ORIGINAL ARTICLE

Death in the neonatal intensive care unit: changing patterns of end of life care over two decades

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Background: Death remains a common event in the neonatal intensive care unit, and often involves limitation or withdrawal of life sustaining treatment.
Objective: To document changes in the causes of death and its management over the last two decades.
Methods: An audit of infants dying in the neonatal intensive care unit was performed during two epochs (1985–1987 and 1999–2001). The principal diagnoses of infants who died were recorded, as well as their apparent prognoses, and any decisions to limit or withdraw medical treatment.
Results: In epoch 1, 132 infants died out of 1362 admissions (9.7%), and in epoch 2 there were 111 deaths out of 1776 admissions (6.2%; $p<0.001$). Approximately three quarters of infants died after withdrawal of life sustaining treatment in both epochs. There was a significant reduction in the proportion of deaths from chromosomal abnormalities, and from neural tube defects in epoch 2.
Conclusions: There have been substantial changes in the illnesses leading to death in the neonatal intensive care unit. These may reflect the combined effects of prenatal diagnosis and changing community and medical attitudes.

Although death rates have fallen since the inception of neonatal intensive care, the management of dying infants continues to present medical and nursing staff with practical and ethical difficulties. Selective withdrawal of life sustaining treatment from newborn infants was first described in the 1970s,[1] and a number of authors since then have described the extent and nature of this practice around the world.[2–11] There is continued debate about when it is ethical to withdraw life saving treatment from critically ill newborn infants, which treatments may be withdrawn, and how the dying process should be managed. In the last two decades, changes in community and medical attitudes to these issues might be expected to have changed the way that this care is provided. Two recent papers have described changes in patterns of end of life care over that time period.[10 11] Both documented a significant increase in the proportion of deaths that involved decisions to limit or withdraw intensive care. In the mid 1980s, an audit was conducted of all the infants who died in the neonatal unit at the Royal Children's Hospital over a two year period (part of this first audit has been published previously[12]). To define and explore how practices may have changed, a second audit was recently undertaken, and the results compared.

METHODS

The Royal Children's Hospital neonatal unit is a quaternary referral centre for newborn infants with surgical conditions, complex malformations and syndromes, and severe respiratory failure.

An audit was performed of infants who died from July 1985 to June 1987 (epoch 1). The medical records were reviewed by one author (NC), and data were retrieved on the diagnoses of infants who died, the timing and circumstances of their deaths, and their apparent prognoses. (It is usual for our clinicians to document the nature of discussions with parents and the reasons for withdrawal of life sustaining treatment where this occurs.) Where there was any difficulty in interpreting the events surrounding the death of an infant, the treating neonatologist was consulted. A second audit was performed from January 1999 to December 2001 (epoch 2). This audit was conducted over a longer period to compensate for the smaller number of deaths in the second epoch. These medical records were reviewed by two of the authors (DW and JF), and the same data were recorded.

Infants were divided into groups according to their apparent prognoses (as documented in the medical record by their treating neonatologist; table 1). They were also subdivided into discrete groups by diagnosis. The use of analgesic and sedative drugs at, or subsequent to, withdrawal of life sustaining treatment was recorded.

In our intensive care unit, withdrawal of life sustaining treatment is considered when there is little hope of survival or when quality of life is judged to be unacceptably poor. Decisions about withholding or withdrawing life sustaining treatment are made only after consensus is reached between parents and treating medical and nursing staff. It is common practice for newborn infants who are dying despite receiving maximal therapy, and whose death is imminent—that is, within minutes—that treatment is scaled back to allow parents to hold and nurse their baby before death. In this review, where treatment was withdrawn under these circumstances, infants were still classified as category I—that is, death despite all efforts to achieve survival.

Information about the total number of admissions with certain chromosomal disorders and neural tube defects was obtained from the unit's computerised database.

Statistical comparisons were made between the two epochs using Fisher's exact test and Pearson's χ^2 test. The audits were performed in accordance with National Health and Medical Research Council guidelines.

RESULTS

In epoch 1, 132 infants died out of a total of 1362 admissions (9.7%). There was a significant reduction in the proportion of infants dying in epoch 2 (111 deaths from 1776 admissions; 6.2%; $p<0.001$). This corresponds to a reduction in rate from one death per 6 days to one death per 10 days.

Table 1 Classification of infants by prognosis

Category I: infants who died despite all efforts to achieve their survival.
Category II: infants who died after withdrawal of life sustaining treatment.
- Infants who would almost certainly have died even if life sustaining treatment had been continued—for example, an infant with trisomy 13.
- Infants who would almost certainly have survived if life sustaining treatment had been continued—for example, an infant with holoprosencephaly.
- Infants whose survival was not predictable—with life sustaining treatment they might have survived, or might have died—for example, an infant with severe hypoxic ischaemic encephalopathy.

