What is the current evidence in the management of dyspnoea in advanced disease?

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Background

Dyspnoea is a distressing symptom for patients and carers. It is highly prevalent in advanced COPD (90-95%), CHF (60-88%) and cancer (10-70%) [Solano 2006]. The symptomatic treatment of dyspnoea is still limited but research interest is growing to strengthen the evidence.

Aim

To demonstrate the current evidence of pharmacological and non-pharmacological interventions for dyspnoea in advanced diseases (COPD, cancer, CHF, ILD, and MND).

Method

Review of the literature. Sources: MEDLINE (1950-2008), EMBASE (1980-2008), Cochrane databases (1993-2008). Search: RCT, review, guideline combined with terms for dyspnoea; in addition, reference search and related articles link; Study selection: well conducted Systematic Reviews & RCTs. The SIGN classification (Scottish Intercollegiate Guideline Network) was used for grading of evidence and grading of recommendation (appropriateness for clinical practice).

Opioids and walking aids for the management of dyspnoea

Opium: http://www.stromberg-gymnasium.de/unterricht/faecher/chl/interl/seite2.htm
Rollator: http://www.zipperlein.com/catalog/product_info.php/products_id/94

Results

Good evidence for **significant improvement in reducing dyspnoea**:

1. Opioids
2. Pulmonary rehabilitation (COPD)
3. Non-invasive ventilation (COPD, MND)
4. Neuro-muscular electrical stimulation (COPD)
5. Chest-wall vibration (COPD, MND)
6. Walking aids and breathing training (COPD)

Evidence for **no consistent benefical effect** for:

1. Benzodiazepines (COPD, cancer)
2. Oxygen (Cancer, CHF)

Limited data to judge the evidence for:

1. Inhaled furosemide, phenothiazines, antidepressants, heliox
2. Fan, breathlessness service/counselling and support, acupuncture, music, relaxation, psychotherapy

Intervention	Reference	Disease	Design (number of studies/patients)	Level Evid.*	Results	Effect/Grade of recom.*
Pharmacological interventions						
Opioids	Jennings 2001 Abernethy 2003	COPD, Cancer, CHF COPD, Cancer, MND, ILD	**Cochrane SysRev** (18 RCTs) **RCT** (38 pts)	**1++** **1++**	Significant improvement	**+ / A**
Benzodiazepines	Simon 2009	COPD, Cancer	**Cochrane SysRev** (7 RCTs, 1 CCT)	**1++**	No evidence for improvement	**- / B**
Oxygen	Cranston 2008	Cancer, CHF, Kyphoscoliosis	**Cochrane SysRev** (8 RCTs)	**1++**	No consistent beneficial effect	**- / B**
Non-pharmacological interventions						
Pulmonary rehabilitation	Lacasse 2006	COPD	**Cochrane SysRev** (31 RCTs)	**1++**	Significant improvement	**+ / B**
Non-invasive ventilation	Heffernan 2006 Kolodziej 2007	MND COPD	**SysRev** (86 observ. Stud., no RCT) **SysRev** (6 RCTs, 9 non-RCTs)	**2++** **1+**	Potential beneficial effects (MND) Significant improvement (COPD)	**+ / B**
Other 1. Neuro-musc. electrical stimulation 2. Chest wall vibration 3. Walking aids (rollator) 4. Breathing training	Bausewein 2008	1. COPD 2. MND, COPD 3.+4. COPD	**Cochrane SysRev** (47 RCTs)	**1++**	1.+2. strong evidence 3.+4. moderate evidence	**+ / B**

Table – Characteristics of selected reviews/studies demonstrating the evidence for the management of dyspnoea

(SysRev = Systematic review; COPD = Chronic obstructive pulmonary disease; CHF = Chronic heart failure; ILD = Intestinal lung disease; MND = Motor neuron disease; RCT = Randomized controlled trial; CCT = controlled clinical trial) * Levels of Evidence and Grade of Recommendation – SIGN classification (www.sign.ac.uk)

Conclusion

Only a few interventions have shown evidence for the relief of dyspnoea. These interventions were tested mainly in COPD **or** cancer, but rarely in a broad range of diseases – which limits the grade of recommendation (A-D).

Implication for clinical practice:

1. Opioids are the gold standard in the pharmacological management.
2. A broad range of non-pharmacological treatments are recommended.
3. Using benzodiazepines and oxygen only after individual testing (n=1).

Implications for research:

1. Promising interventions should be tested in a broader range of diseases – e.g. rehabilitation, walking aids, support services, inhaled furosemide.
2. Collaboration and multicenter-RCTs are needed.

References

Abernethy AP et al. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. BMJ 2003; 327(7414):523-8.
Bausewein C et al. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. Cochrane Database Syst Rev 2008.
Cranston JM et al. Oxygen therapy for dyspnoea in adults. Cochrane Database Syst Rev 2008.
Heffernan C et al. Management of respiration in MND/ALS patients: an evidence based review. Amyotroph Lateral Scler 2006; 7(1):5-15.
Jennings AL at al. Opioids for the palliation of breathlessness in terminal illness. Cochrane Database Syst Rev 2001.
Kolodziej MA et al. Systematic review of noninvasive positive pressure ventilation in severe stable COPD. Eur Respir J 2007; 30(2):293-306.
Lacasse Y et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2006.
Simon S et al. Benzodiazepines for the relief of breathlessness in malignant and advanced non-malignant diseases in adults (Protocol). Cochrane Database Syst Rev 2008 (Rev in 2009).
Solano JP et al. A comparison of symptom prevalence in far advanced cancer, AIDS, CHF, COPD and renal disease. J Pain Symptom Manage 2006;31(1):58-69.

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