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REGULAR ARTICLE

Comparing minimally invasive and proactive initial management of extremely preterm infants

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ABSTRACT

Aim: In 2005, we changed our minimally invasive departmental policy for infants born before 26 weeks of gestation to a proactive approach. This included structured guidelines as well as intubation and surfactant in the delivery room, if the parents agreed. The aim of this study was to evaluate the effect of this change of policy.

Method: We compared the Ages and Stages Questionnaire (ASQ) scores, mortality rates and use of mechanical ventilation before (1999–2003) and after (2005–2011) the introduction of the new policy.

Results: Twenty-two per cent of 61 infants in the before group had an ASQ *z*-score of <−2 standard deviation at 18 months' corrected age, compared with 26% of 55 infants in the after group. Mortality decreased from 46% to 36% ($p = 0.06$) and the use of mechanical ventilation at any time during admission increased from 64% to 87% ($p < 0.0001$).

Conclusion: We demonstrated that changing our policy to a proactive approach to the initial care of infants born before 26 weeks did not result in a major increase in psychomotor deficit. However, the use of mechanical ventilation increased significantly and survival tended to improve.

INTRODUCTION

Between 1986 and 2005, we followed a minimally invasive treatment strategy for all preterm infants in our department. This included avoiding intubation in the delivery room if possible, early nasal CPAP, and the INSURE (intubation-surfactant-extubation) strategy if the a/A ratio exceeded 0.22 until 1994 (1) or 0.36 thereafter (2). Mechanical ventilation was reserved for infants who developed respiratory insufficiency and was only used for extremely preterm infants after renewed consultation with their parents (3). Over the years, we became concerned that sometimes rescue mechanical ventilation was being provided too late and experience from Sweden suggested that an early active approach was associated with lower mortality rates in the most immature infants (4). In 2005, we decided to introduce an early active strategy for infants with a gestational age <26 weeks if the parents agreed. This involved providing intubation and prophylactic surfactant in the delivery room, followed by mechanical ventilation until the infant was clinically stable. At the same time, we also introduced gestational age-specific guidelines on general care during the first days of life.

Because a more active approach may allow survival of infants with greater risk of brain injury and hence increase the rate of psychomotor deficit, we planned a systematic follow-up. We decided to use a parental questionnaire as we did not have the capacity to carry out formal development tests, for example, using the Bayley Scales of Infant Development, and because we were keen to identify an increased incidence of psychomotor deficit early.

Parental questionnaires, such as the Ages and Stages Questionnaires (ASQ) (5) employed in this study, are increasingly being used, as parents know their children well and studies have proved that they are reliable when it comes to judging their children's actual abilities (6,7).

There are ASQ questionnaires for 19 different ages, ranging from 4 to 60 months, and each consists of six questions in each of the following five domains: communication skills, gross motor skills, fine motor skills, problem-solving skills and personal–social skills. Each of the six questions provides scores ranging from zero for 'no', five for

Key notes

- In 2005, we changed our minimally invasive departmental policy for infants born before 26 weeks to a proactive approach to initial management in the delivery room. At the same time, we provided structured guidelines on the general care.
- The periods before and after the introduction of the policy were compared.
- Psychomotor development at 18 months did not change significantly, but the use of mechanical ventilation increased from 64% to 87% ($p < 0.0001$), and mortality fell from 46% to 36% ($p = 0.06$).

'sometimes' and ten for 'yes'. The maximum total score is 300 for all questionnaires.

This paper reports the results of the ASQ in our population of infants, born with a gestational age of <28 weeks, comparing the period after the change of policy with previously published data from our unit before the policy change (8). We included all infants born before 28 weeks for the ASQ follow-up as we had introduced specific guidelines on the general care for the first day of life for children born before 26 weeks as well as for those born before 28 weeks. The reason for including children with gestational ages of 26 and 27 weeks was to see whether the change in strategy had a rub-off effect on mortality, ventilator days or neurodevelopmental deficit in that group.

MATERIALS AND METHODS

The 2005–2011 group comprised infants with a gestational age of <28 weeks, who were admitted to our neonatology department between November 2005 and September 2011, after being born in our hospital or transferred from another hospital during their first week of their life. We excluded children whose parents did not speak or read Danish, children who were being adopted or in custody or who did not live in the eastern part of Denmark.

