APNEA IN NEWBORN INFANTS: APPROACH TO MANAGEMENT

RAUL C. BANAGALE*, DIETRICH W. ROLOFF* and WILLIAM F. HOWATTb

Section of Newborn Services*, and Section of Pulmonary Diseasesb, Department of Pediatrics, University of Michigan, Ann Arbor, MI 48109 (U.S.A.)

(Received March 1st, 1983)

SUMMARY

Approximately 25% of infants with birth weights less than 1800 g or infants of about 34 weeks gestational age have an apneic episode. This, and the known high incidence of apneas in infants who subsequently are victims of sudden infant death syndrome, has led to aggressive attempts at early identification of newborns with abnormal cardio-respiratory patterns. We have found the pneumocardiogram to be effective in detecting cardio-respiratory abnormality in the newborn, and a very useful tool in the assessment of the effectiveness of pharmacologic therapy of neonatal apnea. Infants who are discharged on a home apnea monitor should be managed, utilizing a coordinated multidisciplinary team approach, that includes 24 h availability of a physician, technician, community health nurse, social worker and, when possible, a member of a parent support group. This paper presents a review of neonatal apnea and our institutional approach to its evaluation and management.

INTRODUCTION

The majority of low birth weight infants have apneic spells (Alden, Mendelkorn, Woodrum, Wennberg, Parks and Hodson, 1972). Approximately 25% of infants with birth weight less than 1800 g or 34 weeks gestation have apneic episodes (Daily, Klaus and Meyer, 1969). Aside from apnea, other forms of cardio-respiratory patterns have been implicated as causes of recur-
rent or chronic hypoxemia in the newborn infant (Westgate, 1982). For these reasons and because available epidemiologic data show a high incidence of apnea in infants (Steinschneider, 1972; Steinschneider, Weinstein and Diamond, 1982) who subsequently were victims of SIDS (Sudden Infant Death Syndrome), in our institution we are aggressively attempting the early identification of newborns with abnormal cardio-respiratory waveforms (Banagale, 1982a).

POPULATION AT RISK AND DIAGNOSTIC WORK-UP

Certain characteristics of premature infants, such as neurological immaturity, immature chemical responses to hypoxia and a propensity to develop intracranial hemorrhage, have predisposed them to develop abnormal cardio-respiratory patterns and SIDS (Stein and Shannon, 1975; Kattwinkel, 1977; Kelly and Shannon, 1982; Rigatto, 1982; Sells, Neff, Bennett and Robinson, 1983). The population of infants at risk for SIDS however is not limited to the preterm infant and includes term newborns as well. This high risk population as a whole comprises a heterogenous group with numerous other factors (Valdes-Dapena, 1980) associated with the pathophysiology of SIDS.

We routinely perform pneumocardiograms (Banagale, 1982) on the following groups who are at risk for SIDS: (a) those with birth weight less than 1800 g or with gestational age less than 34 weeks; (b) those with history of perinatal and/or neonatal asphyxia; (c) siblings of SIDS infants; (d) infants of mothers with narcotic addiction; and (e) those observed to have apnea, bradycardia, and other abnormal breathing patterns. Appropriate diagnostic

