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Terminal Sedation in Palliative Care

Abstract

Terminal sedation is an important procedure which aims at reducing patients' suffering through the reduction of their consciousness. Terminal sedation is used in cases of intractable symptoms in those who are dying imminently. Sedation is distinct from euthanasia, although the distinction between these two procedures may be blurred and may be confusing. Careful consideration, together with the patients, their family and the multidisciplinary team, is of paramount importance.

Key words: palliative sedation, terminal sedation, intractable symptoms, pain, euthanasia, end of life care

Take home messages

- Palliative sedation aims at relief of symptoms not patient's death.
- Morphine is not a sedative drug and should be used only in combination with benzodiazepines.
- Palliative sedation is distinguishable from euthanasia.
- Existential suffering not accompanied by intractable physical symptoms is seen in most countries as insufficient ground to initiate terminal sedation.
- Some patients may need higher doses of sedatives than the other.
- Terminal sedation has usually no influence of the lengths of survival and the time of patients death usually can not be predicted.
- Nurses have an important role in guaranteeing dignity of sedated patients and their families.
- Sedation protocols and practice should be regularly audited in each institution.

Introduction

When the end is near, in the last days of a patient's life, some symptoms may be difficult to control. Drugs that worked before may appear to be

ineffective, either because of their poor absorption from the gastrointestinal tract or subcutaneous injection site or because of the rapid increase in the intensity of symptoms. Pain is not the only symptom that may prove to be uncontrollable at the end of life. When everything else fails and suffering is unbearable, sedation may be the only solution.

Terminal sedation means the use of specific sedative medications to relieve intolerable suffering from refractory symptoms by the reduction of a patient's consciousness [1].

The concept of terminal sedation is not without controversy [2]. As there are no (and will never be) controlled data on the efficiency of this treatment, there is an abundance of discussion by the experts [3–7] and this is equally confusing both for professionals and the general public.

Instead of writing yet another guideline on terminal sedation, we would like to clarify here different aspects of the discussion around terminal sedation, so the reader, equipped with new knowledge and understanding, may better comprehend this debate or even take part in it. This approach should also help readers to form their own point of view. A number of practical comments may help to provide better care at the bedside.

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Which term to use?

Many people object to the term "terminal sedation". To some it suggests that the sedation has something to do with termination and thus is indistinguishable from euthanasia. Because of this, some people have coined different names, such as "palliative sedation", "controlled sedation", "total sedation", "sedation for the distress of the imminently dying" and many others [1]. New terms are invented daily but they only add to the confusion instead of clarifying it. In fact, the term is not the most important issue here. What is important is that it applies to the imminently dying and those with intractable or refractory symptoms. Terms such as "slow euthanasia" should not be used.

When should terminal sedation be used?

In many patients, the imminence of dying can be adequately recognized and the treatment can be started upon this recognition. However, dying is a complicated and somewhat unpredictable process and health care workers, even with all their modern diagnostic means, can be surprised by it. Death may come earlier or later than expected, so the imminence of approaching death is not always clear. In practice, it is left to the discretion of the doctor.

Using exactly the same pharmacological means in different phases of life in the absence of imminent death could be seen as intention of life shortening and is morally indistinguishable from euthanasia.

What are the refractory symptoms?

When symptoms can not be controlled and are causing distress, patients may become unaware of them once they have been sedated. This does not mean that this treatment will or will not shorten a patient's life [8]. However, the concept of the refractoriness of symptoms is also controversial [4]. Can the doctor ever say that everything has been done to control symptoms? When doctors say this, they mean that everything has been done but "within the limitations of time, place, knowledge, resources and patient's directives". If the patient and the family do not want to be referred to a hospital or hospice, the possibilities of treating the patient at home may be limited. The knowledge and experience of the doctor and the nurse at the bedside may also be limited. Do doctors, therefore, always have an obligation to look for more and better solutions or may they "give up" and start sedation? No simple answer exists to this question. The decision should be

proportional to the situation: both to what is available at the time and to what the doctor and nurse, and preferably the whole multidisciplinary team, find important and practicable.

Can psychological distress be seen as a refractory symptom?

This is another point of controversy. Pain, nausea, breathlessness and many other symptoms are seen as "physical symptoms" and there are few doctors who would refrain from sedation in the dying when these symptoms are not relieved [4]. It is different with symptoms such as depression, anxiety and paranoia, as well as delirium and existential distress. Depression in particular is very difficult to comprehend, as many depressed patients have suicidal thoughts or even talk about euthanasia. Appropriate and timely treatment of depression may revert the wish to die. Doctors and nurses sometimes feel a high degree of pressure from patients and families to proceed with sedation, while the feeling is that not only should decisions be taken without such insistence but that pressure may also frequently provoke resistance. There is no doubt that patients' expressing psychological and existential distress suffer sometimes even more than patients with purely "physical" symptoms [9]. Psychological distress usually accompanies the physical symptoms. In one study in Japan, only 1% of sedations were performed due to psychological distress alone [10]. In many if not most countries psychological and existential suffering as stated above do not qualify for sedation.

