Sedation for Intractable Distress of a Dying Patient: Acute Palliative Care and the Principle of Double Effect

ERIC L. KRAKAUER, B RICHARD T. PENSON, A ROBERT D. TRUOG, C LINDA A. KING, B BRUCE A. CHABNER, A THOMAS J. LYNCH, JR. A

A Hematology-Oncology Department and B Palliative Care Service, Massachusetts General Hospital; C Department of Anesthesiology, Children’s Hospital, Boston, Massachusetts, USA

Key Words. Double effect · Palliative care · Propofol · Caregivers · Psychosocial

ABSTRACT

Shortly before his death in 1995, Kenneth B. Schwartz, a cancer patient at Massachusetts General Hospital (MGH), founded The Kenneth B. Schwartz Center at MGH. The Schwartz Center is a nonprofit organization dedicated to supporting and advancing compassionate health care delivery, which provides hope to the patient, support to caregivers, and encourages the healing process. The Center sponsors the Schwartz Center Rounds, a monthly multidisciplinary forum where caregivers reflect on important psychosocial issues faced by patients, their families, and their caregivers, and gain insight and support from fellow staff members.

The case presented is of a young man dying of recurrent epithelioid hemangioendothelioma, distressed with stridor and severe pain, whose poorly controlled symptoms were successfully treated with an infusion of propofol, titrated to provide effective comfort in the last few hours of the patient’s life. The tenet of double effect, which allows aggressive treatment of suffering in spite of foreseeable but unintended consequences, is reviewed. The patient’s parents were invited and contributed to the Rounds, providing compelling testimony to the power of the presence of clinicians at the time of death and the importance of open communication about difficult ethical issues. The Oncologist 2000;5:1:53-62

PRESENTATION OF CASE

Mr. D was a 20-year-old white male who was referred acutely with hemoptysis. He had a two-month history of right-sided chest wall pain. Approximately two weeks prior to admission he developed a deep, nonproductive cough. The patient had been a one-pack-per-day smoker for three years, with no past respiratory illnesses, denied intravenous drug use, and was heterosexually active, monogamous, and used condoms. There were no foreign travels or infectious contacts. A computerized tomography (CT) scan showed pulmonary nodules and a right pleural effusion. A bronchoscopy revealed pearly white nodules in his trachea and bright red blood, but no endobronchial lesions. At mediastinoscopy, frozen section of a precarinal node suggested poorly differentiated adenocarcinoma. However, final pathology revealed high-grade epithelioid hemangioendothelioma.

Mr. D’s only past medical history was of attention deficit disorder. There was a maternal family history of cancer. He lived with his parents and two brothers and worked in a hardware store.

He was commenced on MAID chemotherapy (doxorubicin, ifosfamide with mesna, and dacarbazine). He had severe pain in the right shoulder, which was difficult to control but was helped by a trigger point injection and opioids, though these caused pruritis. Restaging studies completed after two cycles of chemotherapy showed disappearance of the pulmonary nodules and the right pleural effusion and diminution in the hilar and precarinal lymphadenopathy. After six cycles
of MAID, a repeat CT scan showed only small residual lymph nodes of the mediastinum and hilum with clear lung fields. This response was consolidated by high-dose cyclophosphamide and carboplatinum supported by peripheral blood stem cell reinfusion. He was discharged early with minimal toxicity.

A follow-up scan at three months showed asymptomatic pulmonary nodules and one month later he developed bilateral shoulder pain, which became an ongoing chronic pain syndrome. Recurrence was confirmed by a biopsy of a right lung lesion. This was complicated by a pneumothorax, requiring intercostal chest tube placement and talc pleurodesis. He was treated with both Navelbine and interferon-α without significant benefit and the disease progressed with bulky cervical lymphadenopathy. He subsequently presented with an acute headache and sudden-onset right arm weakness with right-sided ptosis. CT and magnetic resonance imaging (MRI) of the head showed two hemorrhagic intracranial masses. Despite dexamethasone and phenytoin he deteriorated and developed an aspiration pneumonia. The dialogue picks up the story of his last week of life.

**We were using larger doses than most house officers and nurses are used to using, so careful explanation and discussion of our management with the team was necessary.**

**Dialogue**

**Facilitator:** Epithelioid hemangioendothelioma is a very unusual type of cancer. *Michael* was the first patient I had ever seen with this cancer. We talked with the connective tissue sarcoma group, who said that it behaves much more like an angiosarcoma or a soft tissue tumor in this setting. There are only a few cases like this in the literature. The tumor tends to occur in younger patients, to be very vascular and involve the liver. Initially, *Michael* had a beautiful response to chemotherapy, which was consolidated with a stem cell transplant.