There was a change in the diagnoses leading to death (table 2). In particular, there was a significant decrease in the proportion of deaths from chromosomal abnormalities. The number of infants dying with each of the major trisomies was lower in epoch 2, and examination of the total number of admissions for these conditions revealed a reduction in admissions for trisomy 18 (seven in epoch 1 versus one in epoch 2) and trisomy 13 (four versus three), but not for trisomy 21 (19 versus 25). Similarly, the reduction in the number of deaths from neural tube defects (15 in epoch 1 versus one in epoch 2) coincided with a decrease in the number of admissions with this condition (41 versus 7).

In both epochs, approximately one quarter of infants died despite maximal treatment, and three quarters died after withdrawal or limitation of life sustaining treatment (table 3). However, the apparent prognoses of infants from whom treatment was withdrawn differed between the two epochs, with an increase in the proportion of infants who would almost certainly have died, and decreases in the proportion of infants who would have survived, or whose prognosis was uncertain.

Most infants received some form of sedative or analgesic medication at the time of, or subsequent to, withdrawal of life sustaining treatment. Withdrawal of life sustaining treatment occurred at a later stage in epoch 2 (table 3).

DISCUSSION

In this pair of audits, we have documented significant changes in the illnesses leading to death in the neonatal intensive care unit and in the apparent prognoses of infants from whom treatment was withdrawn.

More than 75% of deaths in the neonatal intensive care unit in both epochs followed withdrawal or withholding of potentially life saving treatment. This proportion is substantially higher than that described in the early papers on neonatal end of life care (14–30%).[1 2] It is closer to that reported more recently in the Netherlands and United States in surgical neonatal units (46–55%)[3 6] and perinatal units (58–81%).[4 7–9] The relatively high proportion of deaths that followed decisions to withdraw or limit treatment may reflect the referral base of our population. It is also likely to reflect the prevailing philosophy of clinicians. In particular, it is regarded as less than ideal for infants to die on the ventilator away from their parents. Where infants are clearly dying, or going to die despite treatment, discussions are held with parents about the option of palliative care.

Two previous papers have documented changes in end of life care over time.[10 11] Both papers described the changing patterns of death of infants who died in tertiary neonatal intensive care units over a 10 year period, one in the United States and the other in Norway. Singh *et al*[10] saw an increase from 1988 to 1998 in the proportion of dying infants from whom mechanical ventilation was withdrawn (10% *v* 42% of all deaths). Hagen and Hansen[11] described a similar increase in the proportion of deaths associated with decisions to forgo intensive care treatment (23% *v* 64%). In comparison, the proportion of infants from whom potentially life sustaining treatment was withdrawn was unchanged over time in our study. In the study by Singh *et al*, they subdivided infants from whom life sustaining treatment was withdrawn into those who were moribund and those physiologically stable infants who were removed from mechanical ventilation for quality of life reasons. The latter formed a small subgroup of infants, similar to the group of infants in this study who were felt to be likely to survive if life sustaining treatment were continued. In their cohort, about 40% of infants withdrawn from mechanical ventilation were ''stable''.[10] In comparison, in our unit in the recent epoch only 5% of infants who had life sustaining treatment withdrawn were felt to be likely to survive if life sustaining treatment were continued (a further 21% had uncertain prognosis).

The documented decrease in the admission rate, and number of deaths attributable to severe chromosomal disorders, is likely to be partly related to the effect of prenatal diagnosis and termination of pregnancy, although changes in patterns of referral may also have played a role. Local perinatal data over the last two decades reveal an increase in the overall prevalence of trisomies 13, 18, and 21, but a decrease in birth prevalence related to a large increase in termination of pregnancy.[13] However, the admission rate for trisomy 21 remained unchanged and mortality was substantially lower in the second epoch. This correlates with other reports of changes in mortality for infants with Down syndrome,[14] and may be due to changes in community

Table 2 Principal diagnoses of infants who died

	Epoch 1 (n = 132)	Epoch 2 (n = 111)
Complications of prematurity	27 (20.5)	30 (27.0)
Chromosome abnormalities	22 (16.7)	6 (5.4)*
Trisomy 21	5	2
Trisomy 18	7	1
Trisomy 13	4	3
Neural tube defects	15 (11.4)	1 (0.9)*
Severe hypoxic ischaemic encephalopathy	13 (9.8)	11 (9.9)
Pulmonary hypoplasia/diaphragmatic hernia	13 (9.8)	12 (12)
CNS sepsis, intracerebral haemorrhage, major CNS malformations	9 (6.8)	8 (7.2)
Complex congenital heart disease	5 (3.8)	4 (3.6)
Miscellaneous	28 (21.2)	39 (35.1)

Numbers in parentheses are percentage of all deaths for that epoch. The ''miscellaneous'' group in both epochs includes a large number of infants with conditions that are individually uncommon or rare.
*$p<0.01$.
CNS, Central nervous system.

Table 3 Prognosis of infants who died, and circumstances of withdrawal of life sustaining treatment

	Epoch 1 (n = 132)	Epoch 2 (n = 111)
Category I	31 (23.5)	22 (19.8)
Category II	101 (76.5)	89 (80.2)
Death likely (percentage of category II)	42 (41.6)	66 (74.2)†
Death unlikely (percentage of category II)	17 (16.8)	4 (4.5)†
Death uncertain (percentage of category II)	42 (41.6)	19 (21.3)†
Sedative/analgesic use*	58 (66)	76 (85)
Age at time of withdrawal (days)‡	10.4 (1–121)	24.3 (1–226)

Number in parentheses is percentage of total unless otherwise specified. NB data not available on drug use and age at withdrawal for all of the category II patients in epoch 1 (n = 88).
*Use of sedative or analgesic drugs (opioids, benzodiazepines, barbiturates) at, or subsequent to, the time of treatment withdrawal. Percentage is of total number of patients who had potentially life sustaining treatment withdrawn.
†Comparison of three subgroups of category II, $p<0.001$ (Pearson χ^2 test).
‡Values are mean (range).

attitudes. In the 1999–2001 audit, both infants with trisomy 21 who died had other serious illnesses, which led the treating neonatologist to believe that their prognosis was uncertain. In comparison, four of the five infants with trisomy 21 who died during the period of the first audit were thought to be likely to survive if their treatment were continued.

The cause of the decrease in the number of deaths from neural tube defects is likely to be multifactorial. Reduced birth prevalence of neural tube defects has been attributed to increased prenatal diagnosis[15–17] and periconceptional folate supplementation.[17–19] Improvements in postnatal survival for infants born with neural tube defects in Australia may relate to improvements in care, altered criteria for selecting which infants should be actively treated, and/or the effect of selective prenatal termination of more severely affected fetuses.[15] Interestingly, Hagen and Hansen[11] describe an increase in complex congenital malformations in infants who died in their more recent cohort. However, it is difficult to know how this relates to the diagnostic categories used in this study.

The high proportion of infants in this study who were receiving analgesics or sedatives at, or subsequent to, the time of withdrawal of life sustaining treatment is consistent with previous studies in infants and children.[7 20 21] It was not possible to compare the dosage or timing of administration of drugs in the two audits, but the proportion of infants receiving either opioids or sedatives was higher in the second period. This may reflect changes in neonatal pain management over time.

It may be difficult to generalise the results of these audits. The data reflect changes in practice at one neonatal intensive care unit with a highly specialised referral base. Practice might be expected to be quite different in perinatal units. Although every attempt was made to replicate the methods of the earlier study, different people collected data in the two epochs. Furthermore, as it is based on review of medical records, changes in the patterns of documentation over time may have contributed to observed changes.

Despite these limitations, this study provides important insights into end of life care in a neonatal intensive care unit. Although the death rate for newborns admitted to the intensive care unit has fallen, death remains a relatively common event. Most of these deaths follow decisions to limit or withdraw intensive care. These facts underscore the need for a coordinated and systematic approach to palliative care in newborns. The ethical and legal status of some of these decisions remains unclear, and neonatal teams are forced to make decisions in the absence of clear guidelines. It is important that the wider community are engaged in ongoing discussions and debate about the profound ethical challenges involved in neonatal end of life care.

What is already known on this topic

- Death remains a relatively common occurrence in neonatal intensive care
- A significant proportion of deaths follow withdrawal or withholding of life sustaining treatment

What this study adds

- There have been significant changes in the illnesses leading to death in one neonatal intensive care unit over two decades
- There was no change in the proportion of deaths that followed withdrawal of life sustaining treatment

CONTRIBUTORS

DW: data collection, analysis, preparation and editing of manuscript; JF: data collection, revision, and editing manuscript; PD: planning, revision and editing manuscript; NC: data collection, concept, planning, analysis, preparation and editing of manuscript; PL: planning, revision and editing manuscript; PMcD: planning, revision and editing manuscript; JM: planning, analysis, preparation and editing manuscript.

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Ethics approval: This study was performed as a quality assurance audit, and consequently ethics committee approval was not required (as per Australian National Health and Medical Research Council guidelines, http://www.nhmrc.gov.au/issues/pdfcover/qualassu.htm).

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