The agony of agonal respiration: is the last gasp necessary?

R M Perkin, D B Resnik

Gasing respiration in the dying patient is the last respiratory pattern prior to terminal apnoea. The duration of the gasing respiration phase varies; it may be as brief as one or two breaths to a prolonged period of gasing lasting minutes or even hours. Gasing respiration is very abnormal, easy to recognise and distinguish from other respiratory patterns and, in the dying patient who has elected not to be resuscitated, will always result in terminal apnoea.

Gasing respiration is also referred to as agonal respiration and the name is appropriate because the gasing breaths appear uncomfortable and raise concern that the patient is suffering and in agony. Enough uncertainty exists about the influence of gasing respiration on patient wellbeing, that it is appropriate to assume that the gasing breaths are burdensome to patients. Therefore, gasing respiration at the end of life should be treated.

We propose that there is an ethical basis, in rare circumstances, for the use of neuromuscular blockade to suppress prolonged episodes of agonal respiration in the well-sedated patient in order to allow a peaceful and comfortable death.

A 14-year-old female with neuromuscular disease was hospitalised with acute respiratory insufficiency which complicated an episode of pneumonia. On admission, she was obtunded, and at her parents' request, she was intubated and mechanically ventilated. Three weeks after admission, the teenager was awake, alert, and able to communicate, but ventilator dependent. Although her parents wanted to enroll her in a chronic home mechanical ventilation programme, the patient repeatedly and consistently expressed a desire not to be ventilated. Numerous sessions with different individuals established quite clearly that total dependence on a machine was unacceptable to the patient. After long debate, her requests were respected and ventilator support was removed. She died the same day surrounded by friends and family. Prior to terminal apnoea, she experienced a period of gasing respiration that lasted 13 minutes. This respiratory pattern persisted in spite of increasing doses of morphine. A meeting was held with her parents several months later. During this meeting the mother stated that she wished she that the meeting was held with her parents several months later. During this meeting the mother stated that she wished she that the meeting was held with her parents several months later.

Could these scenarios have been avoided? Yes. In these cases, the administration of a neuromuscular blocking agent would have stopped the gasing response and would have allowed these patients to die in peace. But would it be ethically (and perhaps illegal) to do this? In this paper, we will argue that there is an ethical basis, in some rare circumstances, for the use of neuromuscular blocking agents to suppress the gasing response in order to allow patients to die more peacefully and comfortably, when they or their surrogate decision makers have requested palliative care. The last gags of agonal respiration are not necessary and may be avoided. Although many readers may object that suppression of gasing respiration is equivalent to active euthanasia, we shall argue that it can be justified much in the same way that one can justify other medical decisions that may hasten death, such as terminal sedation. While the term, terminal sedation, is being eschewed because of its ambiguous connotations, the indication for fulfilling a patient's expressed wish of being relieved of the perceived burden of consciousness in the presence of intractable suffering is ethically acceptable. A preferred term, total sedation, suggests complete relief of suffering. The provision of total sedation as an ethically acceptable intervention is based on historical imperatives to relieve suffering, especially in the face of imminent death. The goal of administration of a neuromuscular blocking agent is to alleviate the patient's suffering and to provide comfort to the dying patient. Hastening of the patient's death is an unintended, though foreseeable, consequence of suppression of agonal respiration.

END OF LIFE DECISIONS AND PALLIATIVE CARE

Few people would dispute the idea that a dying patient or their legitimate surrogate decision maker should be able to choose treatments that minimise pain, discomfort, and suffering which accompany terminal illnesses and the dying process. A medical paradigm known as palliative care provides a morally sound approach to end of life decisions. Palliative medicine, as opposed to curative medicine, emphasises pain and symptom management and the alleviation of suffering. This approach seeks neither to hasten death nor prolong life; the main goal is...
to take steps to alleviate pain, discomfort, and suffering.\textsuperscript{13} When the decision has been made to adopt this paradigm, it is often appropriate to withdraw or withhold medical interventions that exacerbate or prolong pain and suffering, such as artificial nutrition and hydration, mechanical support of ventilation, or antibiotic therapy.\textsuperscript{7, 17}

