What is the evidence for treating death rattle at end of life?

**Key points**

- The rattling breath common at end of life is seen as a problem despite death rattle being a natural process.
- Nursing and pharmacological approaches used to treat death rattle often fail to give improvements.
- The decision to treat is largely used to address the distress of relatives, not the patients who may experience side-effects from treatment.
- Education and support for relatives might be a better approach until management of death rattle can be improved.

**Author** Paul Beland is hospice specialist nurse, St Nicholas Hospice Care, Bury St Edmunds.

**Abstract** Death rattle is the noisy, rattling breathing that is common in patients at the end of life. Although not thought to cause distress to patients when they are dying, death rattle is undoubtedly distressing for patients’ relatives and friends, and sometimes for health professionals. Although antimuscarinic drugs appear more likely to be effective if used as soon as death rattle begins, they also have adverse effects, which are more likely to be detrimental if the drugs are used too soon. There is little evidence for the superiority of one drug over another or that any pharmacological or nursing intervention is better than doing nothing. This article discusses the rationale around current management of death rattle and whether it is in the best interests of the patient.

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and Hillier, 2008). Hence, treatment for death rattle is often started by clinicians concerned about the distress experienced by others – rather than by the patient – who feel obliged to intervene (Fielding and Long 2014; Hirsch 2011).

The effectiveness of pharmacological and non-drug treatments, use of which differs between institutions (NICE, 2021), is inconsistent and often fails to resolve the symptom (Kolb et al, 2018). This is disappointing for both relatives and professionals alike (Fielding and Long, 2014), and treatments may be more harmful than beneficial for patients (Campbell and Yarandi, 2013).

Causes
Causes of death rattle include the accumulation of saliva and of bronchial mucus as patients become weaker, less conscious and less able to swallow or cough, which leads to noisy, gurgling breathing (Box 1).

Patients who die with brain and/or pulmonary metastases (Kolb et al, 2018), or with neuromuscular disorders or serious head injuries, appear more likely to develop death rattle (Clark and Butler, 2009). This may be partly attributable to dysphagia and aspiration – including that of saliva. Gastric or oropharyngeal contents may also be aspirated into the larynx and lower respiratory tract and, as with dysphagia, result in episodes of coughing, choking and likely pneumonia – itself associated with the development of death rattle (Morita et al, 2004).

Excess pulmonary mucus production may also result from:

- Heart failure;
- Pulmonary oedema;
- Chest infection (Back et al, 2001).

The last is common in advanced cancer. In rare cases, bronchorrhea (the excessive production of watery mucus) with up to 9l of mucus daily can occur; this is usually associated with lung cancer or lung metastases, in which tumour cells cause inflammation of the mucosal surfaces of the lung, resulting in the production of copious mucus (NICE, 2021).

The development of death rattle can be multifactorial, although diagnosing any particular aetiology is difficult and does not appear to be clinically important (Morita et al 2004; Wildiers and Menten, 2002).

Treatment
Death rattle is difficult to manage (Wildiers et al, 2009), but attempts to improve it are usually either:

- Non-pharmacological/physical;
- Pharmacological – using antiserotonin anticholinergic/antimuscarinic drugs (Hirsch, 2011). The terms anticholinergic and antimuscarinic are effectively interchangeable for the scope of this article.

Non-pharmacological approaches are usually recommended as the first step (NICE, 2021).

Box 1. What causes death rattle?

One cause of death rattle is the accumulation of saliva, of which an average of 2l is produced daily by healthy individuals (Rumbold, 2011). Another is the accumulation of bronchial mucus as patients become weaker, experience reduced consciousness (caused by the disease itself or exacerbated by opioid, hypnotic or sedative drugs), and lose their swallowing and cough reflexes (National Institute for Health and Care Excellence (NICE), 2021; Kolb et al 2018) and, with them, their ability to clear secretions from the trachea and oropharynx (Bennett et al, 2002).

Impaired ability to expectorate (Morita et al, 2004) – which may be exacerbated by the increased stickiness of bronchial mucus caused by dehydration (NICE, 2021) – and the inability to protect the airway, results in partial airway obstruction due to pooling of secretions. Even more secretions are produced in reaction to the obstruction; respiratory movement causes them to vibrate, leading to increasingly noisy, gurgling breathing (Clark and Butler, 2009).

