

## Symptom Management In Comfort End-Of-Life Care Of Pneumonia

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Pneumonia is a common end-of-life complication in many progressive chronic conditions, including dementia, malignancy, and neurodegenerative, respiratory, and rheumatologic conditions[1-5]

There are many individuals in various care settings including home, long-term care, and acute care for whom a palliative/comfort-focused approach to life-threatening illness has been chosen. This may reflect the contents of a Health Care Directive, or the consensus-based process of Advance Care Planning. This may also be determined in the context of a rapidly progressive life-threatening illness, through consideration of goals of care along with realistic limitations of possibilities for investigations and interventions.

This document provides a framework for comfort care at the end of life due to a rapidly progressive pneumonia with death expected within hours or a few days. It addresses an approach to a common constellation of symptoms, and considers common concerns of families.

### **Care Setting**

The impact of care settings will be considered, however its main implication will be on possible routes of medication administration. The availability of monitoring, laboratory or diagnostic imaging investigations, oxygen administration, parenteral fluids, or on-site medical coverage should not impact on the ability to provide comfort care in a rapidly unfolding clinical condition where death is imminent. In fact, where such technologies are available, one challenge will be avoiding their unnecessary and perhaps inappropriate use.

### **Fundamental Concepts**

There are some fundamental concepts and overarching principles that are involved in the aggressive pharmacological management of symptoms at end of life, particularly when death is near and severe dyspnea and/or agitation are rapidly worsening.

#### *Medical Emergency*

There are no “do-overs” in managing symptoms at end-of-life, and the ripple effect of a dying person’s unrelieved suffering on family, friends, and staff is substantial in degree and in its persistence. Severe symptoms must be considered as a medical emergency and treated as such; this is perhaps most particularly true of dyspnea, where rapid deterioration and death may occur while treatment efforts are ongoing.

#### *The “Right Dose” Of Medications*

There is no pre-determined best dose or maximum dose for sedatives or opioids; the correct dose is “the one that works” within acceptable adverse effects. Opioids,

benzodiazepines, and neuroleptics (such as methotrimeprazine) are titrated to empirical effect after an initial dose, which is guided by best information.

#### *“Stacking” Medication Doses – Reasonable Timing Of “prn” Intervals*

In severe distress (dyspnea, pain, agitation), a medication is often “stacked” in its dosing in order to quickly achieve or reclaim comfort. This is much like administering a loading dose when running an infusion in order to reach effective serum levels immediately.

Stacking is the aggressive use of intermittent doses, repeating a dose if there is no improvement by the time there should have been, and before there is time for the medication to clear. It is neither reasonable to repeat a dose before its effect can be seen, nor to wait an hour to repeat an ineffective dose which would have peaked after 10 minutes (such as after an intravenous bolus).

Such an approach can be used with opioids and sedatives, which are titrated to empirical effect... it cannot be used for medications whose doses are predetermined by known boundaries of effectiveness and toxicity (such as acetaminophen, antibiotics, etc).

Example:

*An 85 y.o. opioid-naïve resident of a personal care home is dying of pneumonia complicating a long history of dementia. She is short of breath, with a respiratory rate of 50/min. She is given morphine 5 mg subcutaneously.*

In this situation, by 30 minutes there should be some effect seen from the subcutaneous dose. If not, the dose should be repeated (in fact, sometimes the subsequent dose is doubled if severe distress was untouched by the first dose). An order of “q4h prn” would result in 4 hours of severe distress, only to repeat the same ineffective dose which has largely been cleared.

Time ranges in *prn* orders are meaningless and potentially confusing. The *prn* interval should indicate the earliest time that the next dose can be given. For opioids and sedatives this will be determined by the timing of expected effect. A *prn* order indicating an interval of “every 1-2 hours as needed” is no more informative than “every 1 hour as needed”... if the shortest interval is one hour, then every possible interval beyond that is encompassed.

