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RESEARCH

Survival of extremely premature babies in a geographically defined population: prospective cohort study of 1994-9 compared with 2000-5

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ABSTRACT

Objective To assess changes in survival for infants born before 26 completed weeks of gestation.

Design Prospective cohort study in a geographically defined population.

Setting Former Trent health region of the United Kingdom.

Subjects All infants born at 22+0 to 25+6 weeks' gestation to mothers living in the region. Terminations were excluded but all other births of babies alive at the onset of labour or the delivery process were included.

Main outcome measures Outcome for all infants was categorised as stillbirth, death without admission to neonatal intensivecare, death before discharge from neonatal intensivecare, and survival to discharge home in two time periods: 1994-9 and 2000-5 inclusive.

Results The proportion of infants dying in delivery rooms was similar in the two periods, but a significant improvement was seen in the number of infants surviving to discharge (P<0.001). Of 497 infants admitted to neonatal intensive care in 2000-5, 236 (47%) survived to discharge compared with 174/490 (36%) in 1994. These changes were attributable to substantial improvements in the survival of infants born at 24 and 25 weeks. During the 12 years of the study none of the 150 infants born at 22 weeks' gestation survived. Of the infants born at 23 weeks who were admitted to intensive care, there was no significant improvement in survival to discharge in 2000-5 (12/65 (18%) in 2000-5 *v* 15/81 (19%) in 1994-9).

Conclusions Survival of infants born at 24 and 25 weeks of gestation has significantly increased. Although over half the cohort of infants born at 23 weeks wasadmitted to neonatalintensive care, there was no improvement in survival at this gestation. Care for infants born at 22 weeks remained unsuccessful.

INTRODUCTION

In the autumn of 2007 a House of Commons select committee reviewed the legislation on abortion in the United Kingdom.[1] A House of Commons debate on the subject was scheduled for early 2008. Current legislation limits abortion to before 24 weeks' gestation unless there are specific medical issues. It has been suggested that because of improvements in medical care for such babies this limit should be lowered.

During discussions in the select committee it was recognised that published peer reviewed UK evidence is lacking to answer the question of whether the survival of infants born at 23 or 24 weeks has improved in recent years. We compared the survival of infants in a geographically defined population born before 26 weeks' gestation in 1994-9 and 2000-5.

METHODS

Participants

We included in the study infants alive at the onset of labour, born between 1 January 1994 and 31 December 2005 and before 26 completed weeks' gestation, and born to a mother whose normal home address was within the former Trent health region. The Trent region is a geographically defined population of about 4.6 million, with about 55 000 births a year. Sixteen hospitals within the region provide maternity and neonatal services.

Outcome measures

The outcome measures were stillbirth or miscarriage, death without admission to neonatal intensivecare, death before discharge from neonatal intensivecare and survival to discharge home.

Data collection

A register of all babies born at or before 32 weeks or requiring intensive care has existed in Trent since February 1990 (Trent neonatal survey). Five part time neonatal nurses prospectively collect data during regular visits to neonatal units. They record basic information about pregnancy, delivery, and care provided in the neonatal unit for all infants who meet the criteria for entry in the register. Gestation of infants, an essential element of this study, is allocated by using the following hierarchy: mother certain of her dates (most reliable); early dating scan; late dating scan; postnatal examination (least reliable). Clear standard operating procedures ensure a uniform approach to the

recording of data. Systems are also in place to obtain data about babies of Trent origin cared for outside the regional boundaries.[2]

We determined the number of miscarriages or stillbirths and deaths of infants without admission to a neonatal unit from the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI). This is a longstanding national study (recently renamed the Confidential Enquiry into Maternal and Child Health —CEMACH) that collates data from various sources about all infants delivered after 22 weeks' gestation either born dead or who died in the first year of life.[2 3]

Statistical analysis

We compared two periods of six years: 1994-9 and 2000-5 inclusive. We assessed the significance of differences in outcomes between the two reported time periods with χ^2 tests and determined birth rates with the overall regional births data from the Office for National Statistics (ONS). SAS v8.2 software was used for all analyses.

RESULTS

Comparison of time periods

Total births for the two periods were 339 774 in 1994-9 and 317 473 in 2000-5. During the two periods of the study similar numbers of infants in the relevant gestation groups were either born dead or died in delivery rooms (table), suggesting no major change in attitude to care during labour or assessment after birth of these infants. Of the infants born at 22 and 23 weeks, 58% (133/229) and 63% (126/200)died in the delivery room in each of the time periods, respectively, while slightly fewer (13% (59/453) *v* 10% (46/469)) of the infants born at 24 and 25 weeks did so (table).

There was a marked improvement between the two time periods in the survival to discharge of the infants born at 24 and 25 weeks who were admitted to intensive care (figure). This amounted to an improvement from 24% to 41% (P<0.001) in the 24 week group and from 52% to 63% (P=0.016) in the 25 week group. These improvements were not seen in those born at 22 and 23 weeks. In both time periods none of the infants born at 22 weeks and admitted to neonatal intensive-care survived to discharge. The rate of survival to discharge after admission also changed little for infants born at 23 weeks' gestation, being 18.52% in 1994-9 and 18.46% in 2000-5.

