Treatment and outcome of neonates with hypoxic ischaemic encephalopathy at B.P. Koirala Institute of Health Sciences

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Abstract

Introduction: Perinatal asphyxia is an important cause of neonatal deaths and neonatal intensive care unit (NICU) admission.

Objectives: To assess the treatment pattern in neonates having hypoxic ischaemic encephalopathy (HIE) and its relationship with their outcome.

Method: A hospital based prospective study of one year duration was carried out at B.P. Koirala Institute of Health Sciences, Nepal in term neonates with perinatal asphyxia and HIE, enrolled from the paediatric wards and NICU.

Results: Of the 60 term neonates included in the study, 49 (81.7%) were males. The mean birth weight was 2971±421g. HIE was mild in 13 (21.7%) cases, moderate in 27 (45%) cases and severe in 20 (33.3%) cases. Seventeen neonates were admitted to the NICU. Oxygen was required in 45 neonates (mean duration 60.3 hours). Mechanical ventilation and vasopressors were given in 13 and 29 neonates respectively. Most of the neonates received antibiotics for 5 days. Mean duration of hospital stay was 146.2 hours. Thirteen (21.7%) neonates were neurologically abnormal at discharge. Forty one (68%) neonates were discharged from hospital, 06 (10%) expired during the hospital stay and 7 left against medical advice.

Conclusions: In this study at the B. P. Koirala Institute of Health Sciences, 22% neonates with perinatal asphyxia and HIE were neurologically abnormal at the time of discharge and there was a 10% mortality.

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(Key words: Perinatal asphyxia, hypoxaemic ischaemic encephalopathy)

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Introduction

There are more than 9 million deaths annually during the perinatal and neonatal periods, most deaths occurring in developing countries[1]. Each year around 4 million babies are born asphyxiated of whom 1 million die and one million suffer severe neurological complications such as cerebral palsy, mental retardation or epilepsy[2]. Hypoxic ischaemic encephalopathy (HIE) in an asphyxiated neonate can lead to serious long-term problems among survivors[3]. Perinatal asphyxia has an incidence of 0.5–2% of live births[4,5]. It accounts for 30% neonatal deaths in Nepal[6]. Perinatal asphyxia is an important cause of multiorgan dysfunction[7].

Objectives

To assess the treatment pattern in neonates having hypoxic ischaemic encephalopathy (HIE) and its relationship with their outcome.

Method

A prospective observational study was carried out at B.P. Koirala Institute of Health Sciences (BPKIHS) in eastern Nepal from February 2013 to January 2014. The study was approved by the BPKIHS Ethics Committee and prior written informed consent was obtained from the parents or guardian of the neonates. Term babies delivered at BPKIHS, who developed perinatal asphyxia and HIE, in accordance with Levene staging[8] comprised the study population. APGAR scores were assessed at 1, 5 and 10 minutes and resuscitation was carried out in line with the 2005 Neonatal Resuscitation Programme (NRP) guidelines of the American Heart Association and American Academy of Paediatrics[9]. Babies with congenital heart disease, central nervous system abnormalities or sepsis were excluded from the study.

All babies were managed in the neonatal intensive care unit (NICU) according to the hospital protocol which included administration of oxygen, nasal continuous positive airway pressure (NCPAP), mechanical ventilation, intravenous fluids, vitamin K, inotropes and anticonvulsants as needed. Cefotaxime and gentamycin were given to babies at risk of sepsis and to babies requiring mechanical ventilation. Once babies improved, orogastric feeding was started followed by spoon or breast feeding. An electrocardiogram (ECG) was done and 4 ml of venous blood was taken from each neonate within 72 hours of life for routine

haematological and biochemical investigations and cardiac enzyme estimation. A chest X-ray was done in all babies. Along with all the demographics, the investigations, treatment and outcome were noted in a predesigned proforma.

Data were entered in an Excel sheet for analysis. Analysis of Variance (ANOVA) was used to compare the differences in mean of quantitative data among different stages of HIE and Chi-Square test was used to compare proportions.

