

Chapter 2

How Babies Die and Why This Is Important to Clinicians, Researchers, and Parents

Eduard Verhagen and Annie Janvier

Abstract With technological developments and new knowledge, survival for many neonatal conditions has improved. Survival can be either with or without disability, and/or a chronic condition. Decision-making for neonates with uncertain futures is often influenced by considerations of length of survival, disabilities, and quality of life. In this context, deciding if an LSI is of benefit to a patient involves data about outcomes but also value judgments. These are among the hardest decisions of modern medicine. This chapter describes why discovering the evidence about the outcomes of neonates with uncertain futures in the medical literature is complex and describes research and solutions to help clinicians in this context.

In the past, when neonates died because of lack of intensive care units, ethical discussions and decision-making about life sustaining interventions (LSIs) were generally irrelevant. With technological developments and new knowledge, survival for many conditions has improved. Survival can be either with or without disability, and/or a chronic condition. Decision-making for neonates with uncertain futures is often influenced by considerations of length of survival, disabilities, and quality of life. In this context, deciding if an LSI is of benefit to a patient involves data about outcomes but also value judgments. These are among the hardest decisions of modern medicine. This article describes why discovering the evidence

E. Verhagen (✉)

Department of Pediatrics, University Medical Center Groningen, University of Groningen, 9700, RB Groningen, The Netherlands

e-mail: a.a.e.verhagen@umcg.nl

A. Janvier

Department of Pediatrics and Clinical Ethics, Neonatology and Clinical Ethics, Sainte-Justine Hospital, University of Montreal, 3175 Côte-Sainte-Catherine, Montreal, QC H3T 1C4, Canada

e-mail: anniejavier@hotmail.com

© Springer Science+Business Media Dordrecht 2016

E. Verhagen and A. Janvier (eds.), *Ethical Dilemmas for Critically Ill Babies*,

International Library of Ethics, Law, and the New Medicine 65,

DOI 10.1007/978-94-017-7360-7_2

about the outcomes of neonates with uncertain futures in the medical literature is complex and describes research and solutions to help clinicians in this context.

2.1 Values, Policies, and Facts About Survival

In industrialized countries, most neonatal deaths now occur in Neonatal Intensive Care Units (NICUs) and follow a decision to limit LSIs [1–5]. Attitudes of caregivers also influence speculation about these issues and may contribute to variations in survival and health outcomes for critically ill children [5–7]. Different values, cultures, and/or policy statements can lead to wide variations of practice [8]. For example, one of the “gray zones” in neonatology relates to intervention for extremely preterm infants. Neonates born before 22 weeks of gestational age (GA) do not survive. This is true in all publications. But if we examine the literature for survival at 24 weeks of GA, survival is not homogeneous between studies and varies widely in the literature. In some countries—including Germany, Japan, Sweden, and Norway—such a baby would almost always receive active intervention [9–12]. In Canada, the UK, and some hospitals in the U.S., prospective parents are informed about the outcomes of extreme preterm infants and must decide between intensive care and comfort care [13, 14]. In the Netherlands [15] and in some centers in the U.S. [16], intensive care for these babies is generally considered “non beneficial” and neonatologists often recommend comfort care. Not surprisingly, outcomes for babies born at 24 weeks of GA vary widely between countries. Survival for babies born at 24 weeks is 81 % in Japan, 60 % in Canada, 33 % in the UK, and is as low as zero in some centers in the Netherlands.

It is important to note that attitudes and practice regarding the care of extremely preterm babies are changing. For example, only recently in the Netherlands, obstetricians and neonatologists nationwide agreed to offer parents active resuscitation for neonates from a gestational age of 24 weeks onwards. It appears that the mortality rate among neonates with a gestational age of 24 weeks is now decreasing and is becoming more similar to the rates in other European countries actively resuscitating neonates of such a low gestational age [17]. We still need detailed data about the change in policy to understand what we can validly infer from comparison with other outcome studies.

There is an intimate relationship between values, policies, and facts. What information should parents be told: survival data for their center, survival for other centers, or the wide variation of practice between centers? What does informed consent mean in this situation? If parents are told that the chances of their baby’s survival are low, they will be less likely to choose treatment. If they choose comfort care, their baby will die and in turn, will become part of the statistics. A similar variation of practice can be seen for other neonatal conditions necessitating intensive care and linked with uncertain outcomes. Some examples are hypoplastic left heart syndrome, hydrocephaly, severe renal insufficiency, and trisomy 13 and 18.

