obstruction or restrictive lung disease. Hypoventilation can also arise from restriction of chest movement by pleural effusion and ascites. Very small increases in PCO2 can give measurable change in the sensation of dyspnoea.

Hypoxia can be caused by loss of alveoli or small air-conducting bronchioles, leading to reduced or turbulent airflow. It can arise in bronchopneumonia, airflow obstruction, pulmonary congestion and lung collapse. Ventilation-perfusion mismatching, e.g., with pulmonary thromboembolism, can also cause hypoxia.

Besides the neurochemical drives to respiration, the other important mechanisms that impact on dyspnoea are the mechanoreceptors and the ergoreceptors (also called metaboreceptors) (4). These are responsible for the increased ventilation seen in pulmonary congestion (via J-receptors) and the generation of dyspnoea in muscle wasting conditions. Increased work of breathing arises when the "ventilatory pump" is working against a significant strain, e.g., in pneumonia, pulmonary fibrosis, pleural effusion, lymphangitis carcinomatosa, upper airway obstruction, and emphysema. Clinical clues, which help to identify this factor, include the patient favouring the upright position, or stridor.

Decreased neuromuscular power is seen in patients with neurological impairment, e.g., phrenic nerve palsy, cachexia and other wasting disorders (including steroid-induced myopathy). The maximal inspiratory pressure (MIP) is a useful pulmonary function laboratory method of determining neuromuscular power.

ASSESSMENT

Put together, the signals from the peripheral and medullary receptors to the brain processing areas form the "feed-back" system, while the neurogenic flow from the brain to the respiratory muscles are the "feed-forward" system. When an imbalance forms between these

two information flows, the resulting 'error signal' is a key factor in the generation of the sensation of dyspnoea4.

It is important to be aware of non-respiratory causes of dyspnoea, e.g., anaemia, heart failure and pulmonary thromboembolism. With normal ageing, several changes take place -

- Decreased lung elasticity
- Decreased respiratory muscle strength
- Reduced forced vital capacity and peak flow rate
- Increased air-trapping
- Deterioration in gas exchange
- Reduced ventilatory response to hypoxia and hypercapnia
- Increased ventilatory response to exercise.

Bedside assessment of the breathless patient therefore requires several clinical measures:

- Observation of the patient's position and behaviour
- Clinical examination of the chest and heart
- Pulse oximetry
- Simple exercise testing.

Further investigations that may be helpful include -

- Medical imaging (chest radiograph; ultrasound; CT for mediastinal features)
- Response in dynamic lung volumes to bronchodilator
- Flow-volume loop if upper airway obstruction is suspected
- MIP

MANAGEMENT

With the preceding grounding in respiratory physiology and understanding of the pathological mechanisms, it is possible to prepare a rational multimodal plan for management. First, treatable factors should be tackled, e.g., pleural effusion, heart failure, anaemia, and reversible airflow obstruction. If anti-cancer treatments are still feasible (radiation or chemotherapy) then these should be started sooner rather than later.

Agents, which modify the neurochemical drives, are most helpful for symptomatic palliation. These include the opioids, benzodiazepines and oxygen. Systematic review favours oral or subcutaneous morphine but other opioids may have advantages (5). The addition of helium to oxygen (heliox) gives significant improvement to exercise-related dyspnoea in lung cancer (6). Novel approaches, e.g., nebulised frusemide, need further evaluation (7). Non-pharmacological approaches are nearly always helpful, particularly in the early stages. These include psychological therapies, breathing training and acupuncture (8). However, in the terminal stage, the management of dyspnoea requires sensitive use of sedation-inducing drugs, oxygen and nursing care.

REFERENCES

1. Dudgeon DJ, Kristjanson L, Sloan JA, Lertzman M, Clement K.Morit. Dyspnea in cancer patients: prevalence and associated factors. J Pain Symptom Manage 2001;21(2):95-102.
2. Hoskins P, Ahmedzai SH. In: Ahmedzai SH, Muers M, editors. Supportive care in respiratory disease. Chapter 30. Assessment and management of respiratory symptoms of malignant disease. Oxford: Oxford University Press (in press)
3. Bruera E, Neumann CM. In: Ahmedzai SH, Muers M, editors. Supportive care in respiratory disease. Chapter 7. Assessment of dyspnoea in clinical practice and audit. Oxford: Oxford University Press (in press)
4. Gillette MA, Schwartzstein RM. In: Ahmedzai SH, Muers M, editors. Supportive care in respiratory disease. Chapter 6. Mechanisms of dyspnoea. Oxford: Oxford University Press (in press)
5. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE. A systematic review of the use of opioids in the management of dyspnoea. Thorax 2002;57(11):939-44.
6. Ahmedzai SH, Laude E, Robertson A, Troy G, Vora V. A double-blind, randomised, controlled Phase II trial of Heliox28 gas mixture in lung cancer patients with dyspnoea on exertion. Br J Cancer. 2004;90(2):366-71.
7. Nishino T, Ide T, Sudo T, Sato J. Inhaled furosemide greatly alleviates the sensation of experimentally induced dyspnea. Am J Respir Crit Care Med 2000;161(6):1963-7.
8. MacLeod R. In: Ahmedzai SH, Muers M, editors. Supportive care in respiratory disease. Chapter 12. Psychosocial therapies. Oxford: Oxford University Press (in press)