Neonatal End-of-Life Care: A Single-Center NICU Experience in Israel Over a Decade

WHAT’S KNOWN ON THIS SUBJECT: Neonatal mortality rate and causes of death have been relatively stable in recent years. Decision-making practices preceding death of sick neonates affect the circumstances of death. These practices vary worldwide according to the team approach and local population background.

WHAT THIS STUDY ADDS: Although our population is mostly religious, we observed a decline in maximal intensive care along with increasing redirection of care over a decade. Changes in the team approach and increasing level of parental involvement influence type and duration of treatment.

abstract

OBJECTIVES: To follow changes in the causes of neonatal deaths in the NICU at Hadassah Medical Center, Jerusalem, Israel, over a decade; to examine trends regarding types of end-of-life-care provided (primary nonintervention, maximal intensive, and redirection of intensive care, including limitation of care and withdrawal of life-sustaining treatment); and to assess the parental role in the decision-making process given that the majority of the population is religious.

METHODS: All neonates who died between 2000 and 2009 were identified. The causes and circumstances of death were abstracted from the medical records. Trends in end-of-life decisions were compared between 2 time periods: 2000–2004 versus 2005–2009.

RESULTS: Overall, 239 neonates died. The leading cause of death in both study periods was prematurity and its complications (76%). Among term infants, the leading cause of death was congenital anomalies (48%). Fifty-six percent of the infants received maximal intensive care; 28% had redirection of intensive care, of whom 10% had withdrawal of life-sustaining treatment; and 16% had primary nonintervention care. Over the years, maximal intensive care decreased from 65% to 46% (P < .02), whereas redirection of care increased from 19.2% to 37.5% (P < .0005). An active parental role in the end-of-life decision process increased from 38% to 84%.

CONCLUSIONS: Even among religious families of extremely sick neonates, redirection of care is a feasible treatment option, suggesting that apart from survival, quality-of-life considerations emerge as an important factor in the decision-making process for the infant, parents, and caregivers. Pediatrics 2013;131:e1889–e1896
Neonatal mortality, mostly attributed to prematurity, congenital anomalies, and perinatal asphyxia, remains the major component of infant and childhood mortality. In many cases, deaths of severely sick neonates are preceded by discussions between the medical staff and parents to reach end-of-life decisions appropriate for the infant and the family. The commonly used life-sustaining practices include maximal intensive care, redirection of intensive care (limited care or withdrawal of care), and primary nonintervention care. However, decision-making practices have been reported to vary widely from country to country and among different institutions in the same country. These differences are mainly related to prognostic uncertainty and combine the interface between the “disease-oriented” and the “person-oriented” approaches, together with the individual case-related circumstances, namely, the family, the medical team, law, and society.

Over the past few years, the number of high-risk pregnancies and the resulting incidence of severely sick infants in our hospital have increased. Moreover, a change in the department management has occurred, followed by implementation of a protocol-based practice in the delivery room according to which resuscitations are provided to preterm infants only if they are >24 weeks’ gestation or after parental request if they are less mature. In the NICU, families of critically ill newborns are approached, and end-of-life treatment options are thoroughly discussed when the situation is likely to result in a prolonged dying process or survival with profoundly limited capabilities. The protocol was formally enforced in 2006.

In this study, we reviewed all neonatal and postneonatal deaths that occurred over a decade in the NICUs at the 2 Hadassah-Hebrew University Hospitals, Jerusalem, Israel, and we examined the main causes of death, the medical approaches that were provided, and the parental role in the end-of-life decision-making process.

METHODS
This study was conducted at the Hadassah-Hebrew University Hospitals, Jerusalem, a tertiary referral center for the local city population, mainly Jewish and Muslim. The hospital has 2 campuses, and each has a neonatology unit. The average annual combined birth rate is ~11,000. The medical neonatal team comprises senior physicians who rotate between the 2 NICUs. All protocols are common. The ethical decision-making process is based on multidisciplinary formal meetings that include nurses, social workers, and relevant physicians from other fields.

More than 85% of the hospital population is religious; however, there is wide interreligious (traditional, orthodox, ultra-orthodox) and socioeconomic diversity among patients. The religious aspect is indeed relevant to the study objective because religious Jews and Muslims do not believe in active procedures to hasten death.

All neonates who died between January 1, 2000, and December 31, 2009, were identified. Demographic information and causes and circumstances of death were abstracted from the individual medical records. We categorized the end-of-life care approaches into 3 main groups: (1) primary nonintervention, (2) maximal intensive care, and (3) redirection of intensive care that was categorized as either limited care (not intensifying medical treatment) or withdrawal of care. After discussions with parents, the primary nonintervention approach included nutritional supply and analgesia for sick neonates who survived more than a few hours; however, no invasive therapeutic interventions were provided. The limitation of care approach was based on informative and transparent discussions among the parents, physicians, and other legitimate persons chosen by the family (such as a religious authority), which led to developing a consensus that limits care and allows no escalation from a certain point of intensive treatment (ie, no additional changes in the ventilator setting despite hypoxia or hypercarbia, no chest compressions, no additional administration of vasopressors or resuscitation drugs, no surgical intervention). Withdrawal of care meant that all life-sustaining therapies (ie, mechanical ventilation or cardiovascular support) were discontinued and additional care was focused on nutrition and antipain measures only. End-of-life approaches were categorized after a thorough review of each medical record by 2 of the investigators (SE-F and HK). In cases of uncertainty, all 3 authors reviewed the chart, and a final category was determined.

The parental role in the decision-making process was based on summarized discussions that appeared in the medical records and were classified as no involvement, consenting to redirection of care, or requesting either maximal intensive care or the cessation of life-sustaining therapies. If formal detailed discussions with parents were not documented, we assumed that maximal intensive care was given because this was the former treatment policy, considering the fact that religious families would refuse other treatment options. Trends in end-of-life care and parental role were compared over 2 time periods, 2000–2004 versus 2005–2009.

Descriptive statistical analysis was performed according to the variables. Exact $\chi^2$ and $t$ tests were performed to test for associations between categorical and continuous variables, respectively, by using the PASW 18-software of SPSS (IBM SPSS Statistics, IBM Corporation). The study was approved by the institutional review board.
RESULTS

During the 10-year period 2000–2009, there were 96,843 births in our institution, and 239 neonates died during the neonatal period (2.47 deaths per 1000 live births). No significant change in the neonatal death rate was observed over the years, with a range of 1.9 to 3.4 per 1000 live births. The total admission rate to both NICUs was 8349 between 2000 and 2009, ranging from 568 annual admissions in 2000 up to 702 admissions in 2009, and 3.8 death cases per 100 admissions.

Of the 239 deaths, 58% were boys; 62% and 36% were born to Jewish and to Muslim mothers, respectively; 24% belonged to multiple pregnancies (Table 1). All Muslims and 85% of the Jewish families were religious.

Cause of Death

The causes of death according to gestational age (infants born at ≤26, 27–36, and ≥37 weeks of gestation) in the 2 study periods are described in Table 1. Most cases of neonatal death (76%) occurred in preterm infants born at <36 weeks and 6 days; 37% of the entire recorded deaths occurred among infants born at ≤26 weeks. In this group of extreme prematurity (born ≤26 weeks), respiratory system failure (due to respiratory distress syndrome, air leaks, pulmonary hemorrhage, pulmonary hypertension, bronchopulmonary dysplasia) and cardiovascular collapse were noted in 57%, extensive intracranial hemorrhage (ICH) was detected in 45%, 18% had sepsis, and 7% suffered from necrotizing enterocolitis before death.

Among infants born at ≥37 weeks, the predominant cause of death (48%) was congenital malformations (including cardiac 23%, chromosomal 23%, central nervous system 19%, renal 14%, lung 9% anomalies), followed by neonatal asphyxia (19%) and sepsis (7%). An additional 8 neonates (14%) in this group died after renal failure, brain edema, severe anemia, and adrenal insufficiency.

When comparing the incidence of the leading causes of death (respiratory failure, extensive ICH, congenital malformations) in the years 2000–2004 versus 2005–2009, no significant trend of change was observed.

Age at Death

Seven neonates died in the delivery room shortly after birth. Of these, 4 were born extremely premature at <25 weeks, and resuscitation was discontinued because no vital response was detected. Two other preterm infants were born at 25 and 35 weeks’ gestation with anencephaly and hypoplastic lungs secondary to Potter syndrome, respectively, and they received primary nonintervention care. One preterm infant born at 32 weeks’ gestation died after severe asphyxia.

Of the 239 neonatal death cases, 29% died during the first day of life with an additional 13% dying at up to 48 hours of life, 23% died between day 3 and day 7 of life, 22% died between day 8 and day 30 of life, and 14% died after 30 days of life (Table 1, Fig 1).

With regard to the cause and timing of death of neonates admitted to the NICU (N = 232), earlier deaths (<3 days) were clearly related to severe lung disease in preterm infants (60%), whereas later deaths were associated with sepsis and multiorgan failure. Deaths occurring at >30 days of life occurred mostly among extremely preterm infants (49%) and were related to chronic lung disease (57%) and complications of necrotizing enterocolitis (9%).

We detected a significant decrease in death cases occurring during the first week of life, from 72% to 55% (P < .019) when comparing the years 2000–2004 with 2005–2008, with a significant increase in the percentage of postneonatal death occurring after 30 days of age, from 8.4% to 20% (P < .04), respectively (Table 1, Fig 1).

Type of End-of-Life Care

Overall, in 56% of the 239 neonatal death cases (including 5 neonates who died in the delivery room), maximal intensive care was performed from birth to death. In 25%, redirection of care was conducted (from maximal intensive to limited care). Only in 3% of the death cases was redirection of care that eventually ended in withdrawal of life-sustaining treatment implemented. In 18% of the cases (including 2 neonates who died in the delivery room), intensive care treatment was not initiated, and these neonates received nutrition and analgesia if they survived more than a few hours.

The maximal intensive care approach was practiced more often during the years 2000–2004, applied to 65% of the dying infants; however, during the years 2005–2009, this type of care decreased significantly to 46% (P < .02). In parallel, the redirection of care approach increased significantly from
19% to 37.5% (P < .0005) in the years 2000–2004 and 2005–2009, respectively. The least conducted approach was the primary nonintervention care, and no significant change during the 2 time periods was observed: 15% and 17%, respectively (Table 3).

Of the neonates treated with the limited redirection approach, 38% were born at $37$ weeks' gestation. The leading causes of death in this subgroup (41.4%) were congenital anomalies and perinatal asphyxia (14%). The limited redirection approach was conducted in 34.5% of extremely preterm infants ($\leq 26$ weeks) who died, and the main causes of death were extreme respiratory insufficiency and severe intraventricular hemorrhage (IVH). The primary nonintervention approach was mostly initiated in infants born at $>35$ weeks' gestation (58%) with congenital malformations (82%).

Seven infants (3%) died after redirection and withdrawal of care; 3 were extremely preterm infants with severe IVH-ICH, 2 were term infants with cyanotic heart defects and hypoplastic lungs, 1 infant with Down syndrome was born at 28 weeks with complicated cyanotic heart disease, and an infant born at 35 weeks' gestation had sepsis and extended IVH-ICH.

