

# Sudden infant death syndrome, prematurity and sleeping position

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## Abstract

Sudden infant death syndrome (SIDS), an unexpected death of an infant which remains unexplained after a thorough investigation, is the commonest cause of postneonatal mortality in the developed world. Prematurely born infants are at an increased risk of SIDS, particularly if they are slept prone. It is, therefore, important to understand why infants die of SIDS and the effects of prone sleeping position on prematurely born infants. Possible mechanisms of SIDS include failure to arouse, infection and genetic predisposition. Impaired arousal has been described during prone sleeping and in infants exposed to maternal smoking. Infection is associated with an increase in both duration and depth of quiet sleep and arousability is depressed. Infants may be at an increased risk of SIDS because of mutations leading to genetic disorders capable of causing death or having polymorphisms that might predispose to death in critical situations. The prone position has physiological advantages for prematurely born infants with and without respiratory distress in the immediate neonatal period. The few data on convalescent babies demonstrate prone posture has an advantage in improving oxygenation in infants with BPD, but is associated with less spontaneous arousals and more central apnoeas. These data emphasize that practitioners must emphasize to parents the importance of sleeping their prematurely born infants supine at the high-risk age for SIDS.

**Key words:** infection; arousal; genetic predisposition.

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## Introduction

Sudden Infant Death Syndrome (SIDS) is the unexpected death of an infant occurring during the first months after birth, which remains unexplained after thorough investigation, including review of the clinical history, examination of death scene and a postmortem [1]. SIDS is the most common cause of post neonatal mortality and, in industrialized countries, accounts for 40% of all deaths from one month to one year of age [2]. The incidence of SIDS peaks between the second and fifth months after birth; ninety percent of the deaths from SIDS occur by six months of age. Certain infants are at an increased risk of SIDS (Table I) and include those slept prone. As a consequence, there have been national campaigns, such as "Back to Sleep", aimed at reducing prone sleeping. These have resulted in a dramatic reduction in the incidence of SIDS. In the United Kingdom, the SIDS incidence decreased from 1.5-2.0/1000 live births in the mid 1980s to 0.5/1000 live births in 2000 and in the United States

**Table I.** Risk factors

Sleeping position
Prematurity
Male gender
Low birthweight
Maternal smoking
Winter months
Lower socioeconomic status
Poor prenatal care
Young maternal age
Higher parity
Single parenthood
Multiple gestation
Maternal drug abuse
Race (African-American & Native American)

from 1.2 per 1000 live births in 1992 to 0.67 deaths per 1000 live births in 1999 [3]. Yet despite all the publicity, some infants, particularly those born prematurely, are still slept prone. In one series, only 35% of the prematurely born infants were slept non-prone at a corrected age of two months [4]. It is, therefore, important to understand why infants die of SIDS and prematurely born infants are at an increased risk, particularly if they are slept prone. Such information may help to convince parents and care givers that infants, particularly those born prematurely, should not be slept prone at the high-risk age for SIDS. The aims, then, of this review are to discuss possible causes of SIDS, describe the relationship of SIDS to premature birth and highlight the effects of prone sleeping position on prematurely born infants.

### Possible causes of SIDS

#### Failure of arousal

Polygraphic studies have demonstrated that arousals were less common in infants who later died of SIDS than matched control infants [5]. Any impairment in respiratory control and/or arousability could then contribute to processes leading to SIDS [6]. Impaired arousal has been described during sleeping in the prone position and in infants who have been exposed to maternal smoking. Studies have consistently shown that sleeping prone increases the total amount of time spent asleep and, in particular, the amount of quiet sleep and is associated with a decreased number and duration of spontaneous arousals [6]. Healthy term born infants, regardless of their usual sleeping position, were demonstrated to sleep longer with a greater duration of non-rapid eye movement sleep and less

arousals in the prone compared to the supine position when studied at three months of age [6]. In addition, arousal thresholds were significantly higher in both active and quiet sleep when term born infants were studied sleeping prone at two to three months of age [6].

Many studies have demonstrated a strong association between prenatal maternal smoking and SIDS [7]; the effect of smoking is dose dependent. The increase in risk of SIDS in infants whose mothers smoked during pregnancy is between two to four fold, but as high as six fold if there are other risk factors [8-10]. A possible mechanism for this increased risk is poorer arousal, exposure to cigarette smoke has been demonstrated to decrease both spontaneous and evoked arousals from sleep [11]. Premature babies born to mothers who smoked during pregnancy have been shown to have markedly decreased arousals and more apneas during active sleep [12]. Infants whose mothers smoked during pregnancy may have reduced chemoreceptor function; we have demonstrated that such infants have a dampened ventilatory response to added dead space [13]. This may be a manifestation of neurodevelopmental abnormalities in the control of ventilation resulting from prenatal nicotine exposure [14]. Prenatal nicotine exposure results in cell death in the brainstem of animal models [15]. The abnormalities could result from fetal hypoxia, as nicotine is a powerful vasoconstrictor and reduces blood flow to the uterus, as well as having a direct vasoconstrictor effect on the fetus [16]. In addition, fetuses of smoking mothers have raised carboxyhaemoglobin levels, resulting in a decrease in fetal oxygen tension, a shift in the oxygen dissociation curve to the left and a decrease in oxygen delivery to the tissues [17-19]. Nicotine is also a specific neuroteratogen; exposure to nicotine during critical phases of central nervous development resulted in abnormalities of cell replication, cell differentiation and receptor function in rats [20-22].

