epal
An informative read of news, studies, facts & help

Grampians Regional Palliative Care Team

Management of Excess Respiratory Secretions at End of Life

A difficult problem faced at End of Life is managing excess oral and respiratory secretions. This is often referred to by the ugly but apt description 'Death Rattle'. The difficulty is multi-layered. Firstly, it is common, affecting 50% percent of dying patients (Bennett et al, 2002). Secondly, the patient is almost always unconscious, so it is distressing only to family, friends and staff. This has led some to question the need for pharmacotherapy (Campbell & Yarandi, 2013) but this ignores the distress this symptom causes families. Lastly, there is little high quality evidence to support any specific drug regimen.

The rationale for anti-muscarinics at end of life was extrapolated from use in perioperative settings and experimentally with healthy volunteers (Bennett et al, 2002) rather than dying patents. Octreotide has also been theorised to have an antisecretory effect at end of life based on observations of patients receiving it for other indications. For both drug classes, it was hoped that the widespread muscarinic and somatostatin receptors in the salivary glands and bronchial tissue would be inhibited and reduce the volume of secretions and subsequent respiratory noise (Bennett et al, 2002; eTG, 2019).

Although several studies of anti-muscarinic agents like Atropine, Hysoscine Hydrobromide (Hyoscine), Hyoscine butylbromide (Buscopan) and Glycopyrrolate have been published, and some studies have included other agents such as ocreotide, no study comparing all four commonly used anti-muscarinics exists. This has allowed opinion rather than evidence to lead practice guideline development. Although research has been sporadic and contradictory, Wee and Hillier (2008) have twice updated their Cochrane review of the subject (2012; 2017). They included only four sufficiently rigorous studies out of thirty two considered: Wildiers et al (2009); Clark, Currow, Agar, Fazekas, and Abernethy, (2008); plus two German language studies.

The most robust study is Wildiers et al's (2009) randomised control trial (RCT) designed to compare all four commonly used anti-muscarinics but a supply problem prevented the use of Glycopyrrolate. The study was an open label randomised phase III multicentre trial with 333 participants randomised into three intervention groups at each participating centre (Atropine n=115, Hyoscine n=112; Buscopan n=106). They administered one of three drug regimens (below) if a score of 1 or above was obtained. Note the low threshold to commence drug therapy:

- Atropine (n= 115): 500mcg subcut bolus then 3000mcg 24hr infusion.
- Buscopan (n= 106): 20mg subcut bolus then 60mg 24hr infusion.
- Hyoscine (n= 112): 250mcg subcut bolus then 1500mcg 24hr infusion.
- A specific Death Rattle Intensity (DRI) score was their primary measure.
- DRI was assessed 30 minutes, 1hr, 4hrs, 12hrs and every 24hrs until death.
- At 12hrs post, a DRI score of 2 or 3 prompted a repeat bolus and doubling of the infusion dose.
- Dying adults with a DRI score of 1 or more were included (see below).
- Success was measured by any reduction from the initial DRI threshold score of 1 or maintaining a score of 1. A score that remained at 2 or 3 was considered unsuccessful.

Death Rattle Intensity score	Description
0	Not audible
1	Only audible near the patient
2	Clearly audible at the end of the patient's bed in a quiet room
3	Clearly audible at a distance of about 9.5m (from the door) in a quiet room

What were the results?

- No significant difference in response rates between the three arms at 1 hour:
  (Atropine 42%; Buscopan 42%; Hyoscine 37%)
- Repeated dosing improved responses across all three drugs at 24 hours:
- (Atropine 76%; Buscopan 60%; Hyoscine 68%).
- Response improved when drugs started at DRI score of 1 compared to scores of 2 or 3.
- All three drugs given as a loading dose plus 24hr infusion are equally effective in reducing DRI about 40% of the time after one hour and more than 60% of the time after 24 hours.

What does it all mean?

- Drug choices are a complex issue and are based on efficacy, side effect/risk considerations, prescriber familiarity, cost and availability (see below).