The parents filled out the ASQ 10-month questionnaire when the infant was 9 months of corrected age and the ASQ 24-month questionnaire when they were 18 months of corrected age.

We used questionnaires designed for slightly older ages to obtain a normal distribution of the results. The ASQ is designed as a screening tool with focus on children with developmental delay. This means that children who are developed above average tend to achieve the maximum score in the age-appropriate ASQ.

We saw the children in our outpatient clinic when they were 9 and 18 months of corrected age. If the children were considered normal at 18 months of corrected age, no further follow-up was planned. If further follow-up was required, it was continued at our clinic, in the child's primary care centre or following referral to more specialised departments.

To standardise the ASQ results in our 2005–2011 group, we used a control group of randomly chosen age-matched children from the Danish population. The results of this study have been published in a separate paper (9). ASQ total scores were expressed as *z*-scores adjusting for age in days corrected for preterm birth.

The parents of 85 children did not fill out the 24-month ASQ and were contacted by phone and asked about extra help in day care or school and at what chronological age their child was able to walk independently. This chronological age was transformed to the corrected age.

We used ASQ data from a previous study in our unit, covering infants who were born in the hospital or admitted during their first week of life in 1999–2003 (8).

In-hospital mortality, the fraction of infants exposed to mechanical ventilation and the days of mechanical ventilation during the two periods 1999–2003 and 2005–2011 were calculated using the departmental clinical discharge database. Again we selected, without specific exclusions, the infants with a gestational age of <28 weeks born in our hospital or admitted from other hospitals during the first week of life.

The 2005–2011 data showed a discrepancy of 40 infants in the routine clinical discharge database and the dedicated follow-up database. We know that 11 of the babies died, but did not attempt to explore the reason for this difference further, because we could not do the same for the 1999–2003 follow-up data. Therefore, the results in this report on survival and use of mechanical ventilation are based on the hospital discharge database, whereas the results on neurodevelopmental outcome are from the specific 1999–2003 and 2005–2011 databases developed for the two studies.

Statistics: SPSS version 19 was used to calculate the *z*-score of the ASQ total score using the regression coefficients from the Danish national reference to correct for age (9). The two time periods were compared by the *t*-test and the chi-squared test as appropriate.

RESULTS

The mortality in infants born at <26 weeks decreased from 46% in the 1999–2003 group to 36% in the 2005–2011 group (Table 1), but this decrease was not statistically significant ($p = 0.06$). The use of mechanical ventilation at any time during the infants' admission increased from 64% to 87% ($p < 0.0001$) and the mean duration of ventilation also increased (Table 1).

In the 2005–2011 group, 225 of the 290 eligible parents (78%) completed the ASQ 10 months questionnaire at 9 months of corrected age and 160 of the 249 eligible parents (64%) completed the ASQ 24-months questionnaire at 18 months of corrected age (Figs 1 and 2).

Table 1 Mortality and use of mechanical ventilation in the periods 1999–2003 and 2005–2011, calculated from the departmental discharge clinical database (GA = gestational age)

	Infants (N)	Mortality†	Infants in ventilator	Ventilator days in those ventilated (mean and range)
1999–2003				
GA < 26 weeks	188	87 (46%)*	120 (64%)**	10.7 (1–76)
GA 26 and 27 weeks	247	45 (18%)	107 (43%)***	6.6 (1–72)
2005–2011				
GA < 26 weeks	203	74 (36%)*	177 (87%)**	17.2 (1–100)
GA 26 and 27 weeks	252	40 (16%)	127 (50%)***	10.1 (1–97)

†Inborn and outborn admitted who died before discharge/admitted inborn and outborn × 100.
*$p = 0.06$.
**$p < 0.0001$.
***$p = 0.13$.