The time of neonatal and postneonatal death was directly associated with the therapeutic approach practiced; the shortest average lifetime ($3.7 \pm 1.7$ days) was observed in cases in which primary nonintervention care was provided, and the longest average lifetime ($21.3 \pm 5.7$ days) was seen in cases in which redirection and active withdrawal of care were performed (including the period of maximal intensive care treatment). In neonates who received redirection with limited

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TABLE 2 Causes of Death According to Gestational Age at Birth

<table>
<thead>
<tr>
<th>Gestational age at death (wk)</th>
<th>$\leq 26$</th>
<th>27–36</th>
<th>$\geq 37$</th>
<th>$\leq 26$</th>
<th>27–36</th>
<th>$\geq 37$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory complications</td>
<td>26/47 (55%)</td>
<td>13/48 (27%)</td>
<td>1/24 (4%)</td>
<td>24/41 (58%)</td>
<td>11/45 (24%)</td>
<td>1/34 (3%)</td>
</tr>
<tr>
<td>Severe IVH</td>
<td>20/47 (42%)</td>
<td>7/48 (15%)</td>
<td>0</td>
<td>20/41 (49%)</td>
<td>5/45 (11%)</td>
<td>0</td>
</tr>
<tr>
<td>Sepsis</td>
<td>6/47 (13%)</td>
<td>8/48 (17%)</td>
<td>2/24 (8%)</td>
<td>10/41 (24%)</td>
<td>4/45 (9%)</td>
<td>2/34 (6%)</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>2/47 (4%)</td>
<td>3/48 (6%)</td>
<td>0</td>
<td>4/41 (10%)</td>
<td>3/45 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Congenital malformations</td>
<td>4/47 (8%)</td>
<td>21/48 (44%)</td>
<td>11/24 (46%)</td>
<td>2/41 (5%)</td>
<td>25/45 (55%)</td>
<td>17/34 (50%)</td>
</tr>
<tr>
<td>Perinatal asphyxia</td>
<td>0</td>
<td>1/48 (2%)</td>
<td>5/24 (21%)</td>
<td>0</td>
<td>1/45 (2%)</td>
<td>6/34 (18%)</td>
</tr>
<tr>
<td>Metabolic disease</td>
<td>0</td>
<td>2/48 (4%)</td>
<td>1/24 (4%)</td>
<td>0</td>
<td>1/45 (2%)</td>
<td>2/34 (6%)</td>
</tr>
</tbody>
</table>

*Some infants had $>1$ cause leading to death.*
intensive care or maximal intensive care, the length of life was similar, 13.5 ± 3.7 and 13.9 ± 5.6 days, respectively.

Type of Care and Parental Role in the End-of-Life Decision Process

The association between the type of care given and parental involvement in the end-of-life process, as depicted in the patients’ records, is shown in Table 3. When the redirection of care approach was applied, detailed documentation describing the end-of-life decision process and the resultant decision was found in almost all cases (96%). In all cases in which medical treatment and support were discontinued upon parental request or recommendation of the neonatal team, documentation was clearly found in the medical chart. However, documentation of parental thoughts and requests and the medical team’s discussion with the parents was profoundly lacking in the group of infants dying while receiving maximal intensive care (Fig 2). Overall, when comparing the years 2000–2004 and 2005–2009, documented discussions with parents, including their thoughts and requests, and the medical team’s concerns and decisions had clearly increased, from 38% to 84%, respectively ($P < .001$).

DISCUSSION

In this study, we have reviewed in detail 239 consecutive death cases that occurred in our NICU over the past decade, focusing on causes and age of death, medical team approach, and parental involvement. To the best of our knowledge, this is the first Israeli publication addressing issues of death circumstances in the NICU, although statistical national data on deaths of infants born at ≤26 weeks were recently reported.12,13 We found that the leading causes of death remained similar throughout the study period and included prematurity and its complications, whereas term neonates died mainly due to congenital anomalies or asphyxia. These findings are consistent with updated data from Europe6 and North America.16

When comparing trends of age at death during 2000–2004 and 2005–2009, we observed that significantly fewer neonates (72% vs 55%) died during the first week of life in the later study period, whereas the rate of older infants at death (≥30 days up to 8 months) had doubled during 2005–2009 (8.4% vs 20%). The decrease in the death rate shortly after birth may reflect more intensive treatment provided to extremely preterm infants born at the

### Table 3

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Years</strong></td>
<td>2000–2004 ($n = 119$)</td>
</tr>
<tr>
<td>Primary nonintervention</td>
<td>18/119 (15%)</td>
</tr>
<tr>
<td>Parental involvement</td>
<td>11/118 (61%)</td>
</tr>
<tr>
<td>Maximal intensive care</td>
<td>78/119 (65%)</td>
</tr>
<tr>
<td>Parental involvement</td>
<td>13/78 (17%)</td>
</tr>
<tr>
<td>Redirection of intensive care (overall)</td>
<td>23/119 (19%)</td>
</tr>
<tr>
<td>Parental involvement</td>
<td>21/23 (91%)</td>
</tr>
<tr>
<td>Limited care</td>
<td>20/23 (87%)</td>
</tr>
<tr>
<td>Parental involvement</td>
<td>17/20 (85%)</td>
</tr>
<tr>
<td>Withdrawal of life-sustaining treatment</td>
<td>3/23 (13%)</td>
</tr>
<tr>
<td>Parental involvement</td>
<td>3/3 (100%)</td>
</tr>
</tbody>
</table>

NS, not significant.

**FIGURE 2**

Type of care provided to dying infants and parental involvement during the end-of-life process.
borderline of viability, because recently factors other than gestational age only are included in the decision process regarding resuscitation of these infants.\textsuperscript{12,17,18} Unfortunately, these decisions are often made under stressful circumstances. Furthermore, previous studies have shown that neonatal-perinatal teams are conflicted by mortality and morbidity data and do not always act in accordance with the basic ethical principles, including the standards of best interest, patient autonomy, surrogate decision-making, and substituted judgment, as would have been done in other life-saving scenarios.\textsuperscript{19}

Most of the infants who died during the postneonatal period included preterm infants who survived the initial complications (particularly respiratory distress syndrome) and later died of bronchopulmonary dysplasia, necrotizing enterocolitis, or late-onset sepsis. Similar results were described by Simpson et al.\textsuperscript{16} Like those authors, we do not have an answer to the question of whether the late deaths reflect increased longevity or prolonged suffering. However, their study setting was different from ours and was based on an outborn neonatal center; as such, referrals from other hospitals were at different neonatal ages and had possibly been exposed to heterogeneous clinical treatments.

The results of the current study also connect the time of death with the end-of-life care approach conducted. As seen, primary nonintervention care was associated with the shortest time to death, followed by maximal intensive care management and redirection, and limited intensive care, with the oldest age at death observed in infants who received withdrawal of care. Our results are in contrast to other studies that found shorter time to death when withdrawal of care was applied.\textsuperscript{6} We believe that this approach tended to be considered relatively late during hospitalization in our NICUs, that is, only when lifesupporting treatments were determined to be ineffective and death seemed imminent, resulting in prolonging life.\textsuperscript{20,21}

The increasing documentation of parents’ thoughts and requests with regard to their dying child demonstrates, in our opinion, the effects of the change in the medical teams’ approach during the past decade, leading to open and clear discussions with parents while explaining all treatment options. Because this was a chart review study, we assumed that if documentation was not found, a discussion did not take place, but this may or may not be true in each case. Because end-of-life decisions and parental involvement were not measured independently, this may explain the higher proportion of “no discussion with parents” in the maximal care group. We hypothesize that the current change, namely, documenting these discussions, which today are protocol-based, was the result of practicing the redirection of care as a valid option for the vast majority of parents, as also experienced by others.\textsuperscript{22} Yet given the retrospective nature of the study, we are unable to determine precisely whether this observation results from an increased willingness to document these decisions in the clinical records rather than from a real change in practices.

