Is Neonatal Intensive Care Justified in All Preterm Infants?

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Abstract

A proactive policy of resuscitation at birth and prompt initiation of intensive care have been shown to be associated with an improvement in the survival of very preterm infants in both institution-based and population-based studies. As a greater percentage of live births were offered intensive care, the survival rate rose progressively in all birth weight and gestation subgroups among extremely low birth weight infants, including those who were born at borderline viability between 23 weeks and 25 weeks of gestational age. Their quality-adjusted survival rate also rose progressively, since the large gains in survival over time had not been offset by significant increases in survival with disability. Cost-effectiveness and cost-utility ratios remained stable overall, with efficiency gains in the smaller infants over time, as more such infants were being born in level III perinatal centers with the regionalization of perinatal-neonatal healthcare programs. National and international surveys of obstetricians and neonatologists on their perception of viability and their management decisions in extremely preterm infants have shown significant variations on the application use of intensive care in those born extremely preterm. If doctors believe that such infants have little prospect for intact survival, their management would be suboptimal or delayed, thus creating a self-fulfilling prophecy. Both developed and developing countries need to develop appropriate policies for initiating and withdrawing intensive care, taking into consideration their own cultural, social, and economic factors.

Among the many neonatal ethical problems, the one that neonatologists are faced with on a regular basis involves the issue of selective non-treatment, that is, clinical decisions made after the birth of a live-born infant to either withhold or withdraw intensive care in certain clinical situations such as in preterm infants of borderline viability (1). Studies have shown great variability in doctors’ attitudes and their management policies for extreme prematurity. There is a tendency for both obstetricians and neonatologists to underestimate the potential for survival and overestimate the risks of disability for extremely preterm infants (2-4). Many neonatologists continue to selectively resuscitate extremely preterm infants at birth, which means that live born infants are left to die through withholding of intensive care. If doctors believe that the infant has little prospect for survival or survival without disability, it is probable that their clinical management would be delayed or less than optimal and may in fact be creating a self-fulfilling prophecy. Both developed and developing countries need to develop appropriate policies for initiating and withdrawing intensive care, taking into consideration their own cultural, social, and economic factors.
Decision to Withhold Intensive Care

Institution-based Studies
In the majority of Level III perinatal centers within developed countries, all infants with a birthweight of more than 500 g or a gestation of 24 weeks or more are offered intensive care. At Monash Medical Centre (MMC) in Australia, we have reported that 10% of 442 extremely preterm live births born at 23-28 weeks gestation over a 10-year period, 1977-1986, were not offered intensive care, 4% had obvious major malformations, and 6% were considered “nonviable,” for which resuscitation at birth was not offered or was not successful (6). The proportion of live births in which treatment was withheld at the time of delivery was 37% at 23 weeks, 17% at 24 weeks, 8% at 25 weeks, 1% at 26 weeks, 1% at 27 weeks, and 0% at 28 weeks. This approach to offering intensive care was considered ahead of its times even in developed countries 20-30 years ago (7). During an identical period, 1977-1986, in another Level III perinatal center within a few kilometers of MMC, 42% of similar live births born at 24-26 weeks gestation were not offered intensive care, all of whom died (6). This accounted for a lower survival rate among their infants born at 23-28 weeks gestation compared with those in MMC (29% vs 44%), as the survival rate among those who were offered intensive care was similar.

Our practice during the 1990 decade was consistent with what the Royal College of Paediatrics and Child Health in the United Kingdom has published in 1997, which stated that it would not be unreasonable to consider withholding treatment in an infant born at 23 weeks and weighing little more than 500 g (8). There is a general consensus in developed countries even to this day that parents of a 22-week infant should be discouraged from seeking active treatment, whereas those of a 25-26 week infant should be encouraged to consent to intensive care (9). It is reasonable not to offer resuscitation for all 23-24 week infants who should be assessed on an individual basis at the time of birth.

Population-based Studies
Population-based studies from a designated geographical region, rather than from a single institution, are essential if the impact of withholding neonatal resuscitation and intensive care for extremely preterm live births in non-Level III hospitals are to be determined. Significant numbers of these “outborn” preterm infants might not be transferred by a neonatal emergency transport service (NETS) to institutions with a neonatal intensive care unit (NICU), and they would die at their hospital of birth. Our research group in the State of Victoria was one of the first to publish the outcome of a population-based extremely low birth weight (ELBW, <1000 g) cohort born in the 1979-80 (10), reporting on their long-term outcome up to 14 years of age (11). In our State, there are three Level III perinatal centers, each with its NICU and a fourth stand-alone NICU in a children’s hospital. There are 20 Level II special-care units and 150 Level I maternity units with small neonatal nurseries attached. The three perinatal centers deliver only about one-quarter of the State’s births. However, 70% of ELBW births were being delivered in the three hospitals even during these early years, indicating that there was already an effective effort being made to identify women with high-risk pregnancies who might deliver an ELBW infant, and they were being referred in utero by midwives and obstetricians in the community for consultation by maternal-fetal medicine specialists within our perinatal centers. For the remaining 30% ELBW infants who were born outside the perinatal centers, less than half (42%) were transferred for neonatal intensive care after birth; those not referred, with very few exceptions, died. The perinatal mortality rate of ELBW infants was significantly lower in those born in the perinatal centers compared with those born elsewhere (72% vs 93%) as were the stillbirth rate (36% vs 59%) and neonatal death rate (56% vs 82%) (12,13).