Pharmacological
The pharmacological treatment of death rattle has mainly been directed at reducing the secretion of saliva and bronchial mucus by using antimuscarinic drugs (Hirsch, 2011). Their effectiveness in treating death rattle has been extrapolated from their use in drying secretions during anaesthesia (Bennett et al, 2002). NICE (2021) advised that if non-pharmacological interventions do not improve death rattle, or it is causing distress to patients or their relatives, clinicians should consider using either hyoscine hydrobromide, hyoscine butylbromide (Buscopen), glycophytonium (bromide) or atropine subcutaneously (citing EMRPCC, 2013). NICE (2021) recommends giving an initial bolus subcutaneous injection of an antimuscarinic drug to address death rattle, followed by continuous subcutaneous infusion (CSCI), using a syringe driver.

Twycross et al (2021) have observed that administration of these drugs via CSCI is typically initiated at around the same time as the first or second pro re nata (PRN) dose is given. They have advised increasing the CSCI dose if two or more PRN doses – usually given every four hours as required (NICE, 2021) – are needed each day. It is still the case that there is evidence to support single doses of these drugs, but evidence to
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**Box 2. Antimuscarinic drugs for relieving death rattle**

- Hyoscine hydrobromide
- Hyoscine butylbromide (Buscopan)
- Glycopyrronium
- Atropine

Hyoscine hydrobromide

The usual PRN dose of hyoscine hydrobromide – often referred to simply as hyoscine – is 400 micrograms (μg) to be administered subcutaneously (Wilcock et al, 2020); it is more effectively administered via CSCI (800-2400 micrograms over 24 hours), due to its short duration of action (Wildiers and Menten, 2002). Both hyoscine hydrobromide and atropine cross the blood–brain barrier (Watson et al, 2016) and can cause negative central nervous system effects – including confusion, agitation and delirium or sedation – especially in older people (NICE, 2021; NICE, 2015; EMRPCC, 2013).

**Hyoscine butylbromide**

Hyoscine butylbromide is derived from, and has similar effects to, hyoscine hydrobromide (Wildiers et al, 2009), with similarly rapid onset but short duration of antisecretory action (less than two hours) when given subcutaneously (Hirsch, 2011; Bennett et al, 2002). The usual PRN dose of hyoscine butylbromide is 20mg to be administered subcutaneously, or 20-120mg over 24 hours via CSCI (Wilcock et al, 2020). In common with glycopyrronium and hyoscine, butylbromide does not easily cross the blood–brain barrier and so avoids adverse effects on the central nervous system (NICE, 2021).

**Glycopyrronium**

Glycopyrronium has, at over six hours, the longest duration of response of the selected drugs. The usual bolus dose of glycopyrronium is 200-400μg to be administered subcutaneously, which takes up to 45 minutes to take effect (NICE, 2021); 400μg is likely to give faster results (Bennett et al, 2002). Its usual 24-hour dose via CSCI is 600-1200μg (Wilcock et al, 2020).

NICE (2021) reports that subcutaneous atropine, hyoscine hydrobromide and hyoscine butylbromide start to take effect within 15 minutes of administration and, as such, may be preferred to glycopyrronium if rapid action is needed.

**Drug choice**

Generally, the choice between hyoscine butylbromide or glycopyrronium largely depends on availability (NICE, 2021), with hyoscine butylbromide more widely used in the UK because it is cheaper (Twycross et al, 2021). However, hyoscine butylbromide is generally regarded (especially at doses of >40mg) as being incompatible with the antiemetic cyclizine in a CSCI (NICE, 2021), in which case glycopyrronium should be used if both cyclizine and an antisecretory drug are needed. The prokinetic effects of the antiemetic metoclopramide are blocked by antimuscarinics, so their concurrent use should be avoided and an alternative anti-emetic used if needed (Twycross et al, 2021).

In end-stage renal failure, hyoscine hydrobromide carries an increased risk of delirium. Twycross et al (2021) have advised using either hyoscine butylbromide (at usual doses) or halved doses of glycopyrronium, the elimination of which is significantly prolonged in renal failure (Hirsch, 2011).

**Drug effectiveness**

NICE (2021) has advised:

- Changing the drug if death rattle persists beyond 12 hours – the length of time these medicines may take to become effective;
- Stopping if unacceptable side-effects intervene;
- Considering the risks, as well as the benefits, of these drugs before deciding whether to use them;
- Attempting to alleviate relatives’ distress by explaining that patients who are unconscious are unlikely to be distressed by death rattle.

