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ORIGINAL ARTICLE

Sleep-related risk and worrying behaviours: a retrospective review of a tertiary centre's experience

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Abstract

This retrospective study aims at helping physicians select babies considered at risk for fatal events during sleep. It does so by describing the clinical features and outcome of worrying infants' behaviour during sleep, with the activation of an emergency medical service and/or emergency department, subsequently referred to the Centre for Paediatric Sleep Medicine and sudden infant death syndrome, Regina Margherita Children's Hospital, Turin, Italy. We analysed the medical records of infants < 12 months whose parents reported they had worrying behaviour during sleep in the period 1 January 2009– 31 December 2015. Regional guidelines suggest performing anamnesis and capillary blood gas analysis in case of apparent life-threatening events. There were 33 males, average age 55 ± 54.37 days. On arrival at the emergency medical service/emergency department 97 % infants were asymptomatic; 61 % patients had a capillary blood gas analysis as suggested by the regional guidelines. A clear acid-base disorder was observed in two infants, asymptomatic at medical evaluation, that had assumed an unsafe sleeping position. Two patients presented recurrence of the episode at 3 months.

Conclusions: Most worrying infant behaviour during sleep can be related to paraphysiological phenomena; capillary blood gas analysis and anamnesis are pivotal to identify the cases at risk of fatal events.

What is Known:
- *Events that happen during sleep often frighten the parents of newborns. This fear may be induced by the fact that Sudden Infant Death Syndrome typically occurs during sleep.*
- *This tragic event is unpredictable by any clinical features or findings in instrumental examinations and cannot be prevented with an early resuscitation.*

What is New:
- *In our retrospective study, most worrying infant behaviour during sleep can be related to paraphysiological phenomena.*
- *Capillary blood gas analysis and anamnesis collection were crucial to identify the only two life-threatening events.*

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Keywords Sleep · Infants · SIDS · Cardiorespiratory monitor · Capillary blood gas analysis

Abbreviations

AAP	American Academy of Pediatrics
ALTE	Apparent life-threatening events
BRUE	Brief resolved unexplained event
CBG	Capillary blood gas analysis
CPR	Cardiopulmonary resuscitation
ECG	Electrocardiogram
ED	Emergency department
EMS	Emergency medical services
SIDS	Sudden infant death syndrome

Introduction

Parents of newborn infants are often frightened by events that happen during sleeping hours, as previously reported by Kahn and Carrol [4, 10]. This anxiety is mainly based on the fact that the sudden infant death syndrome (SIDS), the main cause of sudden infant death in Western countries, typically occurs during sleep. Unfortunately, there are no clinical features or findings in instrumental examinations that can predict this tragic event, nor can it be prevented with early resuscitation [6, 9, 14, 18].

Krous et al. [12] reported 29 SIDS (6 %) in infants with absent vital signs, that were resuscitated by an emergency service and admitted to hospital, in a retrospective 15-year population-based study on 454 infant deaths attributed to SIDS. The authors did not identify any factor that could have reliably predicted these cases so as to allow for an earlier and more effective cardiopulmonary resuscitation (CPR) and survival without permanent brain injury.

The dramatic drop in the incidence of SIDS cases in Western countries can be attributed only to there having been disseminated *safe sleeping rules* (supine positioning, avoiding exposure to smoke, the promotion of breastfeeding, room-sharing without bedsharing or overheating), in public education campaigns [15]. Nevertheless, parents often use commercial movement sound monitors to monitor their sleeping baby, even if this has been discouraged by the National Institute of Health [16]. It has been reported that these devices may go into a state of *"alarm"* even when the infant is in a state of complete well-being, thus creating a vicious circle of fear. Nowadays, the use of low-cost smartphone web applications, able to monitor infants' vital signs, is spreading worldwide. Therefore, instrumental monitoring of infant sleep is most likely to become commonplace, even there is no scientific evidence as to its utility [2].

Parents who continuously observe their infants sleeping (themselves or with electronic devices) note several different phenomena, including difficulty in waking up, unusual movements, colour change, shallow breathing, apnoea and/or periodic breathing. All of which may well be normal for the infant's age [4, 13] (i.e. central apnoea), but can be very alarming for a non-professional observer and even for health providers who are not well-versed in paediatric sleep medicine. So as to reassure these parents/observers, instrumental examinations like an electroencephalogram, electrocardiogram, cardiorespiratory monitoring and/or polysomnography are often performed. This enhances the sense of anxiety in parents causing discomfort to the infant and leads to additional costs for health services.