Good care of the dying involves administration of medications such as analgesics, sedatives, and anti-emetics, in order to minimize the suffering associated with pain, dyspnoea, delirium, convulsions, and other terminal complications encountered in the dying patient.\textsuperscript{6, 7} For such patients it is ethically appropriate gradually to increase the dosage of narcotics and sedatives to relieve pain and other symptoms, even to dosages that might also shorten the patient’s life.\textsuperscript{8, 9}

**CAUSING OR HASTENING DEATH**

So far much of what we have said is fairly non-controversial, but controversies begin to arise when one considers whether it is acceptable to implement treatment plans that cause or hasten death. What do we mean by “cause or hasten” death? The difference between causing death and merely hastening it is a matter of degree. A person who smokes two packs a day of cigarettes and drinks a fifth of whisky every night is likely to shorten her life by years, and we might say that the person “is hastening” her own death. If she stops smoking and drinking, we would say that she is attempting to “prolong” her life. If, on the other hand, that same person takes an overdose of alcohol and sedatives, we would say that the person caused her own death.

Does it make much of a difference, from a moral point of view, whether one causes or merely hastens death? Common sense seems to dictate that there should be some difference between causing and hastening death: there is a difference between taking an overdose of drugs and alcohol and having a lifestyle that may lead to an early demise. The first case takes away life altogether; the second may merely take away years of life. There are also, however, many borderline cases where “hastening death” is not very different from “causing death”. For example, consider the man who poisons his aging mother by giving her small doses of poison in her food over a six-month period until she dies. Is this better than giving her one massive dose of poison that leads to immediate death? We think not. Indeed, death by slow poisoning may be worse than death by quick poisoning because it causes more pain and suffering. Thus, although people often speak of a difference between “hastening death” and “causing death” this difference is, at best, a matter of degree, not a matter of kind. Many procedures that involve the refusal of treatment, such as withdrawing a patient from a ventilator or stopping artificial hydration or nutrition, cause or hasten death. Clinicians and ethicists have few moral reservations about these procedures because they merely allow the patient to die “naturally”. One might describe these cases as “letting die” but not as “killing”.\textsuperscript{11} If a patient with terminal lung cancer dies after being weaned from a ventilator, many would argue that the patient’s disease caused his death, not the physician. On the other hand, if the patient is not on life support but is suffering greatly and the physician assists the patient in dying by administering a lethal dose of a narcotic or a neuromuscular blocking agent, then we would say that the physician caused the patient’s death. Most people would describe this kind of assistance in dying as “euthanasia”. The physician might also play a key role in causing the patient’s death if the physician helps the patient to kill himself by providing the patient with the means necessary to bring about death. Most people would describe this type of aid in dying as “physician assisted suicide”. Those who believe that doctors should not kill their patients object to euthanasia and physician assisted suicide but may endorse withholding/withdrawing/refusing medical treatment.\textsuperscript{12}

A person who “hastens” death does play a role in causing the death but that is not the same thing as saying the person is the cause of the death. For any death there will be many different causal factors but we assign some more weight than others for medical, legal, or moral reasons. When we ask: “What is the cause of death?” we are trying to assign medical, legal, or moral responsibility for the death. A person who hastens death may or may not be medically, legally, or morally responsible for the death, depending on the circumstances. For example, if a man is terminally ill with cancer and his wife poisons him with arsenic over a period of days, she has hastened his death and is properly the cause of the death. She could be properly charged with murder. But a person who withholds food and fluids from a man with terminal cancer (upon his request) certainly also hastens the man’s death but that person is not the cause of the death and probably should not be charged with murder.

**PLANNING AND DELIBERATION**

The physician develops and implements a plan for bringing about the death of the patient. For example, if a physician carefully determined the dosage of morphine necessary to cause death, deliberated about her actions, and administered that dose and the patient died, we would say that the physician intended to bring about the death of the patient. If the physician was satisfied that the patient died naturally, that the patient died as a result of a heart attack, or that the patient died as a result of a stroke, we would say that the physician intended to bring about the death of the patient. If the physician was satisfied that the patient died as a result of the physician’s actions, we would say that the physician intended to bring about the death of the patient.

