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Sudden infant death syndrome and perinatal risk factors

Research Article

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Abstract: Aim. This paper examines the incidence and possible prenatal and postnatal risk factors for the emergence of the sudden infant death syndrome (SIDS) in the Bjelovar-Bilogora County in Croatia. Material and methods. Data on epidemiological and public health prenatal and postnatal risk factors in infants who died of SIDS were retrospectively processed for the period between 1st January 1991 and 31st December 2011 in the area of the Bjelovar-Bilogora County. Results. SIDS incidence in the investigated period amounted to 0.6% (between 1991 and 2001 it amounted to 0.8%, whereas between 2001 and 2011 it amounted to 0.5%). The connection between SIDS emergence and smoking tobacco was confirmed in 80% of cases, death in the prone position in 40%, increased death incidence between the 2nd and the 4th month of child's life in 40%, time of death in early or late morning in 73.3%, positive heredity in 26.7%, parents' age above 30 in 60%, multiparity in 33.3%, male sex of child in 73.3% of cases, while socioeconomic conditions and SIDS emergence according to seasons turned out to be statistically insignificant. Conclusion. Prenatal and postnatal hypoxic factors were risk of SIDS.

Keywords: *Sudden infant death syndrome • Perinatal factors • Postnatal factors • Bjelovar-Bilogora County • Croatia*

1. Introduction

Sudden infant death syndrome (SIDS), unexpected infant death and crib death are synonyms for sudden, unexplained and unexpected death of an infant below the age of one. The first definition of SIDS was formulated in the year of 1969, and was reformulated in 1984 and again in 2004 as "sudden and unexpected death of a child below the age of one during sleep, whereby the reasons remain unexplained even after appropriate investigation." The aforementioned appropriate investigation refers to a detailed postmortem investigation of the place of death, checkup of possible symptoms or illnesses that the child had had before death and insight into the child's medical history. Differential SIDS diagnosis includes asphyxia or drowning (suffocation), heart rhythm disturbances (arrhythmia), electrolyte imbalance or dehydration, poisoning, trauma, infections (pneumonia, sepsis, meningitis) and congenital malformations [1].

According to numerous research activities, it is obvious that this is a syndrome which results from several factors that are mutually very different, but possibly connected, from prenatal to postnatal period. It has been proven, for example, that protracted intrauterine hypoxia or recurrent hypoxic attack during fetal life affect the development of central nervous system as the most sensitive tissue to hypoxia. Furthermore, ultrastructural changes were found in brain cores (gliosis, apoptosis, structure immaturity), as well as defects in neurotransmitter receptors, especially the serotonergic ones along with carotid body hyperplasia. A biohumoral response to prolonged hypoxic state was confirmed by an increased concentration of various mediators (hypoxanthine, cytokine: IL-1, IL-2, TNF a, erythropoietin). Such results suggest that tissue was exposed to hypoxia for a longer period of time, and not to a postnatal acute hypoxic incident. The previously described impairments of

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regulation mechanisms in recurrent exposure to hypoxia occur when the auto-resuscitation effect to prolonged expiratory apnea and hypoventilation does not appear. Along with other risk factors, this initiates a cascade of fatal changes in the cardiovascular system and sudden death follows [1-4].

The objective of this paper is to determine the occurrence of SIDS in the area of the Bjelovar-Bilogora County between 1st January 1991 and 31st December 2011, as well as identify the connection between SIDS occurrence and prenatal and postnatal risk factors that were previously described in literature in correlation with public health and epidemiology of SIDS.

2. Material and methods

Data on infants who died of SIDS were retrospectively processed for the period between 1st January 1991 and 31st December 2011 in the area of the Bjelovar-Bilogora County that is located in the Northwest Croatia and has 119,743 inhabitants according to the census from 2011. Data sources were postmortem results from the Pathology and Medical History Department of the Pediatric Department of the General Hospital in Bjelovar, as well as the official data of the Croatian Bureau of Statistics (Communication of the Croatian Bureau of Statistics – Natural Change in Population). In personal conversation with parents and based on medical files, socioeconomic conditions (good, medium, bad), smoking during pregnancy (active, active+passive, passive), age of mother and father, parity, interval between pregnancies, course and complications in the current pregnancy, course and possible complications at delivery, birth weight and length; course and outcomes of previous pregnancies and deliveries, gestation age at delivery, possible infections and treatment, time of death, sleep position, diaper state of the infant at the time of death and other factors were examined. Data were analyzed by percentage calculation due to a small sample in the twenty-year material.

3. Results

Between 1st January 1991 and 31st December 2011, 18 SIDS cases were recorded in the area of the Bjelovar-Bilogora County. Three of these cases were not included in the complete analysis, because due to objective reasons we could not collect the most basic data (sex, age, time of death, place of death, data on parents…). However, these cases represent an obligatory part of presenting the incidence of SIDS.

