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Original article

Decisions and outcome for infants born near the limit of viability

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ABSTRACT

Background: Initiation or withholding life support at birth on infants born prematurely near the limit of viability is not an easy decision, with wide variation in practice around the world. Our aim was to review the outcome of preterm infants born near the limit of viability at 23–25 weeks gestation in our institution, with regard to resuscitation decision, survival, and major outcome measures.

Methods: We included all live newborn infants born prematurely at 23–25 weeks gestation at King Faisal Specialist Hospital and Research Centre from January 2006 to December 2015. We collected data on resuscitation decisions, survival, and major neonatal morbidities such as severe brain injury, severe retinopathy of prematurity, and bronchopulmonary dysplasia.

Results: Between January 1, 2006 and December 31, 2015, 97 infants with a gestational age (GA) of 23–25 weeks gestation were admitted; 23, 42, and 32 infants were born at 23, 24, and 25 weeks gestation, respectively. At 23 weeks gestation, full support was initiated in 87% of patients and later on support was withheld in 17.4% of patients, finally 13% of patients survived to discharge. At 24 weeks, full support was initiated in 97.6% of patients, then withheld in 7.1% of patients, and ultimately 59.5% survived. At 25 weeks, full support was initiated in 93.8% of patients, then withheld in 15.6% of patients, and ultimately 62.5% survived. In terms of survival with and without the three major neonatal morbidities, at 23 weeks gestation, no infant survived without any morbidity as compared to 7.1% and 28.1% at 24 and 25 weeks, respectively. The incidence of survival with 1 major morbidity was 8.7%, 30.9%, and 34.4% at 23, 24, and 25 weeks, respectively, the incidence of survival with 2 major morbidities was 0%, 19%, and 0% at 23, 24, and 25 weeks, respectively, and the incidence of survival with 3 major morbidities was 4.3%, 2.4%, and 0% at 23, 24, and 25 weeks, respectively.

Conclusion: In our patient cohort, survival and survival without major neonatal morbidity were very low at 23 weeks gestation, but it improved gradually as gestational age advanced.

1. Introduction

The decision to initiate or withhold life support in infants born near the limit of viability is a hard decision. [1–3]

Although the prognosis is affected by many factors such as by birth weight, gender, multiple pregnancy, and exposure to antenatal steroids [3–5], many recommendations about resuscitation are made solely on gestational age (GA) at birth [2,3,6–11].

In a systematic review of 31 international guidelines for resuscitation decisions of extremely preterm infants, there was a considerable disparity in the recommendations between different countries. In general, most guidelines supported comfort care only at 22 weeks' GA and active care at 25 weeks' GA [12]. Nevertheless, at 23 and 24 weeks of gestation, the recommendations ranged from comfort care to individualized care to routine active treatment [12,13].

In the United States, a consensus statement by the American College of Obstetricians and Gynecologists, recommended all

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measures of neonatal and obstetric care to be considered at 23 weeks of gestation, but no firm recommendation was given for active treatment; however, at 24 weeks of gestation, active treatment was recommended [13,14].

In Saudi Arabia, the religious ruling is "if an infant is born at less than six lunar months (177 days, 25 weeks and 2 days), resuscitation can be offered if deemed beneficial as decided by two specialized physicians" (fatwa # 231) on March 6, 2008 [15].

The aim of our study is to review the outcome of preterm infants born near the limit of viability at 23–25 weeks' gestation in our institution with regard to resuscitation decision, survival, and major outcome measures.

2. Methods

Following approval from the Research Ethics Committee of King Faisal Specialist Hospital and Research Centre (KFSH&RC), we collected data on all live newborn infants born prematurely at 23–25 weeks' gestation at the KFSH&RC, from January 1, 2006 to December 31, 2015. All infants were included even if they had major congenital anomalies. Infants were identified from the NICU database and delivery room logbook; the medical records of the mothers were reviewed for documented resuscitation decisions based on the GA at birth. Then the medical records of the infants were reviewed to assess the resuscitation decision at birth as documented in the medical chart.

For all infants, we collected the following demographic data: maternal history, maternal age, parity, use of antenatal steroids, gestational age, birth weight, sex, mode of delivery, and Apgar score. The mortality rate was calculated based on the GA for all infants. In survivors, we collected data on major complications of prematurity such as intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD), and severe retinopathy of prematurity (ROP). We chose these morbidities as they were shown to be independently correlated with the long-term outcome at 18 months and 5 years in very low birth weight infants in two large studies [16,17].

