Palliative Meds Info
tel: 01 4912578
palliativemedsinfo@olh.ie

Our Lady's Hospice & Care Services
tel: 01 4912578 Harold's Cross
palliativemedsinfo@olh.ie & Blackrock

Question: What are the treatment options for chronic cough?

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Summary

Any possible underlying causes of chronic cough should be identified and managed before proceeding with treatment. The type of cough should be identified and managed accordingly. Simple interventions such as glycerol or honey can help in the management of chronic cough however some patients may require other medications such as opioids or GABA agonists. It is important that a weak opioid should not be prescribed for the management of cough for those already receiving a strong opioid. If opioids or benzodiazepines are to be used they should be used at the lowest dose and shortest possible time to prevent tolerance and dependence.

What is Cough?

A cough is a physiological protective mechanism but may be as a result of an underlying medical condition.[1] Cough helps to clear central airways of foreign matter, secretions or pus and should generally be encouraged.[2,3] Cough can be productive, characterised by the presence of sputum, or non-productive. A chronic cough is defined as lasting more than 8 weeks.[2] Cough becomes pathological when it is dry (or non-productive), adversely affects sleep or quality of life or causes other symptoms such as muscle strain and vomiting.[3] In patients with cancer the prevalence of cough is 50-80% and is highest in those with lung cancer. Causes of cough should be identified before proceeding with pharmacological therapy.

Causes of Cough

The most common cause of cough is respiratory tract infection.[2] In advanced cancer, chronic cough is most likely caused by endobronchial tumour within the central airways.[2]

Some causes of cough are correctable including smoking, rhinitis (allergic, post-infection or vasomotor), bacterial sinusitis, asthma, gastro-oesophageal reflux (GORD), chronic obstructive pulmonary disease (COPD), angiotensin converting enzyme (ACE) inhibitors.[2] Other causes of cough include bulbar muscle weakness, neuromuscular incoordination, heart failure, vocal cord paralysis, chemotherapy and radiotherapy.[2]

Management of Cough

Correct the correctable

If possible, the cause of the cough should be treated specifically, e.g. antibacterials for infection.[4] However, when the cause of the cough is not amenable to specific treatment or is unknown, measures should be taken to suppress the cough[4]

Pharmacological Treatment

Antitussives can be divided into peripherally-acting and centrally-acting agents.[4] The former include local pharyngeal soothing agents (demulcents) and local anaesthetics and their derivatives.[4] Most centrally-acting antitussives are opioids or opioid derivatives.[4] In palliative care, opioid antitussives are generally used in preference to other drugs.[4] Generally, the evidence supporting the use of antitussives in acute or chronic cough is low-level.[4] For treatment options see Table 1.

