Improved Outcome of Infants Born at less than 24 Weeks of Gestation in Japan

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Abstract

Japan neonatologist association had surveyed of survival rates of infants less than 24 weeks of gestation born during 1995 to 2001 and during 2002 to 2004. There was no survival on 20th and 21st weeks of gestations, while survival rates of 22 and 23 weeks had increased from 18% to 31% and 43% to 56% respectively between two studies time periods. Their follow up data at 5 years old reviled as follows; rates of cerebral palsy (CP) with/without mental retardation (MR), MR only, blindness and infants of any aforementioned neurological sequelos were 17%, 26%, 8% and 44%, respectively. Main causes of death of these infants are mostly due to extreme prematurity including fragile skin and immature immunity. To improve the outcome of infants at 22 to 23 weeks of gestation, meticulous and gentle care is essential while knowing the viability limit based on their up-to-date statistics.

Keywords: ELBW infants; Marginally viable infants; Medical ethics

Introduction

Because of the advancement of obstetrical, perinatal and neonatal managements, outcome of extremely low birth weight (ELBW) infants have been markedly improved and currently survival rate of ELBW infants born at 24 weeks or more gestations became 80% or more in Japan [1-8]. Therefore, if ELBW infant's gestational age is 24 weeks or more, active intervention for those infants is widely accepted in Japan, unless the infant has lethal problems at birth. Since the viability limit of fetus is defined to be 22 completed weeks of gestation in Japan at 1991 based on national statistics of infants less than 24 weeks of gestation, we present Japanese experience on infants at 22 and 23 weeks of gestations, to whom active medical intervention are still on debate [2].

Method and Results

Two nationwide surveys and one institutional data on ELBW infants focused on infants less than 24 weeks of gestation are presented.

Chronological changes of survival rates of ELBW infants in neonatal committee of Japan

Pediatric Association has been conducting nationwide follow up study on ELBW infants every 5 years since 1980 [6-8]. There was no survival less than 500 grams at birth before 1980 but close to half (44%) of such ELBW infants and 85% of ELBW infants above 500 grams at birth have survived on the survey of 2000 (Table 1). When the survival rates of ELBW infants (surveyed in 2005) are categorized by gestational age, there are quite different survival rates between each gestational age group (Table 2). There was no survival on 21 weeks of gestations but survival rate of infants after 22 weeks were increased along with the advancement of gestation as follows: 34% at 22 weeks, 54% at 23 weeks, 77% at 24 weeks, 85% at 25 weeks, 90% at 26 weeks, 92% at 27 weeks and 92% at 28 weeks of gestation. Based on these data, it is apparent that ELBW infants at 21 weeks or less are not viable and infants above 24 weeks of gestation have chance to survive close to 80% or more, which elucidates the importance of infants at 22-23 weeks of gestation. These infants are regarded to be marginal viable, which will require medical and ethical consideration before initiating active interventions.

Survival rates of ELBW infants less than 24 weeks of gestation according to Japan neonatologist association

It has conducted surveys at two separate time periods on survival rates of ELBW infants less than 24 weeks of gestation born during 1995 to 2001 and during 2002 to 2004 respectively [1-8]. Reply rates were 106/198 (55%) and 114/205 (56%) and numbers of enrolled infants were 842 and 580 respectively. There was no survival on 20 and 21 weeks of gestation on both surveys. At 22 and 23 weeks of gestation, survival rates had increased from 18% to 31% and 43% to 56%, respectively (Table 3), which was a statistically significant (P<0.01) improvement in survival rates in two time periods on both 22 weeks and 23 weeks of gestation categories (Figure 1). These data encourage us to pursue further improvement of medical care on these marginally viable infants. Follow up data of neurological sequelos of 386 survivors out of 842 ELBW infants less than 24 weeks of gestation born in 1995-2001 were analyzed by subdividing in birth weight category (Table 4). Incidences of neurological sequelos at 5 years old are as follows: CP (with/without MR), MR only, blindness and infants with any aforementioned sequelos were 17%, 26, 8% and 44% respectively. Though nearly half of such survivors are categorized to be neurologically abnormal, MR defined by IQ less than 70 could be over-diagnosed at 5 years old, since extremely preterm infants are still on the process of maturing even at 5 years old.

Table 1: Chronological Changes of Survival Rate of ELBW infants (Neonatal Committee, Japan Pediatric Association).

