Palliative Pharmacologic Sedation for Terminally Ill Adults

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Review Question

What is the evidence for the benefit of palliative pharmacologic sedation on quality of life, survival, and specific refractory symptoms in terminally ill adults during their last few days of life?

Type of Review

The Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 11), MEDLINE (1946 to November 2014), and EMBASE (1974 to December 2014) were searched using search terms representing the sedative drug names and classes, disease stage, and study designs. Randomized, controlled trials (RCTs), quasi-RCTs, non-RCTs, and observational studies (e.g., before-and-after, interrupted-time-series) with quantitative outcomes were included. Studies with only qualitative outcomes or with no comparison (i.e., no control group or no within-group comparison [e.g., single-arm case series]) were excluded.

Relevance for Nursing

Terminally ill people experience a variety of symptoms in the last hours and days of life, including delirium, agitation, anxiety, terminal restlessness, dyspnea, pain, vomiting, and psychological and physical distress. In the terminal phase of life, these symptoms may become refractory and unable to be controlled by supportive and palliative therapies specifically targeted to these symptoms. Palliative sedation therapy is one potential solution for providing relief from these refractory symptoms. Sedation in terminally ill patients is intended to provide relief from refractory symptoms that are not controlled by other methods. Sedative drugs, such as benzodiazepines, are titrated to achieve the desired level of sedation; the level of sedation can be easily maintained, and the effect is reversible. Therefore, nurses need to understand what evidence exists supporting the benefits of palliative pharmacologic sedation in terms of quality of life, survival, and management of refractory symptoms of terminally ill adults in the final hours or days of life.

Characteristics of the Evidence

International databases were searched in October 2012 and again in December 2014 for studies of terminally ill adults who required sedation to control symptoms. The searches resulted in 6,685 citations to screen. After title and abstract screening, 70 full-text articles were reviewed, resulting in 14 included studies of about 4,000 people. The studies compared sedation versus nonsedation. Most patients in the studies (95%) had cancer. The studies took place in hospices, palliative care units, hospitals, and the home. No randomized or quasi-randomized trials were found, and none are likely to be done. Therefore, the best-quality evidence came from well-designed observational studies. Only one study in this review attempted to reduce selection bias between the groups by matching groups on baseline characteristics. Even if this had been done, the groups likely would have differed significantly in their level of symptom control, with people with more severe symptoms more likely to receive palliative sedation. Therefore, even matching of controls cannot adjust for this confounder. Adjusting for this confounder (and others) would be possible statistically but was not done in any of the reported studies. Because of this, the quality of the evidence was poor.

Summary of Key Evidence

No studies reported on the primary outcome of this review (i.e., quality of life or well-being). Four studies compared the sedated and nonsedated groups for control of symptoms and showed that, despite sedation with the intent to control symptoms, delirium and dyspnea were still troublesome symptoms in these patients in the last few days of life and were significantly worse in the sedated group. Control of other symptoms appeared to be similar in sedated and nonsedated groups. All studies except one compared survival time in the sedated and nonsedated groups and concluded that no statistically significant difference existed between the groups. This is important because extensive discussion has taken place in the literature about whether palliative sedation may shorten life, leading to uncertainty.
by some physicians and nurses about whether to use this treatment for fear of the perception that they were performing a form of euthanasia. The use of time from admission to death in comparative groups may be a weak measure of any potential effect of palliative sedation on shortening life. However, determining what the comparison would be in the group that did not receive sedation is difficult, and time from admission to death may be the only feasible comparative measure. Although meta-analyses were unable to be done for this outcome, and the confidence intervals around the point estimates in individual studies were wide, consistency in this result was seen in all of the studies, with 12 of the 13 studies having a longer survival time in the sedated group.

**Best Practice Recommendations**

Although no evidence exists from RCTs and evidence from observational studies is limited about the efficacy of palliative sedation in terms of a person’s quality of life or symptom control compared with non-sedated people, evidence showed that palliative sedation does not hasten death. This has been a concern of physicians, nurses, and families in prescribing the treatment. However, the evidence comes from low-quality studies and should be interpreted with caution.

**Research Recommendations**

Studies that specifically measure the efficacy of sedation in terms of a patient’s well-being and control of symptoms, compared with non-sedated patients, are required. This therapy is widely used, in continuous deep sedation and intermittent forms, but evidence is lacking on the success of controlling symptoms adequately. Adverse events reporting also needs to be improved to quantify the potential harms of treatment. Description of the depth of sedation, timing, and length of sedation was poorly reported in many studies, and the method of measuring and describing this was inconsistent between studies.

Additional studies should attempt to use control groups that are close in prognostic factors to the intervention group to make the groups as alike as possible, except for the presence of sedation. Alternatively, statistical methods to adjust for differences between intervention and control groups should be used.

**Reference**


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