Breathing Pattern and Transcutaneous Oxygen Tension during Motor Activity in Preterm Infants1-3

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Introduction

Clinical experience with transcutaneous oxygen tension (TcPO2) monitoring in infants has demonstrated previously unsuspected fluctuations in arterial oxygen tension. Little is known of the origin of these fluctuations except that sudden decreases in TcPO2 have been shown to be more frequent when infants are disturbed by routine medical procedures (1, 2) and environmental noises (3). Except in instances where crying results, why such disturbances should cause TcPO2 depression has remained unexplained. In the present work, we examined the hypothesis that changes in breathing pattern accompanying generalized motor activity may account for many of these decreases in TcPO2. Using a new technique for measuring tidal volume in active infants (4), we studied changes in breathing pattern and minute volume in 18 preterm infants during episodes of sustained motor activity. These studies revealed the close association of a distinctive motor activity (squirming) with a pattern of breathing in which we documented Valsalva maneuvers and decreases in minute volume as factors that could lead to arterial hypoxemia. Observations in these 18 infants suggest that changes in breathing pattern associated with squirming occur spontaneously or can be elicited by stimuli from procedures. In 10 infants, we recorded TcPO2 and related both squirming motor activity and the breathing changes during squirming to TcPO2 instability.

Methods

Subjects. Eighteen preterm infants were studied. In the initial group of patients (Group A, 8 patients), we studied changes in respiratory pattern during squirming activity using the techniques described subsequently. In a subsequent group (Group B, 10 patients), we added electromyography and TcPO2 recordings in order to further substantiate muscle activity and relate motor activity and breathing pattern to arterial oxygenation. Patient data are provided in Table 1. Most of the patients had recovered from the acute phase of illnesses that initially required intensive care and were being cared for in the intermediate care area of the neonatal intensive care nursery. All were being monitored with heart rate and chest impedance monitors for apnea and bradycardia. All had had one or more bradycardic episodes within 3 days prior to the study and 7 patients (3 in Group A, 4 in Group B) were receiving theophylline for apnea spells and bradycardia. The remainder were breathing room air. Informed consent from the infants’ parents was obtained for all studies.

Methods. The recording sessions lasted 1 to 2 h. Three infants in Group A and 3 in Group B were studied on 2 occasions. The average total recording time per infant was 111 ± 25 min in Group A and 118 ± 15 min in Group B (mean ± SEM). The infants were studied in a quiet room after a feed while lying supine in their incubator or radiant warming table. Skin temperature was servo-controlled at 36.0 to 36.5°C. During the study, handling of the infants was limited to normal care and procedures needed to maintain recording equipment, such as adding tape to secure leads. Respiratory flow was monitored using a lightweight, self-retaining nasal flowmeter and a Statham PM 15-E pressure transducer (Statham Instruments, Oxnard, CA) (4). The principal features of this system include: 0.35 ml added dead space, added respiratory resistance of 1.3 cm H2O/100 ml/s, and 95% response time to change in flow of 0.02 s. Tidal volume was derived from the integration of flow. The sampling catheter from the CO2 analyzer was held close to the mouth to detect oral breathing. In 5 studies, all in Group A subjects, respiratory efforts were monitored by a respiratory bellows (Beckman Instruments, Irvine, CA) around the abdomen. In the remaining studies, esophageal pressure was measured with an esophageal balloon placed in midthorax and connected to a Statham PM-131 transducer (5). The 90% response time of this system was 0.02 s. Transcutaneous arterial oxygen tension was measured by an electrode (Litton Bionetics, Kensington, MD) in all Group B subjects. Surface electromyography was performed in Group B patients, and included abdominal (9 patients), and submental (8 patients) electromyograms. Electrocardiograms were recorded in all patients.

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investigator observed motor activity and notations of these observations were made on the polygraphic tracings.