TABLE I
DEMONSTRABLE CAUSES OF ABNORMAL NEONATAL CARDIO-RESPIRATORY PATTERNS AND ELEMENTS OF DIAGNOSTIC WORK-UP

<table>
<thead>
<tr>
<th>1. Infection (sepsis, pneumonia and meningitis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. CBC and differential count</td>
</tr>
<tr>
<td>b. cultures (blood, cerebrospinal fluid, and urine)</td>
</tr>
<tr>
<td>c. chest X-ray</td>
</tr>
<tr>
<td>d. blood gases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Glucose and electrolyte imbalance</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. blood sugar</td>
</tr>
<tr>
<td>b. electrolytes including calcium and magnesium</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Cardiac, gastro-esophageal, central nervous system, and upper airway anomaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. EKG and/or echocardiogram</td>
</tr>
<tr>
<td>b. barium esophagram, esophageal manometric and esophageal pH determinations</td>
</tr>
<tr>
<td>c. cranial ultrasound and/or EEG</td>
</tr>
<tr>
<td>d. laryngoscopy, soft-tissue radiography of the neck and bronchoscopy</td>
</tr>
</tbody>
</table>
work-up, as shown in Table I, guided by the pertinent history and physical examination findings, should be undertaken to rule out the commonly treatable causes of cardio-respiratory disturbances in infants. Careful search for the presence of infection, glucose, electrolyte, calcium and magnesium imbalance, severe anemia and polycythemia or hyperviscosity should be done. Chest radiograph, electrocardiogram and echo-cardiogram are useful in the evaluation of a possible cardiac anomaly. When gastro-esophageal reflux is suspected (Herbst, Minton and Book, 1979), barium esophagram, esophageal manometric study and esophageal pH measurements are helpful procedures to confirm the diagnosis. In premature newborns, cranial ultrasounds should be performed to rule out intracranial hemorrhage. Some infants with seizure activity may present with apnea and an electroencephalogram is a useful diagnostic tool. A careful search for the presence of an upper airway obstruction should be accomplished. Laryngoscopy, soft tissue neck radiograph and bronchoscopy should be done when indicated. When no demonstrable or treatable cause can be identified to explain the infant's observed apnea, bradycardia or "cyanotic spells", we perform a pneumocardiogram.

PNEUMOCARDIOGRAM

Pneumocardiogram (PCG), also known as pneumogram, nocturnal cardio-respirography or cardio-pneumogram, is still considered by some investigators as a controversial tool in the assessment of infantile apnea (Brooks, 1982). This is due to some yet unresolved limitations of PCG which include: (1) the absence of a generally accepted definition or terminology of what constitutes abnormal cardio-respiratory patterns, other than the obvious prolonged apnea (American Academy of Pediatrics Task Force on Prolonged Apnea, 1978) and profound bradycardia; (2) some investigators have shown that some infants at risk for SIDS show no abnormality in PCG (Southall, Richards, Rodhen, Alexander, Shinebourne, Arrowsmith, Cree, Fleming, Goncalves and Orme, 1982) and that some infants with obstructive apnea were detected only with the use of an acoustic monitor (Werthammer, Krasner, DiBenedetto and Stark, 1983). However, in the absence of a demonstrable or treatable cause as we have previously delineated, we have found the PCG to be an effective tool in detecting variations in newborn cardio-respiratory waveforms. Such variations or abnormalities may in the future be established as a major cause of chronic or recurrent hypoxemia in newborn infants. We have also found that PCG is more accurate than the combined bed-side observation and conventional apnea devices in detecting significant episodes of abnormal cardio-respiratory patterns (Beaumont and Roloff, 1982).

PCG is simple to perform and provides an objective quantification of respiratory rate, rhythm, relative amplitude of inspiration, frequency and duration of apnea and/or bradycardia (Banagale, 1982a) PCG has also been very useful in the assessment of the effectiveness of pharmacologic (theo-
phylline or caffeine) therapy of neonatal apnea (Banagale, 1982b; Banagale, 1983).

PCG is not a polysomnogram (multi-channel recording of awake and asleep states), rather, it is a two-channel recording that measures electrocardiographic activity (ECG) and respiratory wave forms by an impedance technique, performed at night when long episodes of deep sleep are likely to occur. It requires on the average a 12-h recording onto slow speed magnetic tape. We record PCG with a Healthdyne INFA-DATA® monitor recorder (Healthdyne, Marietta, GA). The recorded tape is reviewed on a specialized computer based playback system using the PMD-12 Respiration Replay-Display System® (Oxford Medical System Limited, Abingdon, Oxon). The system permits visual display and examination of the pneumocardiographic patterns on an oscilloscopic display. A hard copy of the trend recording (360 s/page) which shows heart rate and respiratory waveform is obtained and apnea, bradycardia, and other abnormal breathing patterns are identified, measured, quantitated and analyzed page-by-page. Any data of significant abnormality can be viewed and/or printed out at slower speed (real time = 6 s/page) which shows ECG and respiratory waveform. Figure 1 shows a 312-s segment of a 720-min trend recording. It shows the relative regularity of the respiratory rate (35/min) and the heart rate (140/min).

