

Palliative Sedation With Propofol for an Adolescent With a DNR Order

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Death from cancer is often painful. Usually, the pain can be relieved in ways that allow patients to remain awake and alert until the end. Sometimes, however, the only way to relieve pain is to sedate patients until they are unconscious. This method has been called palliative sedation therapy. Palliative sedation therapy is controversial because it can be misunderstood as euthanasia. We present a case in which an adolescent who is dying of leukemia has intractable pain. Experts in oncology, ethics, pain management, and palliative care discuss the trade-offs associated with different treatment strategies.

THE CASE

Diamond is a 17-year-old girl with relapsed acute lymphoblastic leukemia, 7 months' post-allogeneic bone marrow transplant. Over the past 2 months, her percentage of leukemic blasts has been increasing, and she has no cure-directed chemotherapy available for her current disease. She has been followed by the palliative care team since her relapse and was recently admitted to the hospital for pain control. During this admission, she developed respiratory distress and fever and was diagnosed with bilateral pneumonia. After extensive discussion of the options, Diamond's mother decided to forgo transfer to the ICU and escalation in respiratory support while continuing all other therapeutic interventions, including antibiotics and total parental nutrition. A do-not-attempt-resuscitation order was placed in the chart specifying that Diamond should not be treated with mechanical ventilation or cardiopulmonary resuscitation.

Throughout the course of this admission, the palliative care and pain management teams intensively

treated escalating symptoms of pain and agitation with limited success. Despite significant opioid dose escalation, opioid rotation, and the use of adjuvant medications, Diamond continued to be highly agitated with grunting, moaning, and reports of high levels of pain. Additional strategies included a fentanyl infusion of 1000 µg/hour and then rotation to an equianalgesic dose of hydromorphone. Despite these measures, Diamond remained uncomfortable. A ketamine infusion, scheduled lorazepam, and haloperidol were added, without significant relief of her distress. Diamond's suffering was extremely distressing to her family and the bedside nurses. The palliative care team suggested that Diamond may be a candidate for palliative sedation therapy (PST) using propofol. The medical team had concerns regarding the timing and appropriateness of the decision for PST, because Diamond's pneumonia appeared to be improving with therapy. Her mother was agreeable to PST and asked the team to give her a dose that would quickly "end this suffering." An ethics consult was called to determine the

abstract

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appropriateness of using PST in this young adult patient.

Drs Johnson, Baker, and Anghelescu Comment

The death of one's child is a life-altering experience. Parents may experience negative physical and psychological morbidities, including depression, anxiety, complicated grief, and posttraumatic stress disorder. End-of-life care for dying children is an interdisciplinary effort that includes anticipatory counseling, symptom management, and comprehensive psychosocial, spiritual, and bereavement care. Parents will always remember the last days of their child's life. We do not want Diamond's mother to remember a death marked by suffering and uncontrolled pain. The perception of uncontrolled suffering can cause significant distress to both family and staff. How then to treat patients with refractory symptoms at the end of life?

PST is the use of sedative medications to address intolerable and refractory suffering by a purposeful reduction in patient awareness, even to the point of unconsciousness. Medications commonly used in PST include benzodiazepines, anesthetics (propofol and ketamine), opioids, and antipsychotics often at doses that achieve continuous deep sedation. The goal when initiating PST is comfort, not preservation of function or consciousness. PST is a rarely used intervention of "last resort." The goal is not to hasten death, but to relieve distress from refractory and distressing physical symptoms.¹

In evaluating patients like Diamond, it is important to determine if the difficult-to-manage symptoms are (1) burdensome to the patient and family and (2) truly refractory. Many patients who initially appear to have refractory symptoms will respond to expert consultation from palliative care and pain teams and the maximization of traditional

therapies. Such maximization may include rapid opioid escalation, rotation to an alternative opioid, nonopioid adjuvant medications, nonpharmacologic approaches, or interventional approaches.²⁻⁴ In the vignette, the patient is already followed by the pain and palliative care teams and continues to have high levels of pain and suffering that are distressing to her family. To the extent that Diamond has the capacity to participate in conversations, the medical team should solicit her perspective. Some children may desire family interaction and will tolerate greater levels of pain if doing so comes with greater lucidity.

We recommend that PST be used only when the medical team and family are in consensus that the child is imminently dying, with imminently dying defined as a patient with a terminal diagnosis, unlikely to recover from his/her current illness, and unlikely to survive more than several days or weeks. Although the goal of PST is not to hasten death (ie, euthanasia), there exists a risk of respiratory depression (and death) with the doses needed for adequate relief of suffering in some patients. This potential double effect is rare when PST is used by clinicians adequately trained in this intervention, but it is a consideration when evaluating the appropriateness of PST in pediatric patients.