I’d like to say just a couple of things about *Michael* himself. It’s hard to summarize in just a few sentences what he was like. He was very spirited. He wanted to be very much in control of his life and his disease. He had a passion for going to rock concerts, and we used to talk a lot about the rock concerts he went to. He was very clear about what his wishes were; that’s how he approached every part of his treatment. As you can imagine, that created some issues for a young man, going into transplant, who had to be confined to a hospital room. Approximately 18 months after this treatment he progressed with bone and lung disease which was refractory to chemotherapy. Eventually *Michael* developed disease in the brain and he presented with an acute neurologic syndrome. It became very clear that these were very large metastases that were not going to respond to either radiation or surgery. That’s when we got the Palliative Care Service involved. *Mr. D* was admitted to the Neurology Service where he received wonderful care. Many of his caregivers are here today to comment on what that last admission was like for *Michael*. The point of today’s Rounds is to talk about acute palliative care, the way we provide comfort and care to people in their last days of life in the setting of severe symptoms. We’ve asked four panelists to comment.

**Chaplain:** I wanted to comment from the spiritual, or faith, point of view. I think *Mike* had a very fine blend of faith and rock. He was the kind of person who was very unique, very honest, and told you where he was at, and I found a great deal of faith in his Mom and Dad and in his family and it was very special to be with them and to get to know them. During the final admission here at the hospital, the family called me to give him the anointing, or the Sacrament of the Sick, and *Michael* had been somewhat unresponsive and as I began to pray, I remember him looking over at his dad and saying, “I know that guy’s voice,” and he very much joined in that prayer. I was very touched by how the family and their faith helped them to face the death of their son.

**Social Worker:** What I wanted to comment on was the communication. *Michael* was very outspoken and very clear about what he wanted and really challenged his caregivers to listen to him and to work with him on what he needed from them. I think all of his caregivers took the time to hear what he had to say and was able to involve him as an active participant. We respected his wishes, particularly that he didn’t want to suffer. When his caregivers said, “Well, I don’t know what to do
Palliative Care Nurse: I got involved after he had been in the hospital at the time when the work-up revealed that the disease was refractory to treatment. The staff said, “Okay, we have this young man who’s pretty clear about what he wants and what he doesn’t want and we have a family who’s trying to take care of him,” and the challenge at that point was to decide where was the best place for Michael to be when he died. Should he die in the hospital or do we try to get him home? I think we really talked a lot about that. I talked a lot about that with his mom, who also happens to be a nurse. We talked about being a family provider when you’re also a healthcare giver. It became clear that managing at home would be more of a crisis than it was in the hospital, where we were still trying our best to keep him comfortable. So our concerns shifted from Michael at that point to really looking at the whole family and how this would be for them.

Ward Nurse: I just thought I would review the stages that I felt I went through while caring for Michael. He was only on our floor for 10 days and I was able to care for him for most of that. When I first met him, it was hard to get to know him because he was in so much pain and you really couldn’t get through that. Once we got through that you got to really meet this unique personality. I’m having a hard time here [tears]. What made it really challenging was that he had a strong need to be independent, but was also a young man who was dying and clearly dependent. He wanted to make the decisions about his care, and yet he was at a point where he couldn’t make decisions about his care anymore.

Palliative Care Physician I: I only got to know Mr. D in the last three days of his life, so I had missed a lot of the story of the previous 21 years. I have a rule with myself that I call patients by their surname, unless they ask me to do otherwise, so I’ll call Michael Mr. D. When I went to see Mr. D, he had severe pain in his neck and his back. He had a large mass on the right side of his neck that was compressing his trachea, and he had moderate to severe dyspnea. He already was on a lot of medications for these symptoms, so I was very concerned that he might develop severe or intractable distress for which we would need to be prepared. I try to have a safety net ready for every patient. I wanted to get to know him as best I could and particularly to understand what he wanted, even though he was only able to speak a couple of words at a time because of his dyspnea. I asked if he would prefer to be sedated and comfortable, if it came to a choice, or more awake and tolerate some discomfort. He very clearly went for option A. He said that it was okay if it took being sedated to make sure that he was comfortable.

