Queen's Palliative Medicine
COVID-19 Continuous Palliative Sedation Therapy Guideline

This guideline is intended to clarify the process for safe and appropriate use of continuous palliative sedation therapy (CPST) in the context of refractory symptoms for patients at the end of life with COVID-19. CPST should be provided in consultation with a specialist palliative care team. This guideline does not encompass other forms of sedation used in palliative care including temporary procedural sedation or intermittent sedation.

This guideline has been assembled by the Division of Palliative Medicine, Queens University and adapted from several other palliative sedation frameworks, including the BC Centre for Palliative Care (1), the McMaster Division of Palliative Care (2), and University Health Network Hospitals (3) protocols.

A Queen's Palliative Medicine specialist physician is available on call 24/7 to provide consultation and can be reached via the Kingston General Hospital Switchboard at 613-549-6666 and asking for the palliative consultant to be paged.

Use of CPST in COVID-19 Pandemic

CPST is a specialized medical intervention used to address refractory, irreversible symptoms in the last hours or short days of life that have not responded to other treatments (4, 5). In CPST, medications are carefully titrated and monitored to control the symptom at the lightest sedation level and lowest medication dose possible. CPST is continued until natural death occurs from the underlying condition. When used appropriately, CPST does not hasten death and is distinct from the practice of Medical Assistance in Dying (MAiD) (4, 5).

Early experience in providing end of life care for patients with COVID-19 suggests that some patients may deteriorate rapidly with progressive dyspnea that can be challenging to address (6). CPST may be needed for refractory dyspnea or agitation in this context. A variety of approaches for providing CPST are provided in this guideline in order to provide therapeutic options in the setting of medication shortages.

Definitions

Continuous Palliative Sedation Therapy (CSPT)

CPST is defined as the process of inducing and maintaining sedation, in the last hours and days of life, for the relief of suffering caused by intractable symptoms when all appropriate alternative interventions have failed to provide adequate symptom relief. Death is expected imminently within hours to days (<2 weeks) from progression of the underlying illness.

The intention of CPST is to provide symptom relief and reduce suffering. CPST does not intend to shorten life or to bring about complete loss of consciousness through sedation, although the latter is sometimes necessary to relieve suffering (5). Sedation is induced and maintained proportionately to the level necessary to relieve the refractory symptoms and requires careful monitoring and adjustment of medication dosing to ensure the lowest effective dose is used (4). Used within these guidelines, CPST is an ethically appropriate practice for patients with goals of care focused on symptom management and comfort care.

Refractory Symptoms

Symptoms are deemed refractory when all reasonable and available treatment options to manage a patient's symptoms and relieve their suffering have been explored and provided (5). Refractory symptoms should be differentiated from difficult to manage symptoms. A patient being considered for CPST should be reviewed by a palliative care specialist in order to ensure that all possible options for palliation of symptoms have been explored that are effective within an acceptable time frame or within an acceptable risk benefit ratio to the patient. It is important not to label difficult symptoms as refractory because of lack of knowledge or skill on the part of the healthcare provider(s). The most common indications for palliative sedation are refractory symptoms from agitated delirium, severe dyspnea, seizures and pain (4, 7).

CPST for refractory psychological, social, spiritual and existential distress is controversial (8). Due to significant variation in presentation, complexity and definition of psychological, social and spiritual symptoms, it is recommended that team members with expertise in these areas provide support for assessment and management of patients with distress in these domains, including spiritual care practitioners, mental health professionals, social work, ethicists and palliative care specialists.

Criteria for CPST in COVID-19

All of the following criteria must be met prior to initiation of CPST:(4, 5, 9)

1) Death is imminently expected within hours to days (<2 weeks) from COVID-19

2) Symptoms are refractory to all other treatments that are possible & available within the limited time frame and that the patient can tolerate
3) Input has been obtained from a palliative care specialist
4) Informed consent is obtained from the patient or substitute decision maker if the patient lacks capacity. This includes that they understand the outcome of the underlying illness is imminent death within hours to days, they understand what to expect during the dying process, and they understand that the goal of CPST is to alleviate refractory suffering and not to hasten death.
5) The goals of care of the patient are comfort-focused care. The patient does not wish for CPR, intubation, and critical care supports. This is consistent with no Cardio-Pulmonary Resuscitation (no CPR) or Allow Natural Death (AND) orders.

