

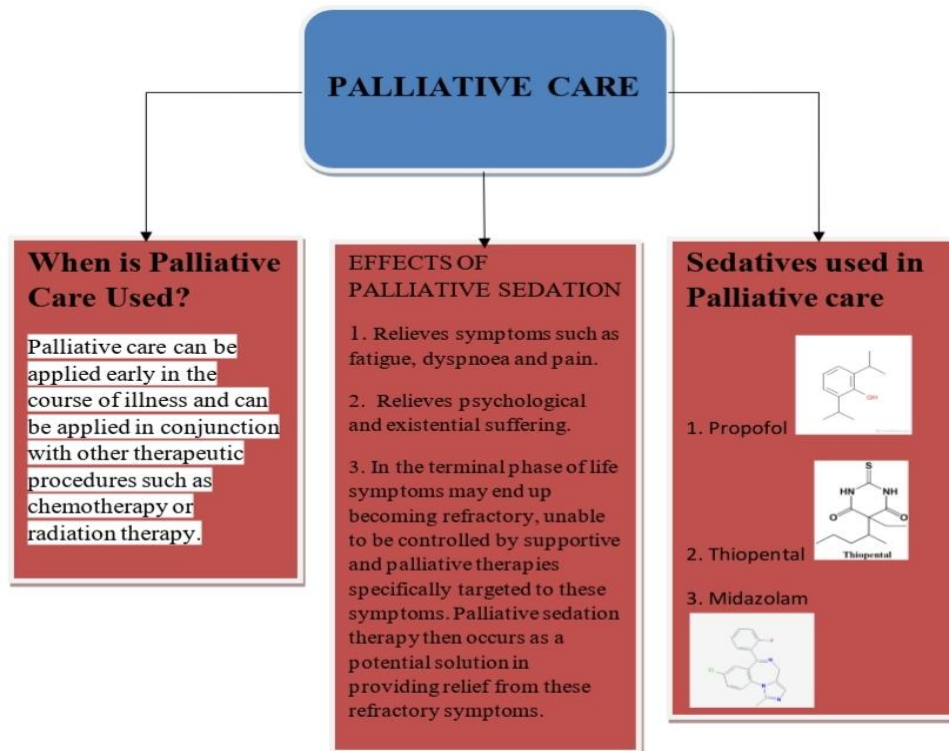
Impact of Sedation in Palliative Care

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Abstract: *Palliative medicine has grown by leaps and bounds in the new millennium. With the increasing acknowledgement of 'Palliative care', new and more exciting studies on Palliative Care are happening. Palliative care is an approach that provides relief to patients and their families that are facing problems related to life-threatening illness. Palliative Sedation is when intentional sedation is used under this care to relieve a dying patient from his/her intolerable suffering from refractory symptoms. Here we debate the importance of Palliative care and Palliative sedation, consider the risks involved, the ethical dilemmas faced while deliberating upon how to improve the services provided under palliative care. We have looked into the various studies that have been conducted and tried to sketch out an outline of the different protocols and definitions regarding palliative care. The risks associated with Palliative care to induce Continuous Deep Sedation (CDS) have also been noted. Studies have always suggested that euthanasia and palliative care by definition are antagonistic, but new studies force us to rethink this approach and think of euthanasia as just another option that should be available to the patient. But no matter what, the patient should always receive palliative care at the highest level.*

Keywords: Sedative, Palliative care, Opioids, Midazolam, Lorazepam



1. Introduction

According to the definition laid out by the World Health Organization (WHO) palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. Dr. Cecily Saunders in the 1950s noted down her observations on the care of dying patients in hospices (1). Her work laid the groundwork for modern palliative care. In 1973 an urologist Balfour Mount (considered the father of palliative care in North America) coined the term "Palliative Care". He also created the first ward for

palliative care at the Royal Victoria Hospital in Montreal. Palliative care can be applied early in the course of illness and can be applied in conjunction with other therapeutic procedures such as chemotherapy or radiation therapy. It is a vital part of treatment as it is necessary to manage distressing clinical complications that will arise out of other therapeutic procedures. Palliative care can be given to anyone suffering from a serious life threatening illness like heart failure, chronic obstructive pulmonary disorder, cancer, dementia and Parkinson's disease. Whether a patient needs palliative care necessarily does not depend on the stage of the illness but more on the point of diagnosis.