We defined disability as severe if the child had cerebral palsy and was unable to walk, low IQ defined as a psychological test score of more than two standard deviations below the mean, or bilateral blindness. Not only did our inborn ELBW infants have a significantly higher survival rate compared with those who were outborn, the inborn survivors had also a significantly lower severe disability rate: 15% vs 50% at 2 years, 15% vs 38% at 5 years, 13% vs 39% at 8 years, and 10% vs 30% at 14 years. Their high disability rate was attributable to suboptimal perinatal care, which was identified in 72% of outborn survivors, secondary to a failure or a delay in initiating intensive care among these outborn infants.
The benefits of a more proactive intensive care policy made available to a higher percentage of live-borns transferred in utero to Level III perinatal centers for management were established when this early regional cohort was compared with later regional cohorts born in 1985-87. Not only was there a significant 50% improvement in ELBW survival rate in 1985-87 compared to 1979-80, but there was a significant reduction in the disability rate among ELBW survivors at our 2-year assessment: severe from 18% to 11%, moderate from 5% to 1%, and mild from 28% to 18% (14). In this study, severe disability was defined as cerebral palsy in children unlikely ever to walk, Bayley Mental Developmental Index (MDI) <69, or bilateral blindness; moderate disability as cerebral palsy in non-ambulant children who were likely to walk or sensorineural deafness requiring amplification; and mild disability as cerebral palsy in ambulant children and Bayley MDI 69-84. The key factor in the improved outcome was the significant increase in the proportion of the State’s ELBW infants was born within the three perinatal centers (from 70% to 77%), where proactive resuscitation and prompt intensive care measures were initiated. Another factor was a greater number of outborn ELBW live births who received proactive resuscitation and prompt intensive care even at the Level II hospitals prior to the arrival of NETS (15). At 5 years of age, severe cerebral palsy was reduced from 3% to 1%, blindness from 7% to 3%, deafness from 6% to 0.5%, IQ score <2SD from 31% to 7%, and IQ score <3SD from 9% to 2% (16).

The proportion of ELBW infants who were inborn at the Level III perinatal centers continued to increase to 84% in 1991-92 and 91% in 1997 (17,18). As a result, a greater number had the benefit of proactive resuscitation and prompt intensive care initiated after birth (19). Table 1 shows that this has resulted in a progressively improved survival rate, as well as an improved adjusted survival rate, secondary to a reduction in the proportion of survivors with disability (20). Another benefit that has been identified is that, in spite of an increase in the consumption of hospital resources that inevitably results from a proactive treatment policy, economic evaluation of efficiency in terms of cost-effectiveness and cost-utility has remained unchanged (21-23).

Table 1. Improving survival and quality-adjusted (QA) survival in a population-based study of extremely low birth weight (ELBW) infants

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*According to ref. 20.

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There was little research data in the 1980-90s on regional population-based cohorts determined by gestational age (24-26). However, in the State of Victoria, we have reported that a proactive treatment policy was associated with an increased survival of extremely preterm infants born at borderline viability down to 23 weeks gestational age, without an increase in the disability rate among survivors (27,28). Over the years 1985-1987, 1991-1992, and 1997, the survival rates were 0%, 10%, and 41% respectively at 23 weeks gestation; 12%, 33%, and 41% at 24 weeks; 28%, 58%, and 73% at 24 weeks; and 45%, 72%, and 88% at 26 weeks. This was primarily a result of an increasing percentage of extremely preterm infants being offered intensive care after birth: from 27% in 1991-1992 to 59% in 1997 at 23 weeks, from 63% to 76% in 24 weeks, from 94% to 98% at 25 weeks, and from 98% to 100% at 26 weeks (29). Our population-based data showed that increased intensive care in the late 1990s for infants at the borderline viability born at 23 to 27 weeks gestation was associated with improved outcomes, at incremental costs that were not excessive compared with more mature infants (30).

Decision to Withdraw Intensive Care

However, a proactive policy to initiate intensive care must take into consideration that a decision to withdraw intensive care might have to be made in selective infants at a later stage in the course of the infant’s treatment. In the event that the
infant's subsequent clinical course indicates that further curative efforts are futile or lack compensating benefit, intensive care should be discontinued and palliative care, which provides symptomatic relief and comfort, should be introduced. This approach, termed “individualized prognostic strategy” has been advocated as an acceptable and preferred mode of operation in the NICU, one that has been endorsed by the Canadian Pediatric Society and the American Academy of Pediatrics (31,32).