Process for providing CPST

- CPST requires comprehensive interprofessional assessment and collaborative decision-making. The essential steps in the decision making, planning and delivery process for CPST include a thorough patient assessment, a review of the goals of care, establishment of informed consent, and development of the CPST care plan. Detailed documentation to support all steps is essential.

- Prior to initiating, discuss with the patient (or SDM) the discontinuation of medications no longer contributing to the patient's comfort, as well as the discontinuation of artificial hydration which may heighten discomfort at end of life due to excessive upper airway secretions or peripheral edema.

- For patients whose refractory symptom is delirium, neuroleptics should be used with CPST medications.

- Patients already on opioids for symptom management should have their opioids continued at current doses but not escalated. **Opioids should NOT be used specifically for CPST** because in order to achieve sedation, toxic doses of opioids may be required, leading to opioid-induced neurotoxicity and respiratory depression, which will cause discomfort and may hasten death (5).

- Ongoing monitoring should be provided for the patient's comfort, level of sedation needed to achieve comfort, and potential adverse effects. We recommend monitoring the level of sedation using the RASS-PAL tool (10; Appendix A).

- Patients should be regularly checked for urinary retention, pressure sores, and other sources of discomfort. Ongoing mouth and bowel care should be provided. Supportive care should be provided to the family.

A **care plan** must be documented that includes:

- Medication orders for CPST (see Pharmacotherapy options below)
- Goal sedation level needed to achieve comfort using the RASS-PAL tool (Appendix A)
- Schedule for monitoring sedation (Appendix A)
- Assessments for symptom control and comfort
- Other medications and treatments to be administered during CPST

Pharmacotherapy Options for Palliative Sedation in COVID-19 (scarcity of resources in pandemic situation may mean that second- or third-line medications need to be used first, and dependent on setting of care)

Notes:

- Patients undergoing CPST require both routine and PRN orders for effective sedation to achieve a sedation level that provides comfort (target RASS-PAL level).
- Neuroleptics should be used with CPST medications whose refractory symptom is delirium.
- Discuss the discontinuation of medications no longer contributing to the patient's comfort as well as intravenous/subcutaneous fluids which are typically not required at end of life and may worsen certain symptoms.

1. FIRST LINE Medications for CPST:

Midazolam continuous infusion

- Loading dose 1-5mg SC/IV
- Then 0.5-1 mg/h SC/IV continuous infusion and 1-5 mg SC/IV q30 mins PRN
- Titrate based on symptomatic response to RASS-PAL score needed to maintain comfort
- Usual dose range is 1-10 mg/h but higher doses may be required in some cases
- Midazolam is the benzodiazepine of choice given its rapid onset and short direction of action allowing for efficient titration. Intermittent dosing is not recommended due to short half-life. Tolerance and tachyphylaxis may result quickly and there should be a low threshold to addition of second- or third-line agents for patients with ongoing refractory symptoms
- Consider adding methotrimeprazine or phenobarbital if doses >10 mg/h are required

2. SECOND LINE Medications for CPST:

Methotrimeprazine

- Loading dose 12.5-25 mg SC
- Then 12.5 mg SC q6h and 12.5 mg SC q2hr prn

- Usual dose range is 25-50 mg q6h
- Titrate up to 300 mg/day total daily dose, based on symptomatic response to RASS-PAL score needed to maintain comfort

Loxapine *(if methotrimeprazine is not available)*

- Loading dose 10 mg SC
- Then 10 mg SC q4h and 5-10 mg SC q4h PRN
- Titrate based on symptomatic response to RASS-PAL score needed to maintain comfort

3. THIRD LINE Medications for CPST:

Phenobarbital

- loading dose 60 mg SC
- Then 60 mg SC q8h and 60 mg q4h PRN
- Usual dose range is 1200-1600 mg/day
- Titrate up based on symptomatic response to RASS-PAL score needed to maintain comfort