According to examined data, the incidence of SIDS in the Bjelovar-Bilogora County amounted to 0.66‰ (compared with total number of liveborn children in this period/year) , whereby it should be stressed that between 1991 and 2001 it amounted to 0.8‰, whereas in the period between 2001 and 2011 it was lower and amounted to 0.5‰, i.e. almost twice as low. The most frequent time of death was in the early or late morning (73.3%), at home (73.3%), and in colder months of the year in 53.3% of cases. At the time of death 40% of infants were in the prone position, 26.7% were in the lateral position and 33.3% in the supine position. Heredity was positive in 26.7% of cases (Table 1).

The course of pregnancy was normal in 86.7%, whereas delivery was normal in 73.3% of cases, with birth weight ranging between 2500 g and 3500 in 46.6% of cases. There were 6.7% of preterm newborns. There were significantly more infant deaths in male infants (73.3%). The exposure of parents to tobacco smoke in any way during the pregnancy (active, passive, active+passive) was present in 80% of cases, there of 36.4% was active, active+passive was present in 36.4% of cases and passive in 27.2% of cases, while the exposure of children to tobacco smoke (passive smoking) was present in 26.7% of cases. There were 26.7% of primigravidae, 20% of secundigravidae, 33.3% of tertigravidae and 20% of quadrigravidae. Socioeconomic status was good in 26.7%, medium in 53.3% and bad in 20% of cases, whereas in 60% of cases one or both parents were aged 30 or above. The mortality of children who were between 0 and 2 months old appeared in 33.3%, between 2 and 4 months in 40%, between 4 and 6 months in 20% and older than 6 months in 6,7% of cases. We were not able to obtain the data on the diaper state of infants at the time of death (except in two cases) (Table 2).

4. Discussion and conclusion

SIDS is, according to its definition, an exclusiveness diagnosis, infant death without a clear and visible cause. SIDS incidence in the world, as well as in Croatia, amounts to around 1 ‰. Native American mothers, inhabitants of Alaska and African American mothers have two to three times higher risk of SIDS occurrence, around 2-3 ‰ [2,3,5]. According to our research, SIDS incidence was lower than the Croatian average, but analyzing the total average, it was almost twice as high in the first examined period until 2001[5], which might be connected with the first years (1991-1995) due to significant immigration and war stress in the Bjelovar-Bilogora County during the Croatian War of Independence.

Table 1. Socioeconomic data and SIDS manner

No.	Seks	Age (mo)	Place of death	Time of death	Month in year	Position	Heredity	Socioec. Status	Pass. smoking
1	f	3.5	home	11:30	December	supine	no	medium	no
2	m	4.5	hospital	6:00	January	lateral	no	good	yes
3	m	3	home	17:15	March	prone	no	bad	no
4	f	1.5	home	6:00	April	supine	no	medium	no
5	f	5.5	home	morning?	August	supine	no	bad	yes
6	m	1.5	hospital	16:50	July	prone	no	medium	no
7	m	2.5	home	morning?	December	supine	no	bad	yes
8	m	1	home	13:00	June	prone	yes	medium	no
9	m	5	home	7:25	January	lateral	no	medium	yes
10	m	2.5	hospital	8:30	October	prone	no	good	no
11	m	6	hospital	9:50	October	prone	no	good	no
12	m	1	home	6:00	November	lateral	yes	medium	no
13	m	3.5	home	0:30	October	prone	yes	good	no
14	m	25 days	home	5:00	July	lateral	yes	medium	no
15	f	2	home	6:45	April	supine	no	medium	no
16	?	?	?	?	?	?	?	?	?
17	?	?	?	?	?	?	?	?	?
18	?	?	?	?	?	?	?	?	?

Table 2. Perinatal risk factors for the occurrence of SIDS

No.	Smoking in pregnancy	Age of mother	Age of father	Parity	Course of pregnancy	Course of delivery	Birth weight (g)	Birth length (cm)	Gestation age
1	no	28	30	3.	NAD	difficult	4360	52	due date
2	act. + pass.	32	30	1.	NAD	NAD	2800	47	due date
3	active	28	30	4.	NAD	NAD	3500	50	due date
4	active	32	31	4.	NAD	prolonged	2500	48	due date
5	act. + pass.	20	22	1.	NAD	NAD	2950	45	due date
6	no	21	28	2.	NAD	NAD	3600	52	due date
7	act. + pass.	27	35	3.	NAD	NAD	2750	50	due date
8	no	36	46	3.	NAD	prolonged	3200	50	37 weeks
9	pasivno	21	29	1.	twins, cerclage	sc,malpositio	2600	47	due date
10	active	20	48	3.	NAD	NAD	3600	48	due date
11	active	22	23	1.	NAD	NAD	3400	50	due date
12	no	22	25	2.	NAD	NAD	3650	54	due date
13	act. + pass.	37	45	3.	twins, s.c.	NAD	2750	51	due date
14	passive	21	29	2.	NAD	NAD	3500	48	due date
15	passive	30	35	4.	NAD	NAD	3000	47	due date
16	?	?	?	?	?	?	?	?	?
17	?	?	?	?	?	?	?	?	?
18	?	?	?	?	?	?	?	?	?