#### *How Do We Know That Opioids Are Not Compromising The Patient?*

A common barrier to the effective use opioids and sedatives in managing terminal dyspnea is the misconception that they will compromise the patient’s respiratory efforts and potentially hasten death. There is no evidence that opioids compromise palliative patients when given in doses proportionate to the degree of distress[6-9]; in fact, there is evidence that they may prolong survival [10, 11]

In comfort care of terminal pneumonia, the clinical context is one of rapid breathing. In the final moments, irregularly spaced apneic episodes interject, resulting in an

erratic pattern with clusters of rapid breaths and increasingly frequent and prolonged apneic episodes. This typically unfolds quickly – over a few seconds to several minutes – following which breathing ceases.

In contrast, excessive opioid doses cause a progressive slowing of breathing which tends to unfold more gradually (unless following a large intravenous bolus), with the respiratory pattern remaining regular. Pupils are generally pinpoint.

This is an important distinction to recognize, as staff and family may be concerned that repeated doses of opioids may contribute to the decline. When administering medications to a patient who is dying, there will invariably be a point at which the patient dies after (but not due to) receiving a medication dose. The above literature evidence and clinical distinction should help reassure that the medications did not compromise the patient.

#### *Considerations In Medication Selection*

- long-acting medication preparations (sustained-release, “CONTIN” preparations, or transdermal fentanyl preparations) should not be used to manage rapidly evolving symptoms
- if death is near and the patient is already on a stable dose of transdermal fentanyl, this should be continued and additional short-acting opioids added for titration of comfort
- specific medication routes and doses are found in the accompanying document “*Medications & Initial Dose Guidelines For Comfort End-Of-Life Care Of Pneumonia*”. Morphine and hydromorphone are the listed opioids, as they are generally available and can be used by a variety of routes
- for the patient with renal insufficiency, hydromorphone may be preferred over morphine due to fewer active metabolites that may accumulate. However, if death is anticipated within a day or two this distinction may not be relevant, as there will not likely be time for metabolite accumulation

#### **Planning For Predictable Situations**

There are predictable (and hence avoidable) issues that may derail a palliative approach in the chosen care setting. This may result in unwanted transfer from long-term care to acute care, or in an inappropriate escalation of investigations and interventions in an acute-care patient. Such issues include:

- availability of needed medications (e.g. formulary or stock considerations, pharmacy budget concerns)
- loss of the oral route of administration
- lack of policy/procedure on needed medications and their administration
- underestimating the precipitous nature of clinical deterioration and escalation of distress
- keeping all team members apprised of goals of care and rationale behind current approach to care. Staff who have not been a part of decision making and related discussions (such as evening and night staff, ancillary staff) may feel uneasy about

aggressive sedation for end-of-life delirium, or rapid escalation of opioids for dyspnea

- being able to “switch gears” to a palliative mode as a cohesive care team, where all team members are aware of the change to palliative circumstances and capable of fulfilling the care expectations
- maintaining ongoing dialogue with family, exploring their concerns, re-framing issues that are not fixable, focusing on realistic goals

Through anticipatory planning and preparation, these issues can be addressed without compromising a comfort-focused approach to care.

### **Specific Symptoms And Concerns**

Specific symptoms and concerns that may arise in the comfort care of end-of-life pneumonia include:

1. Dyspnea (shortness of breath; air hunger)
2. Respiratory congestion
3. Agitated delirium
4. Pain (eg. pleuritic pain, discomfort from immobility, or pain due to pre-existing conditions such as arthritis or malignancy)
5. Supporting and addressing concerns of families – such as decreased intake of food/fluids, concerns about medications such as opioids, need for sedation in terminal delirium, rapid deterioration.

Specific medication routes and doses are found in the accompanying document *“Medications & Initial Dose Guidelines For Comfort End-Of-Life Care Of Pneumonia”*

### **DYSPNEA**

*Dyspnea vs. Tachypnea*

- dyspnea is a **subjective experience** of air hunger (shortness of breath)
- not the same as tachypnea, which is a term describing rapid breathing without consideration of the person’s experience
- the goal of palliation is to ensure that the patient is calm and comfortable as assessed by those at the bedside, not to strive for a specific respiratory rate
- it is important to distinguish the normal physiologic responses to hypoxia and elevated CO<sub>2</sub> (rapid breathing, potentially using accessory muscles, perhaps cyanotic) from the patient’s potential to experience related distress
- the awake patient with a normal respiratory rate who feels as though he/she is suffocating is experiencing dyspnea.
- the experience of an unconscious patient cannot be known; an unconscious patient who is breathing quickly yet appearing calm and comfortable is not likely to be experiencing dyspnea. If there is uncertainty about the comfort of an unconscious patient, treatment with opioids should be provided

