



Fig. 1. Number of ampules supplied by hospital pharmacy services per month.

medications to address terminal secretions in Australia.

There is no doubt that noisy secretions at the end of life are sometimes perceived as very distressing to all those involved with the care of dying patients and further work is required. However, this work needs to focus on objectively identifying which patients are most at risk and once this is clearer, identifying evidence-based approaches to minimizing harm for all those involved: patients, their families, and health professionals.

Katherine Clark, MBBS, MMed, PhD, FRACP, FACHPM
Northern Sydney Cancer and Palliative Care
Network, St Leonards
Sydney, NSW
Australia
E-mail: katherine.clark@health.nsw.gov.au

Northern Clinical School
The University of Sydney, St Leonards
Sydney, NSW
Australia

Caitlin Sheehan, BMed, FRACP, FACHPM
Department of Palliative Care
St George Hospital, Sydney
New South Wales, Australia
Department of Palliative Care
Calvary Health Care Kogarah
Sydney, New South Wales
Australia

David C. Currow, BMed, MPH, PhD, FRACP
The University of Technology
Sydney, NSW, Australia

<https://doi.org/10.1016/j.jpainsymman.2018.10.498>

References

1. 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;56:902–907.

2. 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 Ageing* 2014;43:604–615.

3. Campbell ML, Yarandi HN. Death rattle is not associated with patient respiratory distress: is pharmacologic treatment indicated? *J Palliat Med* 2013;16:1255–1259.

4. Wee B, Hillier R. Interventions for noisy breathing in patients near to death. *Cochrane Database Syst Rev* 2008; CD005177.

Author's Response



To the Editor:

I'm grateful for the interesting comments by an authoritative group of researchers from Australia. I'm trying to respond point by point.

1. They noticed that a proportion of patients who receive an early medication may not develop death rattle (DR) and consequently are exposed to unnecessary harms. They are right, as 40% of patients in the group receiving hyoscine butylbromide late did not develop DR. These percentages reproduce, more or less and with large differences, what it is reported in literature with a prevalence of DR of 60%. In my opinion, considering the low costs and the minimal harms, this should not preclude an optimal use of anticholinergics. Mass vaccination is essential to prevent very rare events; yet no one questions its usefulness. The study was designed also expecting a certain number of patients who would not develop DR. I have to say that it is surprising to recognize unpleasant effects in a dying patient with a low level of consciousness. The paper quoted by colleagues refers to a review assessing the activity of anticholinergic drugs on cognitive function, delirium, physical function, and

mortality, concluding that these drugs have a significant adverse effect on cognitive and physical function, but limited evidence for delirium or mortality outcomes.¹ Of course, dying patients with a lower level of consciousness or sedated do not fit exactly this category because cognitive and physical function are already deeply impaired.

2. Supporting family is an obvious strategy that should be performed in any place where palliative care is available. The decrease of prescriptions of anticholinergic drugs, however, should not be considered as clinically consequential to the benefits, but the result of a strategy privileging communication skills and “normalization” on resolving the problem of DR. Just influencing relatives with communication strategies has even less evidence in scientific terms. Dying with DR is not in line with dignity of death considering many aspects that include environment, lights, rumors, signs, symptoms, tranquility, all together reassuming what we consider as a peaceful death. It is well recognized that the way a loved one dies leaves deep marks in the memories of the relatives, but communication with relatives regards all the aspects of dying, not only “normalization” of DR, of which the benefits should be proven.

3. The controversial effects of anticholinergics and the poor evidence in the treatment of DR are clearly explained by the lack of effect when secretions are already formed.² In this case, the different modality of a timely administration of hyoscine butylbromide provided a relevant outcome, although some patients, estimated to be 40%, could receive a medication

unnecessarily. Unfortunately, we do not have absolute and validated risk factors to select these patients.

To conclude, I think that evidence should be aligned to a good clinical sense and pragmatic studies offer a better adherence to the clinical reality.³ An intriguing aspect deserving interest in the research agenda could be measuring the benefits of supporting family or “normalization” of DR compared with a proactive administration of anticholinergics, that in our study has reduced the development of DR to 6% of patients. Considering that 60% of patients are expected to develop DR, this outcome does not seem irrelevant from a clinical perspective.

Sebastiano Mercadante, MD
Main Regional Center of Pain Relief and
Supportive/Palliative Care
La Maddalena Cancer Center
Palermo, Italy
E-mail: terapiadeldolore@lamaddalenanet.it

<https://doi.org/10.1016/j.jpainsymman.2018.10.497>

References

1. 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 Ageing* 2014;43:604–615.
2. Mercadante S. Death rattle: critical review and research agenda. *Support Care Cancer* 2014;22:571–575.
3. Mercadante S. The benefits of practical clinical trials over traditional randomized clinical trials for opioid management. *Expert Rev Clin Pharmacol* 2018;11:741–742.