Abbreviationes: f-female; m-male; S.C.- sectio caesarea; act-pass-active+passive

74% of SIDS affected children die between the first and the fourth month of life, and 92% in the sixth month of life [6], while SIDS is extremely rare during the first month of life, which was confirmed by our research. In 61% of cases SIDS affected male children [1-4], while in our material this amounted to 73.3% of dead male infants, which is significantly more in comparison with known studies. Researchers stress that the highest risk of SIDS occurrence appears in preterm newborns (children born before the 37th week of pregnancy) and in children with low birth weight (children born with birth weight between 1000 and 1499 grams who have four times the probability. Children with birth weight between 1500 and 2499 grams have three times higher probability for SIDS occurrence, but in our material this data was not confirmed. On the contrary, there was only one preterm newborn and mostly regular birth weights in our population.

It is generally accepted that SIDS that does not result from trauma is preceded by a circulation or respiratory failure [6,7]. The weakness of the diaphragm and auxiliary respiratory musculature is an acute and temporary state, so the diaphragm function may be relatively quickly restored, which possibly explains why SIDS victims do not show signs of respiratory insufficiency directly before death. System infections in the organism demonstrate a link with SIDS pathogenesis [8] and may cause significant reduction of the mitochondrion function (where ATP is generated) in the muscular tissue of the diaphragm [9,10]. The obstruction of upper respiratory tracts most commonly relates to musculature tone loss in the upper respiratory tracts along with missing continual diaphragm movements. These movements, on the other hand, create a recurrent negative thoracic pressure resulting in difficulties in the air flow [11], whereas the musculature weakness of upper respiratory tracts may be caused by a rapid, temporary increase in blood pressure, which may result in unexpected breathing effects. Recurrent obstructive events represent a significant risk for a baby: firstly due to multiple exposures to intermittent hypoxia with sequential obstructions, and secondarily due to recurrent extreme changes in blood pressure.

Around 89% of SIDS victims postmortem showed persistent reticular fibers in the area of pons and medulla, whereas around 50% had an increased number of astroglia in the area of brainstem, which points to insufficient brain histogenesis induced by hypoxia most probably during the prenatal period [12,13]. It takes at least four days for astrogliosis to develop, which suggests that this is not an acute event [14]. It is considered that SIDS includes neurologically compromised newborns who do not possess developed compensation mechanisms during sleep and who experienced hypoxic attacks and alterations of neurotransmitter receptors in brain regions responsible for cardiovascular control during their fetal life [7,15,16]. Protracted prenatal or postnatal hypoxia that is concretely caused by active or passive nicotine intake was found in our material in 80 % of cases, which confirms previous theories of SIDS occurrence and smoking as a significant factor of neurotransmitter system disturbances [3,16].

The effects of sleeping in prone position have been investigated in detail [17]. The hypothesis that prone position overburdens the diaphragm was investigated by Rehan et al. within a study that included 16 healthy children [18]. This study showed that in this position the diaphragm is much thinner and shorter at the endings of inspiratory and expiratory lung volume. They concluded that the lung volume in this position is 15–30% greater, which leads to diaphragm strength being reduced by 40–50%. In the prone position, expired air may again be inhaled, which leads to hypercarbia and also to asphyxia (air saturation drops below 85%, and when it reaches the level of 30–40% brain suffers severe hypoxia, hypoxic coma occurs and auto-resuscitation attempts are often futile) [19], so it is believed that sleeping in supine position reduces the probability of SIDS occurrence. Another mechanism that is considered to be probable is that a child, due to some congenital or acquired defect, cannot use its reflexes to position its head in such position that would allow for unobstructed gas exchange during breathing.

This is exactly the main research target with the stress being put on neurotransmitter systems involved in this signal transduction (including prenatal exposure to tobacco smoke that may damage or modify the development of these transmitters). A change that followed after WHO had given its recommendations related to the advantages of infants sleeping in supine position rather than in prone position, which is connected to SIDS prevention, had led to reduced occurrence of SIDS in the world ranging from 40 % (Argentina) and 83% (Ireland) [20], although SIDS continues to affect children sleeping in supine position. In our material, at the time of death 40% of infants were in the prone position, while 33% of them were in the supine position.

Gene mutations were found that encode potassium, sodium and calcium metabolism that define metabolism in these ionic channels in every fifth child who died of SIDS [20], and it is considered that in 5–10% of cases the aforementioned mechanisms caused SIDS. Some authors mention the following as possible agents: viral myocarditis, congenital aortic stenosis, endocardial fibroelastosis, histocytoid cardiomyiopathy, congenital heart block (associated with mother's lupus

erithematosus) and arrythmogenic right ventricular dysplasia [21], as well as catecholaminergic polymorphic ventricular tachycardia (CPVT) that may develop into arrhythmia and sudden cardiac death [22-24]. The theory that infections cause SIDS is not new, but in 2002 a specific protein was identified in the bacterium *Escherichia coli*, curