



## Managing delirium and psychological symptoms in the last days of life

When delirium occurs in the last days of life it is usually irreversible. Pharmacological treatment is only required for patients experiencing significant distressing symptoms, e.g. hallucinations, agitation. Non-pharmacological interventions should be prioritised, and family/whānau can be guided and supported to help with this. Anxiety and other psychological symptoms are also important to consider and manage, as these can exacerbate delirium and other physical symptoms commonly experienced by patients in the last days of life.

### KEY PRACTICE POINTS:

- Delirium is a prevalent feature in the last days of life where people experience fluctuations in their attention, cognition, awareness and perception
- The cause is usually multifactorial, involving multiple organ failure and other irreversible factors. However, there are some causes or exacerbators of delirium that can be identified and potentially managed, e.g. pain, urinary retention, infection.
- Non-pharmacological strategies are first-line for patients whose symptoms are not causing distress, e.g. re-orientation cues, creating a safe environment with a comfortable room temperature, a low level of noise and adequate lighting. These interventions may be all that is required to support the patient and their family/whānau.
- If pharmacological treatment is required (e.g. for patients with significant agitation or restlessness), subcutaneous haloperidol or midazolam is recommended first-line based on the patient's level of consciousness
- Psychological symptoms, e.g. anxiety, depression, emotional or spiritual distress, are also common in the last days of life and should be managed as they can exacerbate delirium and other physical symptoms, e.g. breathlessness:
  - General supportive measures and non-pharmacological strategies are first-line
  - Conventional treatments such as cognitive behavioural therapy or antidepressants are unlikely to be appropriate in patients with impaired communication and fatigue, and there is insufficient time for them to have an effect
  - Patients currently taking antidepressants for psychological symptoms should continue to do so until swallowing is no longer possible (if they are providing benefit)
  - An antipsychotic or benzodiazepine may be required for some patients if conservative management is unsuccessful

This article is part of a series on managing symptoms in the last days of life. It is recommended to read this article in conjunction with the other articles in the series, particularly: “**Navigating the last days of life: a general practice perspective**”.

## Delirium, agitation and restlessness in the last days of life

Delirium occurring in the last days of life (which may include terminal restlessness or terminal agitation) is reported to occur in some form in up to 90% of people.<sup>1,2</sup> People with delirium typically experience fluctuations in attention, cognition, awareness and perception.<sup>1,3</sup> There are three types of delirium:<sup>2,4,5</sup>

- **Hypoactive delirium** – characterised by drowsiness, inactivity and lack of awareness
- **Hyperactive delirium** – characterised by agitation, hallucinations and restlessness
- **Mixed delirium** – characterised by features of both hypoactive and hyperactive delirium

The cause of delirium in the last days of life is usually multifactorial, involving multiple organ failure and other factors that are now largely irreversible, e.g. hypoxia, metabolic abnormalities.<sup>\*4-6</sup> However, some causes or exacerbating factors of delirium can be managed in the final days, such as pain, urinary retention, certain medicines (e.g. opioids, benzodiazepines, anticholinergics) or substances (e.g. nicotine withdrawal) and infection (see: “Managing symptoms of delirium”).<sup>7-9</sup> People with pre-existing cognitive impairment are at the greatest risk of delirium.<sup>7</sup> Other risk factors include increasing age, immobility and vision or hearing impairment.<sup>4,10</sup>

\* Delirium that occurs during palliative care prior to the last days of life can often be reversed if this is in line with the person’s goals of care, e.g. by correcting metabolic abnormalities, such as hypercalcaemia, hyper/hypoglycaemia and dehydration

Delirium can cause significant distress to the patient and to those supporting them in their last days of life, particularly as this is a time when the patient’s cognition, awareness and ability to communicate is highly valued.<sup>4, 5, 11</sup> Provide information and support to the family/whānau, including the likely causes of delirium, potential symptoms and address any questions or concerns they may have.<sup>4, 12</sup> Reassure patients and their family/whānau that this is a normal part of the dying process.