Therapeutic sedation in the context of palliative care involves a monitored use of medication intended to induce a

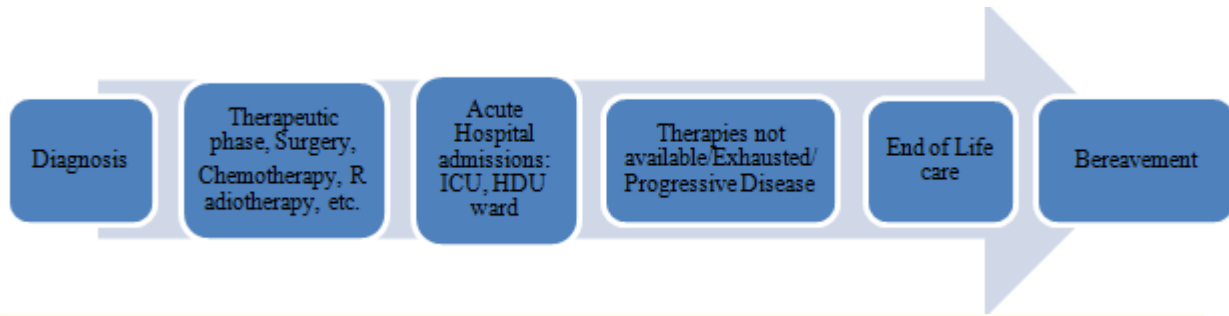
state of reduced or absent consciousness to remove the burden of otherwise intractable and intolerable suffering in a manner that is ethical. Sedation is often a treatment of last resort because of its adverse outcomes and potential risks. This often includes the loss of the patient's ability to interact socially which is something that most patients want to have till the last phases of their decline to death (2). This is the reason why treatments like 'Continuous Deep Sedation' (CDS) are ethically controversial as it often signifies the end of a person's 'biographical life' (the ability to interact meaningfully with other people). We will discuss the various ethical dilemmas related to such treatments in detail in this article. Because of such debates the European Association for Palliative Care (EAPC) Ethics Task Force notes "terminal" or "palliative" sedation in those imminently dying must be distinguished from euthanasia. It observes that in terminal sedation the intention is to relieve intolerable pain and suffering whereas in euthanasia the intention is to kill the patient (3). Such distinctions are important to make because in the absence of well defined guidelines unethical practices might creep in and end up undermining the whole field of palliative medicine. This will lead to extra legal scrutiny and fear of prosecution which might inadvertently affect the level of palliative care received by patients and might lead to patient discomfort or even pain.

In the field of therapeutic sedation one has to focus on the various drugs that are being used to induce sedation. Drugs known as sedatives or tranquilizers are substances that induces sedation by reducing irritability and excitement which can be also classified as psychomotor agitation. These drugs depresses CNS activity and decelerates brain function. Various kind of sedatives do exist but the majority of them deals with the neurotransmitter gamma- aminobutyric acid (GABA). Most sedatives produce beneficial relaxing effects by increasing GABA activity. The medications used for palliative sedation do vary, but benzodiazepines and barbiturates are one of the most favored agents. Sedatives that are mostly used in palliative care are midazolam, lorazepam, Chlorpromazine, Haloperidol, Pentobarbital, Phenobarbital, Thiopental, Propofol (4). The choice of drugs used mostly depend on the institutional policy and clinician preference. Regarding the dose of sedatives used there are no universally accepted guidelines or protocols (5; 6). Clinicians generally do not increase the dose of drugs without explicit evidence of the fact that there is inadequate sedation. So, most clinicians have to unfortunately rely on visual observation. However certain scales such as the Ramsay Sedation scale (7) can be utilized. We can always say that pain control is a complex process that requires multiple titrations of doses overtime. The doses are always advised to be proportional to the pain the patient is currently suffering. Palliative care and the idea of therapeutic sedation is not only about relieving pain of the patients but also to give meaning of life to the patient, manage family bereavement and help patients deal with existential crisis. An interdisciplinary team of professionals gets deployed to help patients and their families manage and get through a

situation that is depressing and fundamentally seems to be unfair. In the end the goal is to ensure that patients who are almost at the end stages of their lives get the dignity they deserve.