In Diamond's case, it would be helpful to have an interdisciplinary team meeting to clarify her prognosis and goals of care. Although it seems that the pneumonia may be responding to therapy, Diamond's progressive leukemia appears life-limiting, and she seems to be at risk for progressive organ dysfunction, coagulopathy, and continued pain from her advancing disease. A team meeting may identify other interventions that may be helpful with symptom management (ie, palliative chemotherapy) and allow the primary team to verbalize their

concerns about the timing and appropriateness of PST. Members of the clinical team may be unfamiliar with the purpose of PST and may not understand that the goal is the relief of suffering and not to hasten death. A clinical ethics consultant or health care ethics committee should be involved.

Before initiating PST, we recommend a family care conference to clarify the family's understanding of their child's prognosis (ie, imminently dying). The team should assess the severity of symptoms and tolerability of the suffering and use shared decision-making approaches to determine if PST is consistent with the patient's and family's preferences and values. It is important to involve the child in an age-appropriate manner and to focus on an objective evaluation of the child's suffering, not the parents'.

Diamond's mother appears receptive to PST and has specifically requested "a dose of something to quickly end this suffering." Among parents whose children have died of cancer, over 10% considered making a request to hasten their child's death, and as high as one-third of parents consider making this request if a child has uncontrolled pain at the end of life.⁵ Clear and comprehensive communication about the purpose of PST (relief of suffering), the risks and benefits of therapy, and the plan for assessing comfort and titrating sedation should be clearly outlined to family and staff. In adult studies on PST, achievement of adequate analgesia may be associated with life prolongation rather than hastening of death.⁶ Objective criteria for monitoring children on PST may help families and clinicians evaluate the level of sedation and, in some circumstances, a trial of sedation may be indicated to determine if it is still indicated.

We generally recommend, when using PST, the withholding and withdrawing of all interventions

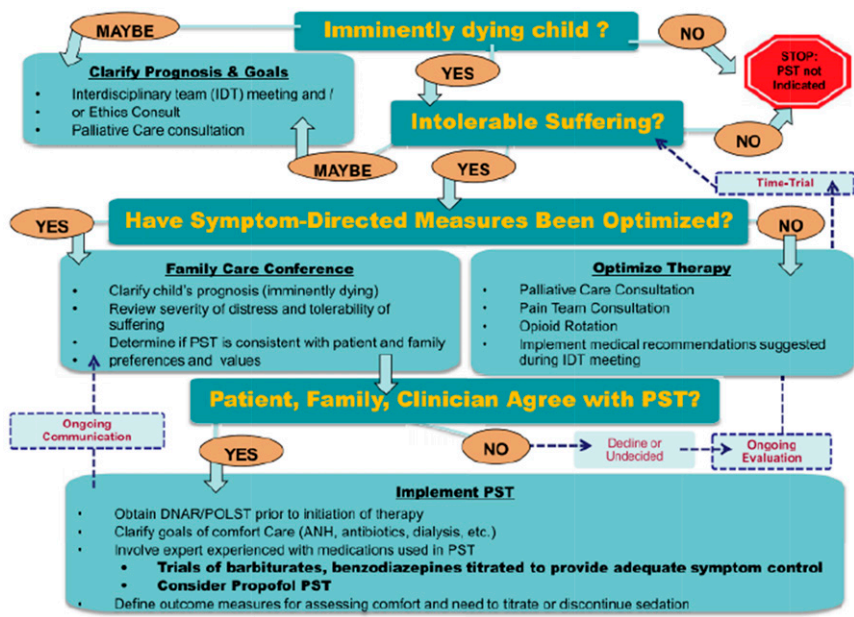


FIGURE 1
 Algorithm for clinicians considering PST. ANH, artificial nutrition and hydration; DNAR, do not attempt resuscitation; IDT, interdisciplinary team; POLST, physician order for life-sustaining treatment. (Reprinted with permission from Johnson LM, Snaman JM, Cupit MC, Baker JN. End-of-life care for hospitalized children. *Pediatr Clin North Am.* 2014;61[4]:842.)

not directly related to optimizing comfort. We discuss other end-of-life preferences and identify the desired location of death. Depending on the availability of local hospice services, PST may be available in the home setting. Alternatively, patients can remain hospitalized in a quiet, private inpatient room without the restrictions that are often associated with an ICU. We encourage pediatric institutions to develop policies and procedures for the use of sedative medications, such as propofol, outside of the ICU or procedural areas when used for PST.

