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Influence of Some recent advances on the morbidity and survival of extremely low birth weight infants (ELBW) at King Khalid University Hospital in Riyadh

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Abstract

The objective of this paper is to examine the survival and associated morbidity of extremely low-birth-weight (ELBW) infants born during 1996-1998, when antenatal steroids and postnatal surfactant had become accepted treatments; and to compare with an earlier period (1991-1993) from our institution. Perinatal and neonatal data on all births delivered at less than 1000 gm at KKUH were analyzed for survival rates and associated morbidity by birth weight and gestational age (GA). The recent cohort (n= 84) of live birth infants, compared to the earlier cohort (n= 86) showed an overall improved survival at discharge (72.6 vs. 30%, p= 0.000). Survival rates improved for 24 to 29-week GA infants, but the survival rate had not improved for ≤ 23 and ≥ 30-week GA infants. Despite such improvement in the survival rate, there was no increase in associated morbidity like NEC, BPD, and sepsis. On the contrary, the rate of ROP, IVH, and perforated NEC have dropped significantly. The use of antenatal steroids, delivery by LSCS, and the postnatal use of surfactant therapy correlated significantly with improved survival.

Introduction

The survival rate of extremely low birth weight (ELBW) infants in the late 1960s was o 1-20% and this increased to 60-80% in the early 1990 [1-2]. The rapid decline in neonatal mortality during the past 4 decades has been attributed to advancements in perinatology and neonatology as well as specific new therapies such as antenatal steroids and exogenous surfactant [3-7]. To the best of our knowledge, the outcome of ELBW infants in tertiary neonatal intensive care units (NICU) in Saudi Arabia has not been reported. To make appropriate perinatal treatment decisions, counsel parents, and plan health-care services, it is vital to have up-to-date mortality and morbidity data. The overall aim of the current study was to examine the survival and the morbidity outcome of ELBW infants during a recent period (1996-1998); when antenatal steroids and surfactant had become accepted treatments in our institution. The results were compared with those from earlier (1991-1993), pre surfactant era. The primary objectives were: (a) to describe the birth weight (BW) specific survival rates of the recent period; (b) to examine the effects of gestational age (GA), BW, sex, mode of delivery, antenatal steroids, and postnatal surfactant on neonatal mortality and morbidity. The secondary objective was to compare the mortality and morbidity between the two time periods.

Methods

We reviewed the obstetric and neonatal records of all infants born at less than 1000 grams at King Khaled University Hospital (KKUH). We included all infants who survived the delivery room resuscitation and were admitted to the NICU during two periods. The first Period extended from 1st of January 1991 to 31st December 1993, and the second from 1st January 1996 to 31st December 1998. We excluded all live born infants who died in the delivery room, those with major and lethal congenital anomalies, and out born babies. We retrospectively collected and entered the obstetric and neonatal data into a database program (Lotus Approach® 97). Obstetric data included gesta-

tional age, mode of delivery, 5 minutes Apgar score. Neonatal data included birth weight, sex, neonatal course during hospitalization till death or discharge, and the cause of death. Major morbidity include hyaline membrane disease (HMD), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH) grades III and IV, patent ductus arteriosus (PDA), culture proven sepsis, and retinopathy of prematurity (ROP) requiring treatment.

We considered death in the first 72 hours of life as early death and BPD as persistent oxygen requirement beyond 28 days postnatal age. We determined the gestational age from the date of the mother's last menstrual period confirmed by early antenatal ultrasound in the majority of cases. In 1994 new technologies like incubators that provide 90% humidity and synchronized ventilators (Baby Log 8000), and new therapies like antenatal steroids and postnatal exogenous natural surfactant (Survanta- ABOT-Lab No 57-992-Z 7) were introduced to our unit.

Statistics: Student t-test was used to compare means in continuous data, and the chi-square and Fisher's exact tests were used for categorical data. We considered a P value of less than 0.05 as significant.

Results

ELBW infants were 0.76% and 0.77% of all live birth in periods 1 and 2 respectively. Among those ELBW infants admitted to the NICU, there was no significant difference between the two periods in the mean birth weight, gestational age, and male to female ratio. The improvement of the perinatal mortality was not statistically significant. There was however, a significant improvement during the second period in the overall NICU survival rate (72.6% Vs 35%), and specifically, the survival of ELBW infants [Table.I]. Such improvement was significant for 24 to 29 weeks of gestational age (GA) and for all birth weight groups [Tables II and III]. Whereas, for GA $\leq 23 \geq 30$ weeks there was no significant improvement in survival [Table II].

The characteristics of all infants who died in the delivery room (DR) in both periods are shown in Table IV. Those died in the DR during period 2 were mostly less than 500 grams at birth and were non-viable.