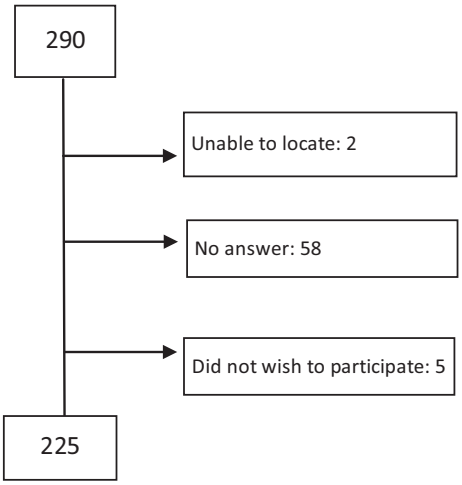

Figure 1 Participants in the Ages and Stages Questionnaire (ASQ) at 9 months' corrected age. (Infants were excluded if they were in custody, were being adopted or their parents did not speak Danish or lived outside the eastern part of Denmark).

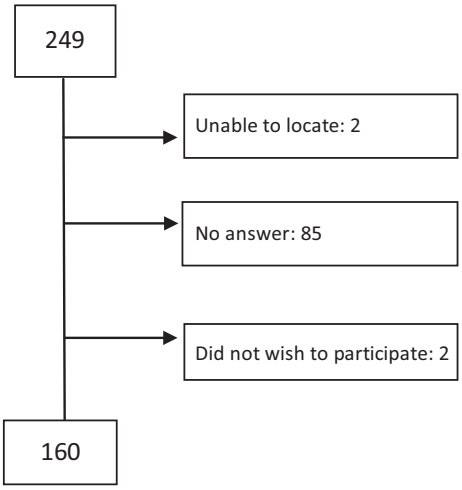

Figure 2 Participants in the Ages and Stages Questionnaire (ASQ) at 18 months' corrected age. (Infants were excluded if they were in custody, were being adopted or their parents did not speak Danish or lived outside the eastern part of Denmark).

Table 2 shows the 2005–2011 ASQ *z*-scores and the 1999–2003 ASQ z- scores at nine and 18 months of corrected age for infants born with a gestational age of <26 weeks and at 26 and 27 weeks. There were 85 nonresponders who did not fill out the ASQ 24-month questionnaire in the 2005–2011 group. We were able to contact 70 by telephone, but 15 could not be reached. The mean gestational age in the responder and nonresponder groups was the same (Table 3). More children in the nonresponder group (17%) were not able to walk independently at the corrected age of 18 months than the number of children who scored zero in the gross motor domain of the ASQ

Table 2 Ages and Stages Questionnaire (ASQ) *z*-score at nine and 18 months' corrected age in the 2005–2011 and 1999–2003 group (GA = gestational age)

	N	ASQ *z*-score mean ± SD	*z*-score −2 SD
9 months' corrected age			
2005–2011			
<26 GA	83	−0.95 ± 1.2	12%
26 and 27 GA	142	−0.75 ± 1.3	16%
18 months' corrected age			
2005–2011			
<26 GA	55	−0.80 ± 1.8	26%
26 and 27 GA	105	−0.56 ± 1.4	16%
Across age (12–60 months)			
1999–2003			
<26 GA	61	−1.3 ± 2.2	22%
26 and 27 GA	57*	−0.9 ± 1.5	13%

*A selected group matched to the <26 gestational age group.

Table 3 Responders and nonresponders in the Ages and Stages Questionnaire (ASQ) at 18 months' corrected age

	Responders	Nonresponders
Number	160	70
Mean gestational age	26.3 (23.9–27.9)	26.2 (24.0–27.7)
Major deficit	Gross motor score = 0 11 (7%)	Not able to walk independently at 18 months 12 (17%)
Minor deficit	ASQ score < −1 SD 34%	Did receive extra help in daily living/day care/school 27 (38%)*

*One no information.

(7%). By the time of the telephone interviews, just two of the 70 children – aged 27 and 44 months corrected age – were not able to walk (Fig. 3). The percentage of children in the ASQ group who had a total ASQ score of <−1 SD was equal to the percentage of children who received extra help in day care or school (Table 3).