This study will hopefully help physicians select babies considered at risk of *fatal events*. It describes the clinical features and outcome of worrying infants' behaviour during sleep, with the activation of an emergency medical service (EMS) and/or emergency department (ED) and subsequently referred to the Centre for Paediatric Sleep Medicine and SIDS, Regina Margherita Children's Hospital, Turin, Italy.

Methods

This retrospective study analysed the medical records of infants < 12 months whose parents reported they had worrying behaviour during sleep in the period 1 January 2009 to 31 December 2015 and had consequently turned to an EMS or ED and will hereafter be referred to the Centre for Paediatric Sleep Medicine and SIDS, Regina Margherita Children's Hospital, Turin, Italy.

In compliance with the Piedmont Region (covering about 4,375,865 inhabitants and 27 paediatric departments) Guidelines, for *Apparent Life-Threatening Events*, all patients admitted were first given a thorough clinical evaluation to exclude any other underlying pathologies. If no diagnosis was reached and the event happened < 24 h from the admission, capillary blood gas analysis (CBG) was carried out and an electrocardiogram (ECG) performed. A 24-h cardiorespiratory monitoring was recorded in ED within 48 h of the event, unless the baby was discharged immediately, in which case monitoring was done by the Centre for the Paediatric Sleep Medicine and SIDS, within this time frame.

Lastly, all the infants were visited in the Centre, and an evaluation of their health status was made on the basis of their anamnesis, physical examination and the 24-h cardiorespiratory recording.

In line with the Centre's policy, a follow-up of at least 3 months was ensured to assess the infants' general condition, any recurrence of the episode and to confirm/contest the diagnosis.

The following data were collected:

- Demographic information
- Parental intervention/action
- Clinical features (i.e. difficulty in waking up, defined as incomplete waking up of the baby or hyporeactivity to normal stimulation, type of respiration, colour change, abnormal movements and activation of a movement alarm monitor)
- Clinical evaluation (cardiorespiratory, neurological examination
- CBG, along with an analysis of glycaemia, electrolytes and haemoglobin
- 24 h cardiorespiratory monitoring
- ECG

Periodic breathing was defined as a breathing pattern characterized by recurrent central apnoea interrupted by breathing efforts [1, 5]. Pathological periodic breathing was defined as a pattern of periodic breathing > 6 standard deviations above the average for gestational age and post-menstrual age and > 10 % time in periodic breathing [17].

In case of loss to follow-up, unreported death was excluded as the Centre provides an active surveillance of sudden unexpected infant death in the range 0–2 years over the whole Region of Piedmont.

Results

A total of 70/799 infants visited in the Centre after ED/EMS activation were identified as having worrying behaviour during sleep. All infants were visited within 24 h from the event. There were 33 males and 37 females; average age was 55 ± 54.37 days. There were 63 term babies and 7 preterm (according to the WHO definition of term pregnancy). A total of 44/70 infants were put on their back to sleep by their parents.

Parents' intervention/action

During the episodes, parents applied the following manoeuvres (information available from 67/70 parents): all the parents had held their infant in their arms (100 %), 18 % of them reported having shaken their child and 11 % had slapped their baby's back.

The infants' general health and capillary blood gas analysis (CBG) on admission to the ED or EMS arrival

Our retrospective review of clinical records revealed that 68/70 babies were asymptomatic at the time of their first medical evaluation (EMS or ED), in as much as they had completely recovered from the episode and were in good general health. The two remaining infants still had hyporeactivity. A total of 43/70 had a CBG, glycemia and analysis of electrolytes and haemoglobin in the ED (CBG was not carried out in 27/70 cases).

Glycemia, electrolytes and haemoglobin were within the normal range in all cases. The CBG was normal in 38. Two out of five of the remaining cases had an acid-base disorder, i.e. 1 had a severe respiratory acidosis (pH 7.23, pCO_2 58 mmHg, HCO_3 23.6 mEq/L) and the other an extremely severe mixed acidosis (pH 6.9, pCO_2 52.6 mmHg, HCO_3 9.3 mEq/L). Both infants were asymptomatic at the first medical examination.

ECG and cardiorespiratory monitoring

The electrocardiogram, performed in 66/70 patients, was in the normal range in all cases. No ECG was performed in 4/70.

A total of 58/70 infants were admitted to the Paediatric Ward (average hospitalisation 6.5 days ± 3.08 days), 4/70 were kept under observation for a few hours, 8/70 were discharged immediately after clinical examination. During the consultation in our Centre, all 70 infants underwent 24 h cardiorespiratory recording within 48 h from the event. A total of 11/70 infants had periodic breathing, but only in 3/11 cases did the parents note it, whilst in 5/11, the parents were worried by the presence of noisy breathing (5/11), 1 other infant had difficulty in waking up, another shallow breathing and a movement sound monitor activated in the third. No pathological periodic breathing was recorded.