Use of resources

The total number of days spent on the neonatal unit rose during the second period in relation to births at each week of gestation except for babies admitted at 22 weeks. It was only in this group that there seemed to have been a move to less aggressive care (table).

DISCUSSION

This analysis of data from the Trent region of the UK showed no improvement in the survival of babies admitted to neonatal intensive care born before

Comparison of outcomes and days of care for extremely premature infants alive at onset of labour in Trent, 1994-9 and 2000-5

	Gestational age (completed weeks)				
Outcome	22	23	24	25	Total
Alive at onset of labour					
1994-9	142	206	237	270	855
2000-5	119	164	258	256	797
1994-2005	261	370	495	526	1652
Live births (% of infants alive at the onset of labour)					
1994-9	81 (57)	148 (72)	198 (84)	255 (94)	682 (80)
2000-5	69 (60)	131 (80)	227 (88)	242 (95)	669 (84)
1994-2005	150	279	425	497	1351
Admitted to neonatal intensive care (% of live births)					
1994-9	15 (19)	81 (55)	165 (83)	229 (90)	490 (72)
2000-5	9 (13)	65 (50)	198 (87)	225 (93)	497 (74)
1994-2005	24 (16)	146 (52)	363 (85)	454 (91)	987 (73)
Survived to discharge (% of admissions)					
1994-9	0	15 (19)	40 (24)	119 (52)	174 (36)
2000-5	0	12 (18)	82 (41)	142 (63)	236 (47)
1994-2005	0	27 (18)	122 (34)	261 (57)	410 (42)
Total days of care					
1994-9	58	1851	7432	12 043	21 384
2000-5	18	2241	11 581	18 462	32 302
1994-2005	76	4092	19 013	30 505	53 686
Mean days of care/admitted baby					
1994-9	3.9	22.9	45.0	52.6	43.6
2000-2005	2.0	34.5	58.5	82.1	65.0
1994-2005	3.2	28.0	52.4	67.2	54.4

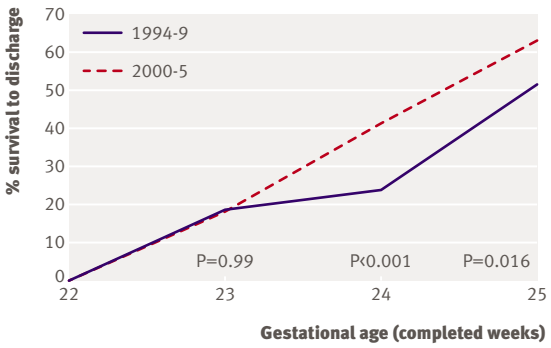
24 weeks' gestation. In those born at 24 and 25 weeks, however, there was a markedly different pattern of improving survival. This suggests a significant improvement in the care of these slightly more mature infants. Evidence gathering by the recent House of Commons Science and Technology Committee in October and November 2007 highlighted the lack of published peer reviewed data regarding the survival of infants born at 23 and 24 weeks' gestation in the UK.[4] The minority report published by the committee criticised the EPICure dataset for presenting outcomes of babies alive at birth rather than the survival of those admitted to intensive care.[1]

Our findings cannot be explained by a change in obstetric practice or neonatal resuscitation practice as similar numbers died in the delivery room in both time periods (1994-9 and 2000-5). These deaths are a mixture of infants who were born dead, born too sick to be successfully resuscitated, or treated conservatively with agreement between parents and staff. We have no robust mechanism for differentiating those deaths that occurred because aggressive resuscitation failed from those where such resuscitation was considered inappropriate. Despite a slight fall (from 55% to 50%) in the proportion of infants who were admitted to a neonatal unit at 23 weeks' gestation, our results indicate no change in the attitude to those admitted. In 1994-9, 78/81 infants (96%) received intensive care compared with 62/65 infants in 2000-5 (95%) (P=0.78). The remaining infants received palliative care alone.

When clinicians consider the appropriateness of intensive care for extremely premature infants they often use the survival figures and developmental outcomes of the EPICure study.[5] This study was a prospective cohort study of all infants born at 20-25 completed weeks' gestation in the UK and Ireland during a 10 month period beginning in March 1995. It provided valuable data on chances of survival for extremely premature infants. With significant improvements in technology and altered attitudes of those caring for these infants these data may no longer be applicable to current infants and the EPICure study has recently been repeated.