The attending neonatologist has the primary role as an advocate for the infant and medical advisor to the parents, whereas the parents act as surrogates for their infant. The shift in emphasis from curative to palliative care requires consensus among all those involved in the care of the infant, both medical and nursing staff, as well as consent from the parents who should be closely involved in this widely shared decision-making process.

At Monash Medical Centre, in the 1981-1987 period, intensive care was withdrawn prior to death in 65% of 316 deaths (33). Among these infants, death was considered to be inevitable in the short term even with the continuation of neonatal intensive care in 70% of the cases. In the remainder, the risk of severe brain damage was considered to be so great that death was considered preferable to a life with major disability. Therefore in our NICU, full treatment until death is uncommon and occurred in only one-third of cases. This experience was not unique as studies from the United Kingdom and New Zealand showed that 70-80% of deaths in their NICUs follow a deliberate withdrawal of life sustaining treatment (34,35).

Principles of Selective Withdrawal of Intensive Care

There are three clinical situations in which selective withdrawal of intensive care is appropriate (1). There are few who would disagree withdrawal of intensive care is morally and ethically acceptable when death is considered to be inevitable and the infant is in the process of dying whatever treatment is provided. Intensive care would be considered in these cases a futile exercise and not in the best interest of the infant. Examples in this category include those infants with severe respiratory failure or fulminating sepsis who have persistent or worsening hypoxemia, acidosis, and hypotension unresponsive to ventilatory and inotropic support. There is no obligation to provide futile medical care in such cases, as no infant with progressive multiple organ failure survives even without withholding cardiopulmonary resuscitation (2). It is appropriate also to consider withdrawal of intensive care even when death is not inevitable with continued treatment, but there is a significantly high risk of severe physical and mental disability should the infant survive. Such a decision should not raise too many moral and ethical problems if the infant’s development of self awareness and intentional action is believed to be virtually impossible or there is no prospect of the infant ever being able to act on his or her own behalf.

One scenario is that of an extremely preterm infant with large, bilateral parenchymal hemorrhages, infarcts, and/or leukomalacia in the brain (3). More controversial an issue is when survival with moderate disability is possible with treatment, but the infant is likely to suffer persistent pain, require recurrent hospitalization and invasive treatment throughout life, and to experience early death in childhood or early adulthood. This situation may arise with a preterm infant with severe chronic lung disease non-responsive to dexamethasone and with no prospect of being weaned from mechanical ventilation, but for whom lung transplant is still considered an experimental option.

The one principle with which all the guidelines proposed in the United Kingdom, Canada, USA, and Australia, is that if continued life for the infant with treatment is a worse outcome than death, then the principle of primum non nocere imposes a professional, moral, and humanitarian duty upon neonatologists to withhold or withdraw life sustaining treatment. Infants cannot benefit from such treatment and death is not the worst outcome for them if they cannot be rescued from irreversible medical deterioration and death, cannot have life prolonged without major sensorineural sequelae, and cannot be relieved of ongoing pain and suffering. When the process of dying is being artificially prolonged, most would agree that the harm of continued treatment exceeds any potential benefit. However, decisions based on quality of life considerations are more difficult as there is inevitably imprecision in predicting the risk of intolerable disability or suffering.

Medico-legal Perspective

Very few cases of selective non-treatment have reached the courts. It is considered appropriate for these difficult decisions to be made within the context of the infant/neonatologist/par-
ent relationship and experience has shown that there is no excessive abuse in such private decision-making processes. The legal position appears to recognize the importance of respecting parental decisions but emphasizes that the law court has the right to intervene and overrule a decision if that is necessary to protect the best interests of the infant. The British legal system, for example, had upheld selective non-treatment in the three categories of neonatal conditions referred to previously. Firstly, selective non-treatment was ruled to be legally acceptable when death was inevitable in the case of a hydrocephalic preterm infant on the verge of death. Secondly, legal precedence for selective non-treatment for an infant with severe brain damage, who was neither dying nor in severe pain, was found in a case presenting to court with a high risk of multiple sensorineural disabilities. Thirdly, selective non-treatment was considered lawful in an infant where the benefits of life with treatment failed to outweigh the burdens of a “demonstrably awful life” of pain and suffering.