2. Discussion

In this article we are going to delve into the details of modern palliative care, the use of therapeutic sedation in palliative care and sedative drugs used for sedation. We are also going to focus on the moral and ethical dilemmas that are associated with palliative sedation and will differentiate clearly between terminal sedation and euthanasia. Dr. Cicely Saunders first noted down her ideas about modern hospice care in the late 1950s based on her observation of dying patients. Thus palliative care began with a focus on the care for the terminally ill. She held the belief that only an interdisciplinary team can relieve the "total pain" of a dying person and his or her family. An American Psychiatrist in the 1960s, Elisabeth Kübler-Ross faced fierce criticism and resistance with respect to the treatment of patients at the end of life. Her book, 'On Death and Dying' brought a revolution in the field of palliative care. Her work helped to humanize how dying patients were acknowledged and cared. Dr. Balfour Mount was the person who first coined the term 'palliative care'. He was a surgical oncologist with The Royal Victoria Hospital of Mc Gill University in Montreal. He used the term palliative care because the word 'hospice' carried negative connotations in French culture. He incorporated Dr. Saunders' innovation in academic teaching hospitals. He was one of the first who demonstrated what it really meant to provide holistic care for patients with chronic or life-limiting diseases, and how that care involved managing the physical, psychological, social and spiritual distress faced by the patients and their families (1). The concept of using interdisciplinary teams is still very much at the core of modern palliative care. The definition of "palliative care" as put forward by the National Quality Forum and endorsed by the National Hospice and Palliative Care Organization (NHPCO) reads: "Palliative care refers to patient- and family centered care that optimizes quality of life by anticipating, preventing and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and facilitating patient autonomy, access to information, and choice." The alleviation of pain and suffering is integral to the vision of quality end of life care. Palliative care is family centered but in cases where family interests or preferences directly contravene the best interests of the patient, the needs of the patient are deemed primary. Palliative care can be given simultaneously as the treatments meant to cure or treat the disease. Palliative care can be administered at any point in the course of the patient's treatment, at the time of diagnosis, throughout the treatment, during follow-up, and at end of life situations.



Continuum of palliative care throughout illness trajectory and beyond. ICU = Intensive care unit, HDU = high dependency unit (8)

Palliative sedation (PS) is a therapeutic path that is only followed in those rare circumstances where the patient is resistant to any other form of treatment. Palliative Sedation is the use of medications to lower the consciousness of the patient so that the patient has limited to no awareness of suffering that is *intractable* and *intolerable*. The terms ‘intractable’ and ‘intolerable’ needs to be defined for better understanding. **Intolerable suffering** is suffering that only the patient can perceive and identify as unbearable or intolerable. It is the duty of the healthcare team to use reliable assessment methods to determine the level of patient’s suffering. When the patient is unable to communicate, these assessments needs to be evaluated in consultation with the families of the patient to determine whether the patient would declare his/her suffering to be ‘intolerable’ if conscious. **Intractable suffering** is suffering to which there is no adequate response. All trialed interventions do not have any adequate response and additional interventions are impractical or unavailable(9).The European Association for Palliative Care (EAPC) considers sedation as a necessary and indispensable therapy which is to be employed in the care of selected palliative care patients with otherwise refractory distress. But the application of such approach requires prudence, due caution and good clinical practice (2).The term “refractory” can be used when symptoms cannot be relieved adequately by conventional therapy that does not compromise consciousness. Overlooking potential risks and problematic practices can lead to unethical practice of Palliative Sedation (PS) which might end up undermining the credibility of responsible clinicians and institutions or in the worst circumstances the discipline of palliative medicine in general. Sedation is employed in palliative care in several settings:

- 1) Transient sedation for noxious procedures
- 2) Sedation in care of burn victims
- 3) Sedation in end of life weaning from ventilator support
- 4) Sedation for management of refractory symptoms in patients suffering from terminal illness.
- 5) Emergency sedation
- 6) Respite sedation
- 7) Sedation for psychological and existential suffering

Intensivists in palliative care often face a dilemma as they have to balance providing analgesia and sedation for terminally ill patients. If they are administering too little they provide inadequate palliative care as a result patients suffer. If they are administering too much they might face prosecution for committing euthanasia. Increasing legal scrutiny may have the unintended effect of fear of prosecution which might lead to under treatment of patients (10) Relating doses of sedative medicine there are no

universally accepted guideline or protocols. So doses of medications should not be increased unless there is absolute evidence of inadequate sedation. Some clinicians depend on direct visual observation to determine depth of sedation others might use the Ramsay sedation scale (7) the intra-operative sedation scale (11) and the Richmond Agitation-Sedation scale (12).