He already was on a dilaudid i.v. drip at 12 mg/h, which is a fairly high dose, and on oral morphine. The two together are equivalent to about 100 mg/h of i.v. morphine. The dose isn’t as important as other things, like how long someone has been on it, whether the symptoms are controlled, and whether unacceptable side effects are occurring. He had not been on high-dose narcotics very long. He also was on gabapentin, clonazepam, and haloperidol, as well as dexamethasone. We changed all medications to i.v. because he wasn’t swallowing reliably. We increased the dilaudid drip and added prn dilaudid bolus doses. We started intravenous diazepam. Initially, I think there was some improvement. I don’t think his symptoms were under excellent control, but I think he was a little improved.

But then quite quickly things really got worse and he developed very severe dyspnea. On examination he had stridor, which made me concerned that there was compromise of his large airway from the mass in the neck. Now, a lot of what we do is sitting and talking with people, and we take more time than one can routinely on other services. But here was a situation where we needed to move fast and protect a dying patient from a lot of suffering. This is what I call “acute palliative care.” So, we increased the opioid (dilaudid) and the benzodiazepine (diazepam) doses rapidly. By then, we were using larger doses than most house officers and nurses are used to using, so careful explanation and discussion of our management with the team were necessary. Although we are a consult service, we often ask permission of the responsible physician to write the orders ourselves in this type of situation. Ultimately, the dilaudid drip was at 65 mg/h and this was supplemented with 15-mg i.v. bolus every 30 minutes as needed. A diazepam drip was started and titrated quickly to 20 mg/h with 15-mg i.v. bolus every 30 minutes as needed. The result was that Mr. D would nod off to sleep for 30 to 45 minutes after dilaudid and diazepam bolus doses.
and his respiratory rate would fall from the forties to the twenties. For a few minutes, he would seem comfortable. But within 30 or 40 minutes he would wake up and immediately become severely dyspneic and distressed with a respiratory rate in the forties.

In my two years on the Palliative Care Service at MGH, I have had only two cases where we really had a hard time making sure a patient was comfortable. In the first situation, like this one, I felt that I needed to use a general anesthetic agent to sedate a dying patient in terrible distress that was not controlled by huge doses of standard agents. Use of a general anesthetic agent outside of the ICU and the OR for a patient who is not mechanically ventilated is unorthodox, and I was not able to muster the support necessary to do so. But in Mr. D’s case, with the help of some great people from nursing and pharmacy and a wonderful neurology resident, we were able to use such a medication.

As I was increasing Mr. D’s medications rapidly to try to control his dyspnea and pain and beginning to work on obtaining an anesthetic agent, I took some time to discuss with Mr. D’s parents the principle of double effect (see Discussion). Very briefly, the principle of double effect applied to palliative care states that, if desired by a terminally ill patient or a surrogate decision-maker, medications intended solely to provide relief from severe pain may be used even at the risk of unforeseen but unintended side effects. For example, high-dose opioids may be given to relieve severe pain or dyspnea even at the risk of unforeseen but unintended sedation, hypotension, respiratory depression, and even hastening of death. The issue of what is intended in the action is the key to whether it is morally defensible. In Mr. D’s case, based on what he had told me about his wishes and the care he would like to receive, I decided that it was acceptable to use a general anesthetic agent to sedate him and thereby make him comfortable, because opioids and benzodiazepines were not working. Thus, my intention was to sedate him. I knew that use of an anesthetic induction agent such as propofol risked unintended but clearly foreseeable side effects including death and I discussed this with Mr. D’s parents. With a lot of courage and with love for their son, they asked me to proceed with this plan. What high doses of opioid and benzodiazepine did not do, propofol did rapidly. It needed a little bit of titration, but for the last six hours of Michael’s life, he was sedated and comfortable. His symptoms that we hadn’t been able to control any other way were under control. I feel that, while this sort of situation—intractable distress of a dying patient—is rare, it is a very serious situation when it happens. I’d like to have the use of a powerful and reliable sedative like propofol for just this kind of situation. Thanks to Mr. D, who showed us how important and effective this kind of medication can be, we are developing a protocol for use of this type of drug in the future to protect other dying patients from intolerable distress.

Facilitator: We’re very fortunate to have with us today Dr. Bob Truog. Bob is from the Children’s Hospital and has published on this topic in the New England Journal of Medicine. He is going to share with us his thoughts on hearing Mike’s presentation.