DISCUSSION

The change of delivery room policy was followed by a marked increase in the use of mechanical ventilation and perhaps contributed to improved survival rates among infants with a gestational age of <26 weeks. It was reassuring that there was no evidence of increased psychomotor deficit. While the risk of ASQ score below −2 SD showed a small increase from 22% to 26%, the mean *z*-score improved from −1.3 ± 2.2 to −0.8 ± 1.8, indicating overall an unchanged risk of developmental deficit.

There were only few surviving infants with a gestational age of 23 weeks in both groups and no infants with a gestational age of 22 weeks. Our results were calculated on inborn and outborn infants admitted to our department

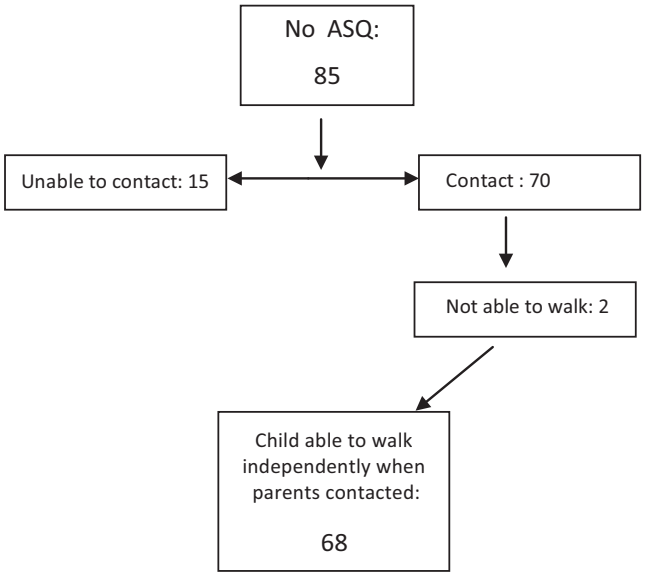

Figure 3 Nonresponders for the Ages and Stages Questionnaire (ASQ) at 18 months' corrected age.

within their first week of life and, in spite of the more proactive approach in the latter period, the number of admissions did not change significantly.

Our study has some strengths. Firstly, it was planned as a quality control measure, using the previous 1999–2003 study as a reference, and was put in place when the change of policy was implemented. Secondly, parental questionnaires are unbiased in the sense that parental judgments are unlikely to be influenced by knowledge of the nature of the comparison.

This quality control measure is possible, due to the low cost and simplicity of parental questionnaires, even when hospitals do not routinely provide formal developmental testing. This model may be of interest to others working in similar conditions and deciding on major changes in treatment policy. However, it should be noted that even comparing 5-year periods in a relatively large neonatal unit will have limited statistical power to detect changes.

The comparison with the 1999–2003 data from our unit had limitations, apart from the limited statistical power. The previous reference study was carried out at one point in time, and, as a result, the children varied in age, from 12 to 60 months. The follow-up rate in the 1999–2003 cohort was higher, perhaps because the study included a telephone interview with questions on maternal education and child handicap. Furthermore, the reference group in 1999–2003 was local, not national, with a considerably higher maternal education. The analysis may have overcorrected for this difference and, as a result, the estimated deficit may have appeared smaller than it really was.

The main weakness is the relatively low follow-up rate. This is partly a result of the structure of the neonatal service in our region, where extremely preterm infants are transferred to step-down units before they are discharged home and these units are responsible for follow-ups. The children only return to us for a few appointments and some parents may think these are unnecessary and decide not to attend. Most of the nonresponders in the 18-month follow-up group were contactable by phone and, although there was some evidence of more motor delay or abnormality in this group, few were severely motor disabled and their cognitive skills did not appear to be too different. Overall, this was reassuring. We did not attempt to include the nonresponders in the 1999–2003 comparison group because a similar telephone interview was not carried out in the previous study.

