

GUIDELINE**Title:** Palliative Sedation**Date Approved:** September, 2006**Approved By:** Palliative Care Clinical Practice Guideline Committee**A. PURPOSE:**

- To provide guidance when considering **Palliative Sedation** as a form of palliation for intractable symptoms in 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.
- 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 patients.
- Although the guideline has not been piloted among target users, it reflects current practice in the Capital Health Regional 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" .
- 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 Palliative Care Guidelines Committee.
- The guideline was evaluated using the AGREE Instrument.
- Health benefits, risks and cost were taken into consideration in the developing the guideline.
- The guideline was not externally reviewed.
- The guideline was issued in 2005 and will be updated in accordance the Clinical Practice Guidelines 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 common reported target symptoms are: hyperactive delirium, dyspnea and pain (2)(3)(4)(5)(6)(7).
- Midazolam is known to be the most frequently reported individual drug for inducing Palliative Sedation (6)(8).

E. DEFINITION:

- **Palliative Sedation** is a process of inducing and maintaining deep sleep in order to **relieve refractory symptoms** in the palliative care setting (9)(10).
- 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(9)(11).
- Symptoms are defined as **refractory** if 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(12)(13). 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 (9). Considering the presence of refractory symptoms and proximity of death, it is best to limit **Palliative Sedation** to deep and continuous sedation. This reflects our current clinical practice.

F. ETHICAL VALIDITY:

- The ethical validity of Palliative Sedation has been questioned because of the perception that it may hasten death. However, recent evidence does not demonstrate any shortening of survival in appropriately selected patients who receive Palliative Sedation (7)(14)(15). It should be emphasized that the intention of this practice is exclusively to relieve the refractory symptoms.

G. CRITERIA:

- When considering **Palliative Sedation** for the patient, the following criteria must be met:
 - 1) The presence of **refractory symptoms**
 - 2) The proximity of death: the presence of an illness that does not allow any realistic possibility for recovery and where death is expected within hours to days (i.e. less a week) (4)(5)(7)(14).
 - 3) The presence of the informed wishes of the patient or his/her surrogate decision maker
 - 4) The patient or his/her surrogate decision maker is in agreement on the expected outcome of his/her illness and the goal of care being his/her comfort.
 - 5) A do not resuscitate order must be in effect.

H. COURSE OF ACTION:

Recommendation 1: In considering the use of Palliative Sedation, the attending physician should ensure that the patient is assessed by a physician expert in symptom management (9)(12).

Following points should be cleared:

- Non-pharmacological approaches, such as distraction and relaxation techniques in the case of anxiety/dyspnea, have been maximized.
- All other pharmacological treatments, such as appropriate titration of opioids in the case of dyspnea or appropriate dosing of neuroleptics for delirium, have been maximized.

- A thorough assessment has been conducted to identify and treat reversible problems.
- Temporary respite sedation has been considered in the event of a potentially reversible delirium, or in the case of extreme psychological distress.
- Palliative Sedation for psycho-existential distress in the presence of proximity of death has been reported in the literature by a number of centres, However Palliative Sedation for psycho-existential distress in isolation from other refractory symptoms as listed above has never been reported from our experience (4) (5) (29). It is recommended to consider obtaining an ethics consult if palliative sedation for psycho-existential distress as the only refractory symptom is being contemplated (See Addendum: Palliative Sedation for psycho-existential distress).

Recommendation 2: The attending physician, or a physician expert in consultation with attending team, should discuss with patient, his/her surrogate decision maker and an appropriate team member of health care providers the option of Palliative Sedation based on the recommendations of a physician expert in symptom management(16)(17).

- Insufficient information and unclear goal of care may be associated with dissatisfaction and emotional burden to the caregivers.
- The target level of consciousness of “Palliative Sedation” is deep sedation: no facial expression of discomfort.
- Ensure that active and appropriate palliation for discomfort should be continued when “Palliative Sedation” is implemented, for example: opioids.
- The distinction between Palliative Sedation and euthanasia, which intentionally induces death as a result of administering a lethal dose of medication, should be discussed.
- 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: the likelihood of noisy respiration, peripheral cyanosis, and decreased urinary output. Distant family members may need to be contacted. Funeral arrangement should be in place.