Data analysis. The qualitative description of motor activity and breathing pattern was on the basis of extensive notes taken at the time of the studies, which were supplemented and confirmed by retrospective review of the polygraphic records. In the retrospective review, the presence or absence of generalized motor activity was assessed on the basis of behavioral observations and body movement artifacts in the electrocardiograms (in all subjects) as well as on increased electromyographic activity (in Group B). In describing our findings, we use the term squirming to indicate sustained spontaneous respiratory changes previously associated with hypoxemia; therefore, we excluded from the quantitative analysis of breathing pattern all episodes of crying, prolonged apnea (>10 s), hiccapping, and suctioning to clear secretsions from the airway when these events occurred in addition to squirming. Cases in which crying appeared after the decrease in \( \text{TCPo2} \) and after 1 min of motor activity were not included. A control period of 1 min prior to onset of squirming lasted from 5 s to 2 min. Some were preceded or followed by bouts of crying. Most episodes of squirming were presumed to be spontaneous because there was no identifiable precipitating stimulus. However, squirming episodes were particularly frequent when we handled the infants at the beginning and at the end of recording sessions. Stimuli such as passing or adjusting the esophageal balloon, tapping or untaping electrodes, wiping the skin with alcohol, or suctioning secretsions from the airway usually elicited squirming. These infants had varied medical histories and some were receiving theophylline, and yet we could identify no predisposing factors for squirming other than sensory stimulation.

Breathing pattern during squirming episodes. The principal features of the respiratory pattern during squirming can be seen in figures 1 and 2. These features included a slowed rate, decreased minute volume, increased variability in the timing and force of respiratory efforts, and increased peak inspiratory and expiratory flow rates with markedly shortened expiratory times. The most distinctive feature of this pattern was sudden cessation of flow during expiration, creating a "plateau" configuration in the tidal volume trace. These plateau in the tidal volume trace usually coincided with increased esophageal pressure of 10 to 20 cm \( H_2O \) and increased activity in the abdominal electromyograms. We used the term "Valsalva breath" for this pattern because of its similarity to a Valsalva maneuver. The end-expira-
Fig. 1. Polygraphic tracings and behavioral observations showing an episode of squirming motor activity and associated respiratory changes in a preterm infant. Tracings are: electrocardiogram, CO₂ sampled at the mouth, nasal air flow, integrated flow (Vt), esophageal pressure, and submental and abdominal muscle electromyograms. Onset of squirming episode first appears as submental muscle electromyographic activity (arrow A), soon followed by abdominal muscle electromyographic activity (arrow B), movement artifacts in the electrocardiographic baseline and observations of leg flexion and “flushed face.” Note changes in the respiratory pattern that appear simultaneously with the motor activity. These respiratory changes include shortened expiratory time (Te) compared with that in the control period (Te_c), increased inspiratory and expiratory peak flow, onset of “Valsalva breaths” characterized by plateau configuration of the tidal volume trace (arrow C), increased esophageal pressure (arrow D), and abdominal muscle electromyogram (arrow B). Flat CO₂ trace indicates absent oral air exchange. Stepwise increase in end-expiratory volume necessitated downshifting the tidal volume baseline twice (arrows E and F) to keep it on scale. Note the return to control breathing pattern when squirming motor activity ceases (arrow F).

Fig. 2. Polygraphic tracings illustrating obstructed inspiratory efforts during squirming motor activity. Abbreviations as in figure 1. Onset of squirming occurs at arrow A. Obstructed inspiratory efforts occur at arrows B. These occur in association with “Valsalva breaths” as evidenced by plateau configuration of the tidal volume tracing and absent air flow with positive esophageal pressure excursion.
pattern as described above were identified in the 10 Group B patients (range, 15 to 4 episodes per patient). In 98 instances, TcPO₂ decreased during the episode. It was unchanged in 3 and increased in 3.

Contribution of squirming to large decreases in TcPO₂. Fifty-nine episodes of acute decrease in TcPO₂ ≥ 10 mmHg were identified in the 10 Group B patients (range, 3 to 10 episodes per patient). During or immediately preceding 46 of these episodes, squirming activity occurred. However, in 25 of the 46 episodes, prolonged apnea preceded the squirming and, in some of these or in other episodes, crying (24 of 46) hiccuping (3 of 46) or sucking of the airway (8 of 46) occurred in close temporal association with the squirming. Therefore, in a total of 30 of 46 episodes, multiple factors possibly contributing to TcPO₂ decrease were identified, whereas in 16 of 46 (30%), the breathing pattern associated with squirming could be held solely responsible for the TcPO₂ decrease. These 16 episodes occurred in 8 of the 10 patients.