Diagnosis

At the first medical examination (EMS or ED), none of the duty physicians thought that the episode could have been related to physiological sleep. Their diagnosis is reported in Table 1. On the basis of the clinical features (accurate episode reconstruction, physical examination) and the results of the instrumental examinations, worrying infant behaviour was classified by the Centre as reported in Table 1 along with the diagnosis.

Worrying infant behaviour was mostly interpreted by the Centre as the baby having difficulty in waking up in a total of 28 cases. Eight out of 28 parents reported that the babies were not completely awake and 17/28 reported that their baby's behaviour was inadequate to casual stimulation, 3/28 had noticed an unusual detail, e.g. pallor or eye rolling and, alarmed, had decided to try to wake up their baby.

As aforementioned, 2 /70 infants were asymptomatic at first medical examination but had shown a clear acid-base disorder, which may have been due to a prolonged cardiorespiratory impairment.

Table 1 The diagnosis made by the duty physician at the ED or EMS and worrying infant behaviour defined by the Sleep Centre physicians after evaluation

Diagnosis by ED/EMS	n/N (%)	Behaviour defined by the Sleep Centre	n/N (%)
Respiratory disturbances	*27/70 (39)**	Difficulty in waking up from sleep	10/27 (37)
		Periodic breathing	7/27 (26)
		Noisy breathing during sleep	*4/27 (15)**
		Colour change during sleep	3/27 (11)
		Shallow breathing	1/27 (3.7)
		Parasomnia	1/27 (3.7)
		Activation of a movement sound monitor	1/27 (3.7)
Apparent life-threatening event	*18/70 (26)**	*Difficulty in waking up from sleep*	*9/18 (50)**
		Colour change during sleep	4/18 (23)
		Noisy breathing during sleep	3/18 (17)
		Periodic breathing	1/18(5.5)
		Startles during sleep	1/18(5.5)
Hyporesponsiveness	*7/70 (10)**	Difficulty in waking up from sleep	6/7 (86)
		Positional asphyxia	*1/7 (14)**
Gastrointestinal disorders	3/70 (4.4)	Shallow breathing	1/3 (33)
		Activation of a movement sound monitor	1/3 (33)
		Difficulty in waking up from sleep	1/3 (33)
Others (including no diagnosis)	*15/70 (20)**	Difficulty in waking up from sleep	5/15 (33)
		Noisy breathing during sleep	3/15 (20)
		Startles during sleep	2/15 (13)
		Shallow breathing	1/15 (6.6)
		Activation of a movement sound monitor	1/15(6.6)
		Parasomnia	1/15 (6.6)
		Positional asphyxia	*1/15(6.6)**
		Benign myoclonus of sleep	1/15 (6.6)

ED, emergency department; EMS, emergency medical services

*The two infants at risk of fatal events were diagnosed with hyporesponsiveness and respiratory arrest (in the group "Other") at emergency department; the Sleep Centre defined the same episodes as positional asphyxia. The two infants with recurrent episodes were diagnosed with respiratory disorder and an apparent life-threatening event, at emergency department; the Sleep Centre defined the same episodes as noisy breathing and difficulty in waking up from sleep, respectively

The two infants at risk of fatal events and the two infants with recurrent episodes are shown in italics

The first infant (case 1), born preterm at 32 weeks, was 55 days old on admission and had a respiratory acidosis (pH 7.23, pCO_2 58 mmHg, HCO_3 23.6 mEq/L) after having slept prone faced down on his mother's shoulder for an hour after bottle milk feeding. When the mother put him back into his cradle, she noticed he was hypotonic and unresponsive even to strong stimulations, such as shaking and slapping his back; therefore, she called the emergency service (ES). In the time-lapse between the call and the arrival of the EMS, the child had woken up completely, cried and appeared normal at examination.

The other infant (case 2), 69 days old at admission, born at term, had an extremely severe mixed acidosis (pH 6.9, pCO_2 52.6 mmHg, HCO_3 9.3 mEq/L). His mother was taking a shower after leaving the baby prone in his crib, with his head turned to one side. However, 10 min later after her shower, she found him sleeping prone, face down on his pillow. She immediately turned his face and was frightened by his colour as he was cyanotic with pale lips, she reported having thought he was dead. When she picked him up he was limp and unresponsive to her stimulations. She tried to ventilate him with mouth to mouth respiration and called the EMS. In the time-lapse between the call and their arrival, the child had woken up completely, cried and appeared normal at examination. CBG was almost normal 8 h later without therapy (pH 7.37, pCO_2 32.8 mmHg, HCO_3 18.6 mEq/L). Due to the exceptional features of this case, the baby was kept in the sleep lab overnight and had a complete nocturnal polysomnography, with normal results.