2.1. Definitions

Active treatment: Infants will be considered to have received active treatment if they received any of the following interventions: ventilatory support (invasive or noninvasive), tracheal intubation, surfactant therapy, chest compressions, or epinephrine.

Comfort care: Infants will be considered to have received comfort care only if it was documented in the medical chart that "no resuscitation" decision was made and he/she did not receive any of the treatments described above at or after birth.

Withholding of active care: If the infant received active care at birth, but because of major complication, the management goal was shifted to only comfort care without active treatment or cardiopulmonary resuscitation and such a decision was documented in the medical chart.

GA was determined from the last menstrual period and/or early ultrasound scan. Small for GA was considered as birth weight <10th percentile for age, according to the United States Vital Statistics natality data sets for 2001 and 2002 [18]. IVH was diagnosed with cranial ultrasound scanning performed during the NICU stage, Papile's classification was utilized [19]. PVL denotes periventricular echogenicity on cranial ultrasound scan. Severe brain injury was defined as Papile's grade 3 and 4 IVH and PVL. ROP was defined using the International Classification of ROP [20]. Severe ROP was defined as unilateral or bilateral disease of stage 4 or 5, or the receipt of retinal therapy in at least 1 eye. BPD was defined as the need for supplemental oxygen at 36 weeks corrected age [21].

3. Statistical analysis

Outcome measures were evaluated by using descriptive analysis. Continuous variables were reported as mean and range; categorical variables were reported as percentages.

4. Results

Between January 1, 2006 and December 31, 2015, 97 infants with GA of 23–25 weeks were admitted, demographic data are as shown in Table 1.

4.1. Resuscitation decisions and survival

23 weeks: Out of 23 infants born at 23 weeks gestation, 5 infants were diagnosed with major congenital anomalies (21.7%); full support was initiated at birth to 20/23 (87%) infants, while 3 infants received only comfort care; later on, intensive support was withheld on 4 more infants (17.4%) because of poor clinical condition or major brain hemorrhage and they eventually died. Out of the remaining 16 infants, 13 passed away and 3 (13%) infants survived to hospital discharge.

24 weeks: Out of 42 infants born at 24 weeks gestation, 6 (14.3%) were diagnosed with major congenital anomalies; another 2 infants (5%) had very early rupture of membranes at 18 and 20 weeks gestation. One infant received comfort care only at birth, while the remaining 41 infants (97.6%) received full support; later on support was withheld for 3 more infants. Twenty-five infants (59.5%) survived to hospital discharge.

25 weeks: Thirty-two infants were born at 25 weeks gestation, 7 infants (21.9%) were diagnosed with major congenital anomalies and 2 other infants (6.3%) had very early rupture of membranes at 18 weeks gestation. Two infants received comfort care only at birth and in 5 other infants support was withheld later in the NICU. Twenty infants (62.5%) survived to hospital discharge.

4.2. Neonatal morbidities

Severe brain injury was diagnosed in 5 (21.7%) infants, 9 (21.4%), and 9 (28.1%) infants born at 23, 24, and 25 weeks gestation, respectively. Retinal therapy for severe ROP was done in 1 (4.3%), 7 (16.6%), and 2 (6.3%) infants born at 23, 24, and 25 weeks gestation, respectively; all of these infants had grade 3 ROP, none was diagnosed with grade 4 or 5 ROP. BPD was diagnosed in 3 (13%), 22 (52.4%), and 10 (31.3%) infants born at 23, 24, and 25 weeks gestation, respectively.

Survival with and without the three major neonatal morbidities at GA is shown in Table 2.

5. Discussion

In our single center study, resuscitation decisions, survival, and major neonatal morbidities were reported for infants born near the limit of viability. Survival rate was very low at 23 weeks gestation, but it improved as GA advanced. The very low survival rate at 23 weeks could reflect our NICU staff's attitude and treatment goals during this period [15,22]. At this gestational age, 13% of those infants received comfort care only at birth and in another 17% of infants active care was withheld.

With regard to major short-term neonatal morbidities, there was a marked improvement in survival with less morbidities as GA advanced, for example, survival with one or no morbidity at 25 weeks gestation was 62.5% compared to 8% only at 23 weeks.