**REGRET AND REMEDY**

If, for some reason, the patient does not die, the physician has some regret and takes some steps to remedy the situation. If the physician allows the patient to breathe normally after withdrawal of support, then he is not intending to bring about the patient’s death. If the physician is disappointed that the patient does not die after withdrawal of life support and he
takes additional steps to bring about death, such as smothering the patient, then he has clearly intended death. In physician assisted suicide and euthanasia, physicians have some regret if the procedure fails and may take some steps to remedy the situation if it does. For example, a physician may increase the dose of a lethal medication if the initial dose fails to bring about the patient’s death. This kind of action is more appropriately described as “killing” because death is more clearly intended.

Thus, although it is often very difficult to understand human actions and intentions, especially in matters of life and death, we believe that some consideration of intentions is required in order to determine the moral status of end of life decisions. “Killing” implies an intention to cause or hasten death; “letting die” implies no such intention. In both cases, the physician may want or foresee the death of the patient, but there are crucial differences between wanting, foreseeing, and intending.

**TERMINAL SEDATION AND DOUBLE-EFFECT DEATHS**

The waters become a bit murkier when one considers active medical interventions, such as administering opioids or sedatives, which are designed to relieve pain and suffering but may have the foreseeable effect of hastening death. Many advocates for better end of life care argue that “terminal” sedation may be an appropriate way of alleviating pain and suffering in terminally ill patients with intractable pain or extreme physical distress. Under a typical protocol, the physician carefully titrates sedatives and analgesics to the level necessary to achieve comfort and pain and symptom control. Very often patients who are terminally sedated become unconscious and never regain consciousness.

Is terminal sedation a type of euthanasia? According to our analysis, terminal sedation is a type of euthanasia only if the physicians intend to cause or hasten death. How could we tell if a physician intended to bring about death through terminal sedation? This is not an easy question to answer, and many would argue that intentions can be very slippery in these cases. If we follow our earlier analysis, then terminal sedation would be called intentional killing only when: 1) physicians have some regret when the patient is not dying soon enough and they take steps, such as increasing dosages of sedatives and opioids, in the absence of signs or symptoms of suffering, in order to bring about death; 2) physicians plan for the death of their patients and take steps, such as increasing dosages of sedatives and opioids, in order to bring about the patient’s death. If the physician is careful and provides only enough medication to make the patient comfortable and alleviate the patient’s pain and suffering, then we would say that this type of terminal sedation is not euthanasia or killing.

Does terminal sedation hasten death? Although the evidence suggests that terminal sedation does not always hasten death—many patients linger far longer than anyone expects—terminal sedation does hasten death in many cases. Thus, the hastening of death is a foreseeable consequence (or risk) of terminal sedation. If we assume that death is a type of harm, then how can it be morally acceptable to perform an action that one knows may produce a harmful effect? To deal with this question in end of life decisions, many writers have appealed to the rule of double effect. This moral rule has wide application, but has played a particularly important role in the care of the dying, allowing those who are morally opposed to euthanasia and assisted suicide to provide adequate pain relief without violating traditional medical morality or their consciences.

Although variously formulated, the role of double effect specifies that an action with two possible effects, one good (intended) and one bad (harmful), is morally permitted provided that:

1. The goal of the action (or intended effect) is itself good.
2. The intended effect is not achieved by means of the harmful effect.
3. The harmful effect is not intended, only permitted.
4. There is no other way of producing the good (intended) effect.
5. There is a proportionately good reason for allowing the harmful effect.

Terminal sedation can meet all of these conditions, since the goal of terminal sedation is to relieve pain and suffering, which is itself a good goal; the relief of pain and suffering is not achieved by bringing about death (unlike euthanasia or physician assisted suicide); the harmful effect (death) is not intended; there is no other way to relieve pain and suffering other than increasing doses of opioids and sedatives; and relieving intractable pain and suffering in a terminally ill patient is a proportionally good reason for hastening the death of the patient. Although the principle of double effect may free physicians from moral culpability, it does not completely liberate them from legal responsibility. A prosecutor could still attempt to charge a physician with homicide or criminal negligence when death occurs. However, since there is a solid legal basis for palliative care, which aims to relieve suffering, assessing the physician’s intention would still play a key role in any legal action resulting from a double-effect death.