#### Infection

The likelihood that infection plays a part in SIDS is suggested by a number of observations, these include the increased (two to three times) incidence of SIDS in the winter months [23] and the high rate of concurrent upper respiratory infections in infants dying of SIDS. Infection changes both the amount and nature of sleep, with increases in both the duration and depth of quiet sleep; in addition, arousability from quiet sleep was found to be depressed after recent illness [24]. Infection may also be a stress factor that contributes to the death of an already vulnerable infant [23].

### Genetic predisposition

Infants may be at increased risk of SIDS because they have mutations leading to genetic disorders capable of causing death [25]. For example, a testis-specific Y-like gene (TSPYL) localized to chromosome 6q22 has been found in nine families of the Belleville Amish community, the affected infants, who seemed normal at birth, developed signs of visceromotoric dysfunction early in life and died suddenly before 12 months of age [26].

Infants may also be at increased risk of SIDS as they have polymorphisms that might predispose to death in critical situations, that is gene environment interactions [25, 27]. The A985G mutation in medium chain acyl-coA dehydrogenase deficiency, the sodium channel gene (SCN5A) and the serotonin transporter gene mutations are a few examples of such polymorphisms. Genetic polymorphisms in fatty acid oxidation have also been estimated to be present in as many as five per cent of SIDS victims [28]. SCN5A polymorphisms in cardiac ion channels and the potential for lethal arrhythmia from long QT syndrome may result in SIDS. Indeed, it has been noted that certain infants who died of SIDS had a higher level of cardiac conduction abnormalities than infants who died of explained deaths [29] and a correlation has been found between long QT syndrome and SIDS in a subset of deaths [30, 31]. It has been estimated that between four and five percent of SIDS deaths may be associated with SCN5A polymorphisms. The serotonin transport gene was the first gene linked to SIDS vulnerability. Serotonin influences a broad range of physiologic systems, including the regulation of breathing, temperature and sleep-wake cycle and serotonergic receptor binding in the arcuate nucleus, nucleus raphe obscurus, and other medullary regions has been demonstrated to be decreased in SIDS cases [32].

### Prematurity and SIDS

Prematurely born infants account for between 10 and 20% of SIDS cases. Infants born prior to 33 weeks of gestation are sixteen times more likely to die of SIDS than infants born at term. The incidence of SIDS is inversely related to gestational age at birth; the relative risk of SIDS in infants born at prior to 28 weeks of gestation being 3.6, but 1.7 in infants born between 34 and 36 weeks of gestational age [33, 34].

#### Prematurely born infants and effect of sleeping position

##### Advantages of prone sleeping

Prematurely born infants with respiratory distress have better oxygenation, higher tidal volumes and

lung compliance and lower respiratory rates and pulmonary resistance when nursed prone [35]. Immediately following extubation from mechanical ventilation, preterm infants nursed prone rather than supine have been demonstrated to have improved oxygenation, as they have less ventilation perfusion mismatch and asynchronous chest wall movement. The better thoraco-abdominal synchrony in the prone position is due to alterations in chest wall mechanics and respiratory muscle performance. The prone position also has advantages for preterm infants without respiratory distress [36], as they too have higher tidal volumes and more compliant lungs in the prone position. Such infants also have a reduced frequency of central and mixed apnoeas, bradycardias and desaturations when nursed prone. The higher rates of apnoea in the supine position may be due to neck flexion resulting in upper airway obstruction [37]. There is also less gastro-esophageal reflux in the prone position.

There have been few studies of the effect of sleeping position on convalescent prematurely born infants, those that have been undertaken still demonstrate benefits of prone positioning. These benefits include less apnoeas and periodic breathing [38] and superior oxygenation [39]. Amongst prematurely born infants being studied for discharge home, however, the benefit of prone positioning with regard to oxygenation was only seen in infants with chronic lung disease who were still oxygen dependent [40].

##### Disadvantages of prone sleeping

Healthy preterm infants born at a gestational age of 28 to 34 weeks studied at 12 to 57 days slept more in the prone position [41] and asymptomatic infants with a mean gestational age of 32 weeks studied at 36 weeks PMA had more quiet sleep and less awakenings in the prone position [42]. We have recently demonstrated that very prematurely born infants studied at 36 weeks PMA slept longer, spent more time in quiet sleep, had fewer arousals and had more central apnoeas in the prone position [43].

#### SIDS, prematurity and sleeping position

Prematurely born infants slept non-supine are at a much increased risk of SIDS. The odds ratio for SIDS in a prematurely born infant slept prone is 48.8 and side slept is 40.5 [44].

##### Advice to parents

As a consequence of the increased risk of SIDS if prematurely born infants are slept prone, it is clearly important that parents are advised against such a practice. Yet a survey of all neonatal units in the United Kingdom demonstrated that, although all recommended supine sleeping on discharge from

the neonatal unit, approximately forty percent did not discourage prone sleeping [45]. In addition, some additionally recommended side sleeping, although this also has an increased risk of SIDS for prematurely born infants. This inappropriate advice may reflect that clinicians appreciate that prone sleeping has advantages for prematurely born infants in the first weeks after birth as documented above and, also, the then lack of data regarding the effect of sleeping position in prematurely born infants at discharge and at the high risk age for SIDS.

## Conclusion

We have recently demonstrated that prone positioning of prematurely born infants at 36 weeks PMA is associated with greater sleep efficiency, more central apnoeas and less arousals [43]. As a consequence, we recommend that prematurely born infants are slept supine at least at that post menstrual age. Such a practice will mean that oxygen dependent infants will require more supplementary oxygen [40]. Parents need to be appropriately supported and counseled that such a disadvantage is far outweighed by the reduced risk for SIDS.

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