Delivery by lower segment cesarean section (LSCS), antenatal steroids, and postnatal surfactant therapy were associated with higher survival rate [Tables V, VI and VII]. However, the use of synthetic surfactant during the first period did not significantly improve survival. Additionally, gender had no significant effect on survival [Table VIII]. There was no significant difference in the causes of preterm labor during the two periods [Table IX].

Immaturity (50%) was the major cause of early death in the first period, whereas, sepsis (24%) and respiratory failure secondary to chronic lung disease (29%) were the major causes of death in the second period. Despite the 50% improvement in the survival rate of ELBW infants, there was no increase in associated morbidity like NEC, BPD, and sepsis. On the contrary, the rate of ROP, IVH, and perforated NEC dropped significantly [Table X].

Table I: Overall Admissions and survival rates during the two Periods

	First period (1991 – 1993)	**Second period** (1996 – 1998)	**p value**
Total Number of deliveries	13505	12557	N/A
Corrected Perinatal mortality rate	16.7/ 1000	14/ 1000	0.076
Early Neonatal Death	6 /1000	3 /1000	0.000
Total NICU admision	1670	1429	0.013
Total NICU survived	1203 (72%)	1351 (95%)	< 0.05
Total NICU Death	467 (28%)	78 (5%)	<0.05
ELBW < 1000 GM			
All born	103	97	
Died in the DR	17 (16.5%)	13 (13.4%)	0.54
Admitted to NICU	86	84	N/A
Birth Weight (mean) in grams	734.8 $\pm$ 173.76	748 $\pm$ 156.34	0.60
Gestational age (mean) in weeks	25.9 $\pm$ 2.4	26.2 $\pm$ 2.33	0.28
Male : female	45 : 41	41 : 43	0.65
Saudi : Non Saudi	72 : 14	65 : 19	0.296
Survival	30 (35%)	61 (72.6%)	< 0.05
Median duration of hospital stay (days)	96	83	

Table II. Gestational age based survival rate to discharge

Gestational age	First period (%)	Second period (%)	P value
≥30 Weeks	4/5 (80)	7/8 (88)	0.73
27-29 Weeks	12/25 (48)	27/29 (93)	0.000
24-26 Weeks	13/42 (31)	23/32 (72)	0.001
23 Weeks	1/8 (12.5)	4/8 (50)	0.099
< 23 Weeks	0/6 (0)	0/7 (0)	N/A

Table III. Survival rate based on who weight classification

	First period (%)	Second period (%)	P value
< 500 g	0/9 (0)	0/2 (0)	
500 – 750 g	10/36 (27.8)	18/34 (53)	0.03
751 – 999 g	20/41 (48.8)	43/48 (89.6)	<0.05
Total	30/86 (35)	61/84 (72.6)	<0.05

Table IV. Characteristics of ELBW infants died in the delivery room during the two periods

	First period	Second period	P value.
Total number	17 (16.5%)	13 (13.4%)	0.54
Mean BW	644 + 51	513 + 95	
Range BW	560-760	390-740	
Mean GA	25 + 1	24 + 1	
Range GA	23-28	22-26	
< 500 GMS	0 (0%)	8 (62%)	
< 24 weeks	2 (12%)	4 (31%)	
LSCS	2 (12%)	0 (0%)	
Antenatal steroids	0	5	
Lethal anomalies	0	1	
Intubated and resuscitated	17	3	

Table V: Mode of Delivery and survival rate

	First period (%)			Second period (%)			Both periods (%)		
	Total	Survival	P	Total	Survival	P	Total	Survival	P
SVD	77 (90)	23 (30)	0.004	48 (57)	33 (69)	0.36	125	56 (45)	0.000
LSCS	9 (10)	7 (78)		36 (43)	28 (78)		45	35 (78)	
Total	86	30		84	61		170	91	

Table V: Antenatal steriods and survival rate

	First period (%)			Second period (%)			Both periods (%)		
	Total	Survival	P	Total	Survival	P	Total	Survival	P
Steriod *	11 (13)	9 (73)	0.001	60 (71)	53 (88)	0.000	71	62 (87)	0.000
No steriod #	75 (87)	21 (28)		24 (29)	8 (33)		99	29 (29)	
Total	86 (100)	30 (35)		84 (100)	61 (73)		170 (100)	91 (54)	

** All received two doses of 12.5mg of dexamethasone 12 hours apart prior to delivery*
 # Did not receive antenatal dexamethasone except for 3 who received one dose prior to delivery

Table VII: Post natal Surfactant therapy and survival rate

	First period (%)			Second period (%)			Both periods (%)		
	Total	Survival	P	Total	Survival	P	Total	Survival	P
Survanta	0	0	0.120	80 (95)	1 (76)	0.001	80	61	0.000
Exosurfe	13 (15)	7 (54)		0	0		13	7	
No sufactant	73 (85)	23 (32)		4 (5)	0 (0)		77	23	
Total	86	30		84	61		170	91	

Table VIII. Gender and survival rate

	First period (%)			Second period (%)			Both periods (%)		
	Total	Survival	P	Total	Survival	P	Total	Survival	P
Male	45	13 (29)	0.222	41	30 (73)	0.912	86	43 (50)	0.35
Female	41	17 (41)		43	31 (72)		84	48 (57)	
Total	86	30		84	61		170	91	

Table IX. Causes of preterm birth

Causes of preterm Labor	1991 - 1993	1996 – 1998
Idiopathic preterm labor	37 (43%)	30 (36%)
Chorioamnionitis	13 (15%)	10 (12%)
Maternal hypertension +	10 (12%) +	16 (19%)
Antepartum heamorrhage +, +	10 (12%) ++	8 (10%)
Premature rupture of membrane +	33 (38%) +	2o (24%)

+Some had more than one possible cause for the preterm birth

Table X: Morbidity rate

	First period	Second period	P value
NEC + (%)	20 (67)	36 (59)	0.280
CLD (%)	13 (43)	34 (54)	0.1507
SEPSIS (%)	29 (34)	34 (40)	0.4182
ROP (%)	17 (57)	10 (16)	<0.05
MAJOR IVH (%)	11 (36)	6 (10)	<0.05
Perforated NEC (%)	11(36.7)	7 (11.5)	0.0001

+Confirmed NEC by radiological diagnosis

Discussion

The survival rate of ELBW infants has improved substantially since 1965 [8]. Our results showed the same substantial improvement in the survival rate of ELBW where the survival rate increased from 35% to 72.6%. Such survival rate is similar to reports from USA and Japan [9]. In this study, live births survived the delivery room resuscitation were used as the denominator for mortality rates. There has been no significant change in the delivery room resuscitation policy in regard to selective resuscitation. On the contrary, there has been a non-statistically significant decrease in the delivery room mortality of ELBW infants in the recent period (13.4% Vs 16.5%). Additionally, those who died in the delivery room in the recent period were at the margins of viability (less mature and had lower birth weights than those in the previous period). Therefore, the improved survival in the recent period was not related to selective resuscitation policy in the delivery room.

Perinatal management at the lower margin of viability is still a difficult issue and up-to-date outcome statistics is an important factor to consider the overall management. Studies on the efficacy of recent advances in treatment (antenatal steroids and natural surfactant) have reported improved survival. During the recent period of our study the use of antenatal steroids was accepted even for preterm labor at very early gestations. Antenatal steroids were used in 71% in the recent period compared to 13% in the previous period. Similarly postnatal natural surfactant was administered to 95% of the ELBW infants in the recent period compared to only 15% of synthetic surfactant in the previous period. Therefore the recent period represents the outcome after the institution of these recent advances and other new technologies like incubators that provide 90% humidity and synchronized ventilators (Baby Log 8000). The use of antenatal steroids has significantly improved the survival rate of ELBW infants in both periods. Similarly, the use of natural surfactant has significantly improved the survival rate of ELBW infants. The use of synthetic surfactant, however, did not result in significant change in the survival rate. Our finding of higher survival of ELBW infants delivered by LSCS is similar to published reports [10].

Birth weight and gestational age were the most important factors predicting survival. The chance of survival improves most markedly at gestations between 23 and 29 weeks. We reported no survival for infants born with BW below 500 grams. The effect of gender on survival and the male disadvantage has been documented in previous reports [11-15]. In our study the male disadvantage seen in the earlier period was no longer evident in the recent period .The previously reported female advantage may be due to relatively more advanced development for a given gestation as a result of hormonal differences. The administration of antenatal steroids that accelerate maturity of several systems, and exogenous surfactant, may have contributed to the narrowing in the gender difference in maturation. Our findings on the lack of female advantage is similar to the recent findings of Battin et al [16].

Despite the significant increase in the survival rate of ELBW infants in the recent period, the short term morbidity has either not changed (NEC, BPD, and sepsis) or even improved significantly (ROP requiring treatment, major IVH, and perforated NEC). The improved survival and morbidity included those born at the extremes of viability (23-26 weeks) with survival rate of 68% in the recent period. Such improvement is associated with increased use of resources. Although we currently do not have long term outcome data for this group, the decrease in both respiratory and other major morbidity, which correlate with future neuro-developmental outcome is reassuring. The appropriateness of initiating intensive care for those ELBW infants born at the margins of viability (23-25 weeks) is widely discussed. Most physicians, ethicists, and lay persons agree the likelihood of survival is not the only issue that should be considered for marginally viable patients. These issues include the suffering caused by intensive care, the quality of life, the values and preferences of the patients or their surrogates, and the available resources. Both the Canadian Pediatric society and the American Academy of Pediatrics, in association with their obstetric colleagues have published guidelines on the management of threatened birth of an ELBW infant [17]. Yet there is no simple way to address all these issues for marginally viable infants.

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