The Window of Opportunity for Treatment Withdrawal

Dominic Wilkinson, MBBS, BMedSci, MBioeth, DPhil, FRACP

hysicians sometimes refer to a "window of opportunity" for withdrawing life-sustaining treatment in patients with acute severe brain injury. There is a period of critical illness and physiological instability when treatment withdrawal is likely to be followed by death but prognosis is uncertain. If decisions are delayed, greater prognostic certainty can be achieved, but with the risk that the patient is no longer dependent on life support and survives with very severe disability. In this article I draw on the example of birth asphyxia and highlight the role that the window of opportunity sometimes plays in decisions about life-sustaining treatment in intensive care. I outline the potential arguments in favor of and against taking the window into account. I argue that it is, at least sometimes, ethical and appropriate for physicians and parents to be influenced by the window of opportunity in their decisions about life-sustaining treatment.

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In intensive care, it is not uncommon for critically ill patients with poor prognosis to be allowed to die. Most deaths in pediatric and neonatal intensive care units follow decisions of this nature.1-8 Lifesustaining treatment (LST) is sometimes withdrawn or withheld because it is thought highly unlikely that the patient will survive; treatment is futile. Alternatively, treatment is sometimes limited because of predictions of the patient's quality of life.^{2,4,5} The burdens of treatment, illness, and impairment are sufficiently great that it is not believed to be in the patient's best interests to continue active efforts to keep them alive, even though it is possible or even probable that, with treatment, they would survive. 9,10

In the latter case, there is sometimes a sense of urgency about treatment decisions. This particularly applies to acute severe brain injury, for example, following stroke, acute hypoxia-ischemia, or trauma. Some physicians refer to a "window of opportunity" to decide whether to limit LST.¹¹⁻¹⁴ The concern is that, if decisions

Author Affiliations: Program on Ethics and the New Biosciences, Oxford Uehiro Centre for Practical Ethics, and The Ethox Centre, Department of Public Health and Primary Health Care, University of Oxford, Oxford, England.

are deferred or delayed, the patient may no longer be physiologically dependent on intensive care treatments. At that stage, even if decisions are made by family members to limit further intensive care, there is a risk that the patient will survive with very severe impairment.

In this article I will assess some of the ethical questions raised by the window of opportunity in intensive care. I will draw on the example of hypoxic-ischemic encephalopathy in newborn infants and assess the potential arguments in favor of and against the window. I argue that it is, at least sometimes, appropriate for parents and physicians to take into account the window of opportunity in their decisions about LST.

THE WINDOW OF OPPORTUNITY IN BIRTH ASPHYXIA

One condition in which the window of opportunity question is sometimes raised is birth asphyxia, or newborn hypoxicischemic encephalopathy (HIE). Moderate or severe degrees of HIE affect 2 to 4 infants of every 1000 live births. 15-17 Despite the recent development of hypother-

Table 1. Competing Considerations of Early Withdrawal vs Late Withdrawal

Early Withdrawal of Treatment

More uncertainty about prognosis
Lower risk of survival with severe disability because patient is more physiologically unstable
Less time for caregivers to decide; risk of rushed decisions and later regret

Withdrawal of life support easier, with prolonged death and patient suffering less likely

Later Withdrawal of Treatment

Less uncertainty about prognosis
Higher risk of survival with severe disability because patient is less dependent on

More time for surrogates to come to terms with prognosis and decide about treatment

life support

May require consideration of withdrawal of artificial nutrition—more controversial, and may lead to prolonged dying

mia as a form of neuroprotection for asphyxiated infants, almost half of those affected either die in the newborn period or survive with severe impairment, including cerebral palsy, global developmental delay, blindness, and deafness. ^{18,19}

Given the poor outcome for many infants with HIE, it is unsurprising that parents and physicians sometimes question whether LST should continue. Most deaths in infants with HIE in developed countries follow decisions to limit LST. ^{2,16,20} Deaths usually occur in the first few days after birth, when infants are dependent on mechanical ventilation and/or inotropic support. Perinatal hypoxia-ischemia leads to early multiorgan failure in many infants with HIE, ²¹ with improvement often occurring after 72 hours. ^{22,23} Prior to this point, withdrawal of LST is likely (though not certain) to lead to the infant dying quickly.

