Intensive Care and the Very Low Birth Weight Infant

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Infants of very low birth weight (VLBW) are, for the most part, potentially normal at birth but, because of immaturity of structure and function of many organs, are at risk from death or permanent handicap. A recent survey[1] of world literature suggested that the improvement in the outcome for these babies, which has occurred over the past ten years, was due to perinatal intensive care. To date, information concerning the survival of VLBW infants from Irish hospitals is limited, apart from Halli-day's review[2] of babies less than 1000 g.

In the Coombe Lying-in Hospital[3] during the past decade the neonatal death rate for normal babies has fallen from 6.2 to 1.2 per thousand, but complete data concerning VLBW infants have not been reported. The present study was undertaken in order to determine and compare the survival and neonatal morbidity of the VLBW infants bom in the Coombe Lying-in Hospital in two four-year periods, the latter four years during which intensive care methods were introduced with the main changes being the more rational use of mechanical ventilation and the introduction of parenteral nutrition.

Subjects and Methods

Between 1973 and 1980, a total of 59,250 live born infants were delivered in the Coombe Lying-in Hospital, of whom 417 (0.7%) weighed between 501-1500 g. The present report using mothers' and infants' records, compares the survival and early morbidity of the 206 VLBW infants born between 1973-76 with that of the 211 born between 1977-80. Nineteen VLBW infants born in the first period and twenty-five in the second period were excluded from the analysis because of lethal congenital anomalies.

Neonatal Care: Similar resuscitative measures were employed after delivery during the two periods with the more severely asphyxiated infants being intubated and hand ventilated. In the nursery, standard neonatal care was given throughout the two periods with regard to temperature control, administration of Vitamin κ] and the use of antibiotics for infants with clinical evidence of sepsis. Jaundice was treated with phototherapy and an exchange transfusion was usually performed if the serum bilirubin exceeded 17*u*mol/100g. birth weight (Img/100g birth weight).

Blood glucose levels were monitored in a similar manner during both periods with Dextrostix and laboratory determinations when necessary. Serum calcium, urea, electrolyte and bilirubin estimations were performed only when clinically indicated in the first period, while more frequent routine monitoring was carried out in the second period.

Management of Respiratory Problems: Idiopathic respiratory distress syndrome (1RDS) was defined as the presence of two of the following features after four hours of age (or earlier if death had occurred before that time): grunting respirations, costal recession or a respiratory rate of greater than 60/minute.

Table 1 summarises the changes which took place in the management of respiratory problems in the two four-year periods. The indications for the use of Continuous Positive Airways Pressure (CPAP) or mechanical ventilation were not clearly defined in the first period during which 25 infants were assisted with CPAP and a further 14 were mechanically ventilated. In the second period, babies considered viable

Table 1
Management of Respiratory Distress

	'73	'74	'75	'76	'77	'78	'79	'80
Treatment								
O_2 Hood	+ + +	+ +	+ +	+ +	+	+	+	+
CPAP Gregory Box	-	+ +	+ +	+ +	+ +	+	-	-
Nasal	-	-	-	-	-	+-	+ +	+ +
ETT	-	+	+	+	+	+	+	+
Ventilation IPPV	-	-	+	+	+ +	+ +	+ + +	+ + +
IMV	-	-	-	-	-	+ +	+ + +	+ + +
Reverse I: E Ratio	-	-	-	-	-	-	-	+
Monitoring								
Inspired 0^ Concentration —	-	+	+	+	+ +	+ + +	+ + + +	+ + + +
Arterial Blood Gas Analysis —	-	+	+	+	+ +	+ + + +	+ + + +	+ + + +
Umbilical Arterial Catheter —	-	+	+	+	+ +	+ +	+ + +	+ + +
Transcutaneous p0; Monitor —	-	-	-	-	-	-	-	+

Number of pluses indicate in a representative fashion the frequency with which a mode of treatment or monitoring occurred.

Abbreviations

CPAP Continuous positive airways pressure.
ETT Endotracheal tube.
IPPV Intermittent positive pressure ventilation.
IMV Intermittent mandatory ventilation
I:E Ratio, insipiratory:expiratory ratio.

were commenced on CPAP if an arterial oxygen tension of 6.5 kPa (50 mmHg) was not obtained in an inspired oxygen concentration of 35%. Mechanical ventilation was instituted for severe apnoea, poor respiratory effort associated with a deterioration in the clinical condition or a PaCO; greater than 7.5 kPa (55 mmHg). The inspired oxygen concentration was adjusted to maintain the arterial oxygen tension between 6.5 and 10.5 kPa (50-80 mmHg). After 1976, neonatal ventilators with facilities for IPPV with positive end expiratory pressure were used while ventilators with a capacity for a reversed inspiratory/expiratory ratio were introduced in 1980.

Apnoea of prematurity, defined as a cessation of breathing for greater than 15 seconds, was treated with stimulation and oxygen and with bag and mask ventilation when necessary during both periods. Severe recurrent apnoea was treated with mechanical ventilation during the latter period.

The diagnosis of pneumonia, pneumothorax and bronchopulmonary dysplasia were made on clinical and radiological grounds. The presence of patent ductus arteriosus was established on ausculatatory findings together with hyperdynamic arterial pulsations on palpation. Necrotizing enterocolitis (NEC) was diagnosed on radiological, operative or autopsy evidence together with appropriate clinical findings.

Management of Nutrition: Babies with respiratory distress throughout the eight-year period were given fluids intravenously until it was considered that feeds would be tolerated. In the initial years, these feeds were administered by the nasogastric route, whereas after 1977, most babies were fed continuously by a transpyloric tube. When respiratory distress was severe, or when feeds were not tolerated, parenteral nutrition using Vamin and Intralipid as well as dextrose, electrolytes and vitamins were introduced. Parenterai nutrition was discontinued when 50-75% of the caloric intake was being administered by the enteral route.

Statistical Analysis: Statistical significance was evaluated using Students' t test and X^2 analysis as deemed appropriate.

Results

The mean age and parity of mothers during the two study periods were similar. Table 2 summarises the mode of delivery and neonatal condition according to the maternal complication that precipitated premature delivery. The incidence of maternal complications was similar during the two study periods even though a definitive cause for premature delivery was made more frequently ($p<0.05$) in the second four

Table 2
Summary of Outcome of Pregnancy According to Maternal Complication

	No Complication		APH		Cervical Incompetence		Multiple Pregnancy		PET/Hypertension		Idiopathic RIUG		Rh. Isoimmunization		Total	
Years	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80	1973-76	1977-80
N	42*	25	59	53	34	41	32	28	14	23	5	13	1	3	187	186
Gestation (Wks)																
Mean±S.D.	28.3±2.4	27.2±3.2	28.1±2.5	27.3±2	28.2±2.4	29.0±2.9	29.0±3.6	29.6±2.0	34.7±2.9**	32.6±2.1	34.6±1.3	35.0±1.9	36	30.3±0.6	29.1±3.5	28.5±3.1
Range	22-34	22-33	23-34	21-33	22-33	23-34	24-37	26-34	29-39	29-35	33-37	32-39	36	30-31	22-39	21-38
Birth Weight (g)																
Mean±S.D.	1150±270	1030±330	1100±260	1010±270	1130±270	1180±260	1030±300	1150±230	1290±180	1290±240	1340±180	1260±180	1360	1290±100	1130±270	1130±280
Range	560-1500	510-1500	550-1500	510-1500	570-1500	570-1500	550-1500	620-1500	900-1500	510-1500	1020-1500	900-1460	1360	1230-1400	550-1500	510-1500
Delivery																
Vertex	30(71%)	22(88%)	44(75%)	28(53%)	20(59%)	32(78%)	18(56%)	11(31%)	8(57%)*	2(23%)	3(60%)	4(31%)	0	2(67%)	121(65%)	101(54%)
Breech	10(24%)	3(12%)	13(22%)	19(36%)	14(41%)*	8(20%)	13(41%)	11(31%)	0	1(4%)	2(40%)*	0	0	0	54(29%)	42(23%)
C.S.	2(5%)	0	2(3%)	6(11%)	0	1(2%)	1(3%)*	6(22%)	6(43%)**	20(87%)	0 **	9(69%)	1(100%)	1(33%)	12(6%)**	43(23%)
Intrauterine Growth																
SGA	0	0	2(3%)	0	1(3%)	4(10%)	3(9%)	6(21%)	12(86%)*	13(57%)	5(100%)	13(100%)	1(100%)	0	24(13%)	36(19%)
Sex																
% Male	56	48	49	60	59	44	41	54	36	48	40	62	100	33	49	52
Survival	15(36%)	10(40%)	19(32%)	21(40%)	10(19%)**	26(63%)	14(44%)	17(61%)	11(79%)	22(96%)	4(80%)	12(92%)	1(100%)	2(67%)	74(40%)***	110(59%)

Abbreviations: APH = Antepartum Haemorrhage, PET = Pre-Eclampsia, RIUG = Retarded Intrauterine Growth
Rh. = Rhesus, C.S. = Caesarean section.
Statistics: * = $p<0.05$ ** = $p<0.01$ *** = $p<0.001$.

years. The overall gestational age was similar in both periods, though the mean gestational age of babies born to mothers with pre-eclampsia (PET) or hypertension was less ($p<0.01$) during the latter four years. More babies were born by Caesarean section (CS) between 1977-1980 ($p<0.01$); this increase occurred among mothers whose pregnancies had been complicated by PET or hypertension ($p<0.01$), idiopathic retarded intrauterine growth ($p<0.01$) or multiple pregnancy ($p<0.05$). The overall proportion of babies who were found to be small for gestational age (SGA)[4] was similar throughout the study, apart from those pregnancies that had been complicated by PET or hypertension during the latter four years when the proportion of SGA babies was significantly reduced ($p<0.05$).

There was a highly significant improvement ($p<0.001$) in survival between the two periods. However, when analysed according to maternal complication, the increased survival was only related to those infants whose mothers had cervical incompetence.

There was a significant improvement ($p<0.001$) in the survival of babies weighing more than 750 g in the latter four years (Table 3): this increase occurred especially among infants born at 26-27 weeks and at 30-31 weeks gestation (Table 4). The increased survival was found particularly among males (31% to 55%; $p<0.001$), whereas no significant increase was found in the survival rate of female infants (48 to 66%; p = N.S.). The survival rate of SGA infants was significantly better ($p<0.001$) than that of infants who were found to be appropriate weight for gestation (AGA) during both periods. While a significant increase ($p<0.001$) occurred in the survival of AGA infants in the latter four years, this increase was not noted in SGA infants.

Babies delivered by CS during each four year period were found to be significantly heavier and more mature ($p<0.001$) than either vertex or breech delivered infants; in the second four years the breech born infants were found to be significantly lighter ($p<0.05$) than the vertex deliveries even though the gestational age of both groups was similar. The survival of babies delivered by CS was better than that of either vertex deliveries both during the first ($p<0.05$) and second ($p<0.002$) periods, or of breech born babies during either period ($p<0.001$). Furthermore, the survival of vertex delivered infants was better than that of breech delivered babies both during the first ($p<0.05$) and second ($p<0.01$) periods even though an improved survival ($p<0.05$) was only noted among the vertex deliveries in the second four years.

Sixty-eight per cent of the deaths during the eight year period occurred during the first 24 hours and only 6% of babies died after the first week. Intraventricular cerebral haemorrhage and hyaline membrane disease were the commonest causes of death in normal babies: 82% during 1973-76 and 60% during 1977-80. There were four post neonatal deaths in the early period and two in the latter (Table 5).

Table 3
28-Day Survival Rate by Birthweight

Weight (g)	1973-76	1977-80	
501-750	0/23 (0%)	1/25 (4%)	N.S
751-1000	6/42 (14%)	12/30 (40%)	p<0.05
1001-1250	17/41 (41%)	38/59 (64%)	p<0.05
1251-1500	52/81 (64%)	59/72 (82%)	p<0.05

Table 4
28-day Survival Rate by Gestational Age

Gestation (Wks)	1973-76	1977-80	
<24	0/4 (0%)	0/7 (0%)	N.S
24-25	1/16 (6%)	0/17 (0%)	N.S.
26-27	4/49 (8%)	12/32 (38%)	p<0.001
28-29	21/48 (44%)	28/52 (54%)	N.S.
30-31	12/24 (50%)	31/34 (91%)	p<0.001
32-33	22/28 (79%)	18/22 (82%)	N.S.
>33	15/17 (88%)	22/23 (96%)	N.S.

Table 5
Post-Neonatal Deaths

Year of Birth	Age at Death (Mos)	Cause of Death
1973	5	Bronchopneumonia Gastroenteritis
1973	2½	"Cot Death"
1974	51	Burns
1976	3	Bronchopulmonary Dysplasia
		Bronchopneumonia
1977	9	Bronchopulmonary Dysplasia
1979	3	Bronchopneumonia Gastroenteritis

The incidence of idiopathic respiratory distress syndrome and recurrent apnoea did not alter significantly during the two four year periods but the treatment changed considerably (Table 6), with an increase in the number receiving mechanical ventilation in the second four year period. During the early period, no mechanically ventilated baby survived but, following the introduction of neonatal ventilators and more specific indications for their use, 47% survived, representing 31% of allsurvivors during the latter period.

Table 6

Respiratory	Disorders—		Treatment
1973-76	I977-80		
N = 128	N=112		
O_2 Only 91 (71%)	9	(8%)	
CPAP 23 (18%)	27	(24%)	
IPPV 14 (11%)	76	(69%)	p<0.001

Neonatal intensive care produced a highly significant increase in pulmonary complications and patent ductus^arteri-osus (Table 7). However, there was no significant increase in the incidence of NEC. The other main feature of intensive care was the provision of parenteral nutrition with amino acids and fat to babies with severe respiratory distress and to those who were unable to maintain adequate caloric intake orally. In the early period, only one baby received Vamin and Intralipid, compared with 28 babies in the latter four years, during which time a further 27 babies received Vamin alone.

Discussion

Most studies of neonatal mortality have recorded a lower survival rate among male infants.[5] In the present study, the survival of male infants increased with the introduction of intensive care, so that since 1977 there has been no significant difference between the survival rate of male and female infants. This selective improvement in male survival among low birth weight infants has also been reported recently from Western Australia.[6] The results presented

Table 7
Neonatal Morbidity

	1973-76		1977-80	
	N = 187		186	
Pneumonia	8 (4%)		43 (23%)	p<0.001
Pneumothorax	4 (2%)		14 (8%)	p<0.05
Bronchopulmonary Dysplasia	1 (1%)		9 (5%)	p<0.05
Patent Ductus Arteriosus	13 (7%)		46 (25%)	p<0.001
Necrotizing Enterocolitis	2 (1%)	7	(4%)	N.S.

support other reports that neonatal intensive care greatly improves the survival of the VLBW infant.[7,8] The improved survival in our unit was such that between 1977 and 1980 the proportion of survivors weighing between 751 and 1,000 g was similar to that of babies of birth weight 1,001-1,250 g, before intensive care was introduced.

Babies delivered by Caesarean section appeared at first to have a better survival rate than those delivered vaginally. However, it should be noted that these babies were significantly heavier and of greater gestational age than those delivered vaginally, so that the improved survival was more likely to have been due to the greater gestational age and birth weight than the mode of delivery. The higher incidence of Caesarean section in the second period was due to an increased awareness of the improved survival of the VLBW infants so that mothers who developed serious ante-natal complications were electively delivered prematurely before intra-uterine death occurred.