Follow-up

A total of 3 infants were lost to follow-up, as their parents did not come for the check-up, nor did they answer the telephone. Only two patients had another episode (cases 3 and 4): the first

had had difficulty in waking up after bottle feeding and the other had had a noisy breathing episode. They were followed-up until disappearance of the episodes, which did not lead to any pathological outcome. Table 2 summarizes the characteristics of the two infants with a prolonged cardiorespiratory impairment and the two patients with recurrent episodes.

Discussion

In the present study, we found that the parents of 70 infants were so worried about their babies' behaviour that they called the emergency services. All parents reported that their child had been sleeping at the time of the event. We rely on their judgement, as in the age range covered by our study group the discrimination between wakefulness and sleep is mainly based on behavioural features such as wide open eyes and breathing patterns [8].

In most cases, the parents were alarmed by their baby having difficulty in waking up from sleep, e.g. the infants with hyporeactivity did not show the usual response to common stimuli provided by their parents who, when they took them into their arms, noted they were limp, which is however a normal condition in physiological sleep. Gentle stimulation often did not suffice to bring their babies out of their deep sleep. Indeed, repeated and even stronger stimulation were required to wake them up in most cases. In a few cases, the infants returned to normoreactivity only in the ED, where there was more and stronger environmental stimulation (bright lights, noise). At this point, the children appeared *completely normal* and most of them were asymptomatic at medical examination.

Moreover, the benignity of these events was confirmed by there being no abnormal findings in CBG or the 24-h cardiorespiratory monitoring, as well as by the positive outcome. The very low number of recurrences at 3 months and the lack of pathological findings at the end of the follow-up, e.g. none of the infants suffered from epilepsy, seem to suggest that the behaviour observed by parents, even if alarming, should be considered paraphysiological for the infants' age, and disappear as the baby grows up and develops more mature neurological competences. With time, parents get used to their infant's behaviour during sleep, especially if supported by adequate professional advice at the time of the evaluation [21].

Interestingly, none of the emergency physicians who had first visited the babies were of the opinion that the hyporesponsivity at waking up from sleep, reported by parents, could have been related to a nonpathological condition. This data confirms that even physicians have difficulty in interpreting physiological sleep phenomena. In the past, the constellation of unexpected events occurring both during wake and sleep that are frightening to the observer were known as apparent life-threatening events (ALTE) [4, 10, 21, 22]. This term has now been replaced by the American Academy of Paediatrics by the use of *Brief Resolved Unexplained Event (BRUE)* [19].

The first criteria to diagnose a BRUE is that the event lasts < 1 min [19]. In our study, based on the most accurate environmental reconstruction of the incident as possible, all cases lasted much longer from the onset of the event to normalization. Secondly, an event is considered a *BRUE* only if there is no other likely explanation after a complete anamnesis and physical examination [19]. In these cases, the guidelines suggest the episode should be named with the *symptoms that characterize it*. For example, the finding of periodic breathing automatically excludes a diagnosis of BRUE [19]. Consequently, a worrying infant's episode due to age-specific variability in physiological sleep [21] cannot be considered a BRUE [19].

Unfortunately, the ED physicians respected the Piedmont Region Guidelines for carrying out a CBG in ALTE in only 43/70 cases; most CBG resulted normal and in only two infants did we observe real life-threatening episodes: in these

Table 2 The characteristics of the two infants at risk for SIDS and the other two with recurrent worrying sleep behaviour

Characteristic	Case 1	Case 2	Case 3	Case 4
Gender	Male	Male	Male	Female
Age	55 days	60 days	60 days	30 days
Born at gestational age	32 weeks	40 weeks	38 weeks	39 weeks
Parents' intervention	Shaking, back slapping	Mouth to mouth respiration	Holding in the arms, back slapping	Holding in arms
Condition at EMS/ED admission	Normal	Normal	Normal	Normal
CBG	pH 7.23, pCO_2 58 mmHg, HCO_3 23.6 mEq/L	pH 6.9, pCO_2 52.6 mmHg, HCO_3 9.3 mEq/L	Not performed	Normal
ECG	Normal	Normal	Normal	Normal
Cardiorespiratory monitoring	Normal	Normal	Normal	Normal
Follow-up	Normal	Normal	Normal	Normal
Risk factors for unsafe sleep	Prone position on his mother's shoulder	Prone position	None	None