Dr. Truog: Thank you for inviting me over. I guess maybe I should start by asking, “Why has the use of propofol drawn so much attention and concern?”

The issue of what is intended in the action [double effect] is the key to whether it is morally defensible.
The use of barbiturates in palliative care has been a problem because they’ve been so closely associated with the practice of euthanasia. When necessary to relieve nonphysical suffering. This last indication was the most controversial.

I agree that the use of both barbiturates and propofol can be justified under the rubric of double effect. I think that the difficulties and misunderstandings surrounding the use of these agents have come about for several reasons. First, these are potent sedatives that work very rapidly and with profound effect. Second, the use of barbiturates in palliative care has been a problem because they’ve been so closely associated with the practice of euthanasia. For example, they are used to perform capital punishment. They are the drugs of choice in Holland for performing euthanasia. And they have been recommended in the United States for assisting suicide. So there’s a very strong association that people have between barbiturates and euthanasia, and I think that association has carried over to the use of propofol. But, I would very much agree with Eric, that I think their use can be justified under the rubric of double effect in exactly the same way that the other sedatives and analgesics are currently used.

But, just in closing, let me say that I think your points about standardizing the practice here are excellent ideas. I’m on the Ethics Committee for the American Society of Anesthesiologists, and yesterday I received an e-mail from an anesthesiologist at a large medical center that I won’t name here. The e-mail reads, “I am faced with the unfortunate task of addressing the use of propofol used on a patient care floor, not ICU, that was used in an unusual terminal patient for uncontrollable pain during the terminal hours of her life. The drug was mistakenly released by the pharmacy in the middle of the night. I was not informed until the next morning. The patient did not expire of a cardiopulmonary arrest but was receiving very large doses of fentanyl, ativan, and morphine in addition to the titrated propofol in the hands of non-intensivists/anesthesiologists. Other agents were not effective that had been tried in the past. I am now faced with politically strong oncologists who may wish to continue the precedent that has been set.” He goes on to say “I am preparing a presentation for our medical board to try and dissuade the continued use of this drug on a regular floor.” This anesthesiologist is asking for advice from the Ethics Committee of the American Society of Anesthesiologists. So I think this is a timely issue. Thank you.

Ward Nurse: Although propofol’s not a drug I’m familiar with, I had a lot of support from everyone, from the residents to the nurse manager, to Michael’s parents, I mean everyone came and checked on me. Everyone made sure I knew what I was doing. It’s not a drug that I have ever administered before. I didn’t feel in any way that by administering it to him I was setting in effect a chain of events that led to his death. I felt that I was giving him comfort in his final hours.

Chaplain: Yes, you could really sense a lot of emotional and spiritual anxiety among family, friends, and staff that were in that room. It really was only through the intervention that has been described that I feel a great deal of spiritual peace was reintroduced and allowed an attitude of, “Yes, this was the time to let Michael go in peace.” It could be done because now the family, the friends, staff were back at peace again seeing him pain free.

Mr. D’s Father: Dr. L, you talked with Michael one time and explained to him the use of Navelbine. It took about 45 minutes. When you finished you said to Michael, “How does that sound?” And he said, “Sounds like you said the same thing in 45 minutes that Dr. A said in 10.” Michael liked to get to the point. As his parents, I’d like to get to the point. We got just about everything we needed from the Mass General. The doctors were fantastic. You were honest with us. You gave us your opinion. When we asked about operating on Michael, we were led to the right decision, and after we made it we were told that we had made the right decision and we needed to hear that, as his parents.

When you talked with him, you’d ask him about rock concerts and about his life. He felt important and we needed to know that. Dr. K, when it got to the end and you were considering using propofol, you told us that it would take his discomfort away, but that it could hasten his death. We needed to hear that honestly and I think that’s important from the parent’s standpoint. We needed to know the truth. No matter how hard it is, you need to hear it and hear it right away. You’re making life-and-death decisions with your child, and that, to
me, means a whole lot. I think the nursing staff is fantastic. They made us feel important. They got to know us. I know you want to refer to him as Michael D, Mr. D. But it was nice to know that the staff called him Mike. That I was Joe and my wife was Donna. That was important to us. You know, giving him a radio with a station he wanted to listen to or his favorite food, peaches. Little things really made a huge difference. My wife would like to tell you about the experience she had with her mother and how it was different with Michael.