RAMSAY SEDATION SCALE	
Score	Level of Sedation
1	Patient is anxious, agitated, restless or both
2	Patient is co-operative, oriented and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk, response to light, tactile or auditory stimulus
5	Patient exhibits sluggish response to light, tactile or loud auditory stimulus
6	Patient exhibits no response

Source:-13

Richmond Agitation-Sedation Scale		
	Target RASS Value	RASS Description
+4	Combative	Combative, violent, immediate danger to staff
+3	Very Agitated	Pulls or removes tube or catheters, very aggressive
+2	Agitated	Frequent movement without purpose, resists ventilator
+1	Restless	Anxious and apprehensive but no aggressive movements
0	Alert and Calm	
-1	Drowsy	Not fully alert but has sustained response to voice (eye opening and contact greater than 10 seconds)
-2	Light Sedation	Brief response to voice (eye opening and contact less than 10 seconds)
-3	Moderate Sedation	Response to voice in the form of movement or eye opening
-4	Deep Sedation	There is movement or eye opening as response to physical stimuli, but no response to voice
-5	Unarousable	There is no response to physical stimuli or voice

Source:-13

Sedation is usually recommended for patients with intolerable distress due to physical symptoms, when there is a lack of other methods for relief within the required time frame, and there is risk for refractoriness. Continuous Deep Sedation (CDS) is only considered if the patient is in the terminal stages with expected prognosis of hours or days at most.

Continuous Deep Sedation (CDS) can be selected if:-

- 1) The suffering is intense
- 2) Suffering due to refractory causes
- 3) Death is expected within a few hours or days
- 4) The patient has explicitly expressed his/her wish for CDS
- 5) If an end of life catastrophic event occurs such as massive hemorrhage or asphyxia. (2)

The practice of sedation in palliative care naturally begs us to give attention to the various sedative drugs used in the process. We know sedatives or tranquilizer is a substance that induces sedation by reducing irritability and excitement (psychomotor agitation). This depresses CNS activity and decelerates brain function. Various kinds of sedatives do exist but the majority of them deals with the neurotransmitter gamma- aminobutyric acid (GABA). Most sedatives produce beneficial relaxing effects by increasing GABA activity. A postal survey conducted on 61 Palliative care experts in 1996 gives us an idea of the drugs and dosages used for sedation. Out of 96 patients for whom drug lists were reported, 37% were reported to receive one drug for sedation, 30% received two drugs, and 28% received three drugs. Three-quarters of Canadian and all respondents from UK received midazolam. All US patients received lorazepam. Opioid were given to 40 patients. The opioids used include morphine, diamorphine, hydromorphone, fentanyl and methadone. The dose was given for 30 patients and, when converted into parenteral morphine equivalents, the doses ranged from 150mg/24 hours to greater than 5g/24 hours, with a median dose of 525 mg/24 hours. Over 60% of these patients had either pain or respiratory distress reported as the major symptom requiring “terminal sedation” (14).

Benzodiazepines such as midazolam are the most frequently prescribed sedative drugs for palliative care of patients with refractory symptoms. However, because many physicians fear that sedation might cause shortening of a terminal patient’s life, they hesitate to use this therapeutic measure. In a review on Palliative pharmacological sedation for terminally ill patients (15) we have noted that terminal restlessness is an agitated delirium that appears to occur in some people during the last few days of life (16). In The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) it is indicated that during the last three days of their life, 80% of dying hospitalized patients had severe fatigue, 50% severe dyspnoea, and 40% severe pain (17). In another study, we have observed that the most commonly reported symptoms were fatigue, dyspnoea, and dry mouth, with the most distressing being fatigue, dyspnoea, and pain (18). Other distressing symptoms reported in this and other studies of the same nature were noisy breathing, excess respiratory secretions, agitation, anxiety, constipation, nausea and vomiting, anorexia, incontinence, pressure sores, and insomnia (e.g. 19; 20). In the terminal phase of life (i.e. when the disease is progressive, far advanced, incurable, and death is imminent), these symptoms may end up becoming refractory, unable to be controlled by supportive and palliative therapies specifically targeted to these symptoms. Palliative sedation therapy then occurs as a potential solution in providing relief from these refractory symptoms. While discussing the use of sedation in palliative care it is also imperative that we point out the risks that might be associated with the aforementioned practice. From the beginning the practice was controversial; critics either conflated the practice with euthanasia or ‘mercy killing’. Many critics argued that the adjective ‘terminal’ in the term “terminal sedation” is not merely an indicator of time denoting the final phase of patient’s life but the intended purpose of the intervention itself. Because the term was deemed confusing and ambiguous the term ‘terminal sedation’ was abandoned altogether and the term ‘palliative sedation’ found its way into scholarly literature. In a study done in Japan by Tatsuya Morita et.al it was revealed that there are risks of inappropriate use of sedation in cases with potentially treatable psychiatric disorders. It was seen that less than 40% of physicians considered psychiatric intervention a strong possibility in patients who have shown signs of delirium and depression which was considered by experienced liaison psychiatrists to be intrinsically treatable. Moreover approximately half of them chose continuous Deep Sedation as a potential option. The study also revealed that physicians suffering from emotional exhaustion were less confident of psychological intervention and had a more favorable view of use of CDS suffering from refractory physical and psychological distress (20). Ten Have et.al noted that there were statistical variations in the prevalence studies done on palliative sedation. It was observed that there are striking differences in the reported prevalence of sedation in terminally ill patients ranging from as low as 1% to as high as 88%. He ascribed these inconsistencies to ‘terminological polysemy’. It means that the definitions of palliative sedation used in the prevalence studies are different or there are no definitions at all. Guidelines, protocols on problems such as whether to consult patient and