### Assessment of delirium

A clinical diagnosis of delirium can be made based on symptom history, pattern recognition and any other relevant information from the family/whānau or carers.<sup>1, 4</sup> Validated tools are available to help assess patients for delirium, e.g.

**Confusion Assessment Method (CAM), 4AT.**<sup>1,4</sup> However, these are often not practical or possible to apply in the last days of life, particularly for those with limited communication or fluctuating levels of consciousness.<sup>1,4, 13</sup>

As a general approach, ask the patient (if possible) or their family/whānau about features of delirium, including any:<sup>1,4</sup>

- Acute change in mental status and whether this fluctuates throughout the day
- Increase in distractions, disorientation, disorganised thinking or other cognitive changes, e.g. hallucinations, aggression
- Changes in consciousness or activity, e.g. lethargy, stupor, hypervigilance, difficulty sleeping

Repetitive plucking of bed sheets or clothing, groaning and facial grimacing can be signs of delirium in the last days of life.<sup>4,5, 14</sup> Some patients may also experience auditory or visual hallucinations, which can be distressing for them and their family/whānau.<sup>2, 14, 15</sup> However, these should be distinguished from the positive spiritual visions and experiences that can occur at end of life which are generally comforting and reassuring to patients, and do not require medical intervention.

## Managing symptoms of delirium

When deciding on an appropriate treatment plan, consider the patient’s emotional, spiritual, social and physical needs.

First consider any reversible causes or exacerbators of delirium, which can be treated.<sup>8, 9, 13</sup> These may include:

- **Pain** – ensure adequate pain relief.<sup>9, 13</sup> For further information, see: “**Managing pain in the last days of life**”.
- **Constipation/faecal impaction or urinary retention** – consider use of laxatives/an enema (if possible) or urinary catheterisation if not already in place.<sup>14, 16</sup>
- **Medicines**, e.g. corticosteroids, anticholinergics, opioids, benzodiazepines – consider discontinuation or if the medicine is required, lower doses or switching to an alternative medicine.<sup>11, 13</sup>
- **Other substances**. If the patient’s symptoms are likely caused by nicotine withdrawal, consider use of nicotine replacement patches.<sup>6</sup> A benzodiazepine is often useful for patients with alcohol withdrawal.<sup>17</sup>
- **Infection** (e.g. urinary or respiratory tract infection) – antibiotics may improve the symptoms of delirium if treatment is considered appropriate.<sup>4, 10</sup>
- **Psychological causes**, e.g. fear, anxiety or spiritual distress – use non-pharmacological management strategies, considering what interventions (if any) have helped them to overcome this in the past.<sup>7, 13</sup> Antidepressants should not be introduced as there is insufficient time for them to have an effect.<sup>18</sup> For further

information on the management of psychological symptoms, see: "Support the patient's mental health and wellbeing needs".

### Prioritise non-pharmacological interventions

Evidence suggests that non-pharmacological interventions are preferable to pharmacological treatments in patients experiencing mild symptoms of delirium.<sup>19, 20</sup> Ideally, non-pharmacological management strategies will have been discussed with the patient and their family/whānau prior to the last days of life so that a plan is already in place (i.e. advance care planning, see: [www.hqsc.govt.nz/our-work/advance-care-planning/](http://www.hqsc.govt.nz/our-work/advance-care-planning/)).