	Glycopyrrolate	Hyoscine	Buscopan	Atropine
Onset (IM data)	30-40 mins	3-5 mins	10 mins	< 20 mins
Peak Action (IM data)	30-45 mins	20-60 mins	15 mins	20 mins
Half life	1 ½ Hrs	1-4 Hrs	1-5 Hrs	2-3 Hrs
Duration	7 Hrs	1-9 Hrs	2 Hrs	4 hrs
PBS Listing	No	No	Yes	Yes

- The four anti-muscarinics are equally (in)effective and have similar side effect/risk profiles except for the ability of Hyoscine and Atropine to cross the blood-brain barrier and potentially increase agitation and contribute to delirium.
- In addition, Atropine has a slightly higher cardiac side effect profile but this is probably irrelevant for most patients in this situation.
- To complicate things further Hyoscine H is sometimes unavailable in Australia.
- At Ballarat Health Services, the Care of the Dying Management Plan symptom control algorithm uses either Glycopyrrolate or Buscopan as the anti-muscarinics of choice in part because of their lack of central side effect.
- The existing algorithm is based on relatively poor evidence but Wildiers et al (2009) offers the best evidence currently available.
- If a patient is at home or in residential care, Buscopan is preferred because of PBS listing.
- ***Routinely using the DRI score and having a very low threshold to commence anti-muscarinics would probably improve outcomes.***

References

Back, I. N., Jenkins, K., Blower, A., & Beckhelling, J. (2001). A study comparing hyoscine hydrobromide and glycopyrrolate in the treatment of death rattle. *Palliative Medicine, 15*: 329-336.

Bennett, M., Lucas, V., Brennan, M., Hughes, A., O'Donnell, V., & Wee, B.; Association for Palliative Medicine's Science Committee. (2002). using anti-muscarinic drugs in the management of death rattle: evidence based guidelines for palliative care. *Palliative Medicine. 16, (5):* 369-74.

Campbell, M.L & Yarandi, H.N. (2013). Death rattle is not associated with patient respiratory distress: Is pharmacological treatment indicated? *Journal of Palliative Medicine, 16, (10)*: 1255-1259.

Clark, K., Currow, D. C., Agar, M., Fazekas, B. S. & Abernethy, A. P. (2008). A pilot phase II randomised, cross-over, double-blinded, controlled efficacy study of octreotide versus hyoscine hydrobromide for control of noisy breathing at the end-of-life. *Journal of Pain & Palliative Care Pharmacotherapy, 22, (2)*: 131-137.

Heisler, M., Hamilton, G., Abbott, A., Chengalaram, A., Koceja, T. & Gerkin, R. (2013). Randomized double-blind trial of sublingual atropine vs. placebo for the management of death rattle. *Journal of Pain and Symptom Management, 45, (1):* 14-22.

Hughes, A., Wilcock, A., Corcoran, R., Lucas, V. & King, A. (2000). Audit of three anti-muscarinic drugs for managing retained secretions. *Palliative Medicine, 14*: 221-222.

eTG. (2019). Palliative Care online version. Therapeutic Guidelines, Melbourne, Australia: Author.

Wildiers, H., Dhaenekint, C., Demeulenaere, P., Clement, P.M.J., Desmet, M., Van Nuffelen, R., Gielen, J., Van Droogenbroeck, E., Geurs, F., Lobelle, J. & Menten, J. (2009). Atropine, Buscopanutylbromide, or Scopolomine are equally effective for the treatment of death rattle in terminal care. *Journal of Pain and Symptom Management, 38, (1):* 124-133.

Wee B, Hillier R. (2008). Interventions for noisy breathing in patients near to death. *Cochrane Database of Systematic Reviews. 2008 Issue 1*; Art. *No.: DOI: 10.1002/14651858.CD005177.pub2.*

Lawrence Habegger
Nurse Practitioner

CONTACTS

Grampians Regional Palliative Care Team
Ph 5320 3553 Fax 5320 6493

Central Grampians Palliative Care
Ph 5352 9328 Fax 5352 9425

Gandarra Palliative Care Unit
Ph 5320 3895 Fax 5320 3763

Ballarat Hospice Care Inc
Ph 5333 1118 Fax 5333 1119

Djerriwarrh Palliative Care
Ph 5367 2000 Fax 5367 4274

Grampians Region Palliative Care Consortium
Ph: 0428 737 330