SHORT REPORT

Preterm mortality and morbidity over 25 years

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Changing preterm population variables have masked improvements in neonatal survival over time. Increased use of antenatal steroids, caesarean section, and surfactant may have reduced the likelihood of mortality and periventricular haemorrhage by a third and doubled that of chronic lung disease, persistent duct, and septicaemia.

Mortality and morbidity for preterm infants has improved over the past three decades, but changes in admission policies and population mix have made these changes difficult to quantify. The introduction of antenatal steroids and surfactant therapy have been shown to be highly effective in clinical trials,^{1 2} but their efficacy “in the field” is less clear. Ideally, to answer these questions, one would use a clinical database collected in a standardised manner from a large geographically defined population over time. Although such attempts have been made, they generate cohorts containing only very high risk infants, or cover only a short period.³

The availability of a clinical database of preterm babies admitted to a single regional unit over 25 years makes it possible to correct for population variables and to examine the effects of changes in treatment.

POPULATION AND METHODS

Over 25 years, a clinical database has been maintained for all infants born alive at 34 weeks gestation or less and admitted to the Mersey Regional Neonatal Unit at Liverpool Maternity Hospital and later Liverpool Women’s Hospital, Liverpool, UK. It includes: year of birth, birth weight, gestation, sex, multiple birth, and where booked for delivery (population variables); clinical interventions such as antenatal steroids, rate of caesarean section, surfactant therapy (treatment variables); and mortality and morbidity data such as periventricular haemorrhage on ultrasound scan (PVH), chronic lung disease (CLD), persistent arterial duct (PDA), and septicaemia. For this study, only infants of <31 weeks gestation are considered, and the data analysed in five five-year blocks. Using logistic regression, with each outcome in turn as the dependent variable, and a dummy variable representing each five-year period after the first as independent variables, odds ratios (ORs) for each outcome for each period were derived. Associations were sought between the outcomes and the population and treatment variables.

To examine the changes in the likelihood of outcomes over time allowing for changes in the population variables, logistic regression was used with the outcome as the dependent variable, and those population variables showing significant association with the outcome and dummy variables representing each five-year period as independent variables. The OR for each outcome in each five-year period compared with the first (1980–1984) was derived, adjusted for population factors. By entering treatment variables also, their contribution to outcomes could be seen.

RESULTS

Between 1 January 1980 and 31 December 2004, 3726 infants born at <31 weeks were admitted. Infants of <28 weeks, with a birth weight <1000 g, from multiple births or inborn, increased significantly over time, as did those whose mothers received steroids, were born by caesarean section, or received surfactant.

There were significant changes in ORs for the outcomes over time (table 1). Population and treatment variables were significantly associated with mortality and morbidities. Multiple birth did not correlate significantly with any of the outcomes, and male sex only correlated with mortality. The ORs from logistic regressions adjusting for population variables showed significant differences from the unadjusted values over the five periods, for mortality between 1990 and 2004, and mortality and/or CLD in the period 2000–04. Adjustment for treatment variables resulted in significant changes in the ORs for outcomes. The changes indicate that the ORs for mortality and PVH would have been about one third higher without the treatment interventions. Similarly the ORs for CLD, PDA, and septicaemia would have been about half their recent values. The OR for mortality and/or CLD no longer differed from 1 in any time period.

DISCUSSION

Variation in population and treatment variables is probably due to a changing population resulting from reorganisations of neonatal care regionally, a move to a new hospital in 1995, and the introduction of new treatments. There was a steady reduction in mortality and PVH over the five periods, but with a significant rise in mortality during 1995–99. Mortality and PVH rates correlated significantly with treatment variables. When these increases were controlled for, the OR for mortality increased in the most recent period from 0.22 to 0.31, suggesting that the likelihood of mortality would be about one third higher if these treatments were not used as at present. A similar effect is seen for PVH (0.53 to 0.83). Why a higher mortality was seen in the period 1995–99 is uncertain, but during this time the surfactant type exclusively used on the unit had been switched to pumactant, later shown to be associated with a higher mortality than poractant alfa, which was used in 2000–04.⁴

The OR for CLD increased over time to 5.47. Controlling for treatments reduced the OR to 2.73, indicating that they may have accounted for around half of the CLD rate seen recently. When mortality and/or CLD is examined, the OR is only significantly different from 1 in 1995–99, and all differences disappear after treatments are controlled for. This suggests that treatments increase the OR for CLD by reducing mortality.