**Decision-making Process**

The importance of less medical paternalism and more informed parental involvement in the decision-making process of selective non-treatment must be emphasized. The neonatologist should never make unilateral decisions regarding the right to die. Adequate and consistent parental communication carried out by medical and nursing staff must begin with the admission of all infants into the NICU so that trust can be developed between the parents and staff irrespective of outcome (36). An open-visiting policy for families is essential to promote such parental contact (37). A realistic assessment of the infant’s clinical condition should be given by the neonatologist to the parents as soon as possible. The medical facts should be presented with an honest, sympathetic, and caring attitude. Often the information has to be repeated and reinforced by the entire staff. Otherwise, misunderstandings and unrealistic expectations can lead to confusion, suspicions, bitterness, and frank hostility. As with most medical decisions made by neonatologists that require parental informed consent, much of the discussion on selective non-treatment depends on trust in the knowledge, judgment, and integrity of the doctor. When a consensus has been reached by the NICU staff that selective non-treatment is an appropriate option to raise with the parents, one or more intense and intimate meetings would be required so that the crucial set of discussions could take place and in which a decision could be reached on the matter. These meetings usually involve both of the parents, the attending neonatologist, a nurse representative and a non-medical staff member who can act as the parents’ advocate, such as a medical social worker.

**Palliative Care**

The neonatologist’s duty does not end with the decision for selective non-treatment. The principles and guidelines for palliative care demand that basic nursing care should continue with the emphasis to provide comfort to the infant. Electronic monitoring of physiological parameters, diagnostic investigations (such as X-rays and blood tests), medications (including oxygen and antibiotics), and therapeutic procedures (including resuscitation, all forms of assisted ventilation and intravenous infusion) which might prolong the dying process, should be discontinued. Prolonged terminal weaning, defined as a stepwise or gradual decreasing of ventilator support over a period of hours, is considered inappropriate. Dragging out the withdrawal serves only to prolong the dying process and any attendant suffering. The argument that the sudden withdrawal of ventilator support resembles an intentional killing does not hold merit, as in both cases, a treatment on which the infant depends for life is being discontinued and death is the expected outcome. The infant should be nursed in a normal cot and warmth provided by light clothing. If the infant has apparent distress, symptomatic relief should be provided, such as suctioning to remove oropharyngeal secretions and sedation with normal therapeutic doses of morphine as needed, even if the pain relief measures may inadvertently shorten the dying process.

A controversial issue involves the withdrawal of enteral nutrition and hydration during palliative care. Preterm or sick infants require gavage feeding and although it has been advocated that this feeding method is part of medical treatment and should therefore be discontinued during palliative care, others consider it as basic nursing care which must not be withheld under any circumstances (38). A number of court decisions have supported the withdrawal of nutrition thus equating the administration of artificial nutrition with other medical procedures (39). Precedence has been set in a British court on the legality of
withholding gavage feeding. Nevertheless, most neonatologists would be reluctant not to provide gavage feeding, even when it might be lawful and appears to be in the infant’s best interest. There is an obvious perception of a moral difference between withdrawing ventilatory support and withholding fluids or nutrition with selective non-treatment. The underlying principle is that naturally or artificially administered hydration and nutrition may be given or withheld, depending on the infant’s comfort.

Parents need a quiet place to be with their infant during the dying process. They may wish that other family members and religious advisors be present. Hospice concepts have been applied to neonatal care by providing a family room that is private yet close to the NICU and by training NICU staff in more supportive approaches towards the families (40,41). Such a program allows the staff to cope better with the dying infants offered selective non-treatment and facilitates the grieving process in the parents. In certain circumstances, withdrawal of intensive care may be arranged to take place in the home, so that death can occur in a more comforting environment for the family.

Roles of Infant Bioethics Committee

The functions of infant bioethics committees include (a) education of staff and parents on relevant ethical principles and provision of literature and resources, (b) policy development and establishment of ethical principles, (c) prospective review through consultation in cases being considered for selective non-treatment and resolution of disagreements among staff and families, and (d) retrospective review of relevant medical records to determine the appropriateness of hospital policies and whether these policies are being followed (42,43). A concern has been expressed that when they attempt to fulfill so many roles, they will do nothing well. The general opinion is that such committees should serve only on an advisory basis without authority to implement any decision. An important function of an infant bioethics committee or consultative group is to provide ethical solace and support for neonatologists who have to face difficult and disturbing decisions.

Conclusions

This review has shown from both our institution-based and population-based studies that a proactive policy of resuscitation at birth and prompt initiation of intensive care improves survival and quality-adjusted survival, not only for ELBW infants but also in those very preterm infants at borderline viability. In most developed countries, this means intensive care being routinely offered to all who have reached 24 weeks gestation. Limited resources in developing countries however necessitate a different intervention point, which may be 26 weeks or even 28 weeks. Continued advances made in the knowledge and technology in neonatal intensive care will result in ongoing revisions of current medico-legal and ethical guidelines. The principles behind decision-making on initiating and withdrawing intensive care will however remain interpersonal and intimate, respectful to the infants’ lives and their parents’ autonomy, and sensitive to the emotional concerns of parents and staff.

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