Lorazepam (alternative benzodiazepine)

- Initial dosage: 1-4 mg SC/SL and 1-2 mg SC/SL q4h PRN
- Usual dose range is 1-4 mg SC/SL q2-4h (buccal route may have inconsistent absorption and require doses of 1-8 mg SL q2-4h PRN)
- Titrate based on symptomatic response to RASS-PAL score needed to maintain comfort

Propofol continuous infusion

- Use limited to a setting with appropriate personnel for administration, monitoring and support and patient must have intravenous access (e.g. Palliative Care Unit or ICU)
- Loading dose 10 mg IV q 5min PRN to achieve sedation level needed for comfort
- Then 0.6 mg/kg/min continuous infusion and 10 mg bolus q 15min prn based on symptomatic response to RASS-PAL score needed to maintain comfort
- Usual dose range is 1-3 mg/kg/h and rates higher than 6 mg/kg/h would be rarely needed

Ketamine continuous infusion

- Use limited to a setting with appropriate personnel for administration, monitoring and support (e.g. Palliative Care Unit or ICU)
- Pre-dose with neuroleptic or benzodiazepine to reduce risk of psychomimetic effects
- Start initial infusion at 0.1 mg/kg/h IV/SC

- Titrate by 0.05 mg/kg/h every 1 hr PRN up to 0.5 mg/kg/h based on symptomatic response to RASS-PAL score needed to maintain comfort
- In some cases, it may be necessary to titrate up to 2 mg/kg/h

MONITORING requirements

- After initiating CPST, assess level of sedation every 30 mins until sedation level needed for comfort is achieved, then q4h and PRN.
- Document target sedation level needed for comfort using a standardized tool such as RASS-PAL.
- If dose modifications are required due to recurrent refractory symptoms, monitor q30 mins until sedation level is again achieved and then q4h and PRN.
- Due to surge possible in a pandemic situation, frequent monitoring may not be reliably available. In these cases, best clinical judgement in the context of resource scarcity should direct monitoring intensity and frequency.

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APPENDIX A

Richmond Agitation Sedation Scale – Palliative Version (RASS-PAL)
for assessing and monitoring level of sedation (Bush et al. BMC Palliative Care 2014)

Richmond Agitation-Sedation Scale - Palliative version (RASS-PAL)[9]

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff (e.g. throwing items); +/- attempting to get out of bed or chair	
+3	Very agitated	Pulls or removes lines (e.g. IV/SQ/Oxygen tubing) or catheter(s); aggressive, +/- attempting to get out of bed or chair	
+2	Agitated	Frequent non-purposeful movement, +/- attempting to get out of bed or chair	
+1	Restless	Occasional non-purposeful movement, but movements not aggressive or vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* **(10 seconds or longer)**	Verbal Stimulation
-2	Light sedation	Briefly awakens with eye contact to *voice* **(less than 10 seconds)**	
-3	Moderate sedation	Any movement (eye or body) or eye opening to *voice* **(but no eye contact)**	
-4	Deep sedation	No response to voice , but any movement (eye or body) or eye opening to *stimulation by light touch*	Gentle Physical Stimulation
-5	Not rousable	No response to *voice or stimulation by light touch*	

Procedure for RASS-PAL Assessment[9]

1. Observe patient for **20 seconds.**	
a. Patient is alert, restless, or agitated **for more than 10 seconds** **NOTE:** If patient is alert, restless, or agitated for less than 10 seconds and is otherwise drowsy, then score patient according to your assessment for the majority of the observation period	Score 0 to +4
2. If not alert, greet patient and call patient by name and *say* to open eyes and look at speaker.	
b. Patient awakens with sustained eye opening and eye contact **(10 seconds or longer).**	Score -1
c. Patient awakens with eye opening and eye contact, but not sustained **(less than 10 seconds).**	Score -2
d. Patient has any eye or body movement in response to voice but no eye contact.	Score -3
3. When no response to verbal stimulation, physically stimulate patient by light touch e.g. gently shake shoulder.	
e. Patient has any eye or body movement to gentle physical stimulation.	Score -4
f. Patient has no response to any stimulation.	Score -5