However, prognostication in HIE is challenging.²⁴ There are various tools used to help assess the prognosis of asphyxiated infants including clinical assessment, electrophysiological tests, and imaging of the brain. But most of these tools face the same problem, that early predictions are more fallible than later predictions.¹² For example, magnetic resonance imaging of the brain is recommended for all infants with HIE²⁵ and provides detailed, specific information relating to areas of brain injury and future impairment.^{23,26-28} But early magnetic resonance imaging is significantly less accurate than later imaging.^{29,30} Furthermore, obtaining magnetic resonance imaging may lead to delays in decision making owing to difficulties organizing a scan, arranging transportation, and having it reported.³¹

What are the consequences of delayed prognostication (**Table 1**)? The main one is that infants may no longer be dependent on respiratory support.³² Spontaneous respiratory drive in infants with HIE is related to the severity of injury, degree of brain swelling, and use of sedatives or anticonvulsants.²² There is little available data on respiratory function in asphyxiated infants,³³ and none on the timing of return of spontaneous respiration in such infants. However, in one recent study of infants with moderate or severe HIE treated with hypothermia, 40% of infants were extubated in the first 3 days after

birth.³⁴ If infants are not ventilator dependent, there is the possibility of withdrawal of other (less intensive) forms of treatment, for example, artificial nutrition. The most severely affected infants with HIE usually have impaired ability to coordinate sucking and swallowing and are dependent on artificial nutrition (usually by a nasogastric tube in the short term) to survive. But although some professional guidelines support withdrawal of nutrition, ^{9,35} it is highly contentious, ³⁶⁻³⁹ is not offered in many places, and has been argued to be contrary to the interests of infants. ⁴⁰ If artificial nutrition is withdrawn, it can take 3 weeks or longer for infants to die. ³⁸

WINDOW OF OPPORTUNITY AND DECISION MAKING

The window of opportunity for treatment limitation decisions in infants with HIE has been mentioned in passing by researchers^{32,41} but it does not feature at all in most descriptions of prognostication in HIE. 22-24,42 In a recent study of English neonatologists' views about prognostic tests and decision making in HIE, it was clear that this was an important consideration for at least some physicians caring for infants with asphyxia¹³: "There is a 'window of opportunity' to withdraw with dignity for the child and for the family and if you don't withdraw during that window of opportunity, the child then may start to respond, may then start to breathe, may come off the ventilator and may survive and is profoundly handicapped."13 Another clinician noted the potential effect of this on decisions: "There is some urgency . . . on the one hand you don't want to push parents, you specifically say you don't want them to rush to a decision about anything, on the other hand they need to be aware that there probably is a much greater chance of the child to survive without the ventilator the longer you delay." 13 On the other hand, 2 neonatologists expressed a degree of ambivalence about the idea of a window of opportunity, stating, "I am not sure I quite buy into that personally. . . . The fact that the baby might survive doesn't mean to say that you have made the wrong decision" and "But whether it truly is used in decision making I'm uncertain. I'm not so sure that I use it."13

OBJECTIONS TO THE WINDOW OF OPPORTUNITY IN TREATMENT DECISIONS

Are there reasons to avoid considering the window of opportunity? One general concern relates to quality-of-life judgments. Some clinicians, ethicists, and disability rights advocates contend that a diminished quality of life is not sufficient grounds for withdrawing LST.^{43,44} If it is only permissible to withdraw treatment when death is inevitable, then a window of opportunity cannot arise. However, both professional guidelines and legal cases have supported the relevance of quality-of-life considerations in treatment decisions.^{9,10,45,46}

Specific objections to the window of opportunity include discomfort with the term itself, uncertainty, the burden of treatment, and the doctrine of double effect.

The term itself may partly explain clinicians' disquiet. The phrase potentially connotes that the death of

the patient is opportune, whereas for families (and the infant), death represents a terrible misfortune. It might be thought insensitive to raise or even to contemplate the "opportunity" of death. However, in some instances it may be a greater misfortune if the infant survives.

