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Original Research Article

RISK FACTORS AND CLINICAL PARAMETERS OF APNEA IN NEONATES IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Neonatal apnea is a symptom of postnatal stress, a disease of physiologic immaturity and remains an exceedingly common clinical problem of neonatal respiration. The present study was done among newborns to study the risk factors and clinical parameters in apneic episode. **Materials and Methods:** This prospective study of 40 neonates with neonatal apnea was carried out in a tertiary care hospital in maharashtra. Details on risk factors, clinical parameters and diagnostic tests were collected. **Result:** 207 episodes of apneas occurred in 40 neonates in one year. The incidence of babies with apneas was 57 per thousand admissions and the incidence in preterms was 18.5%. The following factors were found to contribute to development of apneas in neonates were flexion of neck (62.5%), Hypoglycemia (50%) acidosis (40%), RDS (25%), intracranial bleeds (25%), post-feed, anaemia, culture proved sepsis, birth asphyxia, and pneumonia. The mean number of apneas per infant was 5.17 + 4.92. Blood gases was normal in 24 babies (60%) and the rest showed respiratory acidosis (12.5%, n=5), metabolic acidosis (12.5%, n = 5) and a mixture of respiratory and metabolic acidosis (15.0%, n = 6). Blood gases demonstrated acidosis in a total of 16 patients (40%). The mean heart rate was 76.31 + 26.158/min. Cyanosis was present in 33 babies out of 40 babies (82.5%). **Conclusion:** Flexion of neck, Hypoglycemia, acidosis, RDS, intracranial bleeds, post-feed, anaemia, culture proved sepsis, birth asphyxia, and pneumonia are important risk factors for apnea in infants.

INTRODUCTION

Neonatal apnea is a symptom of postnatal stress, a disease of physiologic immaturity and remains an exceedingly common clinical problem of neonatal respiration. With the first breath, the newborn infant must change instantly from irregular fetal breathing movements irrelevant to the gas exchange, to the self-sustained rhythmic pattern crucial for extra uterine survival. Apneic episodes occur frequently in premature infants. Incidence of apnea is inversely related to the gestational age of the neonate. About 25% of all newborns weighing less than 1800gms (gestation ≤ 34 weeks) will have at least one apneic episode. These spells generally occur in the first week of life, more commonly in the first 1 or 2 days Postnatally, most of the episodes disappear by 37 weeks postconceptional age. The apneic episode warrants an immediate treatment as there will be cerebral hypoxia and hypoperfusion that is expected to adversely affect the survival and subsequent neurodevelopment.[1]

Before the availability of infant ventilators, neonates who failed to sail through the transition from fetal to extra uterine life died shortly after birth. With smaller babies now forming a large percentage of neonatal intensive care units, the management of neonatal apnea is an important part of clinical workload. About 10 to 12% of Indian babies are born preterm as compared to 5 to 7% incidence in the West.[2] Thus, neonatal apnea is a major diagnostic challenge and a therapeutic exercise in NICUs.

Due to its significant contribution to the morbidity and mortality in the low-birth-weight infants, various aggressive approaches in the prevention and therapy of apnea have come up. In general, identifiable, and treatable causes such as infection, hypoxia, hypoglycaemia, hypothermia, and others should be

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corrected. For each episode, tactile stimulation, positive pressure ventilation (bag and mask) and mechanical ventilation should be provided as may be required. The pharmacological approach to the management of this problem is to administer drugs that stimulate respiration in the neonate. Several drugs such as theophylline, caffeine, doxapram and nikethamide have been used. The present study was done among newborns to study the risk factors and clinical parameters in apneic episode.

MATERIALS AND METHODS

This prospective study of 40 neonates with neonatal apnea was carried out in a level II/III Neonatal Intensive Care Unit (NICU) in Niramay hospital and research centre, in Satara, maharashtra, after obtaining IEC clearance. The duration of study was one year from April 2011 to April 2012. On admission to NICU, all babies receive the routine neonatal care consisting of cord care, eyecare, administration of Vit.K and stabilization of temperature. Oxygen and parenteral fluids are supplemented as per indications. The babies are footprinted for identification and New Ballard score was done for maturity. Weight recording of all babies done once daily as a routine. A detailed antenatal history including all maternal factors, birth history including need for resuscitation, the type of resuscitation was recorded. A written consent was taken from parents on admission for all the procedure done in NICU. Gestational assessment (post conceptional age) was done by modified Dubowitz method.

A routine clinical examination including cardiovascular, respiratory, abdominal, and neurological assessment is done on admission and every day thereafter. Monitoring of temperature is done 12hourly, or more frequently if indicated. A recording of BSL, BP, SaO2 is done on all babies on admission. Minimum handling of neonate is done.

Selection Criteria: Any neonate admitted in NICU was selected to the study on first episode of apnea. The babies that were monitored for the selection were: 1. All babies less than 34 weeks post conceptional age. 2. Term or preterm babies with sepsis. 3. Babies with intracranial bleeds, birth asphyxia. Neonatal apnea was defined as the cessation of breathing for more than 20 seconds or if less than 20 seconds, accompanied by bradycardia (with heart rate less than 100/min) and /or cyanosis.

Exclusion Criteria

All babies discharged against medical advice before the completion of study period were excluded from the study.

Period of follow up: Up to 37 weeks post conceptional age, or up to a period of at least two weeks from the last apnea. A pilot study consisting of 9 neonates with apnea was conducted to look for the feasibility of the study and to prepare a complete protocol for the proper conduct of the study. The recording of the apnea was done with apnea monitors and observation by the nursing staff/doctors. Every day the total number of apneas, time of occurrence of the apnea were noted in addition to the following detail. Heart rate, Duration of apnea, Day of 1stapneic episode, Presence of cyanosis, Relation of apnea to feeds, Posture of the baby during episode (particularly position of neck: flexion or extension), Blood pressure, Temperature (rectal), Pulse oximetry, Arterial blood gases, Routine hemogram for Hb, Total counts. Septic work up: blood culture. Chest radiograph and sonography of brain. Routine clinical examination for a possible cause. Data analysis was done in MS Excel software and results presented in percentages and statistical significance as p value.

RESULTS

The 40 neonates fulfilling inclusion criteria were analysed for the role of various etiological factors contributing to apneic episodes. There were 712 admissions in the study period of one year and the number of preterm admitted during the said period is 302. Average incidence of apnea is 56 per thousand admissions and figures for incidence in preterm is 18.5%. The study group consisted of 26 males (65%) and 14 females (35%). The mean gestational age ranged from 28 to 37 weeks. The mean gestational age was 31.38 +/- 2.72 weeks. The birth weight of babies was ranging from 740gms to 1980gms, with mean of 1271.5+/-287.69gms. Of them, 18 babies (45%) were Small for gestational age (SGA) and 22 babies (55%) were Appropriate for gestational age (AGA).

[Table 1] shows the Distribution of risk factors and patterns of findings on investigations in apneic patients (n=40). Table 2 shows the clinical parameters in the study. Table 3 shows the correlation of apnea features with cyanosis and sonography finding.

Apnea and clinical parameters: We studied a total 207 apneas in 40 neonates. The mean number of apneas per infant was 5.17 + 4.92. Number of apneas was ranging from minimum of one apnea to a maximum of 22 apneas per infant. The first apnea appeared right from first postnatal day up to 17thday. The mean of first day of apnea was 3.87 + 3.61 and the median was day 3 of life. Duration of apnea was lasting from 20 seconds to 240 seconds with a mean of 41.99 + 33.99 seconds. The mean duration of longest apnea of each baby was 62.0 + 43.217 seconds. The bradycardia (heart rate <100/min) was observed in all apneas with a minimum of heart rate of 10/min to a maximum of 96.0 min during the episode. The mean heart rate was 76.31 + 26.158/min. Cyanosis was present in 33 babies out of 40 babies (82.5%). The blood pressure recorded by Doppler method showed the values for systolic BP ranging from 43 to 76 mm of Hg with a mean of 56.4 + S.D. 10.203 mm of Hg and for diastolic BP ranging

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from 15 to 50 mm of Hg with a mean of 33.65 + S.D. 6.705 mm of Hg. The pulse oximetry showed that SaO2 was ranging from 75.0% to 95.0% with a mean SaO2 88.075 + 4.703%.