Wee and Hillier (2008) and Hirsch (2011) also cautioned that, although some drugs may be worth trying, their effectiveness is difficult to establish. A later paper by Arcand (2015) highlighted controversy about the usefulness of antimuscarinics in the treatment of death rattle. For example, it cited Bennett et al (2002), which found that a single subcutaneous dose of hyoscine hydrobromide, hyoscine butylbromide or glycopyrronium led to an improvement in death rattle in 35-54% of patients, but that about 20% of patients with death rattle received no benefit from these drugs – possibly due to bronchial secretions overproduced as a reaction to pulmonary oedema or infection.

NICE (2021) cite Wee and Hillier (2008) as having compared hyoscine hydrobromide with normal saline and found no statistically significant difference between the guide doses administered by CSCI is lacking (Bennett et al, 2002). These drugs are still the most common treatments for death rattle (Clark and Butler, 2009), with around three-quarters of people with death rattle receiving them (Wildiers and Menten, 2002). Several antisecretory drugs have been used (Wildiers et al, 2009) (Box 2), of which hyoscine hydrobromide, hyoscine butylbromide and glycopyrro-
two in terms of their effect on death rattle, while a large study by Wildiers (2007) cited by Wee and Hillier (2008) comparing atropine, hyoscine hydrobromide and hyoscine butylbromide found no difference in their effectiveness.

An audit of hyoscine hydrobromide, glycopyrrokonium and hyoscine butylbromide found no apparent difference in their effect on alleviating death rattle (Hirsch, 2011). Similarly, a quantitative systematic review by Kolb et al (2018) found that, in trials comparing several drugs, no marked differences in effectiveness were identified; in one trial, hyoscine hydrobromide was shown to be superior to glycopyrrokonium, while another demonstrated the contrary.

Kolb et al (2018) found the quality of the evidence to be moderate to very low, and evidence for drug treatment of death rattle was ambivalent; ranging from 27% to 86.4% effectiveness and from 22% to 58% for no effect. These wide ranges are attributable to a lack of objective or consistent outcome measures. This heterogeneity was why Wee and Hillier (2008) could not perform a meta-analysis in their Cochrane review; a decade later this was still the case for Kolb et al (2018).

Adverse effects All this matters because, in addition to their desired effects, antimuscarinic drugs commonly cause a range of adverse effects, which can include dry mouth, urinary retention, constipation, agitation, delirium or sedation (Clark and Butler, 2009) (Box 3). It cannot be known to what extent some of these effects occur in people who are dying (NICE, 2021), but they may go unnoticed in patients with reduced consciousness who are unable to communicate (Hirsch, 2011).

Premature use of these drugs in patients who are conscious may cause unacceptable dryness of the mouth and throat (Arcand, 2015).

Hydration The degree to which the giving of artificial hydration may contribute to patients developing death rattle is a contentious issue. NICE (2015) reported considerable diversity of practice as to whether parenteral fluids are continued, reduced, stopped or withheld. It observed that, in clinical situations other than end-of-life care, troublesome respiratory secretions are generally managed by increasing hydration to inhibit mucus from collecting and to enhance the upward ciliary movement of mucus from the respiratory tract. However, NICE (2015) conceded that for patients who are dying, the risk of artificial hydration contributing to pulmonary oedema and worsening pulmonary secretions is impossible to ignore, citing Clark and Butler (2009).

The argument against artificial hydration – and one that many health professionals support – is that the more fluid there is in the body, the more likely it is that fluid will collect in the lungs and worsen respiratory secretions (Davies et al, 2018). This phenomenon is more likely still when patients experience the hypoalbuminaemia that is common in those who are dying (Watson et al 2016). However, Lokker et al (2014) and Davies et al (2018) reported that researchers have found no correlation between hydration and the incidence of death rattle. Peripheral oedema, ascites and pleural effusion, and their association with death rattle, have been investigated in studies that found no such relationship (Kolb et al, 2018; Morita et al, 2004).

In their study, Krishna et al (2010) observed no notable difference in death rattle between patients who were hydrated and those who were not; Davies et al (2018) also found the incidence of death rattle to be similar in artificially hydrated and non-hydrated participants. Davies et al (2018) identified a notable delay in the need to use antisecretory medication in their participants who were artificially hydrated. The authors noted that their study was not statistically powered to compare differences in outcomes between their study groups, and the results should be treated with caution, but their data still suggested to them that, although artificial hydration might not reduce the incidence of death rattle, it might delay its onset.

