ORIGINAL ARTICLE

Nosocomial Bacterial Sepsis in Babies Weighing 1000-1499 g in Kelantan

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Summary

From January to December 1992, 92 babies weighing 1000 - 1499gm here to referred as very low birth weight (VLBW) were admitted to NICU (Neonatal Intensive Care Unit), Hospital University Sains Malaysia (HUSM). Sixty babies were inborn giving a VLBW rate of 7.5 per 1000 live births. Incidence of nosocomial sepsis was 32.6% (30/92) of whom 43.3% (13/30) died. Eighty percent (24/30) of the septic babies had blood culture positive for gram negative organisms of which 40% (12/30) were sensitive only to imipenem. Ventilator support within 24 hours of life was required in 41.3% (38/94) babies of whom 42% (16/38) babies developed nosocomial sepsis. Delayed initiation of feeding was significantly associated with nosocomial sepsis. A strict asepsis policy and early feeding of the VLBW infant are essential components of any strategy to prevent of sepsis due to nosocomial infection.

Key Words: Malaysia, Neonate, Nosocomial sepsis, Very low birth weight babies (VLBW).

Introduction

Nosocomial sepsis in the immunologically immature VLBW babies during post-natal care has remained an important cause of morbidity and mortality and has resulted in a prolonged hospital stay[1,2]. VLBW babies are at risk of nosocomial sepsis due to various factors. These include invasive procedures, the widespread use of broad spectrum antibiotics, weakening of physical barriers and inability to mount an appropriate immunological response. The problem is exacerbated in the nursery setting by shortage of staff and high workload[3]. Invasive live saving procedures such as endotracheal intubation, umbilical vessel catheterisation, oral or endotracheal suction, intravenous infusion and surgery are related to nosocomial sepsis[4,5,6]. Among low birth weight babies the incidence of nosocomial sepsis varies and may be as high as 37%[2].

A NICU in a developing country faces the formidable challenge of controlling nosocomial infection. Hospital University Sains Malaysia is one of the two referral centres for the state with a population of 1.4 million mainly rural based people. There are only 5-6 staff nurse per shift to take care of approximately 50 babies including 6 to 7 ventilated babies. In the year 1992, there were 8004 deliveries of whom 1718 babies required care in NICU. Along with referred admission 2129 babies were admitted to NICU. Overcrowding even with good weight babies is common. The purpose of this study is to describe the spectrum of micro-organism and predisposing factors of nosocomial infections in VLBW admitted to neonatal unit.

Materials and Methods

All babies (n=92) with birth weight 1000-1499 grams admitted to NICU, HUSM during the 12 month period from January to December 1992 were included

in this study. Data was collected from the admission, ventilation and death registers. Ballard scoring was used if the mother was unsure of her date for gestational assessment gestation. Sepsis was defined as a positive blood culture in a clinically septic baby with one or more of the following additional features: (1) presence of more than 20% band cells on the blood film (2) thrombocytopenia < 100 x 10^9 /l and (3) C-reactive protein > 20 mg/100 ml. Nosocomial sepsis was defined as sepsis occurring after 48 hours of age. Five babies in the study population were treated for sepsis on clinical grounds, were not defined as sepsis.

All babies were admitted to NICU and were started on intravenous fluid therapy immediately after admission. Penicillin and gentamycin were administered in babies with intra-partum risk of sepsis or if symptomatic. Indwelling arterial line was placed in babies requiring more than 0.4 of inspired oxygen. The feeding with infant formula were started at discretion of the physician. The known features of sepsis were recorded. Abnormal blood sugar homeostasis was defined as blood sugar less than 2.2 mmol/l or more than 8 mmol/l. All babies with sepsis were investigated with blood culture, total white cell count, differential count, creactive protein.

The data were analysed using statistical software EPI info and SPSS. Continuos variables were analysed with the Students t test when normally distributed and with Mann Whitney test if not. Chi-square test was used for categorical variables. To study the association of the nosocomial sepsis and possible risk factors, we calculated odds ratio and 95% confidence intervals by univariate analysis. Factors associated with p value less than 0.5 were further analysed by multiple logistic regression. Statistical significance was defined a p value less than or equal to 0.05.

Results

Patients: In the year 1992, 92 babies with 1000-1499 gram were admitted to NICU. Sixty VLBW babies were delivered in this hospital giving a live birth-rate of 7.5 per 1000 for 1000-1499 grams babies. There were 45 (49%) male and 47 (51%) female infants. Of 92 VLBW babies 24 (26%) were small for gestational age and 8 (8.7%) babies were born at term. Twenty (21.7%) were twins and 23 (25%) were delivered by caesarean section. Statistically comparable demographic characteristics are presented in Table I for the infants in the septic and non-septic subgroups.