Our survival figures for the whole period 1994-2005 are similar to those reported from 1995 by the EPICure group.[5] In the EPICure study, deaths in the delivery room accounted for 84%, 46%, 22%, and 16% of infants born alive at 22, 23, 24, and 25 weeks' gestation, respectively. The corresponding figures in our study were 84%, 48%, 15%, and 9%. Similarly, survival to discharge occurred in 9%, 20%, 34%, and 52% of the EPICure infants admitted to a neonatal intensive care unit at 22, 23, 24, and 25 weeks' gestation, respectively, with our corresponding figures being 0%, 18%, 34%, and 57%. Follow-up data from the EPICure cohort have indicated high rates of long term morbidity among children born at 23 and 24 weeks' gestation.[6,7]

As a geographical region Trent is reasonably representative of the UK as a whole.[8] It is therefore unlikely that our data are substantially at variance with



Percentage survival to discharge by gestational age for infants admitted to neonatal intensivecare, 1994-9 compared with 2000-5

outcomes of neonatal intensive care across the UK. There are few other population based studies of this type from around the world but those from northern Europe have reported similar rates of survival.[9,10] In Scandinavia rates are generally a little higher, with the best of these reporting 40% survival at 23 weeks for babies admitted to intensive care.[11-13] Data from studies with different methods (such as based only on live births) are difficult to compare because of inconsistencies in the way babies at the margin of viability are classified.[14] We consider that data from single centre studies are impossible to interpret as improved outcomes are more likely to reflect inclusion and selection bias than differences in approaches to management or availability of resources.[15] The use of resources associated with the care provided to babies in our study, however, markedly increased between the two time periods. This trend has major implications for the neonatal service as a whole.

Strengths of study

We used up to date information with robust methods of data collection. Experienced trained research nurses collected data from each unit for the Trent neonatal survey. Data verification procedures, such as auditing a proportion of the forms, double data entry, and the collection of data for infants moving outside of the region for care, also maximised the quality and completeness of the data. The geographical basis of the population studied—that is, data from the entire region—increases statistical precision and removes some of the potential for bias in the results of an observational study.[16] For example, if during the study period there was a change in referral pattern with more infants who survived delivery being referred to tertiary centres, bias might be introduced if data were analysed only from tertiary units. We also used the CESDI database of stillbirths and deaths in the delivery room to ensure that we knew and appropriately classified the outcome of all infants alive at the onset of labour or delivery. The correct classification of infants as being live born but dying before admission to the neonatal unit is an important point that can reflect the ethical viewpoint of the staff resuscitating the infant. This is often overlooked in comparisons of survival rates of premature infants.[17]

WHAT IS ALREADY KNOWN ON THIS TOPIC

Survival rates in infants born before 26 weeks' gestation are relatively low

Recent reports from individual centres of improved survival of extremely premature babies are hard to interpret because of inclusion bias and variation in case mix

WHAT THIS STUDY ADDS

By looking at changes in survival over time in a whole population this study provides data free of inclusion bias and case mix effects

Survival rates in infants born at 24 and 25 weeks' gestation have clearly improved in the past 12 years

Survival rates in those born at 23 weeks' gestation have not changed, and intensive care for babies born at 22 weeks remains unsuccessful

The approach to estimation of expected date of delivery and gestation changed over the period of the study, with most current pregnancies undergoing a dating scan compared with perhaps 50% at the start of the study period. Such a change clearly has the potential to introduce systematic bias. However, over the whole 12 year period just eight trained and experienced nurses who used the same algorithm throughout collected data for this work. We think that our results are unlikely to simply represent a different approach to classification of gestation in the two time periods.

Weaknesses

There was a relatively small number of babies born at 22 and 23 weeks' gestation. While this might be why we could not show improving survival in the smallest babies, the similarity of the survival rates at 22 and 23 weeks is compelling. Application of a retrospective calculation of sample size shows that the cohort was large enough to detect a difference of 13% in the survival rates of the infants born at 23 weeks in the two periods.

Our findings concur with the view of Hack and Fanaroff, who suggested in 2000 that the limit of viability had been reached.[18] Large improvements in the survival to discharge of admitted babies born at 24 and 25 weeks (to 41% and 63%, respectively) in the most recent time period suggests that a blanket policy of not resuscitating these infants is inappropriate. Such an approach is currently pursued in the Netherlands, but in the UK a widespread consultation has suggested guidelines for the approach to individual infants based on gestational age.[19] Recent guidance from the American Academy of Pediatrics also concurs with this approach, recommending honest and open joint decision making between parents and clinicians.[20]

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Contributors: JSD, ESD, BNM, and DJF developed the idea for the paper and drafted the paper. ESD and DJF designed the study. BM performed the statistical analysis, and JSD, ESD, BM, and DJF interpreted the results. All authors revised the paper critically and approved the final manuscript. DJF is the guarantor.

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Ethical approval: Local research ethics committee approval was obtained for each of the centres at the beginning of the Trent Neonatal Survey. In 2004 approval was obtained from the Trent multicentre research ethics committee. The neonatal survey obtained section 60 approval under the Health and Social Care Act for its programmes in 2002. The Patient Information Advisory Group also gave approval for collection of data without consent.

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