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Survival rates of ELBW infants at Tokyo Women’s Medical University (TWMU)

TWMU has been reporting relatively high survival rate of ELBW infants in the past and the data was regarded to be the benchmark on caring ELBW infants in Japan [1,3,4,7-9]. The data of TWMU on ELBW infants was also quoted in the textbook of Avery’s Neonatology (6th edition) as the leading result on infants at 22-23 weeks of gestation [10]. Survival rates of ELBW infants cared at TWMU in 1984 to 2004 are shown in table 5 by gestational age categories. There was no survival at 21 weeks of gestation but were 56% and 42% survival at 22nd and 23rd weeks of gestation, respectively. When gestation age goes up to 24 and 25 weeks of gestation, survival rates of such infants were markedly improved to 77% and 92% respectively. It is clear that there is the apparent difference between 23rd and 24th weeks of gestation in regards to the survival rate, which is the important data on the discussion of the viability limit [1] (Figure 2).

Discussion

Since the survival of infants less than 22 weeks of gestation is negligible, it will be appropriate to recommend no active intervention on such infants unless there is strong parental wish because of the only hand, if gestational age goes up to 24 weeks, survival rate increases close to 80%. Therefore, it is also appropriate to recommend active intervention unless there are apparent medical conditions to relate with lethal outcome or with severe neurological sequel. How we deal with so-called marginal viable infants of 22 and 23 weeks of gestations are

Table 2: Numbers of Births and Mortality Rates According to Gestational Age born in Japan in 2005.

<table>
<thead>
<tr>
<th>Gestational Age (Weeks)</th>
<th>No. of Survival</th>
<th>No. of Admission</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0/8 [0/0]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>0/10 [0/10]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>0/14 [0/14]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>0/17 [0/17]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>0/18 [0/18]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>0/19 [0/19]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>0/20 [0/20]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>0/21 [0/21]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>0/22 [0/22]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>0/23 [0/23]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>0/24 [0/24]</td>
<td>0% [0/0]</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>269/330 (82)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Improvement of survival rate of infants at 22^nd week of gestation in two time periods.

Figure 2: Mortality rate by gestational age (October 1984 to September 2002 in Tokyo Women’s Medical University) (n=240).

Table 3: Survival rates of infants less than 24 weeks of gestation (born between 1995-2001 at 112 hospitals of Japan neonatologists network) [repeated study born between 2002-2004].

<table>
<thead>
<tr>
<th>Gestational weeks</th>
<th>n (%)</th>
<th>n (%)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Born alive</td>
<td>Died before of postnatal life 28 d</td>
<td>Died during NICU stay</td>
</tr>
<tr>
<td>22</td>
<td>97</td>
<td>57 (58.6)</td>
<td>64 (66.6)</td>
</tr>
<tr>
<td>23</td>
<td>282</td>
<td>112 (39.7)</td>
<td>129 (45.8)</td>
</tr>
<tr>
<td>24</td>
<td>423</td>
<td>77 (18.2)</td>
<td>99 (23.4)</td>
</tr>
<tr>
<td>25</td>
<td>501</td>
<td>56 (11.2)</td>
<td>73 (23.4)</td>
</tr>
<tr>
<td>26</td>
<td>542</td>
<td>35 (6.5)</td>
<td>56 (10.3)</td>
</tr>
<tr>
<td>27</td>
<td>408</td>
<td>22 (5.4)</td>
<td>32 (7.8)</td>
</tr>
<tr>
<td>=&gt;28</td>
<td>809</td>
<td>37 (3.9)</td>
<td>67 (8.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>2 (66.7)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>Total</td>
<td>3065</td>
<td>398 (13.0)</td>
<td>522 (17.0)</td>
</tr>
</tbody>
</table>

Table 4: Survival and neurological sequel rates of infants less than 24 weeks of gestation (born in 1995-2001, followed up to 5 years old).

