Alberta Health Services

Edmonton Zone Palliative Care Program

Title: **Palliative Sedation GUIDELINE**

Date Approved: **Original version in September 2006 and revised in October 2015**

Approved By: ***Edmonton Zone Palliative Care Program, Practice Development and Quality Committee***

Date of Next Review: **October 2018**

A. PURPOSE:

To provide guidance when considering **Palliative Sedation** as a form of palliation for intractable symptoms in an appropriate setting and time frame.

B. STAKEHOLDER INVOLVEMENT:

- This guideline was developed by health care professionals with expertise in palliative care. The disciplines of nursing, pharmacy and medicine were represented with additional consultation with ethics and spiritual care
- Patients' views and preferences were not specifically sought in developing the guideline, given the medically frail nature of this population. However, the guidelines reflect the developers' observations of patients' experiences
- The guideline is intended for use by palliative care consultants, as well as other physicians and nurses involved in the care of palliative care patients
- Although the guideline has not been piloted among target users, it reflects current practice in the Edmonton Zone Palliative Care Program

C. DEVELOPMENT:

- The articles were identified through a search of MEDLINE from 1985 to 2005, using the search term "sedation"; subject heading "palliative care", "terminal care", "delirium", "neoplasm", "hypnosis", and "sedative"; combined with "refractory symptom", subject heading "palliative care", "pain", "intractable", limits "human", "English language"
- An additional Pub Med search (2005 - July 15, 2015) using the search term "Palliative Sedation" and "English language": 506 references were found, of which 28 were clinical trials
- Developers' article collections on this topic were perused, as well as the articles' reference lists
- Both clinical case reports and review articles were used as sources of information
- Recommendations were formulated by consensus among the members of the Practice Development and Quality Committee
- The guideline was evaluated using the AGREE instrument
- Health benefits, risks and costs were taken into consideration in developing the guideline
- The guideline was not externally reviewed
- The guideline was issued in 2015 and will be updated in accordance with the Practice Development and Quality Committee process

D. BACKGROUND:

The presence of severe suffering refractory to standard treatment and "sedation" as a means of controlling these symptoms in the palliative care setting has been recognized in the literature since 1990 (1).

The target symptoms that require "Palliative Sedation" vary depending on the setting of care and definition of this practice. The most commonly reported target symptoms are: hyperactive delirium, dyspnea and pain (2)(3)(4)(5)(6)(7)(8).
Midazolam is the most frequently reported individual drug for inducing Palliative Sedation (6)(8)(9)(10).

E. DEFINITION:

Palliative Sedation is a process of inducing and maintaining deep sleep in order to relieve **refractory symptoms** in patients with an anticipated **life expectancy of hours to days** (12)(14). Although "terminal sedation" has long been used to describe this practice, **Palliative Sedation** is thought to be a more appropriate term due to the possibility of misinterpreting the intention of sedation as being "termination" of life (12)(14).

Symptoms are defined as refractory when all other possible treatments have failed, or it is estimated by team consensus, based on repeated and careful assessments by skilled experts, that no methods are available for alleviation within the time frame and risk-benefit ratio that the patient can tolerate (15)(16). Team consensus stands for the consensus among patient, family members, attending physician, and multi-professional care providers.

Various levels and durations of sedation have been described: mild sedation (i.e. "conscious" or "proportional" sedation) versus deep sedation (i.e. "total" or "heavy" sedation), and intermittent sedation (i.e. "controlled", "night", "respite" or "temporary" sedation) versus continuous sedation (12). Considering the presence of refractory symptoms and proximity of death, it is best to limit the definition of **Palliative Sedation** to deep and continuous sedation. This reflects the current clinical practice in the Edmonton Zone Palliative Care Program.

F. ETHICAL VALIDITY:

The ethical validity of **Palliative Sedation** has been questioned because of the perception that it may hasten death. However, recent published evidence does not demonstrate any shortening effects on survival in appropriately selected patients who receive **Palliative Sedation** (7)(8)(17)(21). The intention of Palliative Sedation is exclusively to relieve refractory symptoms; while the intention of euthanasia is to hasten death (18). It is this intention of **Palliative Sedation** that distinguishes it ethically from euthanasia. **Palliative Sedation** is ethically different from euthanasia because it is only offered when: a) death is considered near and b) symptoms are refractory and the distress associated with them is severe enough to justify suppression of consciousness. A separate discussion regarding other end-of-life decisions, such as artificial hydration and feeding should occur before initiating **Palliative Sedation**. Taken together, these factors result in an understanding of **Palliative Sedation** that clearly distinguishes it from euthanasia or practices that are ethically equivalent to euthanasia.

G. CRITERIA:

- When considering **Palliative Sedation** for the patient, the following criteria must be met:

1) **Refractory** symptoms are present.