### *Interventions For Dyspnea At The End Of Life*

- non-pharmacological interventions include calm reassurance, elevating head of bed, cool air with an open window or a fan
- short-acting formulations of opioids are the main pharmacologic palliative intervention (i.e. immediate-release morphine or hydromorphone rather than long-acting tablets or transdermal fentanyl)
- methotrimeprazine is often helpful in providing additional sedation and anxiolysis without significantly adding to the respiratory depressant effects of opioids [12]
- benzodiazepines such as lorazepam may also help with anxiety in the context of dyspnea, however the literature does not consistently show benefit in dyspnea itself. Benzodiazepines are more likely to potentiate the respiratory depressant effects of opioids than neuroleptics such as methotrimeprazine; if additional sedation is needed during rapid escalation of opioid doses, methotrimeprazine is preferred.

### *The Role Of Supplemental Oxygen In Palliation Of Dyspnea At End Of Life*

- in the unconscious patient who appears calm and comfortable yet is breathing quickly, supplemental oxygen does not have a role in end-of-life palliation.
- the potential benefit of oxygen in relieving the experience of breathlessness at the end of life is controversial [13], however **comfort can be achieved without supplemental oxygen** using opioids such as morphine or hydromorphone as well as methotrimeprazine or a benzodiazepine such as lorazepam.

### *The Role Of Oxygen Monitoring In Palliation Of Dyspnea At End Of Life*

- in general, there is no role for the monitoring of oxygen saturation or PaO<sub>2</sub> in comfort-focused care at the end of life
- if the patient appears comfortable, oxygen levels are irrelevant and should not influence care
- if the patient appears uncomfortable, comfort should be pursued through titration of opioids and sedatives regardless of oxygen levels

## **RESPIRATORY CONGESTION/SECRETIONS**

- this refers to deep pulmonary secretions which accumulate due to weak cough and a terminal lower respiratory infection; sometimes referred to as the “death rattle”
- although the unconscious patient would not be aware of secretions, they are disturbing to those at the bedside
- prevalence as high as 92% [14]

### *Interventions For Secretions At The End Of Life*

- subcutaneous or intravenous scopolamine is the primary pharmacological intervention for secretions at the end of life

- in the absence of the subcutaneous or intravenous route, the 0.6 mg/ml injectable scopolamine preparation can be administered nasally; its nasal bioavailability approximates the subcutaneous route [15, 16]

### **AGITATED DELIRIUM IN AT THE END OF LIFE**

- delirium reaches a prevalence of 80% or more in the final days [17, 18]
- an agitated state of paranoia and combativeness is very upsetting for those at the bedside, and the patient would be devastated if aware of his/her actions
- etiology is likely multifactorial; when death is near there is not an opportunity to determine and reverse the underlying cause(s)
- mild delirium may not need treatment if the patient is not distressed and the family prefers wakefulness with mild confusion rather than sedation.
- palliative management of moderate to severe agitation when death is near involves aggressive use of sedatives such as methotrimeprazine and lorazepam (often in combination), with the goal of care being that the patient remains unconscious until death occurs from the underlying condition. **It will not be possible to fine-tune sedation to a balance of being calm yet interactive**, and pursuit of this unrealistic goal will only ensure unacceptable restlessness
- once the patient is calm, this allows family to visit, talk to the patient, pray, play favourite music or read favourite books... this would not be possible if the patient remained highly agitated
- some family members may arrive having missed the opportunity for meaningful interaction. They should be supported in having private time alone with the patient should they wish, without other family members present. This might not be an intuitive step for families, and encouragement from staff may be needed

### **PAIN MANAGEMENT IN END-OF-LIFE PNEUMONIA**

- although pleuritic chest pain and discomfort with cough may be present, pain is not likely to be a symptom of central focus in the final hours or days of a terminal pneumonia, unless it was a preexisting issue
- it is more likely that dyspnea will be the symptom which drives opioid titration, and potential underlying pain will be addressed by this
- there is often uncertainty about whether a patient's restlessness and moaning is related to pain, delirium, or air hunger. If unsure about comfort, then opioids should be considered; the addition of methotrimeprazine may also be helpful, as it has analgesic properties
- as with dyspnea, titration of short-acting preparations of morphine or hydromorphone in doses proportionate to the distress is safe and effective.

