J Palliat Med. 1998 Winter;1(4):315-28.
The double effect of pain medication: separating myth from reality.

Fohr SA

The principle of double effect is used to justify the administration of medication to relieve pain even though it may lead to the unintended, although foreseen, consequence of hastening death by causing respiratory depression. Although a review of the medical literature reveals that the risk of respiratory depression from opioid analgesic is more myth than fact and that there is little evidence that the use of medication to control pain hastens death, the belief in the double effect of pain medication remains widespread. Applying the principle of double effect to end-of-life issues perpetuates this myth and results in the undertreatment of physical suffering at the end of life. The concept of double effect of opioids also has been used in support of legalization of physician-assisted suicide and euthanasia.

The Lancet Oncology. 2003;4(5):312-318
The use of opioids and sedatives at the end of life

Nigel Sykes, Andrew Thorns

Opioids and sedative drugs are commonly used to control symptoms in patients with advanced cancer. However, it is often assumed that the use of these drugs inevitably results in shortening of life. Ethically, this outcome is excused by reference to the doctrine of double effect. In this review, we assess the evidence for patterns of use of opioids and sedatives in palliative care and examine whether the doctrine of double effect is needed to justify their use. We conclude that patients are more likely to receive higher doses of both opioids and sedatives as they get closer to death. However, there is no evidence that initiation of treatment, or increases in dose of opioids or sedatives, is associated with precipitation of death. Thus, we conclude that the doctrine of double effect is not essential for justification of the use of these drugs, and may act as a deterrent to the provision of good symptom control.

Annals of Oncology, Volume 20, Issue 7, 1 July 2009, Pages 1163-1169, Palliative sedation therapy does not hasten death: results from a prospective multicenter study

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Palliative sedation therapy (PST) is indicated for and used to control refractory symptoms in cancer patients undergoing palliative care. We aimed to evaluate whether PST has a detrimental effect on survival in terminally ill patients.

This multicenter, observational, prospective, nonrandomized population-based study evaluated overall survival in two cohorts of hospice patients, one submitted to palliative sedation (A) and the other managed as per routine hospice practice (B). Cohorts were matched for age class, gender, reason for hospice admission, and Karnofsky performance status.

Of the 518 patients enrolled, 267 formed cohort A and 251 cohort B. In total, 25.1% of patients admitted to the participating hospices received PST. Mean and median duration of sedation was 4 (standard deviation 6.0) and 2 days (range 0-43), respectively. Median survival of arm A was 12 days [90% confidence interval (CI) 10-14], while that of arm B was 9 days (90% CI 8-10) (log rank = 0.95, P = 0.330) (unadjusted hazard ratio = 0.92, 90% CI 0.80-1.06).

PST does not shorten life when used to relieve refractory symptoms and does not need the doctrine of double effect to justify its use from an ethical point of view.

N Engl J Med 2010; 363:733-742 Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer

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Despite the fact that fewer patients in the early palliative care group than in the standard care group received aggressive end-of-life care (33% vs. 54%, P=0.05), median survival was longer among patients receiving early palliative care (11.6 months vs. 8.9 months, P=0.02). As compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life but longer survival.