Table 1: Treatment Options for Chronic Cough			
Demulcents: glycerol, honey (e.g. Glycerin, Honey & Lemon)	Stimulate the production of saliva and soothes the oropharynx. The associated swallowing may also interfere with the cough reflex. The sweet taste itself may be antitussive by stimulating the release of endogenous opioids in the brain stem, and this may contribute to the large placebo effect seen in RCTs of demulcents. The antitussive effect of demulcents is generally short-lived.[4]		
Opioids	Opioids act primarily by suppressing the cough reflex centre in the brain stem. Opioids appear less effective for cough due to upper airway disorders, e.g. upper respiratory tract infection, possibly because laryngeal cough involves opioid-insensitive central mechanisms and/or reflects a different reflex (i.e. an expiration reflex).[4]		
Active	Preparations	Dosage regimes	Comments
Dextromethorphan (opioid derivative)	Robitussin dry cough, Benylin non-drowsy dry cough	15mg (10mL) up to four times daily[5,6]	Dextromethorphan has fewer adverse effects than codeine but little evidence to support its effectiveness in severe cough.[7]
Pholcodeine (opioid derivative)	Pholcodex 5mg/5ml solution[8]	10mls every 3-4 hours as required[8]	EMA concluded that the evidence to support concerns of IgE-sensitization to neuromuscular blocking agents is weak; risk:benefit ratio remains favourable.[4]
Codeine (weak opioid)	Codinex 15mg/5ml solution[9]	5-7.5mL up to four times daily[9]	Widely used in practice despite limited evidence.[11] Should not be prescribed if the patient is already on a strong opioid for the management of pain.[2,4]
	Codant 30mg tablets[10]	30mg every 6 hours as required[10]	
Morphine	Immediate release formulations (unlicensed indication)	5–10mg four times daily[4] (but 2.5–5mg four times daily if not switching from codeine)[4]	Effective in some but not all patients; some initially non-responsive showed improvement when dose was increased.[11]
Methadone	Oral Solution (unlicensed indication)	Initially 1–2 mg every 4–6hrs but reduced to twice daily on prolonged use.[12]	Caution is advised due to the risk of accumulation.[12]
GABA agonists	If opioid antitussives are unsatisfactory, GABA agonists may be considered.[4] They may act by interfering with the cough reflex and/or central sensitization which leads to cough hypersensitivity[4]		
Active	Dosage regimes	Comments	
Gabapentin	• 300mg three times daily (TDS), increased up to 600mg TDS[4] • Case reports have used smaller starting doses, e.g. 100mg twice daily[4]	Gabapentin should be initiated at a low dose to prevent dizziness and sedation.[11] Efficacy should be re-assessed after six months of treatment to ensure therapeutic benefit has been achieved.[11]	
Pregabalin	Pregabalin is initiated at low dosage and gradually increased over a one week period to 300mg/day.[11]		
Diazepam	5mg once daily/at bedtime[4]	Caution is advised, prescribed at the lowest dose for the shortest duration to minimise risks of tolerance and dependence.	
Baclofen	10mg TDS or 20mg once daily[4]	Inhibits relaxation of the lower oesophageal sphincter, reducing GORD.[4] Maximum effect seen after 2–4 weeks.[4]	
Other possible treatment options			
Sodium Cromoglicate	10mg inhaled four times daily[4,13]	Reported to improve cough in patients with lung cancer within 36–48h.[4]	
Paroxetine	5-20mg once daily[14]	Case series reports benefit in 5 patients with opioid-resistant cough. Sleepiness was observed in the first days of therapy.[14]	
Nebulised Lidocaine	For information on the use of nebulised lidocaine to treat an intractable cough see Palliative Meds Info document. Available here: http://olh.ie/wp-content/uploads/2014/09/What-is-the-evidence-to-support-the-use-of-nebulised-lidocaine-to-treat-an-intractable-cough-1.pdf		

References:

1. Monograph Cough. Martindale: The complete drug reference. Available from www.medicinescomplete.com. Accessed on the 23/03/17.
2. Twycross R., et al. Symptom management in advanced cancer, 4th Edition. 2009.
3. Monograph Drugs for Cough. Palliative Care Formulary. Available from www.palliativedrugs.com. Accessed on the 23/03/17.
4. Monograph Anti-Tussives. Palliative Care Formulary. Available from www.palliativedrugs.com. Accessed on the 23/03/17.
5. Summary of Product Characteristics Robitussin Dry Cough 7.5mg/5ml Oral Solution. Available from www.hpra.ie. Accessed on the 23/03/17.
6. Summary of Product Characteristics Benylin non-drowsy dry cough syrup. Available from www.hpra.ie. Accessed on the 23/03/17.
7. Monograph Dextrometorphan. Martindale: The complete drug reference. Available from www.medicinescomplete.com. Accessed on the 23/03/17.
8. Summary of Product Characteristics Pholcodex 5mg/5mL oral solution. Available from www.hpra.ie. Accessed on the 23/03/17.
9. Summary of Product Characteristics Codinex 15mg/5mL oral solution. Available from www.hpra.ie. Accessed on the 23/03/17.
10. Summary of Product Characteristics Codant 30mg tablets. Available from www.hrpa.ie. Accessed on the 23/03/17.
11. Weinberger SE, Silvestri RC. Treatment of subacute and chronic cough in adults. Available from www.uptodate.com. Accessed on the 23/03/17.
12. Monograph Methadone. Martindale: The complete drug reference. Available from www.medicinescomplete.com. Accessed on the 23/03/17.
13. Molassiotis A, Smith J, Bennett M, Blackhall F, Taylor D, Zavery B, Harle A, Booton R, Rankin E, Lloyd-Williams M, Morice A. Clinical expert guidelines for the management of cough in lung cancer: report of a UK task group on cough. Cough 2010, 6: 9.
14. Zylicz Z and Krajnik M. What Has Dry Cough in Common With Pruritus? Treatment of Dry Cough with Paroxetine. Journal of Pain and Symptom Management 2004; 27(2) 180-183.