Heart rate and breathing pattern during squirming episodes associated with large TcPO₂ decreases. The 16 squirming episodes in which the exertional breathing pattern appeared to be a primary factor in the ≥ 10 mmHg reduction in TcPO₂ were analyzed in detail. Three of these 16 episodes were apparently precipitated by stimuli (adjusting the electrodes, rubbing the skin, retaping the esophageal catheter). The remaining episodes were apparently spontaneous. Because we lacked definitive criteria for distinguishing spontaneous from stimulus-elicited episodes, we did not consider them separately in the data analysis. The average duration of the 16 episodes was 81.6 s (range, 40 to 149 s). The mean TcPO₂ during the control period preceding the episode was 69.6 (range, 52 to 81 mmHg). The average decrease in TcPO₂ during episodes was 15.39 (range, 12 to 21 mm Hg). On six occasions (in 4 infants) TcPO₂ decreased below 50 mmHg. Control heart rate was 155 (range, 128 to 166 beats/min). It decreased to 114 beats/min during episodes (range, 92 to 172 beats/min) (p ≥ 0.05). During 9 of the 16 episodes (in 5 infants) heart rate decreased to less than 100 beats/min.

The respiratory rate and minute ventilation both decreased substantially during the episode of squirming (table 2). Mean tidal volume was unchanged; however, the variability in Vt was considerably increased during motor activity compared with that of the control period (coefficient of variation = 0.78 versus 0.47, p < 0.05). The duration of Valsalva breaths and obstructive apneas was substantially increased during the spells compared with that of the control period. Valsalva breath duration was positively correlated with the magnitude of TcPO₂ change (r = 0.52, p < 0.05).

Discussion

Although it has been previously reported that respiratory frequency becomes irregular in vigorously active infants, no consistent pattern of change has been suggested and determinations of respiratory air exchange have never been reported. In nonhuman neonates, motor activity has been associated with increased frequency and depth of breathing. In contrast, in human neonates we observed that respiratory frequency and minute volume is reduced during squirming. In addition, we have observed changes in end-expiratory volume, increased respiratory flow rates and decreased expiratory time associated with squirming. Also we have described "Valsalva breaths," which appear to be an important feature of the change in breathing during squirming. During the Valsalva breaths we have shown that there is increased tone in the abdominal wall and increased electromyographic activity of abdominal expiratory muscles. We have further
shown that these changes coincide with raised esophageal pressure. The absence of air flow in this situation implies airway closure. Therefore, the Valsalva breath is similar to the Val-

salva maneuvers that occur during crying (9) or grunting (10), except that expiratory air flow is at no time completely obstructed during crying or grunting. The Valsalva breaths occurring during squirming in infants may not necessarily be maladaptive because, in adults, Valsalva maneuvers during forceful exertions of the extremities are viewed as facilitating limb movements (11, 12).

Obstruction to respiratory air flow was encountered in two different situations during squirming motor activity. Obstruction to expiratory flow occurred during Valsalva breaths, whereas obstruction to inspiratory flow occurred during obstructive apnea (i.e., Mueller maneuvers). The site of obstruction is conjectural but is presumably in the upper airway. In radiographic studies of older infants, Bosma and coworkers (13, 14) noted intermittent airway closure involving both the pharynx and larynx when infants struggle (13) or cry (14). These observations suggest a tendency for muscular constriction of the upper airway during motor activity and crying, a view that is supported by laryngeal electromyographic studies (15). In fact, completely obstructed inspiratory efforts (i.e., obstructive apneoa have been reported in association with crying (14, 16). Given the general similarities of the exertional breathing pattern to crying, it is tempting to speculate that the airway obstruction we saw was on the basis of active airway closure by pharyngeal and laryngeal airway constricting muscles. Alternatively, it is possible that obstruction was secondary to passive closure of the airway during neck flexion, which we saw occurring intermittently during squirming (17).

It has generally been accepted that increased motor activity indicates an increased state of arousal. Furthermore, squirming was not infrequently associated with cry which, again, is usually accepted as a state of arousal. We observed a smooth transition from the silent exertional breathing pattern to crying, suggesting that the two are related behavioral activities that are gradations of a pattern of arousal. Precht and associates (15) reported that gross motor movements occur frequently during State 2 sleep (REM sleep). We do not see this as conflicting with our view, because we interpret the data to mean that episodes of sustained motor activity interrupt sleep, not that infants are sleeping during the motor activity.

The present observations, which relate behavioral arousal (i.e., sustained, generalized motor activity) and sensory stimulation to episodes of obstructive apnea and bradycardia in infants, pose something of a paradox, because previous studies of neonatal apnea and bradycardia, including our own, have tended to implicate sleep as a primary etiologic factor (17, 18). Indeed, sensory stimulation to produce arousal is the most frequently used treatment for apneic spells in infants. The present observations do not discount the role of sleep in many of the apneic spells that occur in infants. On the other hand, the present observations support the concept that there are different forms of neonatal apnea and that these different forms may have fundamentally different underlying physiologic causes.

We have shown an association of squirming with a decrease in TcPo2 in several ways. We observed a decrease in TcPo2 after most squirming episodes. Furthermore, when we scanned the tracings for large decreases in TcPo2, we found a frequent association with squirming. When examining both brief and prolonged episodes of squirming we treated TcPo2 change qualitatively because TcPo2 is a highly damped reflection of arterial Po2, which makes absolute change less relevant (19). In our search for large decreases in TcPo2, the 10 mmHg criterion was arbitrary. Again, considering TcPo2 damping, the change in arterial Po2 was likely larger than the change in TcPo2 during these episodes.

Three factors were likely contributors to the decrease in TcPo2 during squirming episodes. Minute ventilation was decreased by more than 50% during squirming. This was due to multiple factors including obstructed inspiratory efforts and prolongation of the respiratory cycle by Valsalva breaths. A second factor possibly contributing to hypoxemia is intermittent venous shunting. This very likely occurs during the Valsalva breath. Shunting has been demonstrated by Walsh and coworkers (20) and by Lind (21) when infants cry. During the phase of increased thoracic pressure, venous return to the heart is greatly diminished. Consequently, when inspiratory efforts occur, they produce a surge of venous flow to the right atrium creating transient reversal of atrial pressure ratios, which causes right to left shunting. Duration of Valsalva breaths correlated significantly with change in TcPo2, which would support the notion that shunting during these breaths was an important influence on TcPo2. However, it has been pointed out previously (10), that shunting during a Valsalva maneuver is influenced by hemodynamic factors and cannot be predicted by respiratory measures alone. The final factor that could have contributed to the decrease in TcPo2 is increased oxygen consumption associated with motor activity. We have no way of assessing this contribution independent of breathing pattern changes. It may have been a significant factor, particularly in prolonged episodes.

In the present study, a decrease in TcPo2 below 50 mmHg was documented on multiple occasions. The TcPo2 has been reported to decrease during handling of infants in the absence of prolonged apnea, crying, or other accepted explanations for hypoxemia (2, 22, 23). There has been speculation that an altered respiratory pattern may explain this phenomenon (2, 3, 24). We observed that 30% of sudden decreases in TcPo2 were associated with a distinctive "exertional breathing pattern." Furthermore, in many other instances,

**TABLE 2**

<table>
<thead>
<tr>
<th>Respiratory Frequency (breaths/min)</th>
<th>Tidal Volume (ml/kg)</th>
<th>Minute Volume (ml/min/kg)</th>
<th>Duration of Obstructive Apnea (s/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control period</td>
<td>58.3 ± 17.9</td>
<td>5.7 ± 2.5</td>
<td>335.6 ± 141.2</td>
</tr>
<tr>
<td>Squirming</td>
<td>35.1 ± 10.2†</td>
<td>4.9 ± 2.8†</td>
<td>162.2 ± 81.7†</td>
</tr>
</tbody>
</table>

* Data from 16 episodes occurring in 8 patients. Data given are the means of the mean value from each patient (n = 8).
† p < 0.01 (paired t test, n = 8).
‡ p > 0.05 (NS).
this breathing pattern was a possible contributory factor to a rapid decrease in TCPO₂ in addition to prolonged apnea, crying, hiccupps, or airway suctioning. We have identified several aspects of the exertional breathing pattern including Valsalva maneuvers, decreased minute volume, and apnea, each of which would be a likely cause of hypoxemia. Furthermore, the observation that stimulation can cause squirming with the accompanying changes in breathing pattern suggests that the exertional breathing pattern accounts for many of the episodes of decreasing TCPO₂ when preterm infants are handled or disturbed.

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**References**