## CONCERNS OF FAMILIES

### *Decisions: Choices and Non-Choices*

- substitute decision makers should not be made to feel that they are being asked what *they* want done for their loved one... rather, they are being asked what their loved one would choose if he/she were able to in the present situation. Most families will acknowledge that he/she would want a comfort-only approach in a circumstance of rapid deterioration without likelihood of its reversal. They may have trouble deciding on such an approach themselves, however
- families often feel that they are deciding whether or not their loved one lives or dies when they are presented with care choices as death nears
- it is generally helpful to emphasize that the underlying illness and its complications have determined that this is not a survivable situation; any choices about care options are simply presented with an intention to ensure comfort as the natural course of the illness unfolds
- too often, families are asked to make a decision about care which will have no impact on the subsequent course of illness. This may reflect a desire to respect their autonomy in substitute decision making, however autonomy is not strengthened by offering choices which cannot achieve hoped-for goals
- if there is an intervention which reasonable lay-persons may expect but which the present clinical context precludes, the family should be made aware that the intervention is not possibly effective and will not be attempted. For example, there may be hope that attempted CPR may be effective when death is expected to occur from multisystem failure due to a relentless terminal condition. Such interventions should not be presented as choices, only to back-track when the choice is selected.

Rather than:

*"If his heart were to stop, would you want us to try to restart it?"*

A suggested approach could be:

*"As you know, things are changing quickly for him. We can make sure he's comfortable, but I don't believe that he has much time. His systems are shutting down, and this will reach a point where his heart can no longer keep beating. While you may have heard of times where people will try to restart the heart beating with CPR, that can't work in this type of situation, as it's not possible to fix the problems that caused the heart to stop... we won't be attempting that."*

This is no different than explaining why hoped-for surgery cannot be done, or a specific chemotherapy will not be given in a circumstance where it can't work or will be too toxic. In neither of these situations would the intervention be offered and then the offer withdrawn if selected.

### *Feeding And Hydration*

- an understandable and very common concern is that food and fluid intake is compromised at the end of life
- in the terminal phase progressive illness there is virtually always a profound loss of appetite (and therefore an absence of hunger). The literature is clear that the body cannot use calories to become stronger or to gain weight. Instead, it breaks down its own energy stores (muscle/fat/carbohydrates) regardless of caloric intake. Efforts to improve caloric intake by enteral or parenteral means have no role in addressing comfort, functional status, or survival in such end-of-life scenarios
- there is contradictory literature on whether the dying patient feels thirst, and whether fluid administration will even help reduce thirst at this time. In the unconscious patient, the experience of thirst will not be possible. In the awake patient, it is generally felt that attention to mouth care and moistness will address thirst in the final hours/days of life

### *The Precipitous Decline*

- the rapid deterioration in the final days of life can be surprising for many, and upsetting for family members who may feel that they have missed the opportunity to say goodbye
- when a pneumonia develops in the context of progressive physical and cognitive decline, there is little physiologic reserve to blunt or slow a deterioration; this is much like someone being supported by very thin ice... any added burden results in falling through very suddenly
- at times the very medications being given for comfort are blamed for the rapid changes being seen; it may be necessary to review the sequence of changes with family, to reaffirm the imperative of comfort, and to reframe the approach to care as "what would he/she want in these circumstances?"