Sepsis: There were 30 babies diagnosed to have sepsis giving an incidence of sepsis in VLBW babies of 32.6%. The clinical and metabolic features of nosocomial sepsis include apnoea with or without bradycardia (50%), lethargy (76.7%), bleeding (13.3%), feeding intolerance (33.3%), difficulty in weaning (10%), metabolic acidosis (66.7%) and abnormal blood sugar (66.7%). Half of the babies (15/30) developed nosocomial sepsis before the age of day 8 and 86.7% (26/30) before day 16 with a range from day 3 to 42. The average age of the babies at the onset of nosocomial sepsis was 10.7 (SD 7.85) days.

Pathogenic organisms: Gram negative organisms are the commonest pathogen (80%). Gram negative sepsis was confirmed in 75% (12/16) and 85.7% (12/14) of the ventilated and non-ventilated babies respectively. *Klebsiella* sp. was found to be the commonest organism causing sepsis (Table II). Resistance to third generation cephalosporines and aminoglycosides was detected in 45.8% of the gram negative organisms. They were sensitive to imipenem and ciprofloxacin. There were 20 endotracheal secretion cultures performed in the first week of ventilation. In 12 endotracheal suction 13 pathogenic organisms were isolated: *Pseudomonas* sp. in 5, *Klebsiella* sp. in 6, and methiciline resistant *Staphylococcus* aureus in 2. The organism colonising the endotracheal tube did not correlate with those causing sepsis.

Risk factors: The risk factors analysis is presented in Table III. Thirty-eight (41.3%) of the VLBW babies were ventilated within the first 24 hours of age and median duration of ventilation was 6 days (range 1 to 33 days). The indications for ventilation were respiratory distress syndrome in 30 (79%), perinatal asphyxia in 6 (15.8%) and apnoea in 2 (5.2%). Three ventilated babies developed pneumothoraces and two died due to causes unrelated to the pneumothoraces. Nosocomial sepsis developed in 16(42%) ventilated babies at a median age of 9 (range 3 to 42) days.

Table I
Demographic characteristics of VLBW

Variables		Sepsis (n=30)	No sepsis (n=62)	p
MALE/FEMALE		18/12	27/35	0.141
WEIGHT TO GESTATION				
	SGA	14	10	
	AGA	48	20	0.271
GESTATION (WEEKS)@		32.6(3.1)	32.3(2.2)	0.853 #
GESTATION BY GROUPS				
	28 - 30	10	15	
	31 - 33	9	29	
	34 - 36	9	12	
	≥ 37	2	6	0.359
MODE OF DELIVERY				
	Assisted breech	1	5	
	SVD	20	43	
	CS	9	14	0.559
PLACE OF BIRTH				
	HUSM	20	40	
	BBA	3	6	
	DH	2	6	
HOME OR CLINIC		5	10	0.972
TWIN		6	14	0.779
MEAN BIRTH WEIGHT (G)@		1247 (133.39)	1284 (133.38)	0.220
APGAR < 4		6 [10]	9 [6]	0.162
RDS		15	33	0.772
MATERNAL COMPLICATIONS				
	PET	6	10	0.646
	APH	2	4	
	Cervical incompetence	1	1	
	Placenta praevia	1	0	
	VDRL +ve	1	0	
	Chorioamnionitis	0	1	
	Oligohydramnios	0	1	

SGA: small for gestation; AGA: appropriate for gestation; SVD: spontaneous vaginal delivery; CS: caesarean section; HUSM: Hospital USM; BBA: born before arrival to hospital; DH: district hospital; PET: pre-eclampsic toxaemia; APH: anteparum haemorrhage

@ mean(standard deviation) [ ] Record was not available # Mann Whitney test

Table II
Bacteriology of blood culture and mortality in 16 ventilated and 14 non-ventilated babies

Pathogen organism	Ventilated babies n (% Died)	Non-ventilated babies n (% Died)	Total isolates & Mortality (%)
Klebsiella erogenous	6 (66.7)	7 (42.9)	13 (53.8)
Pseudomonus sp.	4 (50)	2 (100)	6 (66.7)
Acinetobacter	2 (50)	0	2 (50)
Escherichia coli	0	2 (0)	2 (0)
MRSA	2 (100)	2 (0)	4 (50)
Others including candida	2 (100)	1 (0)	3 (66.7)

MRSA: Methicilin Resistant Staphylococcus aureus

Forty babies within the first day of life had indwelling arterial lines of which 33 were peripheral lines. The mean duration of arterial line was 5.5 (SD 3.2) days. None of the babies with umbilical arterial catheterisation had sepsis. Sixteen babies (40%) with a peripheral arterial line had sepsis and 6 babies developed sepsis while the catheter was in place. All babies received intravenous fluid therapy from birth.

Only 10 (10.87%) VLBW babies received expressed breast milk during the initiation of feeding. The first feeding was significantly delayed by 4.8 (SD 2.47) days in babies with sepsis than 3 (SD 1.38) days in babies without evidence of sepsis ($p < 0.001$). In a multivariate regression model the delayed feed remained significantly associated with sepsis (Exp ß = 7.77; $p=0.04$).

Outcome: Seventeen babies (60.7%) died of infection related causes of whom 13 babies due to nosocomial sepsis, 3 due to nercotising enterocolitis and 1 to intrauterine infection by cytomegalovirus. The other causes of death were prematurity in 7 (25%), congenital abnormalities in 3 (10.7%) and asphyxia in 1 (3.6%). The mortality rate for nosocomial sepsis was 43.3% (13 deaths). The babies with sepsis stayed in NICU for a mean duration of 31.3 (SD 18.9) days compared to 29.7(SD 15.1) days for babies without sepsis. The mean duration of stay in NICU for babies who survived and died was 36 (SD 10.6) days and 15.3 (SD 17.4) days respectively. The overall 28 days survival rate for these babies was 73.9% and 69% babies could be discharged. Early neonatal, late neonatal and post neonatal deaths in NICU were 39.3%, 46.4% and 13.3% respectively of the total neonatal deaths.

Discussion

Nosocomial infections constitute a growing problem in NICU, especially with a developing unit in a developing country. The incidence of nosocomial bacterial sepsis and mortality rate of sepsis in VLBW babies in our unit was very high. A high prevalence of gram negative organism also featured in this study. Being a retrospective study we could not focus precisely on the reasons for the high incidence of gram negative sepsis in both ventilated and non-ventilated groups. Factors that may be involved in the high prevalence of

Table III
Risk factors and outcome of the VLBW

Variables	Sepsis (n=30)	No sepsis (n=62)	Unadjusted Odds ratio (95% CI)	p
Ventilated within 48 hours of life	22	16	OR: 2.08 (0.78-5.60)	0.105
Duration of ventilation (days)!	10.9 (9.2)	5.6 (4.5)		0.03@
Arterial indwelling catheters:				
Peripheral artery	16	17		
UAC	-	7		
Total	16	24	OR: 1.81 (0.68-4.84)	0.187
Duration arterial indwelling catheters (days)!	6.8 (3.8)	4.7 (2.7)		0.051
Feed started within 72 hours of age	4	38	OR: 0.10 (0.03-0.34)	<0.001
Died	16	12		< 0.001

! mean (standard deviation)
UAC Umbilical artery catheterisation
OR Unadjusted odds ratio
CI confidence interval
@ Mann Whitney test

sepsis and gram negative pathogen include: hand washing attitudes and techniques, overcrowding and under staffing, widespread use of prophylactic broad spectrum antibiotics. In our unit under staffing is a contributing factor, where 2-3 ventilated beds and 6-7 non-ventilated beds are looked after by one nurse. Overcrowding and limited nursing personnel leads to disruption of the chain of sterility. High workload increases the incidence of colonisation with resistant organisms[3]. We noted that early endotracheal colonisation occurs in the ventilated infants. The discipline of sterility in the NICU is of paramount importance[7] including proper skin, eye and umbilical care and a sensible approach to antibiotic policy. Prolonged use of antibiotics is associated with an increased risk of systemic candidiasis[7], and creates 'antibiotic pressure' that select for resistant organisms[3]. A strict antibiotic policy should include the discontinuation of empirical antibiotic therapy after 48-72 hours if there is no evidence of sepsis[8]. Breast milk is also protective against infection including narcotising enterocolitis and therefore the VLBW infants should preferably receive expressed breast milk feeding. Fifty four percent (50/92) babies were starved for more than 72 hours and 52% (26/50) developed sepsis. A similar

observation was made in a retrospective study by Unger A et al [9] who showed a decreased incidence of nercotising enterocolitis, bronchopulmonary dysplasia, and nosocomial infection infants fasted less than 4 days compared to those fasted greater than 4 days.

Evolution of strategies for infection control in our unit was done based on this study. We developed a protocol for antibiotic usage in which the duration of antibiotic was strictly monitored and audited at 48 to 72 hours after initiation. The antibiotics were withdrawn if blood culture was negative. Cephalosporines were strictly reserved for proven meningitis. Trophic feeding was advocated by 48 to 72 hours of life and mothers were encouraged to supply expressed breast milk. Unit also introduced rooming in facilities to promote human milk feed. In addition to these regular hand washing concept is stressed during regular rounds.

This study with its limitation has highlighted the magnitude of gram negative sepsis in VLBW and identified an important observation on the relationship of sepsis with feeding practice. A simple policy of early feeding can be practice without any additional resources. This strategy along with other steps to decrease nosocomial sepsis should decrease VLBW mortality rate, shorten hospital stay, and reduce cost. At present we have undertaken a study on the sepsis in neonate admitted to NICU. In near future we shall be able to compare the data to study the effect of the strategies developed following the present study.

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