NOISY UPPER RESPIRATORY TRACT SECRETIONS: PHARMACOLOGICAL MANAGEMENT

AUTHORS: JASON W BOLAND, ELAINE G BOLAND

Jason Boland; Hull York Medical School, Senior Clinical Lecturer and Honorary Consultant in Palliative Medicine; Care Plus Group and St Andrew's Hospice,

Elaine Boland; Hull and East Yorkshire Hospitals NHS Trust

CORRESPONDING AUTHOR: JASON W BOLAND

Journal: BMJ Supportive & Palliative Care

This article has been accepted for publication in BMJ Supportive & Palliative Care, 2019 following peer review, and the Version of Record can be accessed online at http://dx.doi.org/10.1136/bmjspcare-2019-001791.

NOISY UPPER RESPIRATORY TRACT SECRETIONS: PHARMACOLOGICAL MANAGEMENT

Upper respiratory tract secretion accumulation with noisy breathing (‘death rattle’) is caused by salivary secretions pooling within the hypopharynx. It occurs in people who cannot swallow, usually in the last days of life.[1-3] It is reported in 12–92% of dying patients[3-6]; the weighted mean prevalence is 35%.[5] The noise and secretions can be distressing for some family members and staff.[5-8] They are reportedly not associated with subjective respiratory distress,[4, 5] although those with the problem often have impaired consciousness so patient impact is unclear.[5] Antimuscarinic drugs (e.g. glycopyrronium and hyoscine butylbromide) reduce new secretion formation.[2-4]

Systematic reviews have found no benefit of antimuscarinics over placebo. They advise against their routine use once noisy upper respiratory tract secretions are present.[3, 5, 9] Although they reduce production, they do not remove existing secretions. The idea of preventative prophylactic administration, before secretions occur, for those at risk is tantalising. It is not currently possible to identify those at higher risk of respiratory secretions.[9, 10]

An open-label exploratory study in dying hospice patients with impaired consciousness compared prophylactic hyoscine butylbromide (n=51) with administration after secretions developed (n=81).[11] The loudness of the secretions’ noise was determined by the nurse in charge. Prophylactic hyoscine butylbromide was more effective; 6% had noisy secretions in the prophylactic arm versus 61% in the standard treatment arm. Dose titration did not occur (all received hyoscine

butylbromide as a 20mg stat dose followed by 60mg/day).[11] Onset of death rattle was also delayed in the prophylactic group (12 hours v 36 hours).[11] This was an important exploratory study although it was unblinded and side effects were not reported.[11]

Before implementation into routine clinical practice, data on the benefits and harms of prophylactic antimuscarinics are needed from powered placebo-controlled studies.[12, 13] These are ongoing.[14] Without a blinded placebo comparator arm, bias (e.g. information/observer) is likely to influence the results. A previous uncontrolled, unblinded study of antimuscarinics reported benefit,[15] but this effect no longer remained in controlled blinded studies.[3, 5, 9, 16] This might partly be due to reduction in noisy breathing with placebo.[16] Furthermore, we do not fully understand the natural history of noisy secretions (hence the need for a placebo arm) and antimuscarinic side effects (e.g. constipation, dry mouth, and urinary retention which can also cause distress).[2, 13, 17] Prophylactic hyoscine butylbromide in all dying patients cannot be recommended.[12, 13] It remains important to assess, effectively communicate with the patient's family (even pre-emptively), and use non-pharmacological measures.[1, 3, 6, 12, 18, 19] If pharmacotherapy is indicated, frequent assessment for efficacy and adverse effects is needed, stopping after 12-24 hours if ineffective (although dose titration might be needed).[3, 19] In future studies, an important clinical outcome might be the views, concerns, and distress of family/carers about noisy upper respiratory tract secretions.

Box - Practical management of noisy upper respiratory tract secretions

Consider pre-emptive discussion and preparing relatives and carers about end of life care and related potential symptoms.

Assessment

- Are they *upper* respiratory tract? Or just another cause of the noisy breathing (e.g. chest infection, pulmonary oedema)
- Is anything reversible?
- Do they appear distressing to the patient?
- Are they distressing to relatives/carers?

