Making Opioids Safer at the End-of-Life

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Use of opioids at the end-of-life, particularly when care is being withdrawn, can tread a fine ethical line

A known effect of opioid administration is decreased respiratory drive and minute ventilation (the amount of gas inhaled into the lungs per minute) as well as increased sedation. This presents a challenge at the end-of-life where providing patient comfort and relieving suffering may be at odds with preserving adequate ventilation.

A patient story

Esther (not her real name) is a 70-year-old Kenyan woman who had no history of having received any preventative (primary) care. She presented to a missionary hospital very ill from *Plasmodium falciparum* malaria which had progressed to end-stage renal disease (ESRD). Initially, the patient's family did not want dialysis as services were not available at the missionary hospital and it necessitated transfer two hours away to a tertiary care center in Nairobi.

Several days later, the family wished to pursue dialysis, but the ESRD had progressed to the point where dialysis would have been ineffective, leaving kidney transplantation as the only, but not possible, option. Ventilator-associated pneumonia (VAP) also developed during this time period.

Consequently, it was suggested that care be withdrawn and the patient made comfortable. End-of-life care typically includes terminal extubation (withdrawal of the ventilator tube from the lungs), withdrawal of care (with or without extubation), "comfort measures only" care, and management of acute/chronic pain.

In Esther's case, intravenous fentanyl was chosen for use during withdrawal of care. Fentanyl is a *mu*-opioid receptor agonist that exerts both analgesic and sedative effects. It has advantages over other opioid agents including its rapid onset and short clinical duration of action in small doses, relative hemodynamic stability and minimal parent compound accumulation in the face of renal impairment.

The rule of double effect

Our Kenyan patient is a classic case of the application of the Rule of Double Effect (or RDE). According to a paper by Judith Kennedy Schwarz PhD, RN in the Journal of Hospice and Palliative Nursing (sign-in may be required):

> *"The rule of double effect has its roots within the Roman Catholic tradition of moral theology. It has a long history of use by bioethicists and philosophers as a means to resolve a particular type of ethical conflict in clinical cases. These cases involve a*

> *clinician who must decide whether to act when the proposed action has two known outcomes— – one that is desired, desirable, and the intended effect of the action; and another that is neither desired nor intended, although it may be foreseen."*

RDE is often used to justify the administration of opioids to relieve pain even though it may lead to the unintended, although foreseen, consequence of hastening death by causing respiratory compromise and depression.

According to the Catholic Church, RDE is morally justified if the following four conditions are met:

1. The nature of the act. The act itself must not be intrinsically wrong and not be in a category that is absolutely prohibited (e.g. killing of innocent persons), when considered independently of its consequences.
2. The agent's intention. The agent must intend only the good and not the bad effect; although the bad effect, such as respiratory depression following administration of opioids, may be foreseen but not intended.
3. The distinction between means and effects. The bad effect, such as death, must not be the means used to bring about the good effect, such as the relief of suffering.
4. Proportionality between the good effect and the bad effect. The good results must outweigh the bad effect—the bad effect can be permitted only when there is a proportionally grave reason for permitting the foreseen bad effect.

The application of these conditions can be seen in the following examples:

- Morally Not Justified. Suppose that a terminally ill patient is experiencing intolerable pain and suffering. If the patient's nurse knowingly and intentionally administers a dose of opioids and kills the patient in order to relieve the patient's pain and suffering, the patient's death is intentional and not justified under the Catholic Church interpretation of RDE.
- Morally Justified. However, if the nurse administers the same dose of opioids in order to relieve the patient's pain and suffering, and this results unintentionally with the patient suffering opioid-induced respiratory depression and eventual death, then the nurse's acts are morally justified under the Catholic Church interpretation of RDE.

In the instance of using opioids to manage distress associated with the withdrawal of care, some have suggested that 'suffering' should be anticipated, and aggressively treated, despite concerns about respiratory distress.

Patient monitoring after opioids

With Esther, as well as others receiving opioids in the hospital for pain management, it is essential to monitor respiratory status. Assessment and management of pulmonary mechanics is a multifaceted, complex task often complicated by the lack of an accurate and continuous respiratory monitoring system to guide clinical decision-making. This is especially true when using opioids to manage pain and increase comfort at the end-of-life.

Previously, there has been no accurate and reliable way to quantitatively measure apnea (temporary cessation of breathing), dyspnea (labored breathing), respiratory distress, and changes in ventilation at the end-of-life. Dyspnea is a qualitative subjective experience that can only be perceived by the person experiencing it; respiratory distress is the observable corollary to dyspnea. Dyspnea and respiratory distress are expected during terminal extubation and should be a primary focus of care.

Several methods are currently used in an attempt to monitor respiratory distress and adequacy of ventilation during end-of-life, such as, pulse-oximetry, subjective clinical assessment, end-tidal CO_2($EtCO_2$), monitoring bi-spectral (BIS) index of the EEG, the Richmond Agitation Sedation Scale (RASS), and the COMFORT scale.

All of these are grossly inadequate and do not present a true picture of ventilatory status. $EtCO_2$ monitoring is less reliable in the non-intubated patient. Pulse-oximetry has been described as inadequate because it is a time-lagging indicator of respiratory status. It can become even less useful in the presence of supplemental oxygen. Neither pulse oximetry nor capnography provide a real-time quantitative measurement of true ventilatory status and pulmonary mechanics in the non-intubated patient.

ExSpiron non-invasive respiratory monitor (Photo courtesy of Dr. Schlesinger)

In this case, clinicians were able to monitor Esther's respiratory status after extubation by using a non-invasive respiratory volume monitor (RVM), such as the one shown in the photo. In addition, they used pulse oximetry and watched for changes on the physical exam.

The RVM allowed us to ascertain the minute ventilation of the patient, calculated by respiratory rate (breaths per minute) multiplied by the tidal volume (amount of air measured in milliliters during inspiration and expiration).

By monitoring Esther's minute ventilation, we were able to rapidly titrate to 40% of predicted minute ventilation (based on ideal body weight), below which minute ventilation values would be considered "unsafe." After extubation, fentanyl was given in 25-µg aliquots until the minute ventilation reached the 40 percent mark. The minute ventilation reached the 40 percent threshold after about 5 minutes and the fentanyl administration was stopped. The patient died 15 minutes later.

Patient comfort without committing euthanasia was achieved, and the family was at peace with the process. Importantly, the ICU clinicians and nurses were also at peace with the process.

ABOUT THE AUTHOR

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