2.2 Outcome and Unit Philosophy

Finding survival statistics for fragile neonates and interpreting the data from the values may be difficult, but examining and interpreting long-term outcomes when babies survive can be even harder. Let's return to the example of a baby born at 24 weeks of GA. She develops a large unilateral grade 4 parenchymal hemorrhage at three days of life. Should the physician offer to withdraw LSI because of this finding? What can we find in the literature? What is the positive predictive value (PPV) of future cerebral palsy in preterm babies who survive with such a bleed? The outcomes after this neurological insult vary widely in the literature: from a PPV of 20–85 % [18, 19]. These differences arise in part from value judgments and not only from the NICU care babies receive. In some units, physicians will recommend withdrawing (WD) LSI in this case. In others, physicians will offer to WD LSI. And in others, parents will be informed that this parenchymal hemorrhage will increase the risk of disability for their child. Even in a single NICU with homogeneous values and so-called “neutral disclosure” to parents, different styles of disclosure may influence parents. Some babies die *with* their parenchymal hemorrhage (because of sudden bleeding and cardiovascular collapse) and others die *because* of their parenchymal hemorrhage (LSI are withdrawn for quality of life reasons). Furthermore, some units will not consider WD LSI for a small hemorrhage, but only for a large one, in a more unstable baby. The smaller the hemorrhage, the better the outcomes. Survivors in different units will have different outcomes, mainly because of the philosophy of the unit. Similar variations of practice can be seen for many other conditions where WD of LSI can occur in the NICU: hypoplastic left heart syndrome, severe NEC, severe respiratory insufficiency, hydrocephalus following IVH, seizures in very preterm infants, meningitis with shock, asphyxia with serious seizures, and others.

So how can we interpret statistics for neonates with uncertain futures and decide whether an LSI is in the best interest of our patient? How is it possible to make sense of the medical literature when outcomes are influenced not only by interventions but also by philosophies?

2.3 Description of Circumstances Around the End-of-Life

The circumstances surrounding decisions to withhold or withdraw interventions are rarely explicitly described in publications on neonatal intensive care unit (NICU) outcomes. Most studies do not make the distinction between WD/WH LSI from dying babies, and WD/WH interventions from physiologically stable children for quality-of-life reasons. This is an important distinction, as children who were stable might have lived if intervention had not been withdrawn or withheld.

NICU deaths for fragile neonates should be transparent in the medical literature. Without these distinctions, it is impossible to truly examine the literature, counsel

parents in a meaningful way, examine whether a certain intervention makes a real difference in terms of disability, or compare studies of NICU outcome (between NICUs or in one NICU at different times) in a meaningful way.

We have recently reported a useful method to classify and compare death and dying in the delivery room and NICU using strict definitions of physiology and LSI [20]. There are five ways neonatal deaths can be classified: (1) Some babies die because NICU admission is WH, (2) others die with CPR (No WH or WD), (3) or without CPR but on a respirator (no WD, WH CPR), (4) or because LSI are WD/WH in an unstable patient (baby would have died despite LSI), (5) or because LSI are WH/WD in a physiologically stable patient for quality of life reasons. In this category, many patients may have survived, had LSI been continued. Each unit can categorize their deaths in this manner. We were able to show that almost all NICU deaths in four units in three countries were accompanied by some degree of withholding/withdrawing, but that the physiologic stability of the dying infants varied considerably within and between countries. In addition, we found that dying babies with similar characteristics were treated differently with regard to initiating and increasing comfort medications. This difference in treatment between units suggests that comfort medication was not only directed at the medical condition of the baby but also at the parents and healthcare providers’ comfort and outcome [21]. Uniform classification of deaths is feasible and offers an important step towards transparency about norms and values of stakeholders in decision-making and true comparison of NICU outcomes.

Studies that do describe the circumstances around the decisions about the newborn’s end-of-life report that 25–45 % of NICU deaths are by withdrawing intensive care in stable newborns for quality of life reasons [22, 23]. This high proportion of deaths by ‘elective’ withdrawal seems even more important if we keep in mind that physicians will use outcome reports to counsel parents about decision-making regarding the fetus and/or sick neonate.

Another important step toward more transparency and comparability could be made if we use data about babies who never make it to the NICU in neonatal outcome calculations. A substantial proportion of these babies are often described as “in utero deaths.” There are many ways fetuses die in utero; the most common ways are shown in Table 2.1. In addition, a group of live born babies are not admitted to the NICU for the reasons mentioned in Table 2.1.