Mr. D’s Mother: My mother died of cancer in this hospital the year Michael was born. Her oncologist, who’s still here, was very, very good and very supportive, but the day my mother died, we never saw his face. That was 22 years ago and that always stuck with me. I mentioned that earlier in Michael’s illness because I needed to be sure that somebody would know that that was an issue. This probably healed years of pain from that one instance because, like being surrounded by angels, we got amazing support. The other issue is that I never felt like we weren’t part of your team. I felt like we were working all together and we were very much considered, and that’s very, very important. You always validated our thoughts and feelings. I felt that no matter what decision we made, you would have said, “That’s a good decision,” and that’s so important to hear because we have to live with that. You made us feel comfortable with that. It was like that from the beginning. Once I said to Mike, “Dr. A’s your friend,” and Dr. A said, “No I’m not, I’m his doctor.” But no matter how hard you tried, you’ve been his friends too. It’s meant a lot to us. Not to make this sound like it’s been a great situation, but I can’t imagine it could have been handled any better. We’re very grateful. Thank you, all.

Facilitator: One of the really important things that made this possible was the tremendous integration and teamwork between patient, family, nursing, palliative care, and pharmacy.

Nurse: We met Michael’s needs well, but Michael helped to demand that you meet his needs. For some patients you have to learn how to look for their needs. You have to learn how to extract their needs. They may not be quite ready to respond to you that second, but they hear it and they remember it and maybe later that day or that week or after however long you may have to wait, they will act on it.

Facilitator: Mike’s forthrightness really set the atmosphere for the staff.

Palliative Care Physician II: Michael definitely demanded that we take the time. He had many different ways. He was very engaging. So it was easy for us to spend the time with him and people enjoyed spending time with him. I think your point is great that not all of our patients are able to speak up to the doctors and challenge them in that way or to voice their opinions the way Michael was able to. We have to be able to spend time with patients who aren’t speaking up for themselves the same way.

You told us that it would take his discomfort away, but that it could hasten his death.

Doctor: I am concerned about generalizing from this great case and how that bears on your responsibility in terms of how you use propofol. It was absolutely clear that this was an irreversible condition and that there was great communication. My concern is, what happens in the very rapid medical turnaround situations that most of us are increasingly dealing with and when the clinical situation and consensus are less clear.

Dr. Truog: I can tell you that even in my own intensive care unit, the principles that have been outlined around maintaining a focus upon relief of symptoms and being clear about one’s intentions, are not understood, sometimes even by the people who work with me. It does make me wonder what must be going on in centers that don’t have all the wonderful opportunities that we have to have teaching conferences like this and that don’t have knowledgeable people around like you do here. I worry a great deal about these things and I worried that one unintended effect of the article we wrote might be to promote the widespread use of barbiturates in inappropriate circumstances. Our intentions in the article were to recommend their use in very rare cases and only as an extreme last resort when all else had failed. Unfortunately, others have distorted the intent and findings of our study.

I don’t really want to say more except to acknowledge that in using the principle of double effect to justify sedation (that is, beyond just relief of pain), you’re right up against the edge of the envelope. Because, in most cases, these are not patients who are ever going to wake up again. It is just a matter of keeping them sedated for a matter of
hours or for even a couple of days before they die. I think this scenario does strain the rather rule-oriented approach of the principle. In these circumstances you move beyond strict rules into some gray areas, which I don’t think can be avoided. I think there is a difference between this practice of sedation and overt euthanasia, however. The difference hinges upon whether or not the medications are being titrated to effect. It is this aspect of titration that is an indicator of where the clinician’s intentions lie. If you are titrating to comfort, you are not intending the patient’s death.

**Palliative Care Physician I:** I do agree that there should be controls on the availability of medications like thiopentol or propofol. I think the slippery slope phenomenon is real. I want to clearly distance myself from those who practice euthanasia.

**Palliative Care Physician II:** I think we’re struggling with these issues all the time. Although knowing the principles is helpful, it obviously doesn’t feel that good even when it’s the right thing to do.

**Palliative Care Physician I:** I want to have all the tools to deal with the worst case scenario. I want to be prepared for it and I want to anticipate it. That’s the safety net I want to provide my patients. Whatever it takes. Even if it means admitting a dying patient to the intensive care unit. If a dying patient’s intractable symptoms cannot be controlled in any other setting but the ICU, then that patient, in my opinion, has a strong indication for ICU admission.

**Pharmacist:** I wasn’t involved in the treatment but I certainly support the opinion, from the pharmacy’s standpoint. I think putting a policy in place is a great idea, but policies sometimes give people a false sense of security. We need to use the bureaucracy in a way that will help us.

**Doctor:** What do you see as the maximum amount of narcotic that you’d want to give?

**Palliative Care Physician I:** Well, I take my lead from my patients. There are people who have remarkable tolerance for pain and discomfort and who want to be awake. I just try to keep an eye on the situation. When my own two eyes aren’t there, I rely on nursing staff and house officers to let me know when a patient’s discomfort is becoming too much for that patient. If this occurs, then we treat more. How do I know the proper dose? Certainly, we have to know accepted dosing standards. But most importantly, I look at the patient. I’ll use whatever I need to use to keep a patient comfortable who wants to be comfortable. If it’s up to 5,000 mg/h of morphine, as in Dr. Truog’s case, so be it. That patient clearly was very tolerant to narcotic. Five thousand milligrams per hour—I don’t wish that on any pharmacist. You just have to camp out on the floor!

**Palliative Care Physician II:** There are maybe 15 or 20 common myths about analgesics that are very much a part of the medical and nursing lore. One is that you can’t make people comfortable without sedating them. This is a very special case. Most patients get opiates and can be alert and drive and lead normal lives. We don’t want you to start thinking that opiates equals sedation. Sedation in general is the unfortunate side effect of opiates and we try to use non-sedating agents whenever we can.

**Facilitator:** It’s very different for a physician to write an order and for a pharmacist to mix a drug than it is for a nurse to give the drug. Maybe some of the nurses who do this a lot can comment on how you feel when you’re giving these drugs?

**Nurse:** Yes, it’s one thing to talk about the double effect and show it on an overhead, but when you’re doing it, it’s much more concrete than for physicians who are just writing the orders.

**Nurse:** I have no problem with keeping my patients comfortable, but I think it needs to be closely monitored. I think we need to recognize just how labor intensive end-of-life care is. It’s as hard as waiting to see if someone is going to code. I was able to care for him and feel comfortable in what I was doing and monitor him carefully enough. I could stand there and titrate it up and see how he reacted to it and have enough time to be in there. But that was because my nursing staff took all my other patients from me. I had just him. I would have had three to four other patients besides him. I had doctors who were willing to approach end-of-life care and not deny symptoms and not accept symptoms. I had pharmacists who were coming up every hour on the hour. It was like a code team but for an end-of-life care. Clearly, that’s only okay in exceptional circumstances. The main thing for me was that it was actually controlling his symptoms and was not intended to shorten his life. You walk the line in trying to stay within your own ethics, my own morals, and what I feel is good for the patient. But I didn’t have any difficulty doing that.

**Nurse:** We need to use the bureaucracy in a way that will help us.


Discussion

Acute Palliative Care

Palliative care is comprehensive care focused on alleviating suffering and promoting quality of life for patients living with a life-threatening or terminal illness [2]. Acute palliative care is palliative care made urgent or emergent by the sudden or severe distress of a patient. Such distress is due typically to pain, dyspnea, vomiting, or other physical symptoms. However, acute palliative care may be required for psychiatric problems such as severe anxiety or agitated delirium. Acute palliative care often requires medications such as opioids and benzodiazepines in doses that sometimes risk serious side effects. In such situations, the principle of double effect can help guide treatment decisions. The case described here demonstrates an extreme type of acute palliative care for which the principle of double effect is always relevant: sedation for intractable distress of a dying patient (SIDD Pat).

The Principle of Double Effect

The principle of double effect is a centuries-old doctrine of the Roman Catholic Church for deciding how to act when all possible actions in a given situation risk bad consequences. Its applicability to end-of-life decision making is widely accepted and has been reaffirmed recently by Pope John Paul II [3]. The principle states that an action with two or more possible effects, including at least one possible good effect and others that are bad, is morally permissible if four provisos are met [4, 5]:

- The action must not be immoral in itself.
- The action must be undertaken with the intention of achieving only the good effect. Possible bad effects may be foreseen but must not be intended.
- The action must not achieve the good effect by means of a bad effect.
- The action must be undertaken for a proportionally grave reason (rule of proportionality).