Recommendation 3: If the option of Palliative Sedation is selected by the patient or his/her surrogate decision maker, the attending physician or physician expert 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 surrogate decision maker’s consent
- The agreed goal of care amongst the patient, family, and health care providers.

Recommendation 4: Once consent is obtained for Palliative Sedation, the physician expert in symptom management should arrange for Palliative Sedation and appropriate monitoring of the patient (see Recommended Procedure: Monitoring).

- In the setting of community, see Applicability of this guideline.

Recommendation 5: Attending physician should be aware of following outstanding issues. It is strongly recommended that Regional Palliative Care Consultant be contacted (496-1300) for further assistance when having difficulty managing deep sedation.

- Paradoxical reaction/Poor response to midazolam
 - 1) Sporadic reports and clinical experience alert clinicians 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 (18).
 - 2) Possible misassessment of death proximity should be considered when poor response to midazolam is observed (19)(20).
- A significant increase in midazolam dose when duration of administration exceeds 14 days has been reported (21).

I. APPLICABILITY:

- The ability to apply this guideline is limited to the person (patient) who meets above criteria.
- In the setting of community, following further criteria should be met:
 - 1) The patient has been assessed and admitted to the Palliative Home Care Program.
 - 2) The Palliative Home Care Nurse (PHCN) should discuss the case and be in agreement with the Palliative Resource Coordinator (RC). PHCN will review the patient situation with the RC as soon as “Palliative Sedation” becomes a treatment option for consideration.
 - 3) RC should ensure that PHCN will remain in the home for initiation and stabilization of “Palliative Sedation” and until the patient and family are comfortable.
 - 4) The attending physician must be available to visit the patient and family at home at any time until the patient’s death.
 - 5) The attending physician’s order, including Do Not Resuscitate order, should be in the patient’s home care chart, which should be kept in the home.
 - 6) PHCN will ensure that an infusion pump is available for the patient when required (Community Pharmacy and/or Home Care, Community Care Access). (Refer to site specific teaching package for examples of how to titrate medications with different infusion pumps.)

J. EDITORIAL INDEPENDENCE:

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

K. RECOMMENDED PROCEDURE:

Recommended Procedure

Contraindications

- Hypersensitivity to midazolam or any component of the formulation, including benzyl alcohol (cross –sensitivity with other benzodiazepines may exist) (22)

Preparation

- Prime tubing all the way to the tip of the winged infusion set.
- Initiate a new subcutaneous site according to site specific policy and procedure. Connect the tubing to the pump.
- Confirm availability for additional midazolam.
- Reassess the prescribed medications and ensure the medications are ordered by correct route of administration (i.e. subcutaneous or rectal). All oral medications should be discontinued.
- 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. Due to impaired swallowing due to the sedated state, oral secretions may cause a rattle.

Preparation for Midazolam Infusion and the Rate of Administration

- Midazolam 100 mg in 100 mL mini bag of Dextrose 5% in Water (D5W) or Normal Saline(NS): concentration=1mg/mL
- Initial dosage of midazolam 1-5 mg subcutaneously may be considered for distressed patient.

- Titrate by 1 mg subcutaneously every 5-10 min until patient is sedated, and maintain the dose when patient is sedated appropriately. Do not attempt to decrease the dose unless presence of respiratory depression. The recommended range of the midazolam is 1-10 mg/hour by continuous subcutaneous infusion. However, this may be individualized depending on the patient's needs by supervision of expert in symptom management (See Monitoring).
- Two pre-filled syringes with 2.5 mg (0.5mL) of midazolam for a loading dose, and for priming the 3" winged infusion set, using the midazolam 5 mg/mL injection connection.
- Three pre-filled syringes with 5 mg (1 mL) of midazolam for initial dosage or prn use.
- After Pharmacy hours and for stat orders, refer to site-specific instructions for preparing midazolam, and Quick Response Kit for community patients.
- IV tubing
- Winged infusion set
- Second winged infusion set with injection cap.
- Swabs
- Transparent dressing

Storage and Stability

- Refer to site-specific Parenteral Manual policies and procedures (e.g. CHA Regional Parenteral Manual*).
- At a final concentration of 0.5 mg/mL D5W or NS is stable at room temperature or refrigeration for up to 24 hours when diluted with) (22).
- Midazolam is compatible with NS or D5W, D5NS (22).