<table>
<thead>
<tr>
<th>Gestational Age (Weeks)</th>
<th>No. of survival/No. of admission (survival rate, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>0/1 [0.0]</td>
</tr>
<tr>
<td>22</td>
<td>5/9 [56]</td>
</tr>
<tr>
<td>23</td>
<td>11/26 [42]</td>
</tr>
<tr>
<td>24</td>
<td>27/35 [77]</td>
</tr>
<tr>
<td>25</td>
<td>45/49 [92]</td>
</tr>
<tr>
<td>26</td>
<td>44/54 [82]</td>
</tr>
<tr>
<td>27</td>
<td>48/52 [92]</td>
</tr>
<tr>
<td>28</td>
<td>35/39 [90]</td>
</tr>
<tr>
<td>29</td>
<td>21/23 [91]</td>
</tr>
<tr>
<td>30</td>
<td>19/23 [83]</td>
</tr>
<tr>
<td>TOTAL</td>
<td>14/19 [74]</td>
</tr>
</tbody>
</table>

Table 5: Survival Rate of ELBW infants Tokyo Women’s Medical University (1984-2004).
Nishida H (2002) Marginally viable, fetal infants—who are too young or small to
Nishida H (1993) Outcome of infants born preterm, with special emphasis on

Currently on debate. Though their current survival rates are close to
50%, morbidity is still high and two third of survivors have some degree
of neurological handicap. Therefore, medial decision on treating such
infants at 22nd and 23rd weeks of gestation should be based on the data of
each institute. Our policy of TWMU is to initiate treatments on infants at
22nd and 23rd weeks unless apparent objection is expressed form
parents. Therefore, it is essential to discuss with parents before initiating
active intervention, desirably before birth of the infant. Frequent causes
of death of infants at 22-23 weeks are shown in table 6. One of the most
frequent causes of their death occurs at the time of birth due to asphyxia
and due to no-resuscitation following parents’ will. For better medical
management of these issues, antenatal and perinatal consultations to
parents are mandatory. Main medical reasons of neonatal death after
birth are related with their extreme prematurity, not only of cardio-
respiratory systems but also of skin fragility and immature immunity.
Meticulous care to protect fragile skin and to prevent infection is as
important as cardio-respiratory assist on managing these extreme
premature infants [9]. Specific managements to improve outcome of
infants at 22-23 weeks of gestation are suggested as shown in table
7, though some items quoted on the table are still in debate. Before
birth, exchange information and discussion with obstetricians and
neonatologists are essential, including use of antenatal steroids, timing
of delivery and parents’ will for active intervention. Though caesarian
section at such early gestations are exceptional, it is desirable to deliver
an infant and placenta with connecting umbilical cord as a set covered
by intact fetal membrane for the better cardiovascular stabilization
during and after delivery process [11]. Before cutting umbilical cord,
promoting placental-fetal transfusion by cautious cord milking is
helpful to maintain adequate blood volume of the infant [12]. Often
postnatal steroid administration is essential to stabilize blood pressure
to encounter adrenal cortical insufficiency due to extreme prematurity
and stress [13]. Use of umbilical venous catheter as an infusion route
for the first 5 to 7 days is inevitable to avoid excess handling to keep
peripheral lines [9]. Early enteral instillation of breast milk, especially
Colostrums is useful as bio-protection and gut stimulation [9]. Preventing infection by meticulous care and gentle handling to avoid
excess stress are also very important. Serial C-reactive protein (CRP)
measurements is useful to early detection of infection and moreover,
to reduce unnecessary use of antibiotics [14]. Lastly the optimistic
attitude toward successful survival by avoiding eugenic though is the
most important of all for the success of managing these marginal viable
infants [9].

Conclusion

Current Japanese data on ELBW infants, especially infants less than
24 weeks of gestations are reviewed. Since survival of infants at 21st
week of gestation is exceptional and of infants at 24th week of gestation are close to 80%, it is apparent that infants at 22nd and 23rd weeks of gestation are marginal viable and are on the debate of medical and
ethical discussion for the feasibility of active intervention at NICU in Japan.
Though there are still limited medical knowledge and technology in the
care of infants at 22nd and 23rd weeks of gestation, survival rates of such infants born in 2002-2004 have shown significant improvement from those born in 1990-2001. Therefore, we should continue our
efforts for the intact survival of these extreme premature infants, while
knowing the viability limit based on up-to-date statistics of infants at
22nd and 23rd weeks of gestation.

Acknowledgments

We appreciate Japan Neonatologist Association for their supportive work.

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Comparison of Serum Cortisol Concentrations in Preterm Infants with or without
Late-Onset Circulatory Collapse due to Adrenal Insufficiency of Prematurity.