Table 2.1 Groups of babies who never make it to the NICU: in utero deaths and DR deaths

Stillbirths (dead on arrival to the hospital)
Stillbirths (died in utero because of withholding surgical delivery)
Termination of Pregnancy (TOP) for congenital malformations
“Induction” of labor for risk of extreme prematurity
Small preterms who receive comfort care
Term babies who receive palliative care because of their predicted outcomes
Failed resuscitations

Outcomes for all of these categories of newborns can be influenced by national health policies. For example, a high rate of termination for the “most severe” hypoplastic left heart syndrome will lead to better surgical outcomes for babies with this condition. A decision to do cesarean sections only for fetuses over 25 weeks of GA will likely select bigger non-growth restricted neonates at each GA and will affect outcomes. Another striking example is what happened in Holland in 2007. The Dutch government started offering structural ultrasound at 20 weeks’ gestation for all pregnant women at no extra cost. This has resulted in fewer births of babies with severe anomalies, such as spina bifida (because of termination of pregnancy), which in turn has led to fewer cases of neonatal euthanasia [24]. Another example is the policy statements for treatment of extremely premature infants. In Canada, palliative care is advised in babies born at less than 23 weeks of gestational age, and cesarean section is not recommended below 24 weeks of gestational age [14]. In the United States, gestational age is not mentioned. In the Netherlands, non-intervention is now advised below 24 weeks of gestational age, and between 24 and 25 weeks is defined as the “gray zone” where interventions are optional, depending on parental preferences [15]. The latter policy will result in fewer survivors less than 25 weeks of gestational age, fewer survivors with handicap, and also fewer survivors overall. The policy may also result in less desire to intervene below 25 weeks gestational age, thus contributing to a self-fulfilling prophecy.

For these reasons, we should consider making all fetuses and neonates who are alive at more than 450 g the denominator of all deaths, even if these fetuses are in utero. This classification is more complex than categorizing neonatal deaths and also involves another set of ethical values (and other disciplines).

The examples discussed in this paper underline that national and/or professional healthcare policies can change medical practice and shape patient outcomes. Conversely, outcomes could also influence national health policies and local/personal values. If the prevalence of individuals with disability from prematurity or congenital malformation in our communities decreases, society might adapt. It would be interesting to learn what that might do to health care infrastructure and the availability of support and acceptance of children with disabilities among the public. What effect might this situation have on policy makers and on physicians’ perinatal and counseling and decision-making?

Knowledge about how babies die is important because decisions about WH/WD in the delivery room and in the NICU are in part based on personal, local and/or national values. Those values shape the patient mix, outcome in NICUs, and the context of clinical and ethical decisions. Reflection on those values and on the differences in values between units, as well as proper comparison of outcome data, can take place only if we start including in our calculations data about how babies die and who never makes it to the NICU. Only if we can recognize our biases and make more transparent the true reasoning behind our decision-making processes can we be empowered to respond appropriately and consistently to the needs of sick children and their families.

Today, decisions on when to start WH or WD life supportive interventions in critically ill children are among the most difficult decisions in pediatric practice.

These decisions directly affect the health of our societies. It is difficult to remain neutral when we make these decisions. We expect that full transparency of the circumstances around these decisions will allow us to compare outcomes better, reflect on similarities and differences in end-of-life care, and ultimately make the necessary improvements in the interest of the child.