Examples of non-pharmacological interventions for delirium:<sup>4, 6, 7, 15</sup>

- Implement safety measures, e.g. lower the bed, use a floor sensor mat, remove nearby potentially hazardous objects
- Regularly reposition the patient
- Gentle mouth care, if tolerated
- Close observation (e.g. by a volunteer "sitter" or family/whānau). Having someone always present can help with re-orientation and reduce the patient's fear/anxiety and feeling of isolation.<sup>3</sup>
- Set an ambient room temperature and consider the patient's proximity to heaters or cold draughts
- Ensure adequate lighting, avoid glare from artificial light or sunlight. Use of a night light may be helpful.
- Maintain a low level of noise in the room and reduce negative distraction, e.g. loud television volume
- Place re-orientation cues, e.g. a clock, newspaper, daily schedules, familiar belongings such as photographs or other personal items
- Access to glasses or hearing aids (if required)
- Suggest relaxation or distraction techniques, e.g. gentle touch or massage, aromatherapy, music or radio
- Spiritual or religious guidance or support (if relevant)

Support the use of other complementary techniques or methods that the patient or their family/whānau want to try if they are unlikely to cause harm, e.g. traditional techniques such as Rongoā Māori, Ayurvedic or Chinese herbal medicines.


### Initiate pharmacological treatment as indicated

If non-pharmacological interventions have been inadequate or if the patient is experiencing severe or distressing symptoms, e.g. hallucinations, significant agitation, pharmacological treatment can be initiated.<sup>1, 19</sup>

An antipsychotic (haloperidol) or benzodiazepine (midazolam) administered subcutaneously is recommended

first-line for patients requiring pharmacological treatment for delirium, agitation or restlessness, with the initial choice dependent on consciousness level (Figure 1).<sup>6, 15</sup> Benzodiazepines are particularly useful for patients with agitation and anxiety due to their sedating effects, but they can exacerbate symptoms of delirium at high doses.<sup>9, 10, 16</sup> They are also useful for patients whose symptoms of delirium are caused by alcohol withdrawal.<sup>17</sup> Haloperidol is particularly useful for patients who are also experiencing nausea and vomiting as it is the first-line treatment for this in the last days of life; combining indications means fewer medicines are required.

N.B. Some patients, e.g. those with behavioural and psychological symptoms of dementia, will already be taking oral antipsychotics and require conversion to a subcutaneous formulation.<sup>15</sup>

 **Practice Point:** Anticipatory prescribing of "as needed" subcutaneous doses of haloperidol and/or midazolam is also recommended in patients without symptoms of delirium or who do not yet require pharmacological treatment; if symptoms occur/worsen, the "as needed" dose can be administered and then regular dosing initiated (see regimens below).<sup>15</sup>

### Haloperidol is recommended first-line for patients who are conscious

If the patient is conscious or semi-conscious, 0.5 mg of subcutaneous haloperidol\* should be prescribed and administered stat (subcutaneous injection; unapproved route),<sup>21</sup> with additional doses prescribed on an "as needed" basis, e.g. 0.5 – 1 mg every one to two hours, as needed (to a maximum dose of 5 mg within 24 hours).<sup>15</sup> Ideally, the patient should be reassessed within six hours of initiation to review treatment response.<sup>15</sup>

N.B. Antipsychotics can be associated with restlessness; consider haloperidol as a potential cause if a patient experiences worsening symptoms after treatment initiation.<sup>10, 18</sup> Midazolam can be added early to reduce this effect (or used instead – see below), but do not persist with haloperidol if the patients' distress is worsening.

\* Contraindicated in patients with Parkinson's disease and should be avoided in patients with Lewy body dementia<sup>21</sup>

If there has been inadequate response to treatment with haloperidol after six hours:<sup>15</sup>

- **Switch to midazolam** 2.5 mg, administered subcutaneously (stat), and prescribe additional "as needed" doses, e.g. 2.5 – 5 mg, every 30 minutes, as needed; and/or
- **Add levomepromazine**<sup>†</sup> 6.25 mg, administered subcutaneously, every four to six hours, as needed.



Levomepromazine is a second-line option to haloperidol (with or without midazolam) and is highly sedative. If levomepromazine is used on an “as needed” basis with effect, discontinue haloperidol and convert the daily dose of levomepromazine to a 24-hour dose for continuous subcutaneous infusion, and prescribe additional “as needed” doses.


† Previously known as methotrimeprazine

### **Midazolam is recommended first-line for patients who are unconscious**

If the patient is unconscious, 2.5 mg of subcutaneous midazolam (unapproved indication) should be prescribed and

administered stat, with additional doses prescribed on an “as needed” basis, e.g. 2.5 – 5 mg, every 30 minutes, as needed (to a maximum dose of 20 mg within 24 hours).<sup>15</sup> Ideally, the patient should be reassessed within six hours of initiation to review treatment response.<sup>15</sup>

If treatment is ineffective after six hours, add levomepromazine 6.25 mg administered subcutaneously (stat), and prescribe additional “as needed” doses, e.g. 6.25 mg, every four to six hours, as needed.<sup>15</sup>

 **Practice Point:** Patients already established on high dose anxiolytics may require higher doses of midazolam.<sup>15</sup>

## **Support the patient’s mental health and wellbeing needs**

### ***Nā koutou i tangi, nā tātou katoa***

*When you cry, your tears are shed by us all*

***“Empathy has no script. There is no right way or wrong way to do it. It’s simply listening, holding space, withholding judgement, emotionally connecting, and communicating that incredibly healing message of ‘you’re not alone’” – Brené Brown***

When caring for a patient experiencing psychological distress, the aim is for them, and their family/whānau, to feel comfortable explaining any fears or concerns.<sup>16</sup> Use communication techniques such as asking open questions, active listening and the appropriate use of silences, speech tone and eye contact.<sup>16</sup>

Identifying the cause of the patient’s psychological distress in the last days of life is often difficult as there are usually multiple overlapping causes, such as:<sup>18, 22</sup>

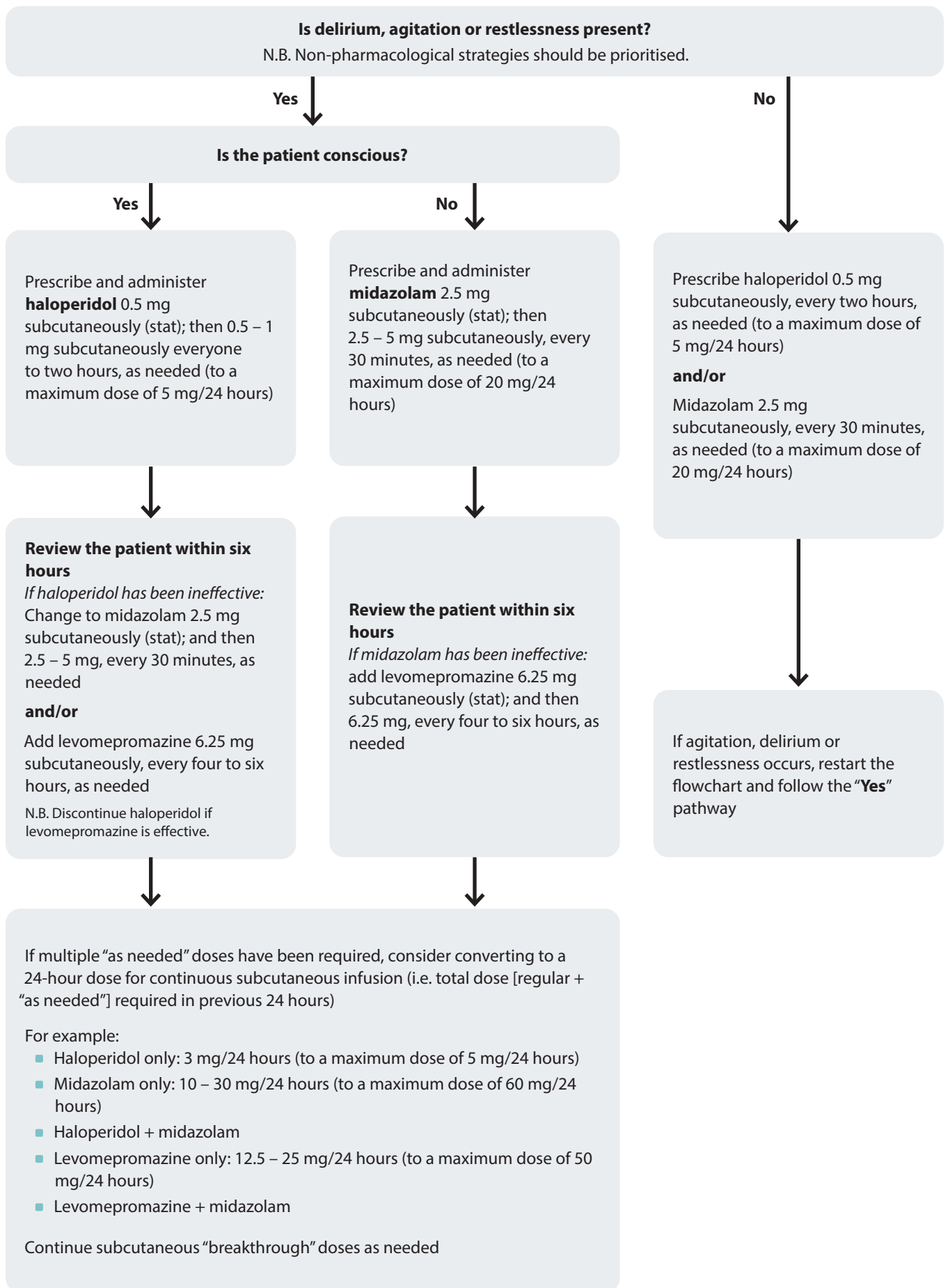
- Fear of pain or other worsening symptoms
- Loss of independence or a sense of burden on carers
- Fear of dying
- Anticipatory grief
- Spirituality concerns
- Contemplating the meaning of life and their purpose
- Concerns about the needs of their family/whānau after they die