Uncertainty

A second reason relates to avoidance of prognostic uncertainty. Uncertainty is a particular problem for prognostication in newborn infants.^{24,47} Observing infants over time to see if they show neurological recovery can reduce this uncertainty.²⁴ For this reason, some authors have recommended that prognostication should be deferred until after the first week of life.²⁴

However, uncertainty is inevitable in decision making for newborns. ^{9,32} The important question is not whether there is uncertainty but whether there is sufficient uncertainty that treatment must continue. Attempting to reduce uncertainty may have costs, and whether that is worthwhile depends on how those costs are weighed against the benefits of avoiding uncertainty. Cochrane has argued⁴⁸ that there is no urgency to make decisions about treatment, for example, in adult patients following a stroke, because there is always the option of withdrawal of artificial nutrition. But given the contentious nature of withdrawal of feeding in newborn infants and the possibility of prolonged suffering, some parents and physicians may choose to withdraw treatment earlier, even at the cost of greater uncertainty. ¹¹

A related objection is that the window of opportunity is not a relevant consideration for treatment decisions because it is not permissible to withdraw treatment from infants who only need short periods of life support. It might be believed that recovery of respiratory drive portends a good prognosis, or a sufficiently good prognosis that treatment withdrawal should not be countenanced. To my knowledge, however, there is no published evidence on the return of spontaneous breathing and prognosis for infants with HIE. Anecdotally, some infants maintain or recover respiratory drive despite very severe patterns of brain injury. ^{13,36,49} It would have been permissible to allow these infants to die if they had still been ventilator dependent.

A second version of this objection relates to the burden of treatment. If an infant will only require a short period of respiratory support, the burden of treatment is relatively minor. It is unpleasant for the infant to have a breathing tube in place, but sedation and analgesia can be provided to reduce any discomfort. In some views, it is only permissible to withdraw or withhold treatment when the burdens of treatment outweigh the benefits; this may not be the case for a short period of life support. But in the face of severe predicted impairment, there are other treatments that may permissibly be withheld that are even less burdensome than a short period of respiratory support. For example, in such infants it is sometimes felt to be acceptable (if the parents choose) to withhold treatment with antibiotics for a respiratory infection. Yet the discomfort and burden associated with a course of antibiotics is minimal. If it is permissible to withhold antibiotics it must be permissible to withdraw mechanical ventilation, even when it would only be required for a short period.

The Doctrine of Double Effect

A more significant concern is that consideration of the window of opportunity potentially conflicts with the doctrine of double effect (DDE). The DDE is widely cited as providing a boundary for permissible actions in end-oflife decisions. 32,50-52 It governs actions that have 2 potential effects, 1 good and 1 bad. According to the DDE, it is impermissible to intend to hasten the death of the patient, but it is permissible to perform acts that unintentionally (or as an adverse effect) hasten death.⁵⁰ The problem is that, if the timing of treatment withdrawal is influenced by whether the infant will die (when extubated), it may appear that death is either intended or is, at least in part, one of the direct goals of extubation. One of the neonatologists interviewed in a recent study suggested, "In some respects the outcome is the outcome . . . you can decide [that] continu[ing] intensive care is not the right thing to do but you are not necessarily doing that so that the baby dies."13

Can the window of opportunity be reframed so that it does not conflict with the DDE? The primary goal of the physician is to respect the interests of the infant. It may be in the best interests of an infant to have treatment withdrawn earlier rather than later, if later withdrawal will lead to survival in a state of severe impairment or to a slow death following withdrawal of artificial nutrition. However, if it is in the best interests of the infant to die, and it is those interests that are the goal of treatment withdrawal, the DDE would still potentially prohibit treatment withdrawal. One of the standard conditions of the DDE is that the good effect is not produced via the bad effect. 53,54 A physician administering morphine to a patient may not do so to serve the best interests of the patient (when the death of the patient is believed to be in their best interests). The physician may, however, give morphine to provide pain relief (a different goal), even if this would also predictably lead to the death of the patient.

A more promising answer, perhaps, is that the physician's goal in withdrawing treatment is not to hasten the infant's death, but to respect parents' request that treatment be withdrawn. If parents are justified in a belief that continuing treatment would not be in the infant's best interests, their wishes should be respected. Parents may choose earlier withdrawal of treatment, partly to avoid the infant's survival with severe impairment. The question may then shift to whether the DDE applies to parental requests as well as to physicians' actions.

On the other hand, perhaps the doctrine itself should be rejected for treatment withdrawal decisions on the basis of predicted quality of life. A full discussion of the DDE is beyond the scope of this article. 53-57 However, one reason to support such a view is that it is permissible to withdraw treatment, though that will lead to the death of the infant. Indeed, if treatment is being withdrawn on the basis of predicted quality of life, the death of the infant must necessarily be judged to be better than continued life and treatment. It seems hypocritical to suggest that this cannot permissibly be one of the goals of action.