In our patient cohort, there was a high incidence of major congenital anomalies, small for GA and very early previable rupture

Table 1
Demographic data of the study participants.

Variable	GA: 23 weeks N = 23	GA: 24 weeks N = 42	GA: 25 weeks N = 32
GA	23 + 3 (SD 2)	24 + 3 (SD 2.3)	25 + 3 (SD 1.9)
BW	Mean 578 (SD 99) Range 420-760	Mean 665 (SD 110) Range 480-1020	Mean 748 (SD 175) Range 400-1090
Male	16 (70%)	24 (57.1%)	14 (43.7%)
Small for age	0	1 (2.4%)	4 (16%)
Congenital anomalies	5 (21.7%)	6 (14.3%)	7 (21.9%)
Antenatal steroids	16 (70%)	34 (81%)	24 (75%)
CS	4 (17.3%)	15 (35.7%)	19 (59.3%)
Active treatment	20 (87%)	41 (97.6%)	30 (93.8%)
Comfort care	3	1	2
Support withheld	4	3	5
Survived	3 (13%)	25 (59.5%)	20 (62.5%)

Value between brackets indicates the percentage, unless otherwise specified.
GA: gestational age, N: number, BW: birth weight, CS: caesarean section, SD: standard deviation.

Table 2
Survival with major neonatal morbidities at gestational age, number (percentage).

GA	23 weeks	24 weeks	25 weeks
Number	23	42	32
Died	20 (87%)	17 (40%)	12 (37.5%)
Survived 3 Morbidities	1 (4.3%)	1 (2.4%)	0 (0%)
Survived 2 Morbidities	0 (0%)	8 (19%)	0 (0%)
Survived 1 Morbidity	2 (8.7%)	13 (30.9%)	11 (34.4%)
Survived 0 Morbidity	0 (0%)	3 (7.1%)	9 (28.1%)

of membranes at ≤ 20 weeks, as we are a major perinatal referral center for such cases, which could affect results. For example, among infants born at 25 weeks gestation, congenital anomalies were diagnosed in 21.9% of infants, while 16% of infants were born small for gestational age. Of those infants, intensive care was not initiated or was withdrawn on 21.9% of infants.

We reported the survival figures of 50 infants near the limit of viability in the 1990s; the survival rate was 29% and 58% at a GA of 23 and 24 weeks, respectively [23,24]. Lower survival rates at 23 weeks gestation in the current cohort could be due to change in caregivers attitude toward less aggressive treatment of infants born at such a low gestational age.

In Saudi Arabia, the Ministry of Health guidelines for neonatal care recommend palliative care for infants born below 24 weeks gestation (personal communication).

Several studies from around the world reported similar trends in survival rates for infants born between 23 and 25 weeks, low survival rates for infants born at 23 weeks gestation were reported from France (1%), Switzerland (4%), the UK (19%), and Australia (20%), while survival rates increased significantly at 25 weeks from the same cohorts to 59%, 61%, 66%, and 76%, respectively [13].

With regard to major short-term morbidities, a similar report from Switzerland showed that survival without the three major morbidities was 15–17% in infants born between 22 and 25 weeks gestation [25].

A major limitation of our paper is that we are reporting short-term data only without a long-term well-structured neurodevelopmental evaluation of the survivors; therefore, we have chosen to analyze the count of 3 morbidities as each of them was independently correlated with a poor long-term outcome [16,17]. The TIPP trial showed that in children without any of the 3 morbidities, the rate of poor long-term outcomes at 18 months was 18%, while rates with any 1, any 2, and all 3 neonatal morbidities were 42%, 62%, and 88%, respectively [16]. While the CAP trial showed that the rates of poor long-term outcome at 5 years in children with none, any 1, any 2, and all 3 morbidities were 11.2%, 22.9%, 43.9%, and 61.5%, respectively [17].

Another limitation is that this was a single-center study with a relatively small sample, so it cannot be generalized to all infants with similar GA. In the future, we hope that we can conduct a larger multicenter or national study for such an infant population.

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Declaration of interest

None.

Ethical statement

We declare that our work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript was prepared in line with the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals.