CBG, capillary blood gas analysis; ECG, electrocardiogram; ED, emergency department; EMS, emergency medical services

cases, the capillary blood gas analysis was the hallmark to distinguish between physiological and pathological status. It is well-known that blood gas analysis is the most reliable indication of fetal oxygenation and an acid-base condition at birth; moreover, it might be helpful in determining the oxygen concentration and whether or not to continue oxygen supplementation in the delivery room [7, 20]. Furthermore, the 2015 update on Paediatric Advanced Life Support recommends monitoring venous or arterial blood gas analysis, serum electrolytes, glucose and calcium concentrations in post-cardiac arrest care to preserve neurologic function, prevent secondary organ injury, diagnose and treat the cause of illness and enable the patient to arrive at a paediatric tertiary care facility in an optimal physiologic state.

The two infants with real life-threatening episodes seemed to have recovered as did the other cases and were even asymptomatic at the first medical evaluation performed by well-trained, experienced physicians. However, the CBG analysis, performed shortly after the event, revealed a severe acidosis, which was most likely an asphyxiating state. We are of the opinion that CBG analysis (covered by the Piedmont Region ALTE protocol) may well be a useful tool to identify those infants who have had a prolonged cardiorespiratory impairment.

Lastly, a thorough analysis of what the parents had witnessed provided vital information on the probable presence of a previous cardiorespiratory impairment due to positional asphyxia. SIDS prevention rules were neglected in both cases, as the two infants had been left sleeping in a prone position, face down on a pillow or the mother's shoulder and were unable to turn their face in response to the hypoxic stimulus. The inability of head-turning or lifting in response to hypoxia is the first step in the putative terminal respiratory pathway associated with the SIDS, so well described by Kinney and Thatch [11]. This is especially true in the case of the baby found face down on the pillow, where it is more than likely that his mother arrived just in time to avoid a catastrophe by chance, as demonstrated by the CBG values which were at a pathological level.

Unfortunately, we are still unable to identify at-risk infants at birth in the first period of their life. Therefore, these cases clearly show the necessity to make all parents aware of the importance of safe sleep at the birth of the baby. Above all, a supine position must be recommended without any exception. As stated in 2016 in a report by the AAP Task Force on the SIDS, "the supine sleep position does not increase the risk of choking and aspiration in infants, even in those with gastroesophageal reflux" [15].

Our experience suggests that an integrated approach is useful to distinguish between physiological and pathological conditions. A description of the clinical features of the event as given by the witnesses and supported by the CBG results and its progress (verified with a 24-h cardiorespiratory monitoring), allowed us to identify episodes pertaining to a physiological condition. Our interpretation was later confirmed by the favourable outcome.

On the other hand, the only two cases with *a real life-threatening event* were sleeping in an unsafe position (face down on the mother's shoulder or on a pillow). The CBG results were of paramount importance to pin-point a serious pathological situation. Lastly, history collection allowed us to explain what had taken place and the consequences on the acid-base status.

We are aware that our study is limited by the fact that it is a retrospective, observational study. Nevertheless, in a recent analysis on ALTE/BRUE, almost 50 % of studies, judged as clinically relevant, were also retrospective [3]. Furthermore, it is a single-centre study; therefore, even if we are the referral Centre for the whole Piedmont Region, there might still be a selection bias. Lastly, 3 of our patients were lost to follow-up. However, given the study design and the active surveillance of sudden infant death carried out throughout the Piedmont Region, we believe that this small drop-out and could be considered negligible.

In conclusion, this study emphasises the following: (a) CBG provides insight into the severity and/or duration of asphyxia; (b) the application of the Piedmont Region ALTE protocol, based on clinical evaluation and blood gas analysis, is useful to distinguish between physiological and pathological conditions in worrying episodes during an infant's sleep; (c) a thorough history collection is mandatory to obtain a reliable reconstruction of frightening behaviour in an infant during sleep; (d) medical training should include details of sleep physiology in the infant, including behaviour that is very age-specific, yet potentially alarming for parents, such as difficulty in waking up, colour change, shallow breathing, apnoea and periodic breathing; (e) currently, the only way to avoid sudden infant death during sleep is to apply safe sleeping rules to the letter.

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Authors' contributions Alessandro Vigo conceptualized and designed the study, wrote the manuscript and approved the final manuscript as submitted.

Oliviero Bruni wrote and critically reviewed the manuscript and approved the final manuscript as submitted.

Giulia Costagliola was involved in the acquisition and the analysis of the data, wrote the manuscript and approved the final manuscript as submitted.

Silvia Noce was involved in the conception of the study, critically reviewed the manuscript and approved the final manuscript as submitted.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in compliance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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