2) Death is expected **within hours to days:** the patient is experiencing an illness that does not allow any realistic possibility for recovery and death is imminent (4)(5)(7)(17). Resources that may assist estimating a survival time of days are available (19)(20).

3) The informed wishes of the patient or his/her alternate decision maker must be clear to all stakeholders.

4) The patient or his/her alternate decision maker understands and acknowledges the expected outcome of his/her illness and that the goal of care is patient's comfort.

5) The Goals of Care Designation (http://www.albertahealthservices.ca/frm-103547.pdf) should be C2,

based on the proximity of death (usually hours to days) with maximal efforts directed at symptom management and comfort. No cardiopulmonary resuscitation would be undertaken, nor should life support interventions be initiated or continued unless directly providing symptom management and comfort.

H. COURSE OF ACTION (Figure 1)**:**

Recommendation 1: In considering the use of **Palliative Sedation**, the prescriber should ensure that the patient is assessed by a palliative care consultant (12)(15).

Recommendation 2: The prescriber, or prescriber with palliative care consultant should discuss the option of **Palliative Sedation** with the patient, his/her alternate decision maker and appropriate health care team (22)(23).

- Insufficient information and unclear goals of care may be associated with dissatisfaction and emotional burden to the caregivers including moral distress
- The target level of consciousness of "**Palliative Sedation**" is deep sedation: no facial expression of discomfort is observed
- Ensure that active and appropriate symptom management continues during **Palliative Sedation,** for example continuing administration appropriate dose of opioids for pain or dyspnea
- The distinction between **Palliative Sedation** and euthanasia, the latter which intentionally induces death as a result of administering a lethal dose of medication, should be discussed (see F. ETHICAL VALIDITY)
- In the situation of family or health care providers not being confident in their skills with **Palliative Sedation**, transferring the patient to a setting that is skilled with this procedure should be considered
- Health care providers should ensure that family members are prepared for their loved one's dying process, including the likelihood of noisy respiration, peripheral cyanosis, and decreased urinary output. Distant family members may need to be contacted. Funeral arrangement should be considered

Recommendation 3: When the option of **Palliative Sedation** is selected by the patient or his/her alternative decision maker, the prescriber or palliative care consultant should ensure that the discussion of the following issues is documented on the health record:

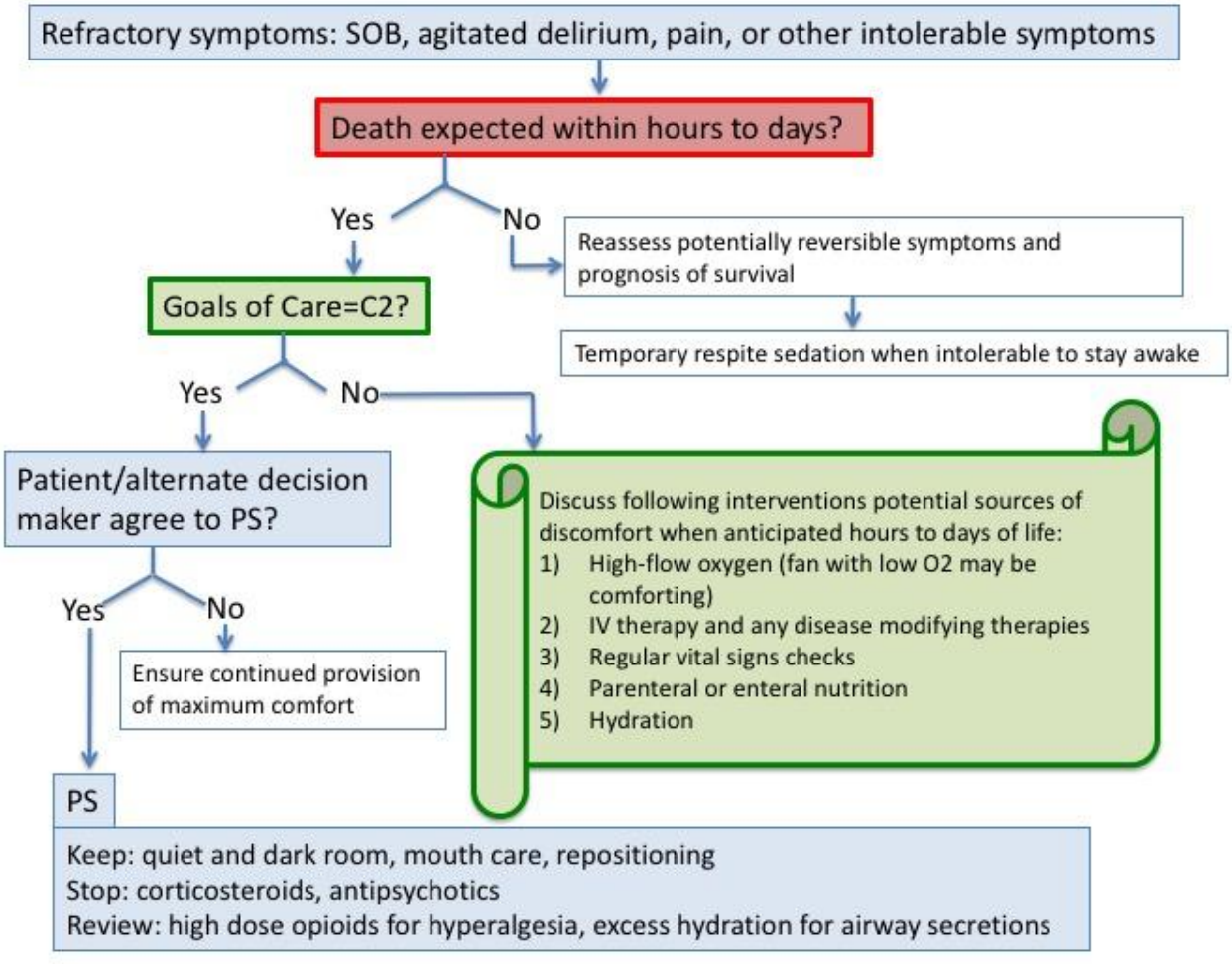
- The criteria and rationale used to determine that the patient is a candidate for **Palliative Sedation**
- The patient or his/her alternate decision maker's consent
- The agreed goals of care amongst the patient, family, and prescribers/health care providers

Recommendation 4: Once consent is obtained for **Palliative Sedation**, the palliative care consult should assist the prescriber in arranging for **Palliative Sedation** and appropriate monitoring of the patient (see Recommended Procedure: Monitoring).

Recommendation 5: The Edmonton Zone palliative care consultant on call should be contacted (780-496-1300 or RAH/UAH/CCI switchboard for palliative care on-call consultant if patient is admitted to one of these facilities) for further assistance when having difficulty managing **Palliative Sedation**.

- Paradoxical reaction/poor response to midazolam:
  1) Sporadic reports and clinical experience alert health care providers to the possibility that midazolam may aggravate the agitation or fail to achieve sedation despite rapid dose increment. The contributing factors for this phenomenon are unclear, but possibly multifactorial such as genetics, smoking and alcohol history, organ function, acidosis, and drug interactions (24).
  2) Possible over-estimation of time of survival should be considered when poor response to midazolam is observed (25)(26).
- A significant increase in midazolam dose when duration of administration exceeds 14 days has been reported (26). At this point, the initial decision should be carefully reviewed with all stakeholders when **Palliative Sedation** exceeds the initial estimated survival time. Other adjuvant for **Palliative Sedation** may be considered when considered appropriate.

Figure 1. Clinical Decision Trees



I. EDITORIAL INDEPENDENCE:

- This guideline was developed without external funding
- The developers have declared an absence of conflict of interest

J. RECOMMENDED PROCEDURE:

Contraindications

Hypersensitivity to midazolam or any component of the formulation, including benzyl alcohol (cross–sensitivity with other benzodiazepines may exist) (28)

Drug interactions

Midazolam is a major substrate of cytochrome enzyme P450-3A4. Concomitant medications that are CYP-3A4 inducers (such as corticosteroids) may result in rapid increment of dosage of midazolam in a short period, whereas CYP-3A4 inhibitors (such as antifungal agents) may cause heavy sedation with a relatively low dose of midazolam (28)

Preparation - general

- Ensure the Goals of Care designation is C2
- All oral medications should be discontinued
- Assess the prescribed medications are necessary, and correct route of administration (i.e. subcutaneous or rectal)
- Foley catheter should be available
- Ensure that the patient is in a safe and quiet environment
- Educate the family and care providers that excessive tactile stimulation, turning and positioning may stimulate arousal of the patient and cause him/her distress. Impaired swallowing due to the sedated state, may cause noisy oropharyngeal secretions

Preparation - midazolam

1. Obtain premixed midazolam: midazolam 100 mg in 100 mL (or 250 mg in 250 mL, depending on the setting, estimated period of Palliative Sedation, and availability) mini bag of Dextrose 5% in Water (D5W) or Normal Saline (NS); concentration = 1 mg/mL (29)
2. Obtain the following equipment and supplies: infusion pump, IV tubing, and subcutaneous infusion set.
3. Initiate a new subcutaneous site according to site specific policy and procedure. Connect the tubing to the pump.
4. Depending on the loading dose prescribed, one pre-filled syringes with 2.5 mg (0.5mL) or 5 mg of midazolam for a loading dose, and another pre-filled syringe with 2.5 mg for priming the 3” winged infusion set, using the midazolam 5 mg/mL injection connection.
5. Prime tubing all the way to the tip of the winged infusion set.
6. Optional: Three pre-filled syringes with 5 mg (1 mL) of midazolam for prn use.