When applied to palliative care, the principle directs that an intervention intended to provide relief from suffering at the end of life is acceptable even at the risk of causing foreseen but unintended side effects. For example, opioids may be given to relieve the pain or dyspnea of a terminally ill patient even at the risk of sedation, respiratory depression, hypotension, and hastening death. If, as in our case, all means of relieving distress short of sedation have been exhausted, then sedation may be the intended good effect. Possible side effects of the sedative, such as respiratory depression, hypotension, and hastening death, may be foreseen, but not intended. The act of giving medication to relieve suffering is not immoral as long as the patient or surrogate request relief and accept the risk of side effects and there are no other safer or simpler means to achieve relief. Such serious side effects must only be risked for a proportionally grave reason such as the relief of suffering of a dying patient who does not wish to suffer. Some patients and families worry that accepting medications for end-of-life suffering that might risk hastening death may be incompatible with their religious beliefs or even a mortal sin. Thus, clear explanation of this principle to patients and families, or involving a chaplain familiar with the principle, can be very comforting. At the same time, the patient’s beliefs, values, and preferences for end-of-life care can be explored.

Sedation for Intractable Distress of a Dying Patient (SIDD Pat)

SIDD Pat is the use of sedating medications to relieve severe symptoms that cannot be controlled adequately despite aggressive efforts without sedation. Such intractable symptoms most commonly are dyspnea or pain but also may include vomiting, myoclonus, delirium, anxiety, or agitation. SIDD Pat for psychological or emotional distress is more controversial than for severe physical symptoms [1]. Use of the term “terminal sedation” is discouraged for two reasons. First, it irremediably connotes sedation intended to terminate or to euthanize. SIDD Pat is intended to relieve intractable distress, not to kill. Second, “terminal sedation” does not convey the indication or proportionally grave reason for sedation: severe, refractory distress of a dying patient.

Various arguments have appeared recently against SIDD Pat as an instance of the principle of double effect and against SIDD Pat in general [4, 6]. Quill, like Orentlicher, argues that double effect “is of limited assistance in evaluating” SIDD Pat.
because sedated patients “die of dehydration or other intervening complications” [4]. In patients like Mr. D, whose death was imminent, this argument is moot. Even if death is not imminent, the fact that a sedated patient is unable to take oral food or fluids should not preclude use of SIDD Pat in appropriate situations for proportionally grave reasons. The disease creates the need for SIDD Pat. If the treatment prevents the patient from eating or drinking, that is a foreseen, unintended, but acceptable side effect of necessary treatment. Orentlicher also argues, remarkably, that “terminal sedation is not only a type of euthanasia; it is also ethically more problematic than either assisted suicide or voluntary euthanasia,” because, unlike assisted suicide or voluntary euthanasia, “terminal sedation can be induced without the patient’s consent or even the patient’s knowledge.” This misses the point that SIDD Pat, like any other major medical intervention, requires a clear indication and informed consent from the patient or surrogate decision maker. With SIDD Pat, the treatment is dictated by and linked to the patient’s specific symptoms. Physician-assisted suicide and euthanasia are more ethically problematic because they break this linkage between treatment and the patient’s symptoms. Death itself becomes the means to symptom control. Thus, physician-assisted suicide and euthanasia are not medical treatments in a traditional sense.

There are little data on the use of SIDD Pat in palliative care [7, 12-14]. The best study to date by Chater and colleagues surveyed 61 palliative care experts of whom 89% felt that “terminal sedation” was sometimes necessary and 77% had used “terminal sedation” within the preceding year [8]. Ninety percent were against legalization of euthanasia. Ninety percent were against legalization of euthanasia.

Various medications and protocols have been used for SIDD Pat [1]. Ideal agents have a rapid onset of action and are easy to titrate, with minimal side effects. Proposed agents include opioids (morphine, dilaudid), benzodiazepines (midazolam, diazepam, lorazepam), neuroleptics (haloperidol, droperidol, chlorpromazine), barbiturates (thiopental, pentobarbital), and other general anesthetic induction agents (propofol, ketamine). In our case, the patient’s distress was refractory to rapidly advanced, high-dose opioid, benzodiazepine, and neuroleptic (droperidol). Among the barbiturates and induction agents that we considered, all but ketamine may cause hypotension, especially if bolus or high doses are used and if other respiratory depressants are used concurrently. The high lipid content of the solution brings with it a risk for infection. Propofol can cause pain on infusion into small peripheral veins. Bolus dosing is undesirable, but when boluses are needed to control very severe symptoms, very quickly, small doses of 10 or 20 mg should be used. The drip rate should be titrated slowly, and a physician or nurse trained in the use of propofol should be present at the