Drug interactions

- Midazolam is a major substrate of cytochrome P450- 3A4. Concomitant medications that are CYP-3A4 inducers may result in rapid increment of dosage of midazolam in a short period, whereas CYP-3A4 inhibitors may cause heavy sedation with a relatively low dosage of midazolam (22).

Monitoring

- Ensure patient achieves deep sedation: no facial expression of discomfort, glazed eyes, eye lid reflex may be absent, present or absent response to mild prodding (23)(24)(25).
- Local reactions
 - 1) SC infusions: refer to the Intermittent SC Injections** and Hypodermoclysis Administration Clinical Practice Guidelines***
 - 2) Observe for local reactions, bleeding, redness and swelling
- Re-assess if additional midazolam from pharmacy is needed based on the infusion rate.
- The attending physician should be informed when the maximum dose range of midazolam is being reached.
- Ensure that the patient receives regular analgesics during the sedated stage.
- Alertness/Sedation Scale may be used as a guide for monitoring the level of the sedation (23). (See Appendix 1: NB: this tool was validated on healthy men who did not have any indication of refractory symptoms.)

For Palliative Home Care only

- A Registered Nurse should be available to remain in the home during the titration phase of sedation.
- Once the patient is stably sedated at a stable dose of midazolam, and the Case Manager is leaving the home, the Community Care Access triage nurse and evening/night RN should be informed of patient status and instruct for continuing care.
- The attending physician's order should be in the patient's homecare chart and faxed to the Community Pharmacy supplying the medication.

Appendix 1 (23)

Assessment categories				Composite score level
Responsiveness	Speech	Facial expression	Eyes	
Responds readily to name spoken in normal tone	Normal	Normal	Clear, no ptosis	5 (Alert)
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Responds only after name is called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild prodding or shaking	Few recognizable words	-	-	2
Does not respond to mild prodding or shaking	-	-	-	1 (Deep sleep)

ADDENDUM TO PALLIATIVE SEDATION

Palliative Sedation for psycho-existential distress

1) Issue of undefined terminology

The terminology and definition of a refractory symptom as a reason for palliative sedation have 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) (29). 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) (15) (30) (31) (32) (33). In a survey of 61 palliative care experts from eight countries, the reasons for the use of palliative sedation were listed as follows: pain (20%), anguish (14%), respiratory distress (12%), agitation/delirium/confusion/hallucinations (12%), restlessness (10%), fear/panic/anxiety/terror (10%), and emotional/psychological/spiritual distress (10%) (8). We also acknowledge the recently reported trend for an increased use of palliative sedation for psychological and existential distress between 1995 and 2002 (7).

2) Complex nature of assessment of the symptom in the end of life

The assessment of symptoms becomes increasingly complex in patients who are imminently dying. In this context, the identification of psycho-existential distress as an only reason to consider palliative sedation would be difficult. This speculation is supported by a study reporting that delirium occurs in approximately 90% of patients at the end of life, and by the finding of high incidence of a low Folstein's Mini-Mental State Examination score in hospice patients whose median length of stay (which is equivalent to the life expectancy) is 30 days (34) (35). Palliative sedation for psychosocial-existential distress in isolation from other refractory physical symptoms as listed above has never been reported from our experience (4) (5) (29).

Determining psycho-existential distress as a refractory symptom should be made only after an unsuccessful process of repeated assessment and standard intervention by appropriately skilled inter-disciplinary clinicians when possible. However we acknowledge that access to professionals who are skilled in the management of psycho-existential distress is limited in settings other than the tertiary palliative care unit, and interventions for psycho-existential distress are not as well-defined as they are for most physical symptoms (12). Depression, delirium, anxiety, mental anguish, familial discord, and spiritual issues may contribute to the suffering of psycho-existential distress, and aggressive interventions directed to those conditions are essential prior to conclude that the condition is intractable (36) (37).

3) Conclusion

Based on our experience and currently available evidence, we do not recommend palliative sedation as a mean to alleviate psycho-existential distress as an only refractory symptom in the end of life. Attending team is recommended to utilize the inter-disciplinary professionals' skills to optimize symptoms whenever possible. It is recommended to consider involving ethics consult as long as it is available to the site of patient care for further assessment and research if in case of need of consideration for palliative sedation for psycho-existential distress as an only refractory symptom occurs.

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***Hypodermoclysis Administration