One of the key criticisms of the principle of double effect is that it relies on some understanding of the distinction between intended and unintended effects, since it applies only when death is not intended. Cases where physicians intend to bring about death are best described as “euthanasia” or “assisted suicide” but not “double-effect” death. As we stressed earlier, we believe there is a moral basis for distinguishing between intended and unintended (though perhaps foreseeable) effects. Indeed, even withdrawal of care at the end of life would be morally questionable without this distinction, because death is often a foreseeable and unintended consequence of withdrawal of artificial nutrition, hydration, or ventilation.

**AGONAL RESPIRATION AND SUFFERING**

We have now laid the moral framework for a position and are prepared to show why we think that suppression of agonal respiration may be permitted in some circumstances. To make our point, we need briefly to describe the gasping response. Assessment of breathing patterns can be complicated in dying patients. Severe dyspnoea, especially at the end of life, is extremely difficult to control. Dyspnoea is a subjective experience defined as an uncomfortable awareness of breathing, breathlessness, or distressing shortness of breath which may be associated with extensive secretions, cough, chest pain, fatigue, or air hunger. This symptom can cause the patient and family to be very fearful; dyspnoea conveys the image of suffering. Numerous pharmacological and non-pharmacological interventions can be initiated concurrently to minimise end of life dyspnoea.

Beyond the subjective symptom of dyspnoea exists the respiratory pattern characterised by gasping. Gasping is a brainstem reflex; it is the last respiratory pattern prior to terminal apnoea. Gasping is also referred to as agonal respiration and the name is appropriate because the gasping respirations appear uncomfortable, causing concern that the patient is dyspnoeic and in agony. There is no question that these agonal breaths are distressing for both family and medical staff to observe (see Case discussions). Many parents report that watching their children gasp at the end of life is among the worst experiences of their children’s illness. Many parents can graphically describe the horror they felt when their child appeared to be struggling to breathe at the end of life; they perceived the child to be distressed.
Gasing, or autoressuscitation, is a well-studied physiologic alevent. In response to asphyxia, there is an initial period of apnoea and hyperpnoea, then primary apnoea lasting for 5–15 minutes, or minutes, then a gasping stage. The gasps become progressively weaker and finally result in terminal apnoea unless external support is provided. Gasing respirations are easily recognised as the presence of a rapid inspiratory rise accompanied by a retarded expiratory phase preceding and followed by a cessation of breathing movements. Gasping is a strong indicator of hypoxaemia. In various animal species gasing does not occur unless PaO2 has fallen to <5–15 mmHg and is elicited only by hypoxaemia and not by hypercapnia or acidosis. Gasping has been identified as a very powerful and distressing mechanism, one that is unlikely to be experienced by sedatives. In addition, gasing respirations in the imminently dying patient will not lead to long term survival unless external intervention is also provided, however, the patient, or their surrogate has requested that such external intervention not be used.

Patients who are gasing have profound hypoxaemia, which most likely renders them unconscious. Thus, one might argue that patients who are gasing do not suffer. We agree that given our current knowledge of pain, suffering, and brain function, patients who are gasing are probably not experiencing pain or suffering. We cannot be certain, however, that these patients are not in pain or suffering. It is possible that these patients still have enough brain function to have some awareness of the discomfort and pain of the gasing response. After all, these patients are not yet brain dead; if they were there would be no gasing response. These patients have some level of brain activity and it is at least possible that they can feel pain and suffer.