The number of babies who received mechanical ventilation progressively increased from 1977 to 1980, largely due to a rise in the number of babies ventilated for poor respiratory effort and this incidence is identical to that reported elsewhere.[1] In this latter period, the neonatal course was complicated by a marked increase in pneumonia, pneumothorax and bron-chopulmonary dysplasia but fortunately none of the surviving infants with bronchopulmonary dysplasia required additional oxygen for more than 15 weeks.

Sick pre-term babies have limited endogenous energy resources,[9] so that a period of starvation after birth might be detrimental to cerebral maturation.[10] Total or partial parenteral nutrition (TPN) as a supplement to inadequate oral intake has been found to be successful in improving the nutritional status and growth of pre-term infants.[11,12]

In a recent comparative trial of TPN and gastric feeding among VLBW infants, the incidence of NEC was less among the TPN managed babies while the survival was similar.'[3] In the present report there was no significant increase in the incidence of NEC in the latter period and the considerable improvement in survival may have been partly attributable to the withholding of enteral feeds and the use of TPN in the ill babies who received mechanical ventilation.

The management of the VLBW infants reported here included the prevention and treatment of birth asphyxia, hypoxaemia, hypoglycaemia, hypocalcaemia, hyperbilirubinaemia and sepsis. While all perinatal units with adequate laboratory and radiological facilities should be able to provide such management, the intensive care of VLBW infants now includes the use of mechanical ventilation and parenteral nutrition.[14] The present report suggests that the use of such facilities helps to improve the survival of VLBW infants. However, neonatal intensive care requires the availability not only of ventilators and parenteral feeding but also adequate nursing and medical staff on a 24-hour basis. Babies on ventilators should be nursed on a 1:1 basis by nursing staff skilled in caring for such infants. Similarly, the medical staff should have the expertise to deal with emergency situations that occur, such as the necessity for urgent intubation or insertion of chest drains. Furthermore, it is vital that back-up facilities from both laboratory and radiology departments are constantly and easily available. A neonatal unit should not attempt to provide intensive care without all these facilities. There has been a gradual, but significant increase in the number of nursing and resident medical staff in our unit over the past four years so that the demands of the increased work load required to care for this rising number of surviving VLBW infants were met.

The long term morbidity and handicap rates of VLBW infants is just as important as their increased survival rate. As many of the babies born in the second study period are still too young to have had an accurate estimate of development and intellectual function performed, it is not as yet possible to compare the two periods precisely. Pre-liminary assessment, however, suggests that the incidence of major handicap has not increased significantly despite the improved survival rate of these infants. A more detailed follow-up assessment will be reported later.

Summary

The survival and early morbidity of VLBW infants born in the Coombe Lying-in Hospital in two four year periods were compared. During the latter period intensive care methods were introduced with the main changes being the more rational use of mechanical ventilation and the introduction of parenteral nutrition. There was a highly significant increase ($p<0.001$) in survival between 1977-80 during which 110 of 186 (59%) normal VLBW infants survived, compared with only 74 of 187 (40%) born between 1973-76.

The incidence of idiopathic respiratory distress syndrome and apnoea of prematurity was unchanged during the two periods. During the latter four years there was a significant increase ($p<0.001$) in the use of mechanical ventilation with a resultant increase in pulmonary complications. However, no infant with bronchopulmonary dysplasia required long term oxygen. The incidence of necrotizing entero-colitis did not alter, possibly related to the use of parenteral nutrition in the management of sick VLBW infants. This report suggests that the use of mechanical ventilation and parenteral nutrition improves the survival of VLBW infants, although it increases their early morbidity.

Acknowledgement

This study was supported by a grant from the Coombe Hospital Research Fund to Dr. P. Gray. We are grateful to Dr. E. Tempany for permission to study patients under his care.

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