In summary, PST is an uncommon but important intervention reserved for those children with refractory suffering at the end of life. Although the concept of PST is well described in the adult palliative care and oncology literature, it has received less attention in the pediatric literature, with publications primarily limited to case series and case reports.⁷ Numerous position statements and clinical guidelines for the consideration of PST have

been published by experts in adult palliative care¹; however, there is a dearth of pediatric-specific guidance. Given the particularly complex medical and social situation that often surrounds a dying child, particularly a child with refractory physical symptomatology, there is a great need for new approaches to pain and symptom control. It may be helpful for institutions to develop standard operating procedures and follow a clinical algorithm (Fig 1) when considering a pediatric patient for PST.⁸

Dr Joel Frader Comments

Diamond’s case illustrates tensions between the palliative care team’s recommendation for PST and the medical team’s belief that PST will preclude Diamond’s surviving her acute infection. Frustration and anxiety likely affect the palliative care clinicians because of the patient’s resistance to remarkably high opioid doses. Complicating the situation is the mother’s request for euthanasia. How can ethics consultants help

the parties understand the moral issues and facilitate a plan of action acceptable to most participants in Diamond’s care?

One wonders where to find Diamond’s perspective. Has the mother voiced Diamond’s view, in a kind of substituted judgment (although that term generally does not apply when making decisions for minors)? Or does Diamond’s mother express a “best interest” view of what to do or, alternatively, project the mother’s desire for relief from Diamond’s apparent misery? If we knew more about Diamond’s experience with her cancer and its treatment, what she went through with her transplant, her beliefs about the meaning of her condition and the value she attached to symptom relief or the potential for additional time to interact with family or the world, we might have an easier time deciding on the path ahead. Diamond may have shared some of her views with her parents, friends, pastor, or members of her clinical team, shedding light on her attitudes and preferences. The ethics team should explore whether Diamond left clear indications about what she would want under the circumstances. Although her status as a minor complicates the legal weight one could place on her “advance directives,” surely at age 17, one would have strong moral grounds for respecting her wishes.

Palliative care clinicians have tools to help adolescents explore and articulate their views about how they want to die.^{9,10} Barriers do exist to completing documents or having advance care planning conversations with teenagers,^{11,12} even when everyone agrees that a cure cannot happen and death will come sooner than later. Some families feel that such efforts place too great a burden on the adolescent; some parents insist that they will all “just know the right thing to do when the time comes” and that planning only increases the pain

of ongoing life. Some clinicians repeatedly say it is “too soon” to initiate such communication, although, as happened with Diamond, waiting incurs the risk of the patient losing the capacity to participate. Teenagers may feel reluctant to raise the matter on their own, worrying that talking will upset their parents or even clinicians. Some adolescents, when queried, really do not want to talk about their futures and defer to their parents, although one cannot always identify those patients without asking them directly. Some empirical data suggest that children, like many adults, welcome opportunities to discuss foreseeable death, ask questions, and have a say regarding care they might receive or the way they wish family and friends remember and honor them after death.^{13,14} The ethical challenge involves allowing minors to meaningfully express their views without excessive disruption of the patient’s emotional and social world. In Diamond’s case, not having a clear view of her preferences makes it harder to resolve the tensions surrounding her care.¹⁵

Two ethical issues remain. First, what ought to be the goals of care? The “big picture” suggests prolonging life per se might not serve Diamond’s interests, especially without a reasonable prospect of adequately controlling ongoing pain, delirium, etc. Nothing here suggests that curing pneumonia will lessen her overall symptom burden; indeed, improving her respiratory status might only prolong her suffering. Using PST typically means forgoing other treatments, including routine fluids and nutrition, antibiotics, and other interventions that extend life. Cases like Diamond’s can be complicated because the infusions necessary to provide adequate analgesia and sedation may maintain circulatory integrity longer than family and clinicians appreciate or find comfortable. The ethics team and the

palliative care clinicians must ensure that all involved parties understand how PST might actually delay death.

The second ethical issue is whether professionals may honor Diamond’s mother’s request for a swift end to Diamond’s ordeal. In the United States, the simple answer remains, “no.” Euthanasia equals homicide, a crime in our country (unlike, in specific situations, in the Netherlands and Belgium and a few other jurisdictions). Physician aid-in-dying, legal in some states in the United States, is an altogether different matter in which physicians provide prescriptions for medications that incapacitated adult patients with terminal conditions may take to hasten their own deaths. Even where physician aid-in-dying is legal in the United States, minors cannot participate. Patients like Diamond, with diminished consciousness, lack the capacity to take the death-inducing medicines, even if they are adults.