Results

Sixty term neonates with HIE were enrolled into the study within 72 hours after birth. Of them, 43 (71.7%) neonates required active resuscitation. Of the 43 neonates, 41 required only bag and mask ventilation whilst 2 with severe HIE required endotracheal tube ventilation and chest compressions. Birth details are shown in Table 1.

Table 1: ***Birth details***

Birth details	HIE stage			P value
	1 (mild)	2 (moderate)	3 (severe)	
Resuscitation				
Not needed	03	13	01	0.009
Needed	10	14	19	
Bag and Mask	10	14	15	
Endotracheal tube	0	0	2	
Chest compressions	0	0	2	
Apgar score				
at 1 minute	3.23±0.83	3.11±0.64	2.55±0.6	0.007
at 5 minutes	5.08±0.49	4.78±0.58	4.1±0.79	<0.001
at 10 minutes	7.46±0.88	6.96±0.9	5.5±1.15	<0.001

According to HIE staging, 13 (21.7%) neonates were in mild, 27 (45%) neonates were in moderate and 20 (33.3%) neonates were in severe HIE groups (Table 1).

The Apgar score at 1 minute was less than 3 in 14 patients with a mean Apgar at 1 minute of 2.95. Apgar score at 5 minutes was more than 5 in 3 (5%) newborns and 3-5 in 57 (95%) none of them having a score of less than 3. Similarly, mean Apgar scores at 5 and 10 minutes were 4.62 and 6.58 respectively. The mean Apgar scores at 1 minute, 5 minutes and 10 minutes were statistically significant among different stages of HIE as shown in Table 1.

The treatment details of neonates with HIE are shown in Table 2.

Table 2: ***Treatment details of neonates with HIE***

Treatment detail	Number (%)	Mean ± SD
Oxygen through Head box (hours)		
<48	19 (42.2)	
48-96	20 (44.5)	60.27 ± 54.81
97-240	06 (13.2)	
Oxygen through nasal continuous positive airway pressure (hours)		
<24	08 (47.1)	
24-48	07 (41.1)	25.88 ± 21.96
>48	01 (11.8)	
Bag and tube ventilation (hours)		
<24	11 (64.7)	20.25 ± 23.46
24-72	06 (35.3)	
Mechanical ventilation (hours)		
<24	01 (07.6)	
24-72	06 (46.2)	89.15 ± 62.23
>72	06 (46.2)	
Vasopressors		
Present	29 (48.3)	
Absent	31 (51.7)	
Duration of vasopressors (hours)		
<48	06 (20.7)	
48-96	09 (31.0	103.24 ± 70.57
>96	14 (48.3)	

As shown in Table 2, forty five neonates required oxygen through head box, 17 required bag and tube ventilation 13 required mechanical ventilation and 29 required vasopressors. Antibiotics were given in 56 neonates, 60.7% receiving them for 5 or less days. Mean duration of antibiotics was 6.1 days.

Table 3 shows the univariate analysis of treatment details.

Table 3: ***Univariate analysis of treatment details***

Treatment	HIE stage			P value
	Mild	Moderate	Severe	
Anticonvulsants				
No	13	0	07	<0.001
Yes	0	27	13	
Vasopressors				
Given	0	09	20	<0.001
Not given	13	18	0	
Antibiotics				
Given	09	27	20	<0.001
Not given	04	0	0	
Number of anticonvulsants	0	1.11±0.32	1.15±0.38	0.934
Oxygen head box (hours)	48.85±61.78	64.56±51.35	66.14±58.72	0.681
Continuous positive airway pressure (hrs)	7.25±3.59	29.00±15.10	32.78±25.34	0.146
Bag and tube ventilation (hours)	3.1250±4.0659	4.3333±2.5166	7.0833±4.9926	0.181
Mechanical ventilation(hours)	0	48.00±0.00	92.58±63.70	0.818
Duration of vasopressors(hours)	0	98.78±42.35	105.25±81.05	0.976
Duration of antibiotics (days)	5.89±3.22	6.00±2.02	6.30±5.07	0.944

As shown in table 3 on univariate analysis, requirements of anticonvulsants, vasopressors and antibiotics were significantly associated with HIE stages. However, the number of anticonvulsants required, duration of oxygen by head box, duration of continuous positive airway pressure, duration of bag and tube ventilation, duration of mechanical ventilation and duration of vasopressors and antibiotics were not statistically significant in relation to HIE stages.

