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REVIEW ARTICLE

The role of end-of-life palliative sedation: medical and ethical aspects – Review



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Abstract

Background and objective: Palliative sedation is a medical procedure that has been used for more than 25 years to relieve refractory symptoms not responsive to any previous treatment in patients with no possibility of cure and near the end of life. Many uncertainties persist on the theme regarding definition, indications, decision making, most appropriate place to perform the procedure, most used drugs, need for monitoring, fluids and nutritional support, and possible ethical dilemmas. The objective of this review was to seek a probable consensus among the authors regarding these topics not yet fully defined.

Method: An exploratory search was made in secondary sources, from 1990 to 2016, regarding palliative sedation and its clinical and bioethical implications.

Conclusions: Palliative sedation is an alternative to alleviate end-of-life patient suffering due to refractory symptoms, particularly dyspnea and delirium, after all other treatment options have been exhausted. Decision making involves prior explanations, discussions and agreement of the team, patient, and/or family members. It can be performed in general hospital units, hospices and even at home. Midazolam is the most indicated drug, and neuroleptics may also be required in the presence of delirium. These patients' monitoring is limited to comfort observation, relief of symptoms, and presence of adverse effects. There is no consensus on whether or not to suspend fluid and nutritional support, and the decision must be made with family members. From the bioethical standpoint, the great majority of authors are based on intention and proportionality to distinguish between palliative sedation, euthanasia, or assisted suicide. © 2018 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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PALAVRAS-CHAVESedação paliativa;
Paciente terminal**O papel da sedação paliativa no fim da vida: aspectos médicos e éticos – Revisão****Resumo**

Justificativa e objetivo: Sedação paliativa é um procedimento médico que tem sido empregado há mais de 25 anos com a finalidade de aliviar sintomas refratários que não respondem a tratamento anterior em pacientes sem possibilidade de cura e próximos do fim da vida. Muitas incertezas persistem sobre o tema no que diz respeito à definição, às indicações, à tomada de decisão, ao local mais adequado para fazer o procedimento, aos fármacos mais usados, à necessidade de monitoração, ao apoio hídrico e nutricional e aos possíveis dilemas éticos. O objetivo desta revisão foi o de buscar um provável consenso entre os autores em relação a esses tópicos ainda não totalmente definidos.

Método: Foi feita uma pesquisa exploratória em fontes secundárias, a partir de 1990 até 2016, a respeito de sedação paliativa e suas implicações clínicas e bioéticas.

Conclusões: A sedação paliativa é uma opção para aliviar sofrimento de pacientes no fim da vida, devido a sintomas refratários, especialmente dispneia e delirium, após terem sido esgotadas todas as outras opções de tratamento. A tomada de decisão envolve explicações prévias, discussões e concordância da equipe, pacientes e ou parentes. Pode ser feita em unidades hospitalares gerais ou de retarguarda e mesmo no domicílio. Midazolam é o fármaco mais indicado, podendo ser necessários também neuroleptícos na presença de delirium. A monitoração desses pacientes se resume apenas à observação do conforto, do alívio dos sintomas e da presença de efeitos adversos. Não existe consenso em suspender ou não o apoio hídrico e nutricional; a decisão deve ser tomada junto aos parentes. Do ponto de vista bioético, a grande maioria dos autores se fundamenta na intenção e na proporcionalidade para fazer a distinção entre sedação paliativa, eutanásia ou suicídio assistido.

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Introduction

Palliative sedation (PS) was first reported in the early 1990s and since then an adequate definition has been sought for this procedure, despite the great difficulties of consensus among specialists.¹⁻⁷

The most widely accepted concept of PS among authors is the use of sedative drugs to alleviate intractable symptoms at the end of life.⁸

Intractable or refractory symptoms are considered to be those that, despite multiple efforts, are not possible to be controlled without compromising the patient's consciousness; which harm their well-being, by the great negative effects on the organism, and interfere with the serene process of dying.^{1,9,10}

There are many misconceptions about this procedure with regard to proper patient selection; the ideal moment to start sedation; the most effective drugs for this procedure; the need for monitoring, hydration and nutrition, and the most appropriate place for sedation, among others, which makes decision-making very difficult and complex.