<i>Drugs used in Palliative Sedation and their doses</i>	
Drugs	Suggested Dose
Lorazepam	0.5–2 mg PO, SL, or SC every 1–2 hours or 1–5 mg bolus IV/SC, then CII/CSI at 0.5–1 mg/h; usual maintenance dose, 4–40 mg/d
Haloperidol	0.5–5 mg PO or SC every 2–4 hours or 1–5 mg bolus IV/SC, then CII/CSI at 5 mg/d; usual maintenance dose, 5–15 mg/d
Pentobarbital	60–200 mg PR every 2–4 hours or 2–3 mg/kg bolus IV, then CII at 1 mg/h; titrate upward to maintain sedation
Midazolam	0.5–5 mg bolus IV/SC, then CII/CSI at 0.5–1 mg/h; usual maintenance dose, 20–120 mg/d
Propofol	10 mg/h as CII; may titrate by 10 mg/h every 15– 20 minutes; bolus of 20–50 mg may be used for emergency sedation
Thiopental	5–7 mg/kg bolus IV, then CII at 20 mg/h; usual maintenance dose, 70–180 mg/h
Chlorpromazine	10–25 mg PO, IV, or PR every 2–4 hours
Phenobarbital	200 mg IV/SC bolus, then CII/CSI at 600 mg/d; usual maintenance dose, 600–1,600 mg/d
All Clinicians should consult pharmacy textbooks, pharmacists, and other knowledgeable professionals for further dosing suggestions. PO = oral; PR = per rectum; SL = sublingual; IV = intravenous; SC = subcutaneous; CII = continuous intravenous infusion; CSI = continuous subcutaneous infusion	
Source:(4)	

family, whether to forgo life sustaining interventions or even what drugs to prescribe are all varied and inconsistent (21). According to the definition of palliative care drawn out by WHO, palliative care is an affirmation of life and it is neutral regarding death i.e. it neither hastens nor postpones death. Palliative care is about offering the support systems that helps a patient live as actively as possible until death. This definition is directly in contrast with the definition of euthanasia which is defined as follows: a physician (or other person) intentionally killing a person by the administration of drugs, at that person's voluntary and competent request. The practice of Physician Assisted Suicide (PAS) also needs much discussion which can be defined as: a physician intentionally helping a person to terminate his or her life by providing drugs for self-administration, at that person's voluntary and competent request. There are many controversies and ethical dilemmas related to PSA, in many places PSA can be penalized by civil law. There is also an ongoing debate on withholding of treatment or treatment withdrawal which can be termed as 'Non Treatment Decisions' (NTD). NTD can be defined as: withholding or withdrawing medical treatment from a person either because of medical futility or at that person's voluntary and competent request. In palliative care the intrinsic value is based upon the acknowledgement of a person as an autonomous and unique social individual. The goal is relief and prevention of suffering and improvement of quality of life. It demands a patient-centered approach contingent upon individual and family needs. Now we also need to acknowledge the fact that 'Requests for euthanasia and PAS require respect and careful attention, together with open and sensitive communication in the clinical setting'. But in the case of PAS or euthanasia there is an inherent danger of misjudging the patient's preferences. In a survey of terminally ill patients, 10.6% considered seriously PAS or euthanasia but in a follow up survey after 6 months 50.7% of such patients had changed their minds. Ultimately only 5.6% of the deceased patients had asked the physician for PAS or euthanasia. In clinical practice it has often been observed that patients show ambivalence while there is a wish for hastened death, there is also a will to live and these exist often in parallel or fluctuates. Palliative care staff should be aware of such conditions of patients. They should acknowledge these requests and enter into open dialogue with patients, caregivers, staff members and family members. Although it should be remembered that requests for PAS and euthanasia can be altered by arranging proper provisions for palliative care. Suffering from physical symptoms can be removed; psychosocial and spiritual care can be given. Sedation should be given to patients with intolerable distress caused by physical symptoms given there is an acceptable time frame and no adverse effects. CDS can also be applied but only if the patient is in the terminal phase. Palliative sedation in this stage can also be applied for severe anxiety, demoralization, refractory depression or existential distress. Whatever is the case the decision to start palliative sedation should be a team decision and must be subjected to supervision. While it is quite clear that by definition palliative care can never be compatible with euthanasia Bernheim et al. suggests that the case of Belgium indicates there is a synergistic effect between the two. It is described by a model called the 'integral palliative care' in which euthanasia is being considered just as another option