In-patient management regarding feeding and use of intravenous fluid is shown in table 4.

Table 4: ***Outcome of babies in relation to feeding and intravenous fluid***

Outcome	Number (%)	Mean ± SD
Start of nasogastric feeding (hours)		
<48	02 (04.5)	
48-96	30 (68.2)	103.57 ± 59.49
>96	12 (27.3)	
Start of breast feeding (hours)		
<48	02 (04.8)	
48-96	17 (40.8)	145.33 ± 94.30
97-240	18 (42.9)	
>240	05 (11.9)	
Intravenous fluid (hours)		
<48	04 (06.7)	
48-96	26 (43.3)	131.63 ± 85.53
97-240	25 (41.7)	
>240	05 (08.3)	

Seventeen neonates needed NICU care. Out of them, 06 (35.3%) were in NICU for 48-96 hours and other 06 neonates for 97-240 hours with a mean duration of 118.94 ± 105.90 hours of NICU stay.

The duration of hospital stay was less than 48 hours in 03 (5%) babies, 48-96 hours in 15 (25%) babies, 97-240 hours in 37 (61.6%) babies and more than 240 hours in 05 (8.3%) babies. The mean duration of hospital stay was 146.17 ± 91.3 hours. The condition at discharge is shown in Table 5.

Table 5: ***Condition at discharge***

Treatment	HIE Stage			P value
	Mild	Moderate	Severe	
Outcome				
Death	0	0	06	
Discharge	12	25	04	<0.001
Left against medical advice	01	02	10	
Final Outcome				
Discharged	12	25	04	<0.001
Death/ Left against medical advice	01	02	16	
Anticonvulsant at discharge				
Given	0	10	03	0.007
Not given	12	15	01	
Neurological outcome				
Abnormal	0	10	03	0.007
Normal	12	15	01	
Hospital stay (hours)	123.85±73.7	154.48±60.62	154.15±130.16	0.575
Discharge weight(g)	2666.67±432.93	2937.2±482.39	2518.75±367.07	0.111

As shown in this table, forty one neonates were discharged, 06 expired and 13 neonates left against medical advice (LAMA). Overall mortality was 10%. When the final outcome in regards to discharged and death/ LAMA was analysed by univariate analysis in different HIE stages they were found to be highly significant. Anticonvulsants at discharge and neurological outcome were also significantly related to HIE stage. However, mean duration of hospital stay and mean discharge weight were not significantly related to HIE stage

Discussion

In the present study 60 neonates with HIE were enrolled. Demographic data such as gender, neonatal weight, crown rump length, head circumference, maternal registration status, gestational age, antenatal complications, obstetric problems, maternal age, and maternal weight were evenly distributed in the different HIE groups. Mean duration of hospital stay was 146.2 hours. Forty one neonates improved, 06 expired and 13 neonates who were critically ill left against medical advice due to financial constraints. When the final outcome of discharge and death/LAMA was analysed by univariate analysis in different HIE stages, it was found to be highly significant. HIE severity was significantly associated with outcome. Those with severe HIE required more inotropes and anticonvulsants and were on longer duration on mechanical ventilation.

In the study by Shah P *et al*, the Apgar score at 5 minutes was less than 5 in 63% infants[7]. In the study by Martin-Ancel et al, Apgar score at 1 minute was 3 or less in 30% infants but the Apgar score at 5 minute 3 or less in 14% infants[10]. In our study, the Apgar score at 1 minute was less than 3 in 23% and 3-5 in 77% patients whilst the Apgar score at 5 minutes was more than 5 in 5% infants and 3 to 5 in 95%. In the study by Padayachee N et al., the overall survival rate was 86.7% with 79.6% having normal development[11]. In our study the overall survival rate was 68% and 78.3% had normal development.

Conclusions

In this study at B. P. Koirala Institute of Health Sciences 22% neonates with perinatal asphyxia and HIE were neurologically abnormal at the time of discharge and there was a 10% mortality.

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