Given this lack of certainty, we believe that the morally most defensible position is to err on the side of relieving possible pain and suffering instead of erring on the side of not relieving pain and suffering. There is a great deal we do not know about human sensation, awareness and, nociception, the noxious sensation of pain as such, without regard to its emotional significance. For many years, paediatricians, and neonatologists believed that newborns could not feel any pain and they frequently conducted surgical procedures, such as circumcision, without anaesthesia. In the past scientists took a similar approach to the pain and suffering of animals, but contemporary animal care and use regulations require researchers to do their best to minimise pain, suffering, and distress of animals used in research. At one time physicians did not believe that patients could feel pain during general anaesthesia, but there are now some well-known cases of patients who were awake and felt a great deal of pain during surgery but could not move their bodies or make their suffering known. Finally, failure properly to manage pain—to assess, treat, and manage it—is professional negligence.

One way of justifying our approach to clinical uncertainty regarding pain, discomfort, and suffering is to appeal to a principle of decision theory known as the maximin rule. According to this rule, when one is faced with a decision where the states of the world are uncertain, then one should choose the option that avoids the worst possible outcome. For example, if your choices are “wear a seatbelt” and “don’t wear a seatbelt” and the states of the world are “get in a wreck” and “don’t get in a wreck” you would be advised to wear a seatbelt because 1) getting in a wreck is uncertain, 2) and the worst outcome would be getting in a wreck and not wearing a seatbelt. If we look at pain, and suffering in the gasing patient in the same way, our choices are “provide adequate relief of pain and discomfort” or “don’t provide adequate relief of pain and discomfort”. The states of the world are “the patient can feel pain and discomfort” or “the patient cannot feel pain or discomfort”. Clearly, the worst outcome is one where the patient can feel pain and discomfort but we do not provide adequate relief of pain, and suffering. Moreover, given the mounting evidence about knowledge of the pain, discomfort, distress of patients related to procedures, we have good reasons to believe the patient will suffer and distress in gasing respiration would be very great if the patient has some awareness of these symptoms. Considerable evidence exists which suggests that in many patients, dyspnoea is related to respiratory muscle contraction.

THE ETHICAL BASIS FOR STOPPING AGONAL RESPIRATION

We are now in a position to defend the main thesis of our paper. Since we believe the physicians should err on the side of alleviating pain and suffering, we have good reasons to believe that patients who are gasing do not suffer. We agree that given our current knowledge of pain, suffering, and brain function, patients who are gasing are probably not experiencing pain or suffering. We cannot be certain, however, that these patients are not in pain or suffering. It is possible that these patients still have enough brain function to have some awareness of the discomfort and pain of the gasing response. After all, these patients are not yet brain dead; if they were there would be no gasing response. These patients have some level of brain activity and it is at least possible that they can feel pain and suffer.

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death. Without this distinction, the doctrine of double effect collapses, since there are many bad consequences that people may foresee but not intend. Also, even withdrawal of treatment at the end of life becomes morally problematic without a distinction between “intending death” and “ foreseeing death”. From a legal point of view, a person can be said to intend an outcome, when they take actions to bring it about and desire that it occur, or when the outcome is the natural and probable result of their conduct. The law makes no distinction between physician X who gives a dying patient an overdose of morphine in order to stop their suffering, and physician Y who gives an overdose of morphine in order to win a bet. Both physicians can be charged with murder because they have the required intent to kill. But it is important, from a moral point of view, to distinguish between physician X and physician Y because foreseeing an outcome is not the same as intending it. Although the physician who uses muscle relaxants to stop the gasping response can foresee that the patient will die as a result, this is not his intent any more than a dentist who performs dental work intends that the patient will feel pain. Pain is a natural, probable, and foreseeable result of dental work but the dentist does not deliberately inflict pain or take steps to ensure that his patients feel pain. Indeed, dentists administer analgesics in order to minimise pain. It makes no more sense to say that a dentist “intends that his patients feel pain” than it makes sense to say that “a physician who uses muscle relaxants to stop the gasping response of a terminal patient intends that the patient die”. We realise that the boundary between “intent” and “ foreseeability” can be both murky and contentious, but the other belief that it is a morally important distinction.

The use of neuromuscular blocking drugs immediately before ventilator withdrawal has been suggested to prevent any outward signs of discomfort that might disturb the patient’s family. It is appropriately argued that such an approach cannot be justified. If a patient was given a neuromuscular blocking agent before ventilator withdrawal, she would not be given a chance to breathe on her own. In this circumstance, one could say this would be evidence of planning the patient’s death.