Management

- Discuss and explain noisy respiratory secretions to relatives/carers (and if appropriate the patient) - this can help alleviate distress
- Use non-pharmacological measures, e.g. repositioning
- If distressing, a trial of antimuscarinics could be considered. This should be discussed with relatives, the patient monitored for adverse effects and discontinued after 24 hours if ineffective (dose titration might be needed). If drugs are used, they should be used promptly as they do not remove formed secretions. Refer to local guidelines, either hyoscine butylbromide or glycopyrronium are most common, both given subcutaneously:
    - Hyoscine butylbromide: 20mg stat with 60mg/day. As required doses can continue to be given a maximum of hourly. Maximum usual daily dose is 120mg.
    - Glycopyrronium: 200mcg stat with 800mcg/day. As required doses can be given a maximum of hourly. Maximum usual daily dose is 1200mcg.

REFERENCES:

1. Cherny N, Fallon M, Kaasa S, Portenoy RK and Currow DC. *Oxford textbook of palliative medicine*. Oxford University Press, USA, 2015.

2. Star A and Boland JW. Updates in palliative care - recent advancements in the pharmacological management of symptoms. *Clin Med (Lond)*. 2018; 18: 11-6.

3. Wee B and Hillier R. Interventions for noisy breathing in patients near to death. *Cochrane Database Syst Rev*. 2008: CD005177.

4. Campbell ML and Yarandi HN. Death rattle is not associated with patient respiratory distress: is pharmacologic treatment indicated? *J Palliat Med*. 2013; 16: 1255-9.

5. Lokker ME, van Zuylen L, van der Rijt CC and van der Heide A. Prevalence, impact, and treatment of death rattle: a systematic review. *J Pain Symptom Manage*. 2014; 47: 105-22.

6. Shimizu Y, Miyashita M, Morita T, et al. Care strategy for death rattle in terminally ill cancer patients and their family members: recommendations from a cross-sectional nationwide survey of bereaved family members' perceptions. *J Pain Symptom Manage*. 2014; 48: 2-12.

7. Wee BL, Coleman PG, Hillier R and Holgate SH. The sound of death rattle I: are relatives distressed by hearing this sound? *Palliat Med*. 2006; 20: 171-5.

8. Wee B, Coleman P, Hillier R and Holgate S. Death rattle: its impact on staff and volunteers in palliative care. *Palliat Med*. 2008; 22: 173-6.

9. Kolb H, Snowden A and Stevens E. Systematic review and narrative summary: Treatments for and risk factors associated with respiratory tract secretions (death rattle) in the dying adult. *J Adv Nurs*. 2018; 74: 1446-62.

10. Likar R, Michenthaler MC, Traar R, Molnar M and Neuwersch S. Clinical factors influencing death rattle breathing in palliative care cancer patients : Non-interventional study. *Z Gerontol Geriatr*. 2017; 50: 332-8.

11. Mercadante S, Marinangeli F, Masedu F, et al. Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later. *J Pain Symptom Manage*. 2018. e-publication.

12. Clark K, Sheehan C and Currow DC. Letter to the Editor Re: "Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later". *J Pain Symptom Manage*. 2019; 57: e16-e7.

13. Boland JW, Johnson M and Currow D. Response to "Hyoscine butylbromide for the management of death rattle: sooner rather than later". *J Pain Symptom Manage*. 2018. e-publication.

14. van Esch HJ, van Zuylen L, Oomen-de Hoop E, van der Heide A and van der Rijt CCD. Scopolaminebutyl given prophylactically for death rattle: study protocol of a randomized double-blind placebo-controlled trial in a frail patient population (the SILENCE study). *BMC Palliat Care*. 2018; 17: 105.

15. Protus BM, Grauer PA and Kimbrel JM. Evaluation of atropine 1% ophthalmic solution administered sublingually for the management of terminal respiratory secretions. *Am J Hosp Palliat Care*. 2013; 30: 388-92.

16. Heisler M, Hamilton G, Abbott A, et al. Randomized double-blind trial of sublingual atropine vs. placebo for the management of death rattle. *J Pain Symptom Manage*. 2013; 45: 14-22.

17. Fox C, Smith T, Maidment I, et al. Effect of medications with anti-cholinergic properties on cognitive function, delirium, physical function and mortality: a systematic review. *Age and ageing*. 2014; 43: 604-15.

18. Campbell ML. Assuaging listener distress from patient death rattle. *Ann Palliat Med*. 2018. e-publication.

19. The National Institute for Health and Clinical Excellence (NICE) guideline [NG31]: Care of dying adults in the last days of life. 2015. Accessed 12.01.2019.