In what way is terminal sedation different from euthanasia?

Terminal sedation is distinct from voluntary euthanasia, at least in the definition. Euthanasia is defined as the administration of drugs with the explicit intention of ending a patient's life, at the patient's explicit request [11]. Terminal sedation should have no intentions (neither explicit nor implicit) of ending a patient's life, but rather the reduction of distress due to refractory symptoms and uncontrolled suffering. However, both procedures end with a patient's death and, if there has been no family involved in making decision, the doctor may be the only one to judge whether this was a case of euthanasia or terminal sedation. His intentions may be clear from the records: for example, sedation might have been started with a reasonable dose of benzodiazepines because of increasing and distressing pain

in dying patient (terminal sedation) or a patient who had never received opioids was suddenly treated with a very high bolus dose of morphine (euthanasia?). However, these matters are not always obvious and those doctors who want to conceal something will be very careful in leaving such obvious traces behind. In some cases, therefore, terminal sedation may be very similar to or indistinguishable from euthanasia. As we think that terminal sedation is legitimate in some cases of refractory symptoms at the end of life and euthanasia is not, the banning of both sedation and euthanasia, just because of this lack of distinction, would cause a great deal of suffering and would make dying more frightening and less humane. To avoid this, doctors and nurses should be in close contact with the patient (if possible), the family and their team. Ideally, the decision about sedation should be taken by the multidisciplinary team and should be recorded in detail, including the doctor's intentions. Only in this way can peers and the public afford the doctor acclamation and trust.

In countries where euthanasia has been legalized, this procedure is usually discussed earlier in the course of the disease, when the patient is fully conscious and can make an informed decision. The very last days of a patient's life make euthanasia according to the law very difficult or even impossible because patients may be confused and not competent to take decisions. Therefore, the last days of life, in countries where euthanasia has been legalized, are usually claimed to be the domain of terminal sedation. In the Netherlands, cases of euthanasia have decreased by one third in the last 5 years because of a more widespread use of terminal sedation [12].

Does the principle of double effect apply in cases of terminal sedation?

According to the principle of double effect, effects that would be morally wrong if caused intentionally are permissible if foreseen but unintended [13]. This principle criticised is rooted in a Catholic morality and is accepted worldwide as an important ethical standard. However, in the context of palliative care and terminal sedation, it is heavily criticized [13], usually by proponents of a more liberal approach to euthanasia and intentional death. Sedation may be seen as an adequate control of refractory symptoms (good effect) and hastening death as an unintended, unpredictable but permissible side effect of this treatment (bad effect). Critics say that this principle would be acceptable only if patients received artificial hydration and feeding, which is usually postponed at this time. In the eyes of the

authors, using artificial hydration and food may be seen as disproportionate in the context of imminent dying and may be more of a burden than a relief. This discussion will probably never end.

Are there any hidden dangers in the terminal sedation procedure?

The act of voluntary euthanasia is clear cut and can be well defined [11]. The doctor gives lethal drugs with the intention of ending a patient's life and the patient usually dies directly after the drugs have been administered. Terminal sedation is less easy to define using the same terms [1]. First of all, the drugs administered are not intrinsically lethal. Like many other drugs used in medicine, it is the dose which perhaps causes the patient to die earlier, not the drug itself. The same drugs (benzodiazepines) may be used in low and adequate doses to control symptoms like fear and anxiety. Sedation is not a single well-defined and clear-cut procedure but a whole spectrum ranging from anxiolysis through intermittent to moderate and deep sedation, respiratory depression and death. Because of this, sedation, more than other procedures, is prone to abuse. In those countries where euthanasia is allowed under certain conditions, doctors may abuse terminal sedation as being less laborious, requiring less paperwork and not needing to be reported with the possibility of prosecution. In the Netherlands, where the GPs are backed by consultants in Palliative Medicine, the abuse of terminal sedation in that way happens more often on busy hospital wards, but not at home [14, 15].

Which drugs are used in terminal sedation?

Sedation is principally provided by benzodiazepines. Soluble benzodiazepines, with a short half-life like midazolam, are the drug of choice [1]. The drugs used for terminal sedation are usually administered subcutaneously or intravenously using a syringe driver. However, the administration of benzodiazepines alone may result in a rapid development of tolerance. This in turn may result in intolerable suffering for the patient and the family when the patient should, but is not able to sleep [16]. Usually, adding low doses of morphine or diamorphine makes the development of tolerance to midazolam less rapid as well as avoids development of tolerance to morphine [17–19].

Opioids are not sedatives as such. Sedation by opioids is usually transient and, at high doses, neu-

roexcitation (stimulation of dynorphin A) may have the opposite effect and even preclude sedation. Hospital protocols where morphine is administered (usually intravenously) in increasing doses until a patient's death [14] has little in common with terminal sedation and may be correctly seen as an attempt at euthanasia. In a minority of patients, liver enzymes will be induced by the use of drugs like carbamazepine or smoking to the extent that the metabolism of midazolam will be increased and plasma levels greatly reduced [20, 21]. In these cases, barbiturates or propofol should be used [16]. However, as barbiturates are used as a drug of choice in assisted suicide [22], the use of them within the frame of palliative sedation is not well accepted.