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## Medications & Initial Dose Guidelines For Comfort End-Of-Life Care Of Pneumonia In Adults

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### Comments, Disclaimers, Assumptions:

The suggestions below are not intended to be comprehensive advice applicable to all clinical scenarios; suggested medications and doses must be considered in the unique clinical context. The following specific assumptions apply:

- the prescribing clinician is aware of any medication allergies or intolerances
- the patient is assumed to be opioid-naïve in the doses suggested below; in a patient already on opioids their existing tolerance will need to be considered.
- the doses indicated below are **conservative starting doses**, as there may be some uncertainty about how a medication will be tolerated. These may very well need to be rapidly escalated, as guided by empirical effectiveness, particularly when using opioids to relieve dyspnea or sedatives in agitated delirium.
- the intramuscular and rectal routes are **not** well tolerated and can usually be replaced by subcutaneous or sublingual routes

Medication	Indications	Route	Dose		Interval
			Frail elderly and/or mild symptoms	“Usual” adult and <u>moderate to severe symptoms</u>	
<b>Morphine</b>	<ul style="list-style-type: none"> <li>• Dyspnea</li> <li>• Pain</li> </ul>	Enteral (oral; feeding tube)  <i>OR</i> buccal/sublingual*	2.5 – 5 mg	10 mg	q1h prn (if repeated prn doses needed, add a q4h scheduled dose, usually equal to the effective prn dose)
		Intravenous	1.25 – 2.5 mg	5 – 10 mg	q 15 min. prn
		Subcutaneous	1.25 – 2.5 mg	5 – 10 mg	q 30 min prn
		Nasal Transmucosal**	not recommended; poor bioavailability <sup>1</sup>		
<b>Hydro-morphine</b>	<ul style="list-style-type: none"> <li>• Dyspnea</li> <li>• Pain</li> </ul>	Enteral (oral; feeding tube)  <i>OR</i> buccal/sublingual*	0.5 – 1 mg	2 mg	q1h prn (if repeated prn doses needed, add a q4h scheduled dose, usually equal to the effective prn dose)
		Intravenous	0.25 – 0.5 mg	1 – 2 mg	q 15 min. prn
		Subcutaneous	0.25 – 0.5 mg	1 – 2 mg	q 30 min prn
		Nasal Transmucosal**	0.5 – 1 mg	2 – 4 mg	q 15 min prn

Medication	Indications	Route	Dose		Interval
			Frail elderly and/or mild symptoms	“Usual” adult and moderate to severe symptoms	
Methotrimeprazine (Nozinan®)	<ul style="list-style-type: none"> <li>• Agitated delirium</li> <li>• Supplement opioids in dyspnea; lacks resp. depressant effects</li> <li>• Nausea</li> </ul>	Enteral (oral; feeding tube)	2.5 – 5 mg	10 – 25 mg	q 1h prn
		<b>OR</b>			
		buccal/sublingual*			
		Intravenous	2.5 – 5 mg	10 – 25 mg	q 15 min prn
		Subcutaneous	2.5 – 5 mg	10 – 25 mg	q 30 min prn
Lorazepam	<ul style="list-style-type: none"> <li>• Anxiety</li> <li>• Sedation, often added to methotrimeprazine</li> </ul>	Sublingual (consider dropping into a 1 ml syringe, then drawing up approx 0.5 ml water to dissolve & administer)	0.5 – 1 mg	1 – 2 mg	q1h prn
Scopolamine (0.6 mg/ml injectable)	Resp. secretions at end-of-life	Subcutaneous	0.3– 0.6 mg	0.3 – 0.6 mg	q1h prn (may initially need 2 or 3 back-to-back doses)
		Nasal Tansmucosal <sup>2,3</sup>	0.3– 0.6 mg (0.5 – 1 ml)	0.3– 0.6 mg (0.5 – 1 ml)	q1h prn

\* buccal/sublingual involves administering up to 1-2 ml of the parenteral preparation of medication into the mouth. These small volumes tend to be swallowed reflexively in unresponsive patients, and their bioavailability are similar to the oral route. High concentrations of the drug may be needed in order minimize volume (e.g. morphine 50 mg/ml; hydromorphone 10 mg/ml)

- \*\*
- small volumes of high concentration
  - if dose > 1 ml then divide equally between nostrils
  - Bioavailability ranges from 50 – 80 % and onset of effect ranges from 5 – 20 minutes, depending on the drug
  - May use a 1 ml syringe as a dropper, or an M.A.D. atomizer as outlined in WRHA Palliative Care Program’s guideline on Medication Administration By Mucosal Atomization Device
  - see also <http://www.intranasal.net>

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