From the bioethical point of view, there is a great deal of discussion about the ethical consequences of indicating a state of unconsciousness for a patient close to death and also the need to clearly distinguish PS from euthanasia.¹¹

Because it is a procedure that reduces patients' awareness, often irreversibly, to the detriment of communication with relatives, there are many doubts, many questions,

and a lot of anxiety in the decision making by doctors. This literature review seeks to obtain a probable consensus of opinions among authors on the subject and make it less difficult for professionals to make this decision.

Methods

An exploratory search was made on secondary sources regarding PS and its clinical and bioethical implications.

Data collection was performed through an online search on the specialized electronic sites (Bireme, SciELO, PubMed) for articles in both Portuguese and English, from 1990 to 2016, with emphasis mainly on authors with more publications on the subject of palliative sedation.

The inclusion criteria were publications between 1990 and 2016, dealing with the PS issue and addressing its definitions, selection of patients, decision making in the indication of PS and appropriate locations, drugs used and monitoring of patients under PS, hydric and nutritional support during PS and bioethical aspects related to PS indication. All articles that were unrelated to the queries sought and those that did not reach agreement among the authors for inclusion in the review were excluded from the study.

Of the 54 articles selected, 48 were used, which were analyzed in an integrative way in search of a probable consensus among the authors about each item investigated.

Development

Definition, indications and decision making in PS

The first publications on the use of PS with the intention of reducing consciousness in patients who were suffering at the end of life appeared at the end of the 1980s. Shortly afterwards, discussions began on ethical implications, effects on survival, and the exact significance of this intervention.^{12–15}

The definition of refractory symptoms, proposed in 1994 and still in force, establishes that refractory symptoms are those in which all possible treatments failed or were estimated as useless by team consensus after repeated expert evaluations; i.e. no available method has promoted relief within time and cost-benefit relationship that the patient could tolerate.⁹

The most difficult symptoms to be controlled in the last days of life are delirium and dyspnea, followed by nausea and vomiting.^{16,17}

In a critical review of seven years of experience with patients who died in palliative care units, the authors found that the indication for PS was mainly due to the presence of dyspnea, delirium and anxiety, while pain was a more easily treatable symptom, rarely requiring PS as treatment. These results confirm that dyspnea, delirium, and anxiety have been the main reasons for end-of-life sedation and that there has been a greater increase in the indication of PS to treat psycho-existential symptoms than to treat physical symptoms.¹⁸

PS for psycho-existential suffering in patients with advanced cancer is a focus of strong controversy in the literature, especially since several studies have revealed that the main reason for the desire to anticipate death, assisted suicide or euthanasia in these patients is not simply due to physical, but rather to the psycho-existential suffering with loss of autonomy, dependence, and lack of meaning in life.¹⁹ The authors' argument against the formal indication of PS for psycho-existential problems is that the intensity of psycho-existential distress does not always mean that the patient is on the verge of death. Therefore, this indication should be reserved for exceptionality, after the resources of intermittent sedation and specialized medical, psychological, and/or religious care have been exhausted.^{20,21}

Decision making depends on the severity of refractory symptoms and should be discussed between the health care team, patient and/or relatives. It requires that the patient's suffering be extreme; definitely refractory; that death is possible within hours or days; that the patient's desire is explicit and yet in some catastrophic end-of-life situations, such as massive hemorrhages or suffocation. It is of fundamental importance an open dialog with the relatives to make it clear that it is a indicated procedure in the absence of other means of managing refractory symptoms. And that does not accelerate or delay death, reduces or eliminates the possibility of verbal communication with the family, can be reversible if the patient's clinical conditions allow, and that the ultimate goal is the well-being of the patient.^{17,22–25}

In 2001, the term palliative sedation therapy was defined as the use of sedative medication to relieve intractable and refractory symptoms by reducing the patient's consciousness and classified as moderate, deep, intermittent, continuous,

primary and secondary sedation according to the indications. The authors consider PS to be a combination of five categories: primary, continuous, deep, for physical and psychological symptoms in patients with vital organ failure. The importance of defining PS subcategories aims to improve the accuracy and depth of sedation, which are primary, continuous, and profound for delirium of patients with cancer or secondary, continuous, moderate for patients with lung cancer dyspnea.^{26,27}

Most suitable places for the procedure, drugs used, and monitoring required for PS patients

PS may be performed in general care areas of hospitals, hospices as well as in the patient's home.^{28,29}

Recent literature reviews have shown that PS in patients at home is feasible, free from complications or adverse effects, provided they are selected, and is an option for patients with refractory symptoms who wish to die at home.^{16–30}

The benzodiazepine midazolam is the drug of choice for initiating PS by having easy titration, rapid onset of action, short half-life clearance, specific antagonist, and being able to be combined with other drugs.^{23,26,28,31}

Neuroleptics and chlorpromazine may be indicated and are effective in patients with signs and symptoms of delirium, as well as other drugs already used prior to sedation for symptom relief, such as opioids for pain.²³ However, the use of high dose opioids for pain and dyspnea management instead of producing comfort may cause delirium, sweating, and agitation.²⁶

Monitoring of patients undergoing PS should be based solely and exclusively on patient comfort and management of unpleasant adverse effects. Cardiac, blood pressure and temperature monitoring should be discontinued in order not to increase the stress of relatives. Staff and relatives should be monitored for occasional presence of psychological and/or spiritual stress.^{17,23,28}

Need for hydration and parenteral nutrition support during PS

The decision to continue or not to provide hydration and nutrition during PS generates many conflicts, both clinical and bioethical. Some understand as necessary to continue it because the patient cannot ingest liquids and food while sedated; others admit that discontinuation of food and hydration can shorten death. Many believe that the permanence of both prevents suffering in some way, and an expressive group deems it unnecessary due to the absence of clear benefit, besides being often harmful due to the possibility of generating edema and ascites as a result of hydration. Some authors believe that when an end-of-life patient receives parenteral nutrition and hydration and begins to show refractory symptoms to the point of requiring PS, hydration and nutritional support may be continued or discontinued according to cultural goals and beliefs. Opinions and practices vary widely and reflect on the different attitudes of physicians, bioethicists, patients, relatives, and local standards of good clinical practice and ethics.^{15,23,28,31,32}

Controversy over the use of artificial nutrition in terminally ill patients, including advanced dementia, has remained controversial for many years, requiring discussions of ethical, medical, legal, financial, and institutional concepts that always prioritize patients' interests.³³

A survey of 143 Portuguese oncologists on end-of-life situations revealed that most of them respect patients' autonomy, favors the withdrawal of water and nutritional support at the patients' request, but not at the request of relatives or by their own initiative.³⁴ In 2013, the Royal College of Physicians of London published recommendations for prolonged disorders of consciousness in vegetative states and of minimal awareness, deciding the withdrawal of nutrition and hydration clinically assisted, in these cases supported by judicial decisions.³⁵

This protocol received several criticisms. Authors conclude that recommendations to withdraw nutrition and hydration from these patients are not only harmful to patients and relatives, but represent the means of consensual euthanasia, constituting a major violation of public trust and medical profession integrity.³⁶

Still regarding these recommendations, the authors suggest that physicians withdraw hydration and nutritional support in situations other than vegetative states and minimal awareness; they establish that joint judicial decisions with the medical team should occur in all circumstances, which would provide security to the general public and protection to the vulnerable ones.³⁷

For a Brazilian author, even when it is considered irrelevant that hydration and nutritional support favor the medical prognosis of patients in advanced stage of the disease without a cure perspective, in certain circumstances there will be a decision in favor of maintaining artificial support that respects personal beliefs and provide psychological comfort for the relatives. This could be more beneficial than any improvement in clinical parameters.³⁸

Bioethical implications of PS

One of the most complex discussions about PS concerns its bioethical character; that is, to make very clear the difference between PS, euthanasia, and assisted suicide.

Indications and justifications for PS have been guided by three bioethical fundamentals from the standpoint of principle: double effect, proportionality, and autonomy. The double effect principle is applied to situations in which it is impossible to avoid all harmful actions of an act. The traditional double effect formulation emphasizes four fundamental conditions: the nature of the act, which needs to be good or morally neutral and not forbidden or intrinsically wrong; the intention of the one who does the act, which must be good, that is, while the good effect is desired, evil can be foreseen, tolerated and allowed; the limit between means and effects, which in PS refers to the fact that death should not be the means to obtain the desired effect, which is the alleviation of suffering; and finally the proportionality, in which the good effects need exceed or counterbalance the ill effects.^{21,39–43}

The rigid character of bioethical principle foundations based on the four principles known as autonomy, beneficence, nonmaleficence, and justice has slowly been

replaced by personalistic bioethics. Its principles are based on promoting the integral good to the human being through a perspective that recognizes the being and dignity of a person as absolute values, and places as a fundamental principle the unconditional respect for their inviolability and the protection of free expression based on human rights.^{44–48}

PS for managing intractable symptoms has been considered a human option and of compassion for the conscious and continuous suffering of both the patient and relatives.⁴²

Because PS is ethically permissible under the principles of double effect, proportionality, and autonomy, physicians should have in mind the explicit intention of relieving symptoms rather than causing death; there must be proportional reasons when choosing PS, such as intolerable suffering, refractoriness of suffering, poor general conditions of the patient, and respect for the will of the patient and relatives.⁴³

PS and euthanasia were differentiated based on three aspects: while the explicit objective of PS is the relief of symptoms, that of euthanasia is the death of the patient; in PS, the doses of sedatives are proportional to the effect sought, while in euthanasia the doses of medications are lethal. Finally, while in PS the relief is the symptom with some risk of shortening life, in euthanasia the result is the immediate death of the patient.^{47,48}

PS is not confused with euthanasia or assisted suicide, as the last two practices involve a specific intention to seek the end of life through the deliberate use of lethal doses of sedative drugs or non-therapeutic escalation of doses disproportionate to relieving stressful symptoms.²⁴

The principles of beneficence and nonmaleficence could explain the difference between PS, assisted suicide, and euthanasia, as PS seeks relief from suffering, not death.²⁸

An article recently published questioning whether there is an option for PS at the end of life concluded this is a therapeutic option that makes possible to relieve refractory symptoms. But the decision of applying it and put a patient in irreversible unconsciousness is not free of ethical consequences, which requires a clearer view of the aspects involving it.¹¹

The absence of impact on the survival of patients with PS is enough to distinguish it from assisted suicide.¹⁷

Conclusion

According to the current literature review, which covers important aspects of PS, from its first reports to the present day, consensus can be observed among professionals in many of the variables involved in their practice.

Regardless of the terms used, the definition of PS according to the literature should be based on the treatment of refractory symptoms in patients with non-curable illnesses, short life expectancy, and when no other previous treatment had satisfactory results. The refractory symptoms that most lead to the indication of PS are delirium and dyspnea, followed by vomiting and pain in lower incidence. Existential and psychological symptoms should receive a multidisciplinary team approach. The decision to institute PS depends on the refractoriness and intensity of the symptoms and should be preceded by explanation and discussion of the

health team with patients and/or relatives, in the search for approval and consent of all those involved.

Psycho-existential symptoms have been suggested as an indication for PS, but most authors disagree formally because there are other means to treat such symptoms.

PS has been mainly provided in hospitals and hospices although there are no contraindications for its use at home. Midazolam is the drug of choice for PS, using neuroleptics and chlorpromazine only in cases of delirium and major confusions. Opioids should not be discontinued if the goal is to provide analgesia, but are not indicated for primary sedation due to the adverse effects that may result.

Monitoring of patients under PS only seeks to assess comfort levels, which include absence of pain, relief of symptoms, presence of adverse effects, and degree of sedation. Cardiac monitoring has been discouraged as it increases the risk of stress among relatives.

There is no consensus regarding the maintenance or withdrawal of hydration and nutritional care during PS, even among the team itself, which is perhaps the most controversial point. As long as it is not harmful, this decision must be made together with the relatives, remembering that culturally food is life and for many relatives the cessation of it can shorten life. Ethical aspects are complex and opinions very variable. There is no clear evidence that maintaining artificial nutrition and hydration prolongs life in patients nearing death.

From the ethical standpoint, PS has been the subject of great discussions, since placing a patient in unconsciousness until his death may not be easily distinguishable from assisted suicide and euthanasia.

The ethical principles on which PS is based are derived from bioethical principle foundations: double-effect, proportionality, and autonomy. Because these are rigid principles, which do not regard a person's being and dignity as absolute values, there is a need to show the act's intention (good) and proportionality (good effects exceed or counterbalance the bad ones) in order to be distinguished from physician-assisted suicide and/or euthanasia. It is believed that with the evolution of personalistic bioethics, in which the person's being and dignity are absolute values, this distinction will be easier to make.

Conflicts of interest

The authors declare no conflicts of interest.

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