Apnea and Laboratory parameters: Haemoglobin examination done in all patients showed that 9 babies had haemoglobin of less than 10gms%. The haemoglobin was ranging from a minimum of 6.2gms to a maximum of 17.5gms with a mean of 12.17 + 2.822gms. Total leucocyte counts showed the values ranging from 3500 to 68000 cells/mm3 with a mean of 14510 + SD. 13483/mm3. Hypoglycemia (BSL < 40 mg%) was observed in 20 babies (50%). Blood sugars during the apnea were ranging from 12.0gms% to 403.0gms% with a mean of 83.25 + 97.07 gms%. Blood gases was normal in 24 babies (60%) and the rest showed respiratory acidosis (12.5%, n=5), metabolic acidosis (12.5%, n = 5) and a mixture of respiratory and metabolic acidosis (15.0%, n = 6). Blood gases demonstrated acidosis in a total of 16 patients (40%).

Table 1: Distribution of risk factors and patterns of findings on investigations in apneic patients (n=40).

Parameter			**Parameter**		
Factor	**n**	**%**	**Radiological Findings**	**n**	**%**
Flexion of neck	25	62.5	Normal	25	62.5
Post feed	12	30.0	RDS	10	25.0
Respiratory distress syndrome	10	25.0	Pneumonia	4	10.0
Intracranial bleed	10	25.0	Pneumothorax	1	2.5
Culture proved sepsis	7	17.5	Findings in USG Brain	n	%
Birth asphyxia	5	12.5	Normal	30	75
Pneumonia	4	10.0	Intracranial bleed	10	25
Pneumothorax	1	2.5	Lab parameter	n	%
Type of Acid base distribution	n	%	Haemoglobin (< 10gms%)	4	10
Normal ABG	24	60	Hypoglycemia (BSL≤ 40 mgs%)	20	50
Respiratory acidosis	5	12.5	Acidosis	16	40
Metabolic acidosis	5	12.5			
Respiratory air + metabolic acidosis	6	15.0			

Table 2: Clinical parameters in apnea in the study.

Clinical Parameters	**Min Value**	**Max Value**	**Mean**	**SD**
No. of apneas per infant	1	22	5.17	4.92
Day of first apnea	1	17	3.87	3.61
Duration of apnea in secs	20	240	41.99	33.99
Heart rate per min	10	96	76.31	26.15
Systolic BP	33	76	56.40	10.203
Diastolic BP	15	50	33.65	6.705
SaO2 (%)	75	95	88.075	4.703

Table 3: Correlation of various clinical parameters.

	Cyanosis		
Heart rate	**Present**	**Absent**	**p value**
≤ 60/min	25	1	0.007
>60/min	≤8	6	
	Sonography finding		
Day of first apnea	Normal	I/C bleed	
1st day apnea	8	3	1.00
1st apnea any time thereafter	22	11	
	Cyanosis		
Duration of apnea	Present	Absent	
≤ 20 seconds	2	2	026
< 20 seconds	31	5	

DISCUSSION

There were 712 admissions in the study period of one year and the number of preterms admitted during the study period is 302. Our average incidence of apnea was 56 per thousand admissions and figures for incidence in preterms was 18.5%. Rigatto (1982) has shown that apnea occurred in 23% of preterms in one year study period at Children centre, University of Manitoba, Canada.[3] The incidence of apnea in babies less than 34 weeks (<1800gms) is around 25%.[4] Our study group consisted of more male infants (n = 26,65%) than female infants (n = 14,35%). There is insufficient information regarding the prediction of apnea to either of the sex.

Full term babies and babies above 2500gms were not excluded from the study. Still, the maximum gestational age in our study was 37 weeks and the maximum birth weight was 1900gms. Apnea was more commonly observed in babies less than 34 weeks, and 85% of the babies were less than 34 weeks. The mean gestational age was around 31.38 +- 2.72 weeks. Similarly, babies between 1000–1500gms constituted 62.5% of infants under the study group. We had more SGAs (55%) than AGAs (45%). It has been widely accepted that apnea is more common in preterms and low birth weight infants.[4]

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Our study also showed exclusive occurrence of apnea in preterm and low birth weight group. However, there are no studies comparing the incidence of apnea in AGAs and SGAs so far, though our series showed a greater number of SGAs than AGAs. Neonatal apnea is often associated with ongoing neonatal disease and frequently, combinations of specific factors are operative. These factors may directly or indirectly affect the breathing mechanism of the infant leading apnea.[5] In our study, the following risk factors associated with apnea; supine position of flexion of neck (62.5%), hypoglycaemia (50%), acidosis (40%), RDS (25%), intracranial bleeds (25%) following feeds (23.70%), anaemia (Hb<10gms%) (22.5%), culture proved sepsis (17.5%), birth asphyxia (2.5%).

The preterms lying supine are at the disadvantage of changes in lung mechanism and thus, are at the high risk of apneas. In 1992, Ruth Heimler has demonstrated an increase in the incidence of apnea in supine than while lying prone.[6] In our study 25 babies (62.5%) were lying supine with flexion of neck during the episodes. According to Martin R J, preterm infants while in active sleep, exhibit asynchronous movements of the intercostal muscles in relation to diaphragmatic contraction. The resulting rib cage distortion may cause a decrease in the functional residual capacity and pulmonary oxygen reserve.[7] Controversy regarding the nursing position of the neonates is present since a long time. But the infants in prone position are at risk of SIDS.8 However, so far as apneas are concerned, supine position is better than prone position.

Hypoglycemia (< 40gms%) was seen in 50% of our babies. According to Riggato (1982) the apneas due to hypoglycaemia has almost disappeared and all their infants received prophylactic intravenous 10% glucose.[3] In our NICU we have a greater number of SGAs and additional risk factors like asphyxia, sepsis etc., for explaining higher incidence of hypoglycaemia associated with apnea. Acidemia was observed in 40% of our babies. This included a mixture of respiratory and metabolic acidosis as the commonest (15% of total number of acid base disturbances). The respiratory and metabolic acidosis were 12.5% each.60% of the babies had normal blood gases. Martin P. Samuels has mentioned acidosis as an important risk factor for apnea.[5]

In RDS the more severe the parenchymal involvement, more frequent are the apneic episodes. The mechanism is probably exhaustion of the respiratory pump due to high energy expenditure required to move the diaphragm and achieve an adequate lung volume in face of stiff lung and chest wall distortion.3 There is also hypoxia which significantly contributes to apneic episodes.9 Pneumonia causes hypoxia and stimulate vagal reflexes producing apneic episodes (36). In a study of 118 infants at Children's Centre, University of Manitoba, Canada RDS was observed in 19% of the babies. In our study,10 babies (25%) had RDS, and 4 babies (10%) had pneumonia.