References

[1] Tyson JE, Younes N, Verter J, Wright LL. Viability, morbidity, and resource use among newborns of 501 to 800-g birth weight. J Am Med Assoc 1996;276:1645–51.
[2] Raju TNK, Mercer BM, Burchfield DJ, Joseph Jr GF. Periviable birth: executive summary of a joint workshop by the eunice kennedy shriver national institute of child Health and human development, society for maternal-fetal medicine, American academy of pediatrics, and American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:1083–96.
[3] Rysavy MA, Li L, Bell EF, Das A, Hintz SR, Stoll BJ, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. N Engl J Med 2015 May 7;372:1801–11.
[4] Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive care for extreme prematurity — moving beyond gestational age. N Engl J Med 2008;358:1672–81.
[5] Carlo WA, McDonald SA, Fanaroff AA, Vohr BR, Stoll BJ, Ehrenkranz RA, et al. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. J Am Med Assoc 2011;306:2348–58.
[6] Kaempf 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;117:22–9.
[7] Nuffield Council on Bioethics. Critical care and decisions in fetal and neonatal medicine: ethical issues. London: Nuffield Council on Bioethics; 2006.

[8] Chervenak FA, McCullough LB, Levene MI. An ethically justified, clinically comprehensive approach to peri-viability: gynaecological, obstetric, perinatal and neonatal dimensions. J Obstet Gynaecol 2007;27:3–7.
[9] Raghuveer TS, Cox AJ. Neonatal resuscitation: an update. Am Fam Physician 2011;83:911–8.
[10] Jefferies AL, Kirpalani HM. Counselling and management for anticipated extremely preterm birth. Paediatr Child Health 2012;17:443–6.
[11] Gallagher K, Martin J, Keller M, Marlow N. European variation in decision making and parental involvement during preterm birth. Arch Dis Child Fetal Neonatal Ed 2014;99:F245–9.
[12] Guillen U, Weiss EM, Munson D, Maton P, Jefferies A, Norman M, et al. Guidelines for the management of extremely premature deliveries: a systematic review. Pediatrics 2015;136:343–50.
[13] Patel RM, Rysavy MA, Bell EF, Tyson JE. Survival of infants born at periviable gestational ages. Clin Perinatol 2017;44:287–303.
[14] American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine, Ecker JL, Kaimal A, et al. Periviable birth: interim update. Am J Obstet Gynecol 2016;215. B2–12.
[15] Al-Alaiyan S. The decision not to resuscitate infants born at limit of viability in Saudi Arabia: an Islamic legal opinion. Paediatrics 2009;14:8–10.
[16] Schmidt B, Asztalos EV, Roberts RS, Sauve RS, Whitfield MF. For the trial of Indomethacin Prophylaxis in Preterm (TIPP) Investigators. Impact of Bronchopulmonary Dysplasia, brain injury and sever Retinopathy of Prematurity on the outcome of extremely low-birth-weight infants at 18 months. Results from the trial of prophylaxis in preterms. J Am Med Assoc 2003;289:1124–9.
[17] Schmidt B, Roberts RS, Davis, Doyle LW, Asztalos EV, Opie G, et al. For caffeine for apnea of prematurity (CAP) trial investigators. Prediction of late death or disability at age 5 Years using a count of 3 neonatal morbidities in very low birth weight infants. J Pediatr 2015;167:982–6. e2.
[18] Vital US. Statistics Natality data set for 2001 and 2002. Rockvill, MD: National Center for Health Statistics; 2004.
[19] Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr 1978;92:529–34.
[20] An international classification of retinopathy of prematurity. Pediatrics 1984;74:127–33.
[21] Shennan AT, Dunn MS, Ohlsson A, Lennox K, Hoskins EM. Abnormal pulmonary outcomes in premature infants: prediction from oxygen requirement in the neonatal period. Pediatrics 1988;82:527–32.
[22] Al-Alaiyan S, Al-Hazzani F. The need for hospital-based neonatal palliative care programs in Saudi Arabia. Ann Saudi Med 2009;29:337–41.
[23] Al-Alaiyan S. Call to establish a national lower limit of viability. Ann Saudi Med 2008;28:1–3.
[24] Aqeel A, Al-Deery M, Al-Alaiyan S. Outcome of infants born at the limit of viability: a local experience. Middle East Paediatrics 2001;6:34–7.
[25] Fischer N, Steurer MA, Adams M, Berger TM. Survival rates of extremely preterm infants (gestational age <26 weeks) in Switzerland: impact of the Swiss guidelines for the care of infants born at the limit of viability. Arch Dis Child Fetal Neonatal Ed 2009;94:F407–13.