**The principle of double effect can help guide treatment decisions.**

**Propofol for SIDD Pat**

Propofol (Diprivan, Zeneca; 2.6 diisopropylphenol) is an intravenous general anesthetic agent widely used for induction and maintenance of general anesthesia, conscious sedation for procedures, and sedation of mechanically ventilated patients in the ICU [9]. Its mechanism of action is not well understood but likely involves potentiation of the inhibitory neurotransmitter GABA by inhibiting its uptake. It has a large volume of distribution and readily crosses the blood-brain barrier. It is rapidly cleared from the blood and metabolized in the liver to an inactive glucuronide. Its onset of action (30 sec), duration of action (5 min), and half-life (1 h) are shorter than midazolam and any barbiturate including thiopental. This makes it ideal for SIDD Pat where rapid symptom relief and ease of titration both to maximize comfort and to minimize side effects are crucial. Because liver and renal disease do not significantly affect its pharmacokinetics, it can probably be used safely in patients with these conditions [9].

The level of sedation is easily and quickly controlled by titrating the continuous infusion rate. Its other beneficial properties include anxiolytic, antiemetic, antipruritic, anticonvulsant, antimyoclonic, muscle relaxant, and bronchodilatory effects [10]. Tolerance develops with prolonged use necessitating dose escalation.

Case reports describe effective SIDD Pat using propofol when other efforts had failed [10, 11]. For SIDD Pat, lower doses should be used than for general anesthesia. It can be started as a continuous infusion without a loading bolus at 2.5-5 µg/kg/min (for adults approximately 10-20 mg/h). It can be titrated every 10 min to effect by increments of 10-40 mg/h. The therapeutic dose ranges widely from 5 to 200 mg/h. The usual effective starting dose is 20-50 mg/h. Propofol is supplied as a 10 mg/ml concentration in 100-ml vials. At our institution, it costs $60 for a 100 ml vial or $72 per day for an infusion at 50 mg/h.

Propofol has several important side effects. It is a negative inotrope and peripheral vasodilator and can cause hypotension, especially in patients who are older, dehydrated, or receiving opioids or other negative inotropes or vasodilators. Bolus dosing heightens this risk. Respiratory depression and apnea may occur, especially if bolus or high doses are used and if other respiratory depressants are used concurrently. The high lipid content of the solution brings with it a risk for infection. Propofol can cause pain on infusion into small peripheral veins. Bolus dosing is undesirable, but when boluses are needed to control very severe symptoms, very quickly, small doses of 10 or 20 mg should be used. The drip rate should be titrated slowly, and a physician or nurse trained in the use of propofol should be present at the
bedside while the dose is being titrated to observe the effects and avoid use of more drug than needed for comfort. Concurrent use of other respiratory and cardiovascular depressants should be minimized. However, because propofol has no intrinsic analgesic effect, patients with pain requiring an opioid should continue to receive it. Strict aseptic technique is required in handling propofol, and i.v. tubing should be changed regularly. Large proximal veins or central veins should be used for infusion. Finally, hospital protocols are useful to guide safe use of propofol for SIDD Pat and to help assure that SIDD Pat is used only in those rare cases where a compelling clinical indication exists.

CONCLUSION

Dying patients whose symptoms are sudden or severe require acute palliative care. In rare cases where a patient’s severe symptoms are refractory to aggressive and intensive palliative treatment using standard agents, sedation for intractable distress of a dying patient should be considered. The principle of double effect is an important guide to the use of sedation in this situation. Propofol has many properties that make it an ideal agent for sedation.

In 1846, shortly after demonstrating for the first time that surgery can be performed painlessly, Dr. John Collins Warren soberly described ether anesthesia as “a mode of mitigating human suffering which may become a valuable agent in the hands of careful and well-instructed practitioners” [15]. Agents used for acute palliative care in general and especially for sedation of dying patients with intractable distress are equally valuable modes of mitigating human suffering in the hands of skilled palliative care practitioners.

ACKNOWLEDGMENTS

We wish to particularly acknowledge the involvement of the patient’s family in the Rounds and their contribution, which lent an extra dimension to the communication and caring between patient and staff.

The Discussion is based on a workshop presented at the American Academy of Hospice and Palliative Medicine, 11th Annual Assembly, in Snowbird, Utah, June 1999.

REFERENCES

9 Mirenda J, Broyles G. Propofol as used for sedation in the ICU. Chest 1995;106:539-547.