Whether we should allow euthanasia, for adults or (some) children, in the United States, is quite another issue. Most palliative care clinicians claim good palliative care makes euthanasia unnecessary. Cases like Diamond’s, however, push us to reconsider. Even if we provide effective PST, what purpose do we serve by continuing her existence in an anesthetized state? In Diamond’s case, ending her life swiftly may make sense. It seems ethically justified to hasten death in limited circumstances when continued life provides no benefit; when continued, palliative treatment may, somewhat paradoxically, prolong death; and, most controversially, when the extended life increases the suffering of those providing loving care for the patient. Clearly defining the conditions that permit euthanasia so as to prevent abuse, either of individuals or classes of patients (such as those with disabilities), strikes many as

daunting. Nevertheless, it seems time to try to find agreement on this. Unfortunately, religious and political conflicts in the United States make it unlikely we will see legalization of euthanasia any time soon.

Dr Joanne Wolfe Comments

Let’s consider the unknowns about this case. We do not know the extent to which Diamond, the patient, had the opportunity to participate in decision-making and advance care planning. We do not know whether there are any other loved ones, such as another parent, involved in Diamond’s life. Most importantly, we do not know the patient and family goals of care in the context of her refractory leukemia.

Let’s assume the approach to Diamond’s care has been optimal and unfolded as follows. Diamond’s care has been guided by an interdisciplinary oncology team from the time of diagnosis. She has a longstanding relationship with a social worker, and when she relapsed after transplant, the social worker introduced “Voicing My Choices”¹⁰ to her. They carefully worked through this advance care planning booklet developed by and for adolescents and young adults. In completing the booklet, among other hopes, she indicated that, “If a doctor and another health care provider both decide that I am close to death and likely to die within a short period of time, and life-support treatment would only delay the moment of my death: I would want to have a natural death.” Once completed, Diamond shared this document with her mother. Let’s now assume that at the time of the clinical team’s discussion with Diamond’s mother about her resuscitation status, Diamond was not able to participate in discussions given her profound respiratory distress and high levels of sedation.

The interdisciplinary team meets with her mother and conducts a high-quality goals of care discussion.¹⁶ To

begin, they reflect on Diamond as a person and talk about her strengths and passions. They then use the “ask tell ask” strategy to disclose her poor prognosis. First Diamond’s mother is asked, “Is it ok to talk about how Diamond is doing?” Once her mother agrees, she is told that her daughter has refractory leukemia complicated by severe pneumonia. The team additionally explains that they are worried that if she is intubated she is not likely to get better and they would be facing decisions about discontinuing the ventilator down the road. After this discussion, Diamond’s mother is asked what she thinks would be most important to Diamond in light of this prognosis. Her mother references Diamond’s documentation of her preferences and agrees to the recommendation that a do-not-attempt-resuscitation order be written on her behalf. At the same time, she expresses the hope that Diamond recovers from the pneumonia with continued antibiotics and nutrition support. Her goals are blended, as is not uncommon,¹⁷ and she hopes her daughter lives as long as possible and as well as possible, despite her refractory leukemia.

Fast forward to the current scenario; although the pneumonia is improving, Diamond’s discomfort is escalating. Why is this? The most likely explanation is disease progression potentially resulting in bone and visceral pain, with possible central nervous system involvement as well. Let’s also assume that Diamond is not a candidate for additional disease-directed therapy because of organ dysfunction. Let’s additionally presume that goals of care have been revisited with Diamond’s family and that it has been effectively communicated to them that she is dying from progressive leukemia. Through this discussion, the family now hopes that Diamond lives as comfortably as possible for whatever time she has left. The team

recommends palliative sedation to achieve this goal. The team also recommends, and the family agrees, to discontinue antibiotics and intravenous nutrition so as not to inadvertently prolong her dying.

What about the family’s request to give Diamond a dose that will quickly “end this suffering?” Is this a request for euthanasia? Experience suggests that such requests are not rare when a child’s suffering is extreme. Indeed, in a survey of 141 parents of children who died of cancer, 13% reported that they considered requesting hastened death for their child, and these considerations tended to increase with an increase in the child’s suffering from pain.⁵ Thus, palliative sedation is an especially important intervention when conventional approaches do not achieve patient comfort. If comfort is achieved and Diamond’s final days are peaceful, her family’s grief may also be eased.¹⁸

Dr John D. Lantos Comments

The distinction between palliative sedation and euthanasia is subtle but real. It turns on the intention of the doctor who is administering treatment. The goal of palliative sedation is to relieve suffering. The goal of euthanasia is to cause death. Palliative sedation can sometimes cause death. In the context in which palliative sedation is used, it may be difficult to know whether it caused death or whether death would have occurred anyway. But causation is not the key issue; intention is. That difference in intention may not seem like an adequate safeguard. But, in the context of a dying patient with intractable suffering, doctors have a moral obligation to try to relieve suffering. If that can be done without causing death, it should. If it cannot, then the obligation to relieve suffering is adequate justification for administering a treatment that may also shorten a patient’s life.

ABBREVIATION

PST: palliative sedation therapy

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