Preparation – midazolam infusion

- An initial loading dose of 2.5 or 5 mg may be considered if a patient is restless or agitated.
- Start the subcutaneous infusion of midazolam at 1-5 mg/hour
- Titrate by 1 mg every 10-15 min until the patient is sedated, and maintain the dose when the patient is sedated appropriately. The recommended range of midazolam is 1-10 mg/hour by continuous subcutaneous infusion. However, this may be individualized depending on the patient’s needs and under the supervision of an expert in symptom management (See Monitoring)

Storage and Stability

- Refer to site-specific Parenteral Administration Manual policies and procedures (30)
- Midazolam is compatible with NS, D5W, or D5NS (28)
- At a final concentration of 0.5 mg/mL in D5W or NS, midazolam is stable at room temperature or refrigeration for up to 24 hours (28)

Monitoring

- General monitoring:
  It is generally agreed upon that the quality of **Palliative Sedation** will improve when the effect is monitored. The required depth of sedation should be at the level, which enable patient to be able to tolerate the targeted refractory symptom while all other symptoms are controlled. Therefore, both indices of symptom control and depth of sedation should be monitored simultaneously (31). However, the limited studies for monitoring **Palliative Sedation** effects have been published.

- There are limited instruments studied in palliative care settings:
  1) The depth of sedation and agitation: The Richmond Agitation–Sedation Scale (RASS), a simple observational instrument with was developed and validated in Intensive Care. RASS has not been validated in the **Palliative Sedation** setting. A pilot study in palliative care setting has been reported using modified version of RASS (32). It can guide when caring sedated patients and agitated delirious patients on the continuum of its scale ranging from +4, representing an overly combative, to -5, representing unarousable to both voice and physical stimulation. Ramsay Sedation Scale (1=patient is anxious and agitated or restless, or both; 2=patient is cooperative, oriented, and tranquil; 3=patient responds to commands only; 4=patient exhibits brisk response to light glabellar tap or loud auditory stimulus; 5=patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus; 6=patient exhibits no response) was used in **Palliative Sedation** in home settings (33).
  2) Symptom control: For observation of symptoms for non-communicative patients, adequate measurement instruments such as the Edmonton Symptom Assessment Scale – revised (http://palliative.org/NewPC/_pdfs/tools/ESAS-r.pdf) is recommended to ensure symptoms are adequately controlled. This may be completed by care-givers and family members (31).
- Local reactions:
  1) Subcutaneous infusions: refer to the Intermittent Subcutaneous Injections* and Hypodermoclysis** Administration Clinical Practice Guidelines
     *http://palliative.org/NewPC/_pdfs/management/Edmonton%20Injector%20for%20Intermittent%20Subcutaneous%20Injection.pdf
     **http://palliative.org/NewPC/_pdfs/management/3A7%20Hypodermoclysis%20Admin%20Protocol%20for%20PC%20Patients.pdf
  2) Monitor for local reactions: bleeding, redness, leaking and swelling.
- The attending physician/nurse practitioner should be informed when the maximum dose range of midazolam has being reached
- Ensure that the patient receives regular analgesics when appropriate during **Palliative Sedation**

ADDENDUM TO PALLIATIVE SEDATION

Palliative Sedation for Existential distress

Issue of undefined terminology

The terminology and definition of a refractory symptom as a reason for palliative sedation has not been rigorously established. Accordingly, the reasons for palliative sedation vary between published reports. Currently available literature and our published experience suggest that the most frequent reasons for palliative sedation are agitated delirium, followed by dyspnea (4) (5) (34). **Palliative Sedation** for intractable pain and nausea/vomiting has been reported less commonly in our clinical and published experience (4) (5). Other symptoms such as malaise, insomnia, anxiety, distress, mental anguish, and existential distress have been reported by other groups as reasons for palliative sedation (2) (5) (7) (21) (35) (36) (37) (38). The lack of clear diagnostic criteria in identifying refractory symptoms creates a potential for wide interpretation of “refractory” and the application of **Palliative Sedation**.

Refractory existential suffering

The identification of existential suffering has been a significant concern with respect to the difficulty in clearly defining “refractory existential suffering” and distinguishing this clinically from treatable psychiatric conditions such as depression. Without diagnostic criteria and the difficulty of determining “refractory existential suffering”, providing **Palliative Sedation** for this indication is challenging and open to abuse. In addition, providing **Palliative Sedation** for “refractory existential suffering” as a sole indication (i.e. absence of physical symptoms) risks the use of this practice for patients far removed from the final days of life.

Conclusion

We do not recommend or use **Palliative Sedation** as a treatment to alleviate “existential suffering” as the only refractory symptom in the end of life. The attending team should utilize the interdisciplinary team to address existential distress.

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