### **Managing psychological symptoms for patients in the last days of life**

The initiation of conventional treatments for psychological symptoms, e.g. antidepressants or cognitive behavioural therapy for depression, is not appropriate in the last days of life as there is insufficient time to achieve any benefit, and patient participation will be limited due to fatigue or impaired communication.<sup>3, 18</sup> Patients currently taking antidepressants for psychological symptoms should continue to do so until swallowing is no longer possible (if they are providing benefit).<sup>18</sup>

General supportive and non-pharmacological interventions are appropriate. Additional support may be required for patients with a pre-existing psychological condition.<sup>3</sup> Non-pharmacological strategies may include relaxation or distraction techniques such as listening to music or watching television, aromatherapy, mindfulness-based techniques, reminiscing, spending time with family/whānau or a family pet or therapy animal.<sup>3, 15, 18</sup> Ask about any coping strategies used in the past and whether these could be used again, if appropriate.<sup>7</sup> Patients with spiritual distress may benefit from spiritual or religious guidance or support.<sup>3, 16</sup>


**Some patients with insomnia, anxiety or depression may require pharmacological treatment** with an antipsychotic or benzodiazepine administered subcutaneously, if conservative management is unsuccessful.<sup>3, 18</sup> Opioid doses should not be increased to sedate the patient.



**Figure 1.** Anticipatory prescribing flowchart for delirium, agitation and restlessness. Adapted from *South Island Palliative Care Workstream, 2020*.<sup>15</sup>

## Consider conversion to a continuous subcutaneous infusion

If multiple “as needed” doses of haloperidol, midazolam or levomepromazine have been required, consider converting to a 24-hour dose for continuous subcutaneous infusion, i.e. total (regular + “as needed”) subcutaneous doses required in previous 24 hours (Figure 1).<sup>15</sup> Each of these medicines can be used alone for continuous subcutaneous infusion or combination treatment may also be trialled.<sup>15</sup> Continue subcutaneous “breakthrough” doses as needed.<sup>15</sup>

 Contact the local hospice or palliative care team for advice if the patients symptoms do not respond to appropriate treatment, or if there is unwanted sedation.<sup>8</sup>

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