Apart from benzodiazepines and (dia)morphine, levomepromazine is often used as an adjuvant drug in terminal sedation [23]. It may have an intrinsic analgesic effect complementary to that of opioids; it may have a sedative effect due to its H1 antihistamine effect; and it has an antipsychotic effect which is important in the treatment of people with delirium and agitation. Not unimportant is its powerful antiemetic effect [24]. One of the drawbacks of levomepromazine is a potent anticholinergic effect which usually necessitates introduction of an indwelling bladder catheter. Conscious patients may experience dry mouth.

A specific but rare situation occurs when a patient responds paradoxically to benzodiazepines. This is usually due to a genetic mutation of the receptor protein. The condition appears predominantly in children and young adults [25] but occasionally can be seen in adults. When benzodiazepines induce anxiety instead of controlling it, flumazenil may be considered [26].

What dose can be seen as "adequate" or "proportional" in terminal sedation?

Due to the complexity of situations, there are no fixed doses of sedatives that can be seen as "adequate" or "proportional". The effect of the drug, as always, should be titrated against the desired effects. In some situations, as in distress due to acute bleeding into the trachea, titration can be very rapid. However, these dramatic situations are very rare in Palliative Care.

More commonly, there are hours or days in which to titrate carefully the dose of sedative drugs. Terminal sedation can be best initiated in the afternoon or in the evening, after patients have seen family members and they have seen the patient. Such sedation resembles natural sleep and is less distressing to the surrounding people (think about

the other patients in the bay). The initial dose of sedative will depend on the previous use of benzodiazepines. Higher doses are needed to obtain sedation in those patients who have been using high dose night sedatives for a longer time. Preliminary evaluation of subcutaneous midazolam/morphine administration should be done after 4–6 hours, but one should avoid changing the doses of infused drugs too early. However if the patient is asleep and a-reflexive (deeply sedated) 1–2 hours after administration, the dose is probably too high and should be reduced. Contrary, if the patient is still suffering (being awoken) 4–6 hours after administration, the dose may be too low or liver enzymes have been induced by drugs like carbamazepine and/or smoking and a different strategy should be devised (see about propofol and barbiturates). If necessary, additional single doses of midazolam and morphine can be given subcutaneously. Sometimes failure of sedatives is due to inappropriate absorption from the subcutaneous tissue. In such a case one can see the swelling around the needle insertion. In case of absorption failure the treatment should be continued intravenously.

Is there anything else the doctor should think of considering with terminal sedation?

Preparations for sedation are most important. Are there enough ampoules available (during the weekend?) even if the dose needs to be increased later? Has the patient open his or her bowels recently or is the rectum full of impacted faeces? Is the patient's bladder empty? Sedated patients usually need a bladder catheter, especially when they are going to be sedated with levomepromazine. A full rectum and/or bladder may produce powerful stimuli counteracting the sedating effects of drugs. It is not infrequent that patients who are difficult to sedate receive high doses of sedatives but do not respond to them because of a full bladder. Emptying the bladder may precipitate a patient's deep sedation and even sudden death, so try to insert the catheter before bladder retention.

After the patient is sedated, doctors and nurses should keep checking on the patient and continue to inform the family of any change in condition.

How long it will take?

There are some signs which will say something about the prognosis. While the patients are sedated they do not take fluids and it is usual that the urine volume decreases and the urine becomes more con-

centrated. If patients suffer from considerable oedema, they may mobilize the water from the oedema first. The family should be informed about this. Clinical experience suggests that overweight people combust their fat to water and use this water to perfuse the kidneys, this may result in the same effect as with oedema.

Also clinical experience suggest that when urine production is down to zero and the nurse can be sure the catheter is not blocked, the prognosis is short and there is a considerable likelihood of the patient's dying during the next 24 hours.

The role of the nurse

Nurses do have an important role in the care of terminally ill and imminently dying people. Sedation should be carefully prepared and discussed within the team. Procedures and practice should be frequently audited. The reasons for sedation should be weighted and well considered. Patients' consciousness should not be limited without an important reason. The care should be taken that this last part of life is peaceful and full of dignity. The patient should have time and opportunity to say his good-bys to the family and friends or do things which are important to him. This can be achieved by appropriate timing of the sedation. During the sedation, patients family should be daily informed about patients condition and the nurses should listen to the family members observations and doubt. If needed, the doctor should be asked to elucidate appearing problems.

Conclusion

Terminal sedation is a legally acceptable procedure which is used in many places in the World. Its use is restricted to patients imminently dying and with refractory symptoms. From them most important are pain, breathlessness and delirium. Sedation is not carried out with the intention of shortening a patient's life but is intended to decrease suffering. Sedation is distinguishable from euthanasia. This area is the subject of multiple and confusing discussions and, unfortunately, the distinctions between sedation and euthanasia are sometimes blurred and can not be set in stone. Careful consideration with the patient, family and the multidisciplinary team, as well as the transparent documentation of such cases, will help to illustrate the true intentions of the team.

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