Based on our own experience, that of other investigators (Stein, 1979; Kelly, 1980; Stark, 1982), and from the wide experience of Dr. Eugene Dolanski and associates from Edward W. Saprrow Hospital, Lansing, Michi-
**TABLE II**

**ABNORMAL PNEUMOCARDIOGRAPHIC FINDINGS**

1. Apnea greater than 15 s
2. Periodic breathing* of more than 5% of the total trend recording
3. Bradycardia (recovery time of more than 10 s)
   a. less than 80/min in infants less than 1 month of age
   b. less than 70/min in infants 1–3 months of age
   c. less than 60/min in infants 3–6 months of age
4. Disorganized breathing consisting of irregular respirations with short apneas of less than 15 s accompanied by bradycardia.

*Periodic breathing—three or more respiratory pauses of greater than 3 s, with less than 20 s of normal respiration separating the pauses.

*gan [pers. commun.], we consider the presence of any of the criteria listed in Table II an "abnormal" pneumocardiogram. Figure 2 shows an example of a periodic breathing pattern. It represents a 427-s period periodic breathing on a 558-s segment of a total 720-min trend recording. Figure 3 shows an example of a "short apnea" (apnea less than 15 s). It represents a 12.3-s apneic spell without bradycardia on a 320-s segment of a total 720-min trend recording. Figure 4 shows two "long apneas" (apnea more than 15 s). These are a 19.2-s segment of apnea and a 22.3-s apnea with bradycardia of a total 720-min trend recording. The pneumocardiogram is sensitive to the motion of the electrodes or wires, which produce changes in the DC offset, resulting in artifact patterns (Stark, 1982) as shown in Fig. 5. It represents a 324-s segment of a 720-min trend recording. A (36 s), B (72.5 s), C (48 s) are the

---

**Fig. 2. Periodic breathing of 427 s on a 558-s segment of a 720-min trend recording.**
Fig. 3. A 12.3-s apnea on a 320-s segment of a 720-min trend recording.

Fig. 4. A 317-s segment of a 720-min trend recording showing apnea of 19.2 s duration without bradycardia. The 22.3-s apnea is accompanied by bradycardia of 55/min lasting 24 s.
Specific treatment is instituted depending on the findings in the previously delineated diagnostic work-up. Infants whose abnormal cardio-respiratory pattern does not improve with specific therapy and those infants with abnormal cardio-respiratory patterns without demonstrable cause are started on oral theophylline liquid (theophylline USP, anhydrous, in a non-alcoholic solution), using a loading dose of 6 mg/kg body weight. The maintenance oral dose is 2 mg/kg body weight/dose administered every 12 h. The oral maintenance dose is adjusted to obtain a serum theophylline level of 8–12 μg/ml. We determine serum theophylline level by a micro-scale measurement utilizing high-pressure liquid chromatography (Orcutt, Kozak, Gillman and Cummins, 1977). It is essential that a concomitant serum caffeine measurement be performed because of significant biotransformation of theophylline to caffeine in newborns receiving theophylline (Bada, Kanna, Somani and Tin, 1979; Bory, Baltassault, Porthault, Bethenod, Frederich and Aranda, 1979; Aranda, Grondin and Sasyniuk, 1981; Banagale, 1982a,b). This bio-

Fig. 5. A 324-s segment of a 720-min trend recording with artifact patterns and interruptions of heart rate tracing.

artifact patterns with interruptions in otherwise regular heart rate recording.