Lower ORs for PDA were seen more recently, with the lowest in 1995–99, and were significantly different from the periods immediately before and after. Controlling for treatments led to a halving of ORs after the introduction of surfactants. In 1995–99, the lower likelihood for PDA may be due to the lower activity of pumactant. Increased rates of PDA have been observed with animal derived surfactants.⁵

Abbreviations: CLD, chronic lung disease; PDA, persistent arterial duct; PVH, periventricular haemorrhage

Table 1 Odds ratios (95% confidence intervals) for mortality and morbidities for each five-year period compared with 1980–84.

	Period				
	1980–84	1985–89	1990–94	1995–99	2000–04
Mortality	1.00	0.73 (0.58 to 0.92)	0.46 (0.36 to 0.60)	0.62 (0.50 to 0.86)	0.44 (0.35 to 0.56)
	1.00	0.62 (0.47 to 0.80)	0.26 (0.19 to 0.35)	0.36 (0.28 to 0.46)	0.22 (0.17 to 0.29)
PVH (all)	1.00	0.56 (0.43 to 0.73)	0.34 (0.24 to .47)	0.51 (0.34 to 0.75)	0.31 (0.20 to 0.47)
	1.00	1.25 (1.01 to 1.54)	0.88 (0.71 to 1.09)	0.74 (0.60 to 0.90)	0.62 (0.51 to 0.76)
CLD	1.00	1.25 (1.01 to 1.56)	0.80 (0.64 to 1.01)	0.65 (0.53 to 0.80)	0.53 (0.43 to 0.66)
	1.00	1.21(0.97 to 1.51)	1.07(0.82 to 1.37)	1.04(0.78 to 1.38)	0.83(0.61 to 1.10)
Mortality and/or CLD	1.00	2.56 (1.83 to 3.59)	4.83 (3.49 to 6.69)	5.60 (4.11 to 7.63)	6.00 (4.40 to 8.19)
	1.00	2.56 (1.81 to 3.60)	4.57 (3.27 to 6.39)	5.14 (3.74 to 7.07)	5.47 (3.97 to 7.54)
PDA	1.00	2.55(1.80 to 3.60)	3.07(2.12 to 4.45)	2.62(1.75 to 3.94)	2.73(1.81 to 4.11)
	1.00	1.13 (0.91 to 1.40)	1.26 (1.02 to 1.58)	1.79 (1.47 to 2.19)	1.45 (1.18 to 1.78)
Septicaemia	1.00	1.11 (0.86 to 1.44)	1.06 (0.81 to 1.39)	1.61 (1.26 to 2.06)	1.11 (0.87 to 1.43)
	1.00	1.03 (0.79 to 1.34)	0.98 (0.72 to 1.34)	1.38 (0.97 to 1.97)	0.94 (0.64 to 1.33)
	1.00	0.71 (0.55 to 0.91)	0.65 (0.50 to 0.85)	0.40 (0.31 to 0.52)	0.63 (0.50 to 0.81)
	1.00	0.71 (0.55 to 0.92)	0.66 (0.50 to 0.86)	0.41 (0.32 to 0.54)	0.64 (0.50 to 0.82)
	1.00	0.70(0.54 to 0.90)	0.41(0.30 to 0.58)	0.19(0.13 to 0.29)	0.30(0.20 to 0.44)
	1.00	2.05 (1.63 to 2.59)	3.26 (2.58 to 4.11)	1.95 (1.57 to 2.43)	1.59 (1.27 to 1.99)
	1.00	2.07 (1.64 to 2.62)	3.27 (2.58 to 4.15)	1.91 (1.53 to 2.39)	1.54 (1.22 to 1.94)
	1.00	2.06(1.63 to 2.61)	2.50(1.92 to 3.26)	1.20(0.88 to 1.63)	0.96(0.70 to 1.31)

For each variable, the values on the first line are the unadjusted odds ratios, those on the second line are the odds ratios adjusted for population factors, and those on the third line are the odds ratios adjusted for population and treatment factors.

CLD, Chronic lung disease; PDA, persistent arterial duct; PVH, periventricular haemorrhage.

Septicaemia became more likely up to 1990–94 and then declined. As with CLD and PDA, controlling for the treatments significantly reduced the ORs. The clear fall in OR for septicaemia occurred from 1995 onwards when the unit moved to a new purpose built unit.

This study may have limitations, including selection bias, changes in diagnostic criteria, inadequate correction for changes in population variables, or action of unidentified factors—for example, surfactant type and neonatal facilities.

Using a long term clinical database and correcting for population and treatment variables allows significant changes in outcomes to be determined with confidence. The survival of higher risk infants has caused a rise in CLD, PDA, and septicaemia, associated with increased use of antenatal steroids and postnatal surfactant.

Competing interests: none declared

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