Discussion It hard to disagree with the opinion of Bailie et al (2018) that death rattle is currently poorly managed, or with that of Kolb et al (2018) that its current treatment with antimuscarinic drugs often seems unsatisfactory.

Wee and Hillier’s 2008 Cochrane review found there was little evidence to support any intervention attempting to address death rattle, and that all interventions achieve varying degrees of success.

Kolb et al (2018) concurred that there is no drug treatment – and, also, no non-pharmacological treatment – that is consistently more effective than doing nothing, which means death rattle may be virtually untreatable once it has taken hold. Similarly, Watson et al (2016) observed that, despite the use of all recognised interventions, some patients who are dying continue to breathe distressingly noisily, regardless.

NICE (2015) stated that it is unclear whether drugs are any more effective than non-pharmacological interventions, and concluded that there is insufficient evidence to recommend any drug over another

Box 3. Side effects of antimuscarinic drugs

Common adverse effects include:
- Dry mouth
- Hesitancy of micturition and urinary retention
- Constipation
- Visual disturbances
- Reduced sweating
- Cardiovascular effects
- Drowsiness
- Agitation
- Difficulty in coughing up phlegm from the back of the throat
- Delirium
- Sedation


Treatment of death rattle is largely used to address the distress of relatives, not patients

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in treating death rattle, which according to Lokker et al (2014) and Wildiers et al (2009) may in some cases decrease spontaneously as death approaches. The lack of clear evidence to be guided by when attempting to treat death rattle reflects the paucity of high-quality research in this emotionally challenging and sensitive area (EMRPCC, 2013). This is, in large part, due to the inherent difficulties of research among the dying, including:

- Ethical challenges in accessing, recruiting and monitoring sufficient numbers of dying patients;
- Their inevitable loss to the study;
- The practicability, but subjectivity, of typically the same nurse rating death rattle while treating it and caring for the patient.

Other factors are:

- Variability of drugs, doses and treatment regimens used;
- Inconsistency in measuring death rattle;
- Distress of family members, friends and healthcare workers.

All inhibit objective evaluation of the effectiveness of treatments (Watts et al, 2019; Kolb et al, 2018; Hirsch, 2011; Wildiers et al, 2009; Wee and Hillier, 2008). Hence, patients who are dying and experiencing death rattle are typically treated by health professionals who do not know which treatment, if any, is likely to be most effective.

Furthermore, current treatment is paradoxic. Patients who are dying and have death rattle exhibit no more respiratory distress than those who are dying and do not have it, and the severity of death rattle has no correlation with respiratory distress (Watts et al, 2019; Campbell and Yarandi, 2013). However, even though patients themselves may not seem disturbed by death rattle – and there is little evidence to suggest that they are (Clark and Butler, 2009) – the distress of relatives makes it difficult for clinicians not to intervene, if only for the benefit of those relatives. As a result, the degree to which antimuscarinic drug use is so deeply entrenched in palliative care practice (Wee and Hillier, 2008) means their use is likely to continue (NICE, 2021; NICE, 2015).

However, given the adverse effects of these drugs, Wee and Hillier (2008) considered their use to pose an ethical dilemma; it may be that treatment is not in the patient’s best interests, even if it does confer family members’ support: (Arcand, 2015). NICE (2015) considered the continued use of antimuscarinic drugs in the treatment of death rattle hard to justify, given the lack of evidence for their effectiveness. Yet, once antimuscarinics are started, their use tends to continue in even the absence of therapeutic benefit (Hirsch, 2011).

Hence, it falls to nursing to provide:

- Mouth care for the patient;
- Good communication and explanation for their relatives to reassure them the patient is not distressed by, what may be for their loved ones, the upsetting noise of death rattle (NICE, 2015; Hirsch, 2011).

While we lack effective treatments for death rattle, the best alternative might be to focus on ensuring families receive the information they need to understand that this symptom is a normal part of the dying process (Lokker et al, 2014; Clark and Butler, 2009). More research into its management is still needed, as information and communication alone will not be enough to alleviate the distress of all relatives who hear their loved one’s death rattle (Van Esch et al, 2020).

Conclusion

Death rattle is common in patients at the end of life, and although disturbing to relatives, is not thought to cause distress to the patients themselves. The effectiveness of nursing and pharmaceutical approaches used to manage death rattle is not well supported by the evidence, and treatments can have adverse effects, so their use may not be in the best interests of the patient. Helping families to understand that death rattle is a natural part of dying may be a better course of action until there are more effective ways of managing it.

References


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