MANAGEMENT
transformation of theophylline to caffeine in newborns includes N-methylation at the N7 position, whereas the known metabolic pathway of theophylline in adults involves oxidative reactions such as N-demethylation (N1, N3) and C-8 oxidation. Methylated serum caffeine has potentiating effect and levels as low as 3–4 μg/ml have been shown to regularize abnormal respiratory patterns. The pharmacologic effect of methylated serum caffeine is either due to the therapeutic effect of caffeine alone or due to its additive effect to theophylline leading to a higher total methylxanthine load.

A. Infants discharged without home apnea monitor

An infant whose abnormal breathing pattern has responded to administration of theophylline as evidenced by a normal repeat PCG at 3–7 days after the initiation of therapy is sent home on medication without a home apnea monitor. These infants are followed closely in our High Risk Developmental Follow-Up Clinic and also in the primary care physician's office. Periodic determination of their serum theophylline and caffeine levels is performed. Medication is adjusted to maintain therapeutic serum theophylline levels and the infants are monitored for evidence of drug toxicity (Steinschneider, 1972). The duration of treatment with theophylline has been variable but these infants usually have a normal PCG when theophylline is discontinued at about 44 weeks corrected gestational age (conceptional age). During the process of weaning the infant off medication, he or she may temporarily be placed on a home apnea monitor and the monitor is discontinued when the follow-up PCG is normal without medication. Infants who fail the attempt to discontinue the medication, as evidenced by an abnormal follow-up PCG, are restarted on medication. These infants, as previously indicated, are taken off the apnea monitor when the repeat PCG is normal with medication. Some infants require such trials of weaning 2–4 times before the appropriate response is attained.

It should also be emphasized that premature infants have a remarkably slow elimination of theophylline and caffeine. Theophylline can be detected in the plasma up to 3 days after cessation of theophylline therapy and caffeine can still be detected up to 9 days after treatment (Bory et al., 1979). Therefore, the potentiating effect of methylated caffeine should be considered not only at the initial phase of theophylline therapy, but also during and at the termination of treatment (Banagale, 1982b; Banagale, 1983).

B. Infants discharged on home apnea monitor

There are two groups of infants who are discharged on home apnea monitor: first, those infants whose PCG is abnormal despite adequate serum theophylline and/or caffeine levels; second, surviving twins of SIDS victims and the subsequent siblings of victims of SIDS proven at autopsy.

Infants belonging to the first group predominantly consist of premature infants who, other than their abnormality of cardio-respiratory patterns, are growing, but have not yet met our criteria for discharge. In addition to the
previously mentioned diagnostic work-up, they undergo further evaluation for any other possible unrecognized and treatable cause. When indicated, metabolic and amino acid screen is performed. Polysomnography (Hoppenbrouwers, Hodgman, Harper, Hofmann, Sterman and McGinty, 1977; Kahn, Bloom, Waterschoot, Engelman and Smets, 1982) or performance of brain stem evoked potential may at times be necessary (Westgate, 1982). A few infants have been treated with phenobarbital because of the suggestion of seizure activity on EEG (Watanabe, Hara, Hakamada, Negoro, Sugiura, Matsumoto and Maehara, 1982; Watanabe, Hara, Miyazaki, Hakamada and Kuroyanagi, 1982).

Infants belonging to the second group consist of those who undergo diagnostic work-up based on the history of a sibling dying of SIDS (Kelly, Twannmoh and Shannon, 1982). Because of the high statistical risk factor of this group of infants, coupled with the extreme parental and/or physician anxiety, they are commonly sent home on an apnea monitor even when no treatable cause is found and, in some instances, irrespective of the result of PCG.

The parents of this group of infants undergo an extensive hospital discharge planning which is provided by a coordinated multi-disciplinary team. Table III shows an assessment of the family unit including the parents' understanding of the purposes of home apnea monitoring as well as the home care cost. Evaluation of the extent of insurance coverage for the cost of the equipment, accessories and needed services is undertaken. In Michigan, the Division of Services to Crippled Children (DSCC) has provided financial assistance for medical and nursing care of home apnea monitored infants provided the rigid but appropriate medical criteria for placement of the home apnea monitor are met. The coping ability of the parents, including the other members of the family, is also taken into consideration.

Table IV outlines the in-hospital educational process given to the parents and extended family members (other caretakers). They are taught the appropriate performance of cardiopulmonary resuscitation. A technical personnel or a monitor dealer representative explains the proper use of the monitor including needed supplies and services. Plans on how to handle an emergency situation are also discussed. This includes local emergency services, such as the ambulance company or emergency medical services. The power company is notified to provide priority service to the family in case of

**Table III**

**FAMILY ASSESSMENT**

1. Parents' acceptance and ability to understand advantages and disadvantages of home apnea monitoring
2. Coping ability and family support system
3. Appropriateness of home environment
4. Home care cost
TABLE IV

FAMILY EDUCATION

| 1. Proper use of apnea monitor  |
| 2. Proper performance of cardiopulmonary resuscitation |
| 3. Monitor installation and related services |
| 4. Proper maintenance of record or event data sheet |
| 5. Emergency support plans, especially physician and emergency room accessibility |

Power failure. The parents and other caretakers are also instructed as to the proper maintenance of the record or event data sheet, as well as immediate access to the emergency room.

As shown in Table V, appropriate referrals to the related community agencies are also accomplished to ensure proper follow-up of the infant and the provision of adequate medical and psychosocial support to the parents and their family. The coordinated multi-disciplinary team approach includes the 24-h availability of a physician, technician, community health nurse, social worker and, when possible, a member of a parent support group. There is always a concerted effort to minimize the stress produced by 24-h home apnea monitoring (Black, Hersher, Steinschneider, 1978; Cain, Kelly and Shannon, 1980).

The infant is followed closely in the primary care physician’s office and in the High Risk Developmental Follow-Up Clinic. Accurate therapeutic drug(s) monitoring is performed on infants who are discharged on theophylline and/or phenobarbital.

At present, our criteria in considering an infant ready for discontinuation of the home apnea monitoring consist of: (1) the infant has had no apnea, bradycardia or “cyanotic spells” for at least 2 months; and (2) those infants who have had previously abnormal PCG should have a normal follow-up PCG, preferably two normal PCGs, 1 month apart. During this period, the infant’s cardio-respiratory response to upper respiratory tract infection

TABLE V

COMMUNITY REFERRAL AND FOLLOW-UP

| 1. Home health care, or Visiting Nurse Association |
| 2. Social Services Department |
| 3. Financial aid |
|   a. Division of Services to Crippled Children (DSCC) |
|   b. March of Dimes, American Red Cross, National SIDS Foundation, or other available resources in the community |
| 4. Primary care physician |
| 5. High Risk Developmental Follow-Up Clinic |
| 6. Parent Support Group |
and/or DPT immunization is taken into consideration. Siblings of SIDS victims (even those with normal PCG) are kept on monitor for 6 months. The process and timing of the discontinuation of home apnea monitor is not always consistent because of the above mentioned factors along with the differences in the degree of parental readiness and acceptance of disconnecting the infant from the monitor. The majority of these infants are successfully discontinued from theophylline therapy and home apnea monitor in about 6 months. While the majority (91%) of SIDS deaths occur in the first 6 months of life, the termination of home apnea monitoring and/or theophylline therapy is not a signal to discontinue meticulous follow-up care. These infants continue to be followed closely in the primary care physician’s office and in the High Risk Developmental Follow-Up Care Clinic.

ACKNOWLEDGEMENT

We wish to express our sincere gratitude to Louise Dooley for preparing the manuscript for publication.

REFERENCES


