Risk Factors for Extreme Events in Infants Hospitalized for Apparent Life-threatening Events

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Objective To determine whether known risk factors for cardiorespiratory illnesses will help identify infants who could experience extreme events during an admission for an apparent life-threatening event (ALTE) or later at home.

Study design Retrospective cohort study of all patients admitted for ALTE between 1996 and 2006. Extreme events included central apnea >30 seconds, bradycardia >10 seconds, and desaturation >10 seconds at hemoglobin-oxygen saturation value with pulse oximetry <80%.

Results Of the 625 patients included in the study, 46 (7.4%) had extreme cardiorespiratory events recorded, usually within 24 hours of hospital admission. The most frequent diagnosis was upper respiratory tract infection (URTI, 30 infants). These factors increased the likelihood of having extreme events ($P < .0001$): post-conceptional age <43 weeks (5.2-fold increase), premature birth (6.3-fold), and URTI symptoms (11.2-fold). The most frequent events were extreme desaturations (43/46 infants), preceded by a central apnea. Seven infants had extreme events recorded later during home monitoring (4 with URTI); all 7 infants had sustained extreme events in the hospital.

Conclusion Extreme events were identified mostly in association with symptoms of URTIs, in infants born prematurely, and in infants <43 weeks post-conceptional age. Monitoring with a pulse oximeter should identify infants who sustain these events.
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An apparent life-threatening event (ALTE) is defined as an episode that is frightening to the observer, characterized by some combination of apnea (central or obstructive), color change, marked change in muscle tone, and choking or gagging.[1] A variety of diagnoses are identified after such events, such as an infection or a neurological condition.[2,3] In addition, some infants with ALTE have significant documented cardiorespiratory events when later monitored at home with cardiorespiratory monitors[4,5]; however, there is little information on the occurrence of such events in relation to the initial ALTE.

As the definition of significant cardiorespiratory events has evolved, events previously considered to be significant are now recognized as common in normal healthy infants. The Collaborative Infant Home Monitoring Evaluation (CHIME) study[5] showed that apnea lasting as long as 30 seconds and bradycardia lasting <10 seconds did occur in the group enrolled as "healthy term infants." The term "extreme events" therefore has been introduced for cardiorespiratory events that exceed the aforementioned limits for apnea duration and bradycardia. Data on what constitutes a drop in oxygenation that lies outside the reference range for infants and children is now available.[6-10]

We do not know with certainty what constitutes the risk factors for the occurrence and severity of cardiorespiratory events in infants experiencing an ALTE, whether while in the hospital or, later, at home. Being able to identify infants who are at high risk for extreme cardiorespiratory events would help clinicians who have to decide whether they would hospitalize infants who experienced an event at home. In the CHIME study,[5] the preterm infants were at increased risk of extreme events until 43 weeks post-conceptional age (PCA). Most of these infants, however, were not discharged home with a monitor because of a diagnosis of ALTE. A study conducted by our group between 1990 and 1995 showed that the presence of cardiorespiratory events in hospital was associated with an

See editorial, p 317

ALTE	Apparent life-threatening event	RSV	Respiratory syncytial virus
CHIME	Collaborative Infant Home Monitoring Evaluation	SpO_2	Hemoglobin-oxygen saturation value with pulse oximetry
IQR	Interquartile range	TTI	Transthoracic impedance
PCA	Post-conceptional age	URTI	Upper respiratory tract infection
PICU	Pediatric intensive care unit		

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increased risk of recurrence at home.[4] However, that study did not differentiate between conventional and extreme events, and data on oxygen saturations were often unavailable.

We therefore reviewed our past 10-year experience with infants who have ALTEs. Our objective was to determine whether known risk factors for cardiorespiratory illnesses can help to identify which infants will experience extreme events during an admission for ALTE or, later, at home. The potential risk factors we explored included prematurity (born at <37 weeks of gestation), PCA <43 weeks, male sex, symptoms of an upper respiratory tract infection (URTI), and winter months.

METHODS

Patient Population

This retrospective cohort study included all patients admitted to the Montreal Children's Hospital for an ALTE between April 1996 and March 2006. Our institution is a tertiary pediatric center with, on average, 66 000 emergency department visits annually. Our search strategy consisted of using all the relevant international classification-of-disease codes that best describe the diagnosis of ALTE: "ALTE," "apnea," "blue spell," or "choking episode" and homemade code subdivisions used at our institution. We reviewed the medical records of all the patients identified with the aforementioned search parameters to determine their eligibility for inclusion. We excluded patients who had pre-existing control-of-breathing conditions (congenital central alveolar hypoventilation, myelomeningocele), airway anomalies, cyanotic heart diseases, arrhythmias, and patients already on cardiorespiratory monitors or patients with a tracheostomy. To qualify for inclusion, the reason for consultation had to have been an ALTE. The infant also should have apparently recuperated from the event when he or she was seen in the emergency department. When an infant was seen more than once for the same diagnosis, the first admission was counted as the relevant one.

To determine the proportion of infants coming to the emergency department for ALTE who were eventually admitted to the hospital, we extracted data from our emergency department database. The data, however, were available only from the end of 1999 (77 of the 120 months of the study). For the patients admitted to the hospital, we were able to match the data from the 2 sets on the basis of the medical record number, the admitting diagnoses, and the date of birth.

In-hospital Investigation

All infants admitted with a diagnosis of ALTE undergo a standard investigation[4] and are first monitored with a nonrecording cardiorespiratory monitor (detection of respiration with transthoracic impedance [TTI]) and, usually, a pulse oximeter also. The ward-attending pediatrician will then assess, on the basis of the perceived significance of the event, the need for documented monitoring (with an event-recording monitor), in consultation with the respiratory medicine consulting physician. When an event-recording monitor is used, it is used for the entire duration of the investigation (1 to several days), 24-hours per day. In addition, patients with recurrent clinical events or monitor alarms will have continuous hemoglobin-oxygen saturation recordings performed, with pulse oximetry (SpO_2).

Type of Monitor and Data Acquisition

We used the Smart Monitor 970S or the Smart Monitor 2 (Children's Medical Ventures, Respironics, Murrysville, Pennsylvania), both of which are TTI apnea monitors with memory capabilities to store events that violate the preset alarms. Respiratory and electrocardiographic waveforms were recorded 45 seconds before, and 45 seconds after, violation of the alarm thresholds. The monitor recorded any cessation of respiratory movements for ≥16 seconds and produced an audible alarm with a cessation of respiratory movements for ≥20 seconds and for an immediate drop in heart rate to 80 bpm (first month of life) or 60 bpm. When SpO_2 was to be recorded also, a pulse oximeter was connected to the cardiorespiratory monitor and the pulse oximeter memory was downloaded separately. For the early years of the study period, a Nellcor N200 pulse oximeter (Nellcor, Pleasanton, California) was used; we then used the Radical pulse oximeter with Masimo technology (Masimo Corporation, Irvine, California). With both monitors, the audible alarms were set at SpO_2 of 87%. For the last 2 years of the study, we used the Smart monitor 2PS (Children's Medical Ventures, Respironics, Murrysville, Pennsylvania), which is a thoracic impedance cardiorespiratory monitor with an integrated pulse oximeter that uses Masimo technology.

Data Extracted

All data relevant to the event leading to admission to the hospital, the risk factors, and the investigation undertaken were entered in a data base. For identifying infants who had symptoms of an URTI, we look for such a diagnosis made by the physicians or for the mention of a recent onset of rhinorrhea with or without cough and mild fever. We also collected data on follow-up, including home monitoring and further events, both clinical and documented. For all infants who had recordings in hospital and at home, we reviewed the original recordings to determine the precise duration of the recorded events. Two investigators did the scoring (H.A., A.C.). When the 2 investigators' scores did not correspond, they reviewed the tracings until an agreement was reached.

Definition of Extreme Events

We defined an "extreme event" according to the criteria of the CHIME study.[5] Thus, we defined an extreme apnea as a central apnea lasting >30 seconds and an extreme bradycardia as either a drop in heart rate to <60 bpm for at least 10 seconds for infants <44 weeks postconceptional age (PCA) or as a drop to <50 bpm for at least 10 seconds for infants ≥44 weeks PCA. We defined a significant drop in SpO_2 as a SpO_2