The use of sedation to relieve cancer patients’ suffering at the end of life: addressing critical issues

As oncologists, we have a clinical and ethical responsibility to relieve the suffering of our patients as they approach the end of life. In situations of otherwise intractable suffering, sedation, to induce a state of decreased or absent awareness (unconsciousness), has emerged as a critically important therapeutic option to relieve the burden of otherwise intolerable distress [1, 2]. The aim is to provide adequate relief of distress in a manner that is ethically acceptable to the patient, family and health care providers. Apart from its use for patients undergoing noxious procedures and in weaning from ventilator support, sedation is a treatment of last resort because of its anticipated adverse outcomes and potential risks.

Pragmatically, the anticipated adverse outcomes of sedation for the patient are impairment or loss of the ability to interact (depending on the depth of sedation that is applied). Distress for family members which may relate to several factors, including the impaired ability to interact with the patient, anticipatory grief, confusion or disagreement regarding the indications for the use of sedation, and perceptions that the decision to resort to sedation was precipitous, or perhaps inappropriately delayed, or the perception that sedation directly, or even indirectly, hastens death [3–7].

sedation and hastening death

This issue, as to whether sedation of patients to relieve refractory distress at the end of life hastens death, is significant to all the stakeholders: the patient, their family and the health care providers. The issue is critical to the discourse with patients and their families, informed consent and to the ethical deliberations essential in every case.

Although, several studies indicate that palliative sedation does not hasten the death of patients overall; the evidence supporting this conclusion has, to date, been based on comparative survival data of patients admitted for inpatient hospice care, comparing the survival of those patients who did or did not need sedation to manage refractory suffering [8–12]. These data were indicative, but not conclusive, insofar as there was a possibility that the patient populations were intrinsically different with different prognoses and different anticipated trajectories of demise. The study by Maltoni et al. [13] in this issue of the Annals of Oncology addresses some of these concerns. In their study, Maltoni et al. studied the impact of sedation on survival using patient cohorts which were matched for prognostic variables. Their data indicate that, even when matched for adverse prognostic variables, sedated patients in this setting did not have an accelerated demise. This is an important contribution.

It is important to note that in this study, the vast majority of patients were lightly sedated. Could it be that that light sedation has no effect on survival and that sudden deep sedation does? Could it be that the shortened survival among a subgroup, such as those receiving sudden deep sedation for catastrophic symptoms, is lost in the statistical analysis of the larger group? I doubt that these questions will be answerable by randomized controlled study as it is ethically implausible to randomize patients with catastrophic refractory symptoms at the end of life to a no sedation arm. If there were enough patients who refused sedation for the management of catastrophic symptoms at the end of life, a matched cohort study may provide the answer. In the meantime, we need not be paralyzed by uncertainty. Medicine is not a science of certainty, rather, it is characterized by uncertainties [14]. Clinicians, patients and their families are challenged to find pragmatic, and ethically appropriate, best options despite the uncertainty that exists.

so, what do we tell the patient and their family?

On the basis of these findings we can tell patients, their families or other concerned parties that sedation will not foreshorten life? The answer is yes and no.

- We can now say that the administration of sedation to highly selected patients suffering from refractory distress at the end of life is unlikely to shorten life.
- Even if, in general, there is no foreshortening of survival, this does not preclude the possibility that some individual patients may suffer complications of the sedation process such as respiratory depression, aspiration or hemodynamic compromise. In one of the few studies to report adverse events in patients undergoing sedation in this setting, almost 4% of patients suffered cardiorespiratory arrest or life-threatening aspiration [15]. For immediately preterminal patients with overwhelming distress, this risk will usually be considered trivial relative to the goal of relieving otherwise intolerable suffering. In other circumstances, such as patients requesting short-term sedation to gain relief from severe symptoms, the risks may have significant, or even catastrophic, consequences and risk-reducing precautions (including vital sign monitoring and the availability of an antidote to the sedating agent) are generally indicated.
- When sedation is used, the issue as to whether or not to continue hydration is still an open question. No conclusions regarding the impact of continuation or withdrawal of hydration on survival can be imputed from Maltoni’s study, and this issue is still unresolved.
sedation is never trivial
For oncologists and palliative care specialists, sedation is an important and necessary therapy in the care of selected patients with otherwise refractory and severe distress at the end of life. Since sedation has the capacity to harm as well as to help, the manner in which this therapeutic tool is applied is important. Inattention to potential risks and problematic practices can lead to harmful and unethical practices such as the abusive, injudicious or unskilled use of sedation.

Abuse of palliative sedation occurs when clinicians sedate patients approaching the end of life with the primary goal of hastening the patient’s death [16–23]. Injudicious palliative sedation occurs when sedation is applied with the intent of relieving symptoms but in clinical circumstances which are not appropriate. In this situation, sedation is applied with the intent of relieving distress and is carefully titrated to effect but the indication is inadequate to justify such a radical intervention. This underscores the importance of patient evaluation by a clinician who is expert in the relief of symptoms before resorting to this therapeutic option. Conversely, injudicious withholding of sedation in the management of refractory distress occurs when clinicians defer the use of sedation excessively while persisting with other therapeutic options that do not provide adequate relief. Substandard clinical practice of palliative sedation occurs when sedation is used for an appropriate indication but without the appropriate attention to good clinical care. There can be many reasons for this. It occurs when sedation is started without inadequate consultation with the patient, family members or other staff members; when there is inadequate monitoring of symptom distress or relief and when the dose of sedative is escalated rapidly without titration to effect and use of minimal effective doses.

the case for procedural guidelines
Given the potential for harm to the patient, their family or to the reputation and ethical standing of the treating clinician or institution, prudent application of this approach requires due caution and good clinical practice. Sound procedural guidelines, such as checklists, can reduce the risk of adverse outcomes in medicine [24, 25].

Table 1. Ten universal issues for the development of procedural guidelines in palliative sedation

| 1 | Discussion of potential role of sedation in end of life planning |
| 2 | Clinical indications in which sedation may or should be considered |
| 3 | Patient evaluation and consultation procedures |
| 4 | Consent requirements and procedures |
| 5 | Need to discuss the decision-making process with the patient’s family |
| 6 | Selection of the sedation method |
| 7 | Guidelines for dose titration, patient monitoring and care |
| 8 | Guidance for decisions regarding hydration and nutrition and concomitant medications |
| 9 | The care and informational needs of the patient’s family when the patient is sedated |
| 10 | Care for the medical professionals |

Procedural guidelines for the use of sedation in the management of refractory sedation at the end of life can help guide clinical practice to ensure sedation is used in appropriate setting and to help avoid pitfalls in practice. Examples of procedural guidelines are available on the public domain [1, 7, 16, 26–42]. Based on a review of these guidelines, 10 universally relevant procedural issues can be identified (Table 1). Countries, hospitals and organizations wishing to develop procedural guidelines will soon be aided by a framework for the development of such guidelines based on these 10 universally relevant procedural issues, that is being developed by the European Association for Palliative Care.

N. Cherny*
Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem, Israel
(E-mail: chernyn@netvision.net.il)

references