Intracranial bleeding is a common cause of apnea during the immediate neonatal period. In the study at Children's Centre intracranial bleeding was observed in 20% of babies with apnea. In our study, the intracranial bleeding was observed in 10 babies (25%). Rigatto noted that the babies affected with intracranial bleeding usually have an anoxic insult at birth.[3] Birth asphyxia is known to cause hypoxemia and central depression. It also enhances the release of endogenous opiates causing depression of respiratory drive.[9] In our study, 5 infants (12.5%) had birth asphyxia. In our study, we could not prove any cause and effect between intracranial bleed, day of first apnea and anoxic insult at birth. Feeds can precipitate apnea by producing changes in lung ventilation or lung perfusion, interfering with airway oxygenation, lung, chest wall and vascular reflexes, and by inducing gastro esophageal reflux. Martin et al., has referred to apneas occurring during or soon after nasogastric feeding in a proportion of infants.[5] In our analysis of 207 apneas, 47 apneas (22.7%) were post-feed, 6 apneas (2.89%) were prefeed and 154 apneas (74.39%) occurred in infants not being fed.

We studied a total of 207 apneic episodes in 40 neonates. Apneic spells generally occur in first week of life. In our study, number of apneas per infant was ranging from a minimum of 1 to maximum of 22 per infant with a mean of 5.17 +4.92. Ann Stark has mentioned that if the apneic spells do not occur in the first week, they are unlikely to occur later.[4] But 4 infants in our study had their apneic spells after 7 days of life. However, these apneic spells were severe and related to sepsis.

Apneic episodes of 11-15 seconds duration are classified as mild and those of 16 to 20 seconds as moderate and those over 20 seconds duration as 'prolonged' apnea.10 In our study, the duration was ranging from 20 to 240 seconds with a mean of 41.99 +-33.9 seconds. Daniel. CS (1975) has shown that paediatric pneumogram with continuous recordings of respiration was better and picked up apneic spells of 10 to 19 seconds duration which could not be picked up by the staff and doctors.[11] We used 'apnea alarms' set for 20 seconds as well as recordings by staff for noting duration of apnea.

A newborn with immature respiratory control system reacts to the lack of airflow with bradycardia and diminished gas exchange.[12] The concomitant reduction in the cardiac output is reminiscent of the diving reflex. This sequence of events has an impact on cerebral blood flow and other organ blood flow. Effect of hypoxemia with decreased blood flow to various organ systems, followed by reperfusion causes injury to the developing extrauterine organs. In our study, in all 207 apnea there was bradycardia. Usually, apneas of duration longer than 20 seconds are associated with bradycardia.4 Cyanosis was seen in 33 babies (82.7%). We could prove that there is correlation between cyanosis and bradycardia. However, there was no statistical correlation between duration of apnea and cyanosis in our study.

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David Girling has studied blood pressure recordings and has shown that, during the attack there is rise in pulse pressure with increase in systolic pressure and rarely a fall in diastolic pressure.[12] Pulse pressure increased whenever there is bradycardia. In our study, the mean systolic blood pressure was 56.4 + 10.28 and the mean diastolic blood pressure was 33.62 +6.705.

Pulse oximetry has revolutionized the understanding of apnea and hypoxemia. It is the 'hypoxemic' episodes that are clinically significant than the arrest of 'breathing'. Martin et al., have recommended that some episodic falls in oxygenation may be minor and clinically unrecognized, but others may present as major cyanotic episodes or even cardiorespiratory arrest. It is possible that they result from false in airway oxygenation, which in turn produce pulmonary vasoconstriction, leading to further hypoxemia through development of right to left shunting. To avoid hypoxemic episodes SaO2 should be kept at 95 to 97%. 5Ann. R. Stark has reported that SaO2 less than 80% are inadequate and between 80 to 85% are adequate if PaO2 is greater than 45mm of HG.4 The values above 85% are in general not harmful. Pulse oximetry showed varying range of SaO2 during the episodes.4 patients (10%) had SaO2 less than 80%, 6 patients (15%) between 80 to 85% and 30 patients (75%) had SaO2 above 85%.

CONCLUSION

In conclusion, 207 episodes of apneas occurred in 40 neonates. The incidence of babies with apneas was 57 per thousand admissions and the incidence in preterms was 18.5%. The following factors were found to contribute to development of apneas in neonates were flexion of neck, acidosis, RDS, intracranial bleeds, post-feed, anaemia, culture proved sepsis, birth asphyxia, and pneumonia.

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