Although the information on survival rate and outcome in extremely preterm infants is known, decisions about the end of life of sick infants, especially limiting care or withdrawing of ventilation and providing further palliative care, are made differently within and between countries.\textsuperscript{23,24} Active withdrawal of treatment is common in NICUs in Europe, and half of neonatal deaths occur with this approach in the United Kingdom,\textsuperscript{25} France,\textsuperscript{26} the Netherlands,\textsuperscript{27} Switzerland,\textsuperscript{6,28,29} and Germany.\textsuperscript{9} In a multicenter survey\textsuperscript{7} assessing physician’s end-of-life decisions in NICUs across 7 European countries, physicians from all these countries were found to have “set limits to intensive interventions,” including continuation of current treatment without escalation, withholding of emergency treatment, and withholding of intensive treatment (the latter with the exception of Italy). Clinicians’ decisions to withdraw ventilation were more variable; the rate of physicians in agreement was highest in the Netherlands, the United Kingdom, and Sweden; intermediate in France and Germany; and lowest in Spain and Italy. France and the Netherlands reported giving drugs with the intention to end life.\textsuperscript{7} Conversely, in Latin America, withholding or withdrawing of life support in the NICU are rare events, and treatments with sedatives/narcotics are seldom given to dying infants.\textsuperscript{30} In North America (the United States), the process to withdraw treatment is more formalized; parents and clinicians agree to “reorientate” care, and a second neonatologist is required to review the case before presentation to the hospital’s ethics committee for approval (this step may be a formality but is required by state law).\textsuperscript{31}

Generally, it appears that parents seek to play an active, but not a sole role in the decision-making process regarding their sick infant.\textsuperscript{32,33} Therefore, physicians should support parents during the process, based on clear and informed medical counseling. The involvement of parents in the end-of-life decision-making process also has a favorable impact on long-term parental grief.\textsuperscript{34} Cultural context may influence the preferred type of involvement, varying from physicians largely making the decisions as in Latin America,\textsuperscript{30} to decisions made mostly by parents as in Quebec, Canada.\textsuperscript{35}

Because of the retrospective nature of this study, it was difficult to measure accurately the relationship between the type of care given and the cultural and
religious background of the families. However, because >85% of our Jewish population is religious and all our Arab families are Muslim and religious, we can assume that most neonates who died were born to religious families. The topic of various religious groups and their effect on the treatment approach is beyond the scope of this study. Nonetheless, considering our religious patient population, which is mostly composed of ultra-Orthodox believers who are forbidden to hasten death despite good intentions, we were surprised to find the change in trend toward increasing implementation of the redirection of care approach. This may stem from the fact that the option of not intensifying treatment, medically parallel to the term “passive euthanasia,” is increasingly being accepted by Jewish religious authorities. Involvement of religious authorities, such as a rabbi whom the family relies on, may facilitate the decision-making process by parents, because different opinions of Jewish authorities are recently being heard on the issue of extending the life of a dying newborn, quality of life, and sanctity of life.

Similarly, life sanctity is one of the basic sacred laws in the Islamic religion; one cannot take the life of another. Sickness is considered a test from God and is essentially related to faith. However, in specific circumstances, life withdrawal is an option. Thus, the action of withdrawing or withdrawing care must be thoroughly explained to parents when their child is in an end-of-life situation so that the difference between intention and action while providing redirection of care will be completely understood. Limitations of this study include the fact that it was performed in a single institution; thus, generalization of the findings is restricted. However, because our population is ethnically unique, we believe that the data add another aspect to the wide spectrum of circumstances of NICU deaths. In addition, because this was a retrospective study, we could not link the results with parental education, demographic data, and socioeconomic status, which may be of interest for evaluation in additional prospective studies.

We speculate that the significant increase in applying the redirection of care approach in sick neonates born to religious parents is the result of direct and transparent discussions, as seen in the documented data, when specifically addressing the expected quality of life. Although the infant’s best interest comes first, the potential influence of poor life quality on the family emphasizes the emerging significance of the family interest as well in the decision-making process. Overall, the redirection of care, compared with maximal intensive care for sick infants, is feasible even among religious families.

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