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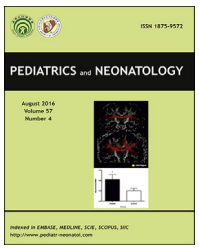

Original Article

Neurodevelopmental outcomes at 3 years old for infants with birth weights under 500 g

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Key Words
extremely low birth weight infants;
stillbirth;
extreme prematurity;
less than 500 g;
survival rate

Background: Marked improvements have been achieved in the survival of extremely low birth weight infants, but survival rates and prognoses of extremely small infants with birth weights ≤500 g remain poor. The aim of this study was to clarify long-term outcomes for surviving infants with birth weights ≤500 g.
Methods: The study population comprised fetuses of gestational age ≥22 weeks, expected live- or stillbirth weight ≤500 g, and birth date between 2003 and 2012. Developmental assessments were performed prospectively at 3 years old.
Results: Data were obtained for 21 fetuses, including 10 live births and 11 stillbirths. Of the 10 live births, median gestational age was 25.2 weeks (range, 22.4–27.1 weeks), median birth weight was 426 g (range, 370–483 g), and two neonates died before discharge. One infant with severe asphyxia died within 12 h and another infant with Down syndrome died at 34 days. The survival rate was thus 80%. All surviving infants were small for gestational age. Seven of the 8 surviving infants (88%) weighed less than 2500 g at a corrected age of 40 weeks. Seven infants were available for developmental assessments at 3 years old. One infant could not be followed. Two of those seven infants (29%) showed normal development, three infants (42%) showed mild neurodevelopmental disability, and two infants (29%) showed severe neurodevelopmental disability. One infant had periventricular leukomalacia and cerebral palsy. Two of the seven infants (29%) had short stature (<3 SD) at 3 years old.

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Conclusion: Although the survival rate among live births was good (80%) in this study, neurodevelopmental outcomes remained poor in infants with birth weights ≤500 g. Further large studies are needed to assess long-term outcomes for extremely small infants.

1. Introduction

With continuing advances in perinatal care, marked improvements in the survival of extremely low birth weight infants have been well documented.[1,2] However, survival rates and prognoses of extremely small infants with birth weight less than 500 g are still poor. Many studies have defined live birth as requiring a birth weight ≥500 g, but increased reporting may account for the increased number of infants with birth weights ≤500 g.[3] Although resuscitation of infants with birth weight ≤400 g was not recommended by the American College of Cardiology/American Heart Association 2005 guidelines,[4] this criterion was discarded in 2015. Although the criteria defining human viability vary between countries, this has recently changed.

Neonatal mortality rates are higher in infants with lower birth weights and greater degree of prematurity.[2,3] Consequently, extending the gestational period and increasing the birth weight is recommended. However, intrauterine growth restriction represents an important risk factor for sudden stillbirth,[5] and inadequate fetal growth may occasionally increase the risk of stillbirth even if the gestational period is extended.

In cases with live- or stillbirth weight ≤500 g, no consensus has been reached and data are lacking on whether early delivery to preempt intrauterine hypoxia is preferable to delaying delivery to obtain maturity and growth even in view of the risk of stillbirth. Moreover, few studies have examined the long-term prognosis in infants with birth weights less than 500 g.[6,7]

Our strategy with regard to the timing of delivery for pregnancies with live- or stillbirth weight ≤500 g is to deliver cases where continued pregnancy would compromise maternal health or where non-reassuring fetal status (NRFS) is identified. Apart from the above-mentioned situations, we opt for expectant management rather than early delivery until 26 weeks of gestation, in anticipation of fetal growth. Beyond 26 weeks of gestation, we consider delivery if fetal growth has ceased. To evaluate our policy, the clinical characteristics of alive and stillborn or dead infants with body weights less than 500 g were compared retrospectively. In addition, to clarify the long-term outcomes of surviving infants with birth weights less than 500 g, developmental assessments were performed prospectively at a corrected age of 18 months old and at 3 years old.

2. Methods

2.1. Study design and patient population

The study population comprised fetuses with gestational age ≥22 weeks and lives- or stillbirth weight ≤500 g delivered between January 1, 2003 and December 31, 2012. Toyohashi Municipal Hospital is a single tertiary perinatal medical center as well as a specialized clinic for all high-risk pregnancies in the East Mikawa district, where the population is approximately 700,000. The average delivery rate is 900–1100 infants per year. About 20 extremely low birth weight infants are admitted to our hospital each year. Our strategy of acute period treatment for extremely low birth weight infants includes: the use of a bronchial tube of maximum possible size; artificial respiration by intermittent positive-pressure ventilation during the acute period; raising the target mean blood pressure to the number of weeks of gestation by means of catecholamines, hydrocortisone, and volume bolus; fentanyl sedation; administration of indomethacin at 12 h after birth to prevent patent ductus arteriosus; glucose and insulin therapy; minimal enteral nutrition at an extremely early period; administration of probiotics; and parenteral nutrition from an early stage.

Table 1a and b show the patient characteristics for live births and stillbirths, respectively. The clinical characteristics of alive and stillborn or dead infants were compared retrospectively.

Finally, to investigate long-term outcomes, developmental assessments were carried out prospectively at 3 years old. Development was assessed using the new Kyoto Scale of Psychological Development (KSPD) test, which yields scores for neurodevelopment. The new KSPD test is a Japanese standard developmental test.[8] This individualized face-to-face test is administered by experienced psychologists to assess child development in the following three areas: posture and movement (fine and gross motor functions); cognitive and adaptation [non-verbal reasoning and visuospatial perceptions assessed using materials (e.g., blocks, miniature cars, and marbles)]; and language and society (interpersonal relationships, socialization, and verbal abilities).[9] Developmental quotient (DQ) was determined using developmental age (as determined from the new KSPD test)/chronological age × 100. We defined DQ ≥ 80 as normal, DQ ≥ 40 and < 80 as indicating mild

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