References

1. Feudtner C, Silveira MJ, Christakis DA. Where do children with complex chronic conditions die? Patterns in Washington State, 1980–1998. *Pediatrics*. 2002;109(4):656–60.
2. Ryan CA, Byrne P, Kuhn S, Tyebkhan J. No resuscitation and withdrawal of therapy in a neonatal and a pediatric intensive care unit in Canada. *J Pediatr*. 1993;123(4):534–8.
3. Sands R, Manning JC, Vyas H, Rashid A. Characteristics of deaths in paediatric intensive care: a 10-year study. *NursCrit Care*. 2009;14(5):235–40.
4. Lago PM, Piva J, Garcia PC, Troster E, Bousso A, Sarno MO, et al. End-of-life practices in seven Brazilian pediatric intensive care units. *Pediatr Crit Care Med*. 2008;9(1):26–31.
5. Verhagen AA, Janvier A, Leuthner SR, Andrews B, Lagatta J, Bos AF, et al. Categorizing neonatal deaths: a cross-cultural study in the United States, Canada, and The Netherlands. *J Pediatr*. 2010;156(1):33–7.
6. Janvier A, Lantos J. Variations of practice in the care of extremely preterm infants. In: Diekema D, Mercurio M, Adam M, editors. *Clinical ethics in pediatrics, a case-based textbook*. Cambridge: Cambridge University Press; 2011. p. 94–100.
7. Gallagher K, Martin J, Keller M, Marlow N. European variation in decision-making and parental involvement during preterm birth. *Arch Dis Child*. 2014;99(3):F245–9.
8. Janvier A, Lantos J. Variations of practice in the care of extremely preterm infants. In: Diekema D, Mercurio M, Adam M, editors. *Clinical ethics in pediatrics, a case-based textbook*. Cambridge University Press, Oxford University Press; 2011. pp. 94–100.
9. Itabashi K, Horiuchi T, Kusuda S, Kabe K, Itani Y, Nakamura T, et al. Mortality rates for extremely low birth weight infants born in Japan in 2005. *Pediatrics*. 2009;123(2):445–50.
10. Sugiura T, Kouwaki M, Togawa Y, Sugimoto M, Togawa T, Koyama N. Neurodevelopmental outcomes at 18 months' corrected age of infants born at 22 weeks of gestation. *Neonatology*. 2011;100(3):228–32.
11. Markestad T, Kaaresen PI, Ronnestad A, Reigstad H, Lossius K, Medbo S, et al. Early death, morbidity, and need of treatment among extremely premature infants. *Pediatrics*. 2005;115(5):1289–98.
12. Serenius F, Sjors G, Blennow M, Fellman V, Holmstrom G, Marsal K, et al. EXPRESS study shows significant regional differences in 1-year outcome of extremely preterm infants in Sweden. *Acta Paediatr*. 2014;103(1):27–37.
13. Holtrop P, Swails T, Riggs T, De Witte D, Klarr J, Pryce C. Resuscitation of infants born at 22 weeks gestation: a 20-year retrospective. *J Perinatol*. 2013;33(3):222–5.
14. Jefferies AL, Kirpalani HM, Canadian Paediatric Society F, Newborn C. Counselling and management for anticipated extremely preterm birth. *Paediatrics Child Health*. 2012;17(8):443–446.
15. de Laat MW, Wiegierinck MM, Walther FJ, Boluyt N, Mol BW, van der Post JA, et al. Practice guideline 'Perinatal management of extremely preterm delivery'. *Ned Tijdschr Geneeskd*. 2010;154:A2701.
16. Kaempff JW, Tomlinson M, Arduza C, Anderson S, Campbell B, Ferguson LA, et al. Medical staff guidelines for periviability pregnancy counseling and medical treatment of extremely premature infants. *Pediatrics*. 2006;117(1):22–9.

17. de Kluiver E, Offringa M, Walther FJ, Duvekot JJ, de Laat MW. Perinatal policy in cases of extreme prematurity; an investigation into the implementation of the guidelines. *Ned Tijdschr Geneeskd*. 2013;157(38):A6362.
18. Hack M, Taylor HG, Drotar D, Schluchter M, Cartar L, Wilson-Costello D, et al. Poor predictive validity of the Bayley Scales of Infant Development for cognitive function of extremely low birth weight children at school age. *Pediatrics*. 2005;116(2):333–41.
19. Schmidt B, Anderson PJ, Doyle LW, Dewey D, Grunau RE, Asztalos EV, et al. Survival without disability to age 5 years after neonatal caffeine therapy for apnea of prematurity. *JAMA*. 2012;307(3):275–82.
20. Verhagen AA, Janvier A, Leuthner SR, Andrews B, Lagatta J, Bos AF, et al. Categorizing neonatal deaths: a cross-cultural study in the United States, Canada, and the Netherlands. *J Pediatr*. 2010;156(1):33–7.
21. Janvier A, Meadow W, Leuthner SR, Andrews B, Lagatta J, Bos A, et al. Whom are we comforting? An analysis of comfort medications delivered to dying neonates. *J Pediatr*. 2011;159(2):206–210.
22. Verhagen AA, Dorscheidt JH, Engels B, Hubben JH, Sauer PJ. End-of-life decisions in Dutch neonatal intensive care units. *Arch Pediatr Adolesc Med*. 2009;163(10):895–901.
23. Berger TM, Hofer A. Causes and circumstances of neonatal deaths in 108 consecutive cases over a 10-year period at the Children's Hospital of Lucerne. *Switz Neonatology*. 2009;95(2):157–63.
24. Verhagen AA. The Groningen protocol for newborn euthanasia; which way did the slippery slope tilt? *J Med Ethics*. 2013;39(5):293–5.



<http://www.springer.com/978-94-017-7359-1>

Ethical Dilemmas for Critically Ill Babies

Verhagen, E.; Janvier, A. (Eds.)

2016, VIII, 96 p., Hardcover

ISBN: 978-94-017-7359-1