Comparing the risk of deficits of 22% and 26% in the two groups to the international literature requires some explanation. First, we used a cut-off of <−2 SD, which in principle corresponds to what is usually termed moderate developmental disability, while <−3 SD may correspond to severe developmental disability. Furthermore, the international literature often uses a complex concept of neurodevelopmental disability (NDI), including sensory disability. Blindness and deafness, however, typically contribute little to the rate of NDI and therefore it is relevant to compare disability rates with our data. In the UK (10) and Sweden (11), the combined categories of moderate and severe overall disability and moderate or severe neurodevelopmental deficits in infants born before a gestational age of 26 weeks were 29% and 33%, respectively (Fig. 4). It should be noted that these were multicenter studies comprising a much larger number of infants in a geographically defined area and that the children were evaluated at older age, which might have resulted in more children in the moderate impairment group. Cognitive performance tests carried out in children with the corrected age of 18–24 months are not a reliable way to predict outcome in individual children, whereas tests carried out at the corrected age of 5 or even 8 years are better (12,13).

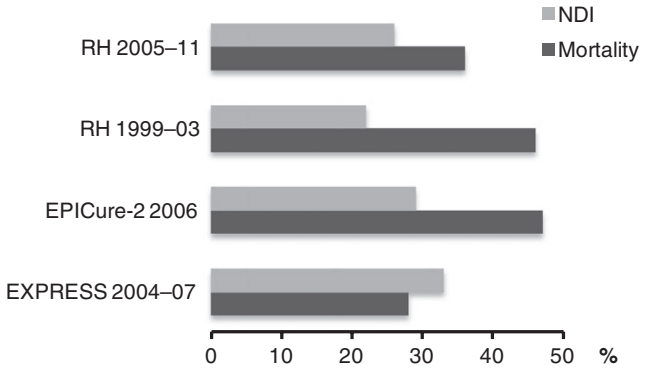

Figure 4 Comparision of mortality and neurodevelopmental impairment (NDI) in three centres. Infants with gestational age of <26 weeks. RH: neonatal department, Rigshospitalet, Copenhagen. Mortality: death in neonatal care. NDI: ASQ total points at 18 months' corrected age <−2 SD. EPICure-2 2006 (10). Mortality: death in neonatal care. NDI: nonimputed data on infants at median 34 months' corrected age. EXPRESS 2004–2007 (11,22). Mortality: death in neonatal care and up to 365 days. NDI: infants at 30 months' corrected age.

However, those children who are severely impaired at 2 years of age remain severely impaired at 5 or 8 years (12,14) and, more importantly for a quality control measure, the rate of deficit does not typically change much.

It is important to identify warning signals without undue delay. However, in our study, the ASQ score at a corrected age of 9 months showed a considerably lower incidence of deficit of 12%. Sutton et al. (15) found that by 1 year, only 11% of children born with a gestational age of 23–27 weeks had major mental deficits. This may suggest that the age of assessment should not be pushed below 12 months.

Is it at all likely that the change in policy would cause increased risk of psychomotor deficit? We were concerned for two reasons. Firstly, a more active early attitude could lead to increase the use of mechanical ventilation – which it did in our study – and mechanical ventilation carries a risk of inadvertent hyperventilation and brain injury (16,17). Secondly, potentially more immature and/or ill infants may survive – which is likely to have happened in our study – and these are more likely to survive with brain injuries than the more mature and less ill infants. Major randomised studies and meta-analyses on early intubation versus expectant management have been published in recent years (18–21). Although the number of infants aged <26 weeks are limited in these studies, there is currently nothing to suggest that prophylactic surfactant strategy provides short-term or long-term benefits when it comes to outcomes such as death or BPD.

We think that the trend towards increased survival in our 2005–2011 cohort is not likely to be explained by the prophylactic surfactant strategy in itself, but was more likely caused by a generally more proactive approach. This included a more structured protocol for the delivery management and care of these small infants, with a focus on resuscitation, thermoregulation, early intravenous parenteral nutrition and management of hypoglycaemia. Finally, parents expressed a wish for an active approach in the great majority of cases and this may well have encouraged us to be more proactive in the following days. As a result of this interpretation, we recently changed our approach back to avoiding intubation in the delivery room if possible.

CONCLUSION

Using parental questionnaires as a follow-up tool in a neonatal department is an easy and cost-effective way to monitor performance. We were able to demonstrate that a major change in policy regarding delivery room management of infants born before 26 weeks did not result in a major increase in psychomotor deficit. However, the use of mechanical ventilation increased significantly and survival tended to improve.

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