Symptom control at the end of life, what about palliative sedation?

Augusto Caraceni
Director Palliative Care, Pain Therapy and Rehabilitation National Cancer Institute of Milan
clinical practice guidelines

ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation†

N. I. Cherny†, on behalf of the ESMO Guidelines Working Group*

† Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem, Israel
Palliative sedation Definition

- The use of sedative medications to relieve intolerable suffering from refractory symptoms by a reduction in patient consciousness (De graef et al 2007)
- “monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering” (EAPC Cherny et al 2009)
- At the end of life
This type of sedation in palliative care

• Is qualified
  – by time course which can be progressive or rapid depending on the clinical situation
  – depth which needs capable monitoring and should be proportionate to the clinical need
  – relationship with prognosis “imminently dying patients” (Hasselaar et al 2009)
## Prevalence

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Prevalence</th>
<th>Setting</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maltoni</td>
<td>2009</td>
<td>25%</td>
<td>Prospective multicenter trial</td>
<td>But DCS only 5.9%</td>
</tr>
<tr>
<td>Maltoni</td>
<td>2012</td>
<td>37 vs 25%</td>
<td>Prospective trial two hospices</td>
<td>Difference not significant after adjusting for case mix characteristics</td>
</tr>
<tr>
<td>Caraceni</td>
<td>2012</td>
<td>64%</td>
<td>Cancer center</td>
<td>Terminal patient referred to PC team for difficult symptoms</td>
</tr>
<tr>
<td>Mercadante</td>
<td>2011</td>
<td>5-36%</td>
<td>Home care</td>
<td>Literature review</td>
</tr>
<tr>
<td>Jasper</td>
<td>2012</td>
<td>13 vs 25%</td>
<td>PCU vs Hospice</td>
<td>Germany</td>
</tr>
<tr>
<td>Claessens</td>
<td>2011</td>
<td>7.5%</td>
<td>8 PCU</td>
<td>Belgium</td>
</tr>
<tr>
<td>Chambaere</td>
<td>2011</td>
<td>14.5%</td>
<td>Population based</td>
<td>Belgium death certificate retrospective study</td>
</tr>
</tbody>
</table>
The prevalence of sedation varies according to

• Objective clinical variability
  – Patient population characteristics, setting of care
  – Definition and type of sedation
• Attitudes and knowledge of care givers
Sedation in the management of refractory symptoms: guidelines for evaluation and treatment

Cherny N., Portenoy R.K.
Are there other options to give relief?

YES

Are the consequences of such interventions tolerable?

YES

The intervention can offer relief in a tolerable time

YES

Refractory symptom

Difficult symptom but Ordinary measures are possible
Indication in 774 patients reported in 10 studies. From a systematic literature review

Maltoni M et al JCO 2012
Indication to sedation at a tertiary cancer center in 51 consecutive cases

<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>Dyspnea and agitation</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>Delirium (hyperactive)</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Agitation</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Dyspnea and delirium</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Pain and agitation</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hemorrhage and agitation</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Caraceni et al Supp Care Cancer 2012
Indication

• Existential/psychological distress
  – Not limited to the terminal phase of the disease
  – Difficult to assess and treat
  – Careful multidisciplinary assessment and monitoring

Maltoni et al  Curr Opin Oncol 2013,
Maltoni et al Ann Oncol 2009
Duration

- Most case series reports durations ranging between a few hours and 2/3 days
- In one prospective study 10% of patients had sedation for more than 10 days and 3% for more than 20 days

Maltoni et al. *Curr Opin Oncol* 2013,
Maltoni et al. *Ann Oncol* 2009
Sedation in acute cancer center

Duration of sedation until death
- median = 45 hours
- 25%-75% = 24-72 hours
- Range = 6-96 hours

Caraceni et al Supp Care Cancer 2012
Impact on survival

• Systematic review of 10 studies
• 1807 patients of whom 621 sedated
• Median survival from 7 to 36.5 days for sedated versus 4 to 39.5 days for non-sedated patients
• Survival is calculated from admission

Maltoni et al  JCO 2012
Effect of continuous deep sedation on survival in patients with advanced cancer (J-Proval): a propensity score-weighted analysis of a prospective cohort study

Maeda I et al Lancet Oncology 2016

- 2426 patients admitted to palliative care institutions (CDS = continuous deep sedation)

<table>
<thead>
<tr>
<th></th>
<th>Median Survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDS</td>
<td>22 days (21 – 24)</td>
</tr>
<tr>
<td>No CDS</td>
<td>26 days (24 – 27)</td>
</tr>
</tbody>
</table>

Palliative sedation: more data and fewer opinions
Difference with euthanasia

- One objective difference has already been mentioned: palliative sedation, in the palliative care of patients with advanced terminal cancer, if appropriately performed, does not hasten death.
Sedation vs Euthanasia

SEDATION
- Intention is to relieve suffering due to refractory symptoms
- The procedure is the use of a sedative drug to reduce consciousness
- The result is the relief of suffering

EUTHANASIA
- The intention is to kill the patient
- The procedure involves a lethal medication
- The result is death

Matersvedt et al Palla Med 2009 EAPC Ethics taskforce
Clinical requirement guidelines

- Identification of refractory symptom
- Prognosis
- Decisional process
- Patient and family communication
- Procedural requirements
  - Monitoring of consciousness level
- Part of Appropriate palliative care
- Palliative care specialist consult
Guidelines

- EAPC recommended framework for the use of sedation in palliative care Pall Med 2009
- Kirk et al Position paper of National Hospice and Palliative Care organization J Pain Sympt Manage 2010
Table 3. European Association of Palliative Care (EAPC) 10-item framework for guidelines in palliative sedation

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommend pre-emptive discussion of potential role of sedation in the end of life care and contingency planning</td>
</tr>
<tr>
<td>Describe the indications in which sedation may or should be considered</td>
</tr>
<tr>
<td>Describe the necessary evaluation and consultation procedures</td>
</tr>
<tr>
<td>Specify consent requirements</td>
</tr>
<tr>
<td>Indicate the need to discuss the decision-making process with the patient’s family</td>
</tr>
<tr>
<td>Present direction for selection of the sedation method</td>
</tr>
<tr>
<td>Present direction for dose titration, patient monitoring, and care</td>
</tr>
<tr>
<td>Guidance for decisions regarding hydration and nutrition and concomitant medications</td>
</tr>
<tr>
<td>The care and informational needs of the patient’s family</td>
</tr>
<tr>
<td>Care for the medical professionals</td>
</tr>
</tbody>
</table>

Adapted from Cherny and Radbruch, Pall Med 2009

“Optimus medicus sit quoque philosophus”
Guidelines


Hasselar JGJ et al Arch Intern Med 2009
National Dutch Guidelines (KNMG)

- Continuous sedation within the context of palliative care is highly complex and requires specialist knowledge. The impact of the problems involved here may be such that consultation and cooperation with other carers, not just organisationally but also in matters of substance, is essential. The committee advises physicians to consult the appropriate expert(s) with specialist knowledge of palliative care in good time.