Table 2. Arguments for and Against Window of Opportunity in Treatment Decisions

Against In Favor

Negative connotations—withdrawal is never opportune There is no window of opportunity because Uncertainty precludes early withdrawal

The burden of a short period of ventilation is minimal, therefore it cannot be in the best interests of the patient to withdraw treatment Patients with severe brain injury (enough to justify withdrawal) do not recover respiratory drive

There is always the option of withdrawal of artificial nutrition

Conflict with the doctrine of double effect—it may imply that the death of the infant is intended

In some situations survival may be a greater misfortune than death

There is a window of opportunity because

Uncertainty is inevitable in newborns and does not always preclude treatment withdrawal

It is sometimes permissible to withdraw treatments of very little burden when the burden of ongoing life is great

There is no good empirical data on recovery of respiratory drive in infants with birth asphyxia; anecdotally, some patients with profound brain injury do recover respiratory drive

Withdrawal of artificial nutrition is controversial and may cause suffering for the infant and family

The intention is to act in the best interests of the patient and to respect parental wishes; if the doctrine permits withdrawal of treatment on the basis of quality of life, it is permissible to take into account the likelihood of the infant dying

Table 2 below provides a summary of potential arguments in favor of and against the window of opportunity in treatment limitation decisions.

INCORPORATING THE WINDOW OF OPPORTUNITY INTO TREATMENT DECISIONS

If it is appropriate to consider the window of opportunity in decisions about life-sustaining treatment, how should parents and physicians decide about the timing of treatment withdrawal? These decisions are particularly difficult because of the conflicting values at stake (Table 1). One possibility that I have explored in detail elsewhere would be to draw on decision theory. However, in practice, this would be extremely difficult to apply because of problems quantifying the probabilities and values of different outcomes. Lagrangian decisions are particularly as the probabilities and values of different outcomes.

More generic guidelines could be generated. This discussion highlights 2 necessary conditions for withdrawal of treatment. The first is that the most likely outcome for the infant is sufficiently severe that it would justify treatment limitation if it were known with certainty⁵⁸; it must be a "fate worse than death." Second, there must be a minimum level of certainty about that outcome. There is no way to express this quantitatively, but one potential way of capturing this is that treatment may be permissibly withdrawn if there is clear and convincing evidence that an infant will be very severely impaired if they survive.⁵⁸

Families will differ in what they judge to be a sufficiently severe outcome and a sufficient level of certainty to warrant withdrawal of treatment. But the two factors are related. The worse the outcome if the infant survives (for example, the longer they are likely to survive and the more suffering they are likely to experience), the greater the amount of uncertainty that could be tolerated.

CONCLUSIONS

The generic features of the window of opportunity are early critical illness with uncertain prognosis and later physiological recovery coinciding with more certain outcome assessment. In this article I have focused on the example of newborn infants with HIE, but similar situations are seen in many forms of acute brain injury, from extremely pre-

mature infants with intraventricular hemorrhage to elderly patients with cerebrovascular accidents.

It is not clear how often or how much this factor influences treatment decisions, but it appears to be an important consideration for at least some clinicians. I have outlined above the potential arguments in favor of and against the window of opportunity playing a role in decisions. Some will oppose the window of opportunity because they reject withdrawal of treatment on the basis of predicted quality of life. Others may oppose it because of the uncertainty associated with early decision making. Nevertheless, it is generally accepted that it is appropriate to take into account the patient's quality of life in judgments about best interests. Complete certainty about prognosis is almost never achievable.

There is a need for better data on the timing and prognostic significance of the return of respiratory drive in infants with HIE. However, there is also sometimes a need to raise the possibility of a window of opportunity for treatment withdrawal with family members. This requires sensitive discussion about prognosis and uncertainty. Decision making should not be rushed, but families should be aware that infants may not die after treatment is withdrawn and that, in some cases, this is more likely if decisions are delayed.

Although dealing with uncertainty can make decisions difficult, when the outcome is sufficiently severe and there is enough certainty about prognosis, it is both ethical and appropriate for parents and physicians to take advantage of the window to withdraw LST.

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Correspondence: Dominic Wilkinson, MBBS, BMedSci, MBioeth, DPhil, FRACP, Oxford Uehiro Centre for Practical Ethics, University of Oxford, Littlegate House, St Ebbes, Oxford OX1 1PT, England (dominic .wilkinson@adelaide.edu.au).

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