In the cases we are describing, however, accepted palliative care is provided to relieve some of the symptoms of dyspnoea but to still allow the patient’s normal breathing pattern to resume. The decision to administer neuromuscular blocking agents would be made only after the patient were no longer breathing normally and had entered the gasping phase.

Finally, it has been argued that the removal of assisted ventilation in the presence of prolonged or irreversible neuromuscular blockade may be justified based on the futility or disproportionate burden of continued treatment, and does not necessarily imply the clinician’s intent to hasten death. We argue in similar fashion; gasping respirations are absolutely futile and possibly burdensome to the patient. Whenever, on the balance of probabilities, they are judged to be a cause of suffering, gasping respirations at the end of life should be treated even if as a result the dying process is shortened.

**OBSTRUCTIONS**

Before closing we would like to consider some certain objections to our view.

**Objection 1:** Patients who are gasping are not in pain nor are they suffering; there is need to provide any palliative medications at this point. They are almost dead and are no longer in any distress.

**Reply:** We concur that there is strong empirical support for this position. If science can one day prove that patients who are gasping have no awareness at all, then we would change our views about administering paralytic agents. But there is still a great deal we do not know about human sensation, awareness, and nociception. Moreover, no patient has ever survived the gasping phase and told us what it feels like. Thus, we cannot be certain that gasping patients are not suffering. If there is a reasonable chance that they are in pain or suffering, then palliative measures are appropriate.

**Objection 2:** Allowing physicians to take measures to stop the gasping response creates a slippery slope toward taking all sorts of measures in the name of alleviating pain and suffering. It is only a short step from administering neuromuscular blocking agents during gasping to more active forms of euthanasia. To stop this slide, physicians must refrain from all actions that are dangerously close to euthanasia or physician assisted suicide.

**Reply:** We agree that slippery slope concerns are present here as well as in other end of life decisions. We also agree that end of life care can be very difficult for patients who are not terminally ill. Moreover, prolonged gasping does not occur in patients who are not gravely ill or capable of being successfully resuscitated. Thus, there is little chance that someone would use our protocol to stop the normal breathing pattern of a patient who was not terminally ill.

**Objection 3:** The principle of double effect may be acceptable in ethics but not in law. A physician who followed your recommendations could be convicted of 2nd or 3rd degree murder, since he or she would be causing the patient’s death and would have the required mental state, such as legal intent, recklessness, or negligence.

**Reply:** As we noted earlier, the principle of double effect does not excuse the physician from all legal responsibility. We think it is highly unlikely, however, that a jury would convict a doctor of murder who followed our recommendations, since the doctor would not be planning to cause death. Moreover, we would argue that a law that prohibits good care for the dying patient is immoral and ought to be revised to allow physicians to stop the gasping response.

**Objection 4:** Since the terminally ill patient in the gasping phase of death is unlikely to be conscious and feeling pain, the use of neuromuscular blocking agents to stop the gasping is beneficial only to those watching the patient die.

**Reply:** Again, one cannot be sure that the patient is not suffering and, therefore, he should be treated. We agree that use of neuromuscular blocking agents would make the patient appear more comfortable and peaceful. Indeed, that is the goal of end of life palliative care. The Institute of Medicine’s definition of a good death is: “A decent or good death is one that is: Free from avoidable distress and suffering for patients, families, and caregivers; in general accord with patients’ families’ wishes; and reasonably consistent with clinical, cultural, and ethical standards.” When death is inevitable and compassionate terminal care is required, not only the patient’s comfort, but also the minimisation of the loved ones’ distress becomes a priority. Research has shown that families are traumatised by a protracted death in which the patient struggles to breathe.

We believe that the use of neuromuscular blocking agents in well-sedated, terminally ill, gasping patients allows fulfilment of all the requirements of the Institute of Medicine’s definition of a good death. Although we do not use neuromuscular blocking agents for this purpose at the current time, we hope this discussion results in dialogue which allows future application.

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