at the end of the palliative care pathway. It can be said while palliative care and euthanasia are two distinct matters they can be considered together when caring for one and the same patient. At the end there is need for recognition of the fact that even if palliative care of the highest level is delivered it will not prevent patients from requesting hastened death, including PAS and euthanasia. As palliative care professionals it is their responsibility to acknowledge and understand the implicit or explicit requests of the patient. Then they should explore these requests and try their best to address the sufferings that underlie these requests (22).

3. Conclusion

Palliative care has come a long way since its days of infancy; the proven efficacy of the care in relieving patients with terminal conditions makes it indispensable to modern medical treatment. One might get the impression that palliative care is lacking in protocols, but it is untrue, the medical journals and textbooks have clear guidelines. The American Academy of Hospice and Palliative Medicine (AAHPM) has clear position statement on palliative sedation including a definition. We know that NHPCO also offers a statement on palliative sedation. Both the WHO and EAPC has clear definitions for palliative care. We have come a long way in terms of research and surveys done on palliative care. But still there are inconsistencies in protocols and guidelines for palliative sedation. To remove such inconsistencies proper research with empirical data needs to be done on patients who undergo palliative sedation. We also need to understand the perspective of the patient, the nature of pain he/she is enduring and also how the idea of imminent death affects the patient. While discussing sedation in patients in terminal stages of their disease, we have faced many ethical dilemmas regarding the morality of it all. Because of the sensitive nature of the subject it is more important to have concrete protocols about conditions especially where the death of the patient is imminent. It is also very important to be very objective and open minded and inform the patient about all the options available. After all the first and foremost duty should be service to the patient. At the end of life the role of palliative care is mainly to relieve suffering of patients and families by providing comprehensive assessment and treatment of the patient's physical, spiritual and psychosocial symptoms. As death approaches naturally aggressive palliation will be provided since the symptom of a patient might worsen. Comfort measures will intensify for the patient and the dying patient's family will be provided with increased support. After the death of the patient has occurred palliative care focuses on bereavement and provides support to the patient's family. Measures should be taken so that the patients' family is able to cope with their loss. We also have to be aware of the fact that with the increasingly ageing population, people living with comorbidities of varying severities, and rising instances of cancer along with the fact that cancer afflicted are living longer because of advances done in the field, and also the recognition of the fact that supportive and symptomatic care is needed in patients suffering from pathophysiological diseases there is going to be an explosion in the need for 'palliative care'. It is therefore quite important that proper importance is given to

palliative care in medical education, healthcare system and society at large. It is absolutely vital that proper resources are allocated to train the manpower needed to deliver the best quality of palliative care. For this to happen it is important to ensure necessary political commitment. Parliamentary sessions dedicated to palliative care, reformation of opioid policies accompanied by healthy debate on these topics by lawyers, physicians and the citizenry. Only then palliative care can reach the benchmark demanded by patients and future needs. In the broadest terms 'care of others' which is integral to human nature is referred to in palliative care. The industrialization of modern medical services has made it lose touch with the innate human aspect of it, but it also has lent efficiency to the system. It is important while moving forward to hold onto the advances that have been made and rejuvenate the more human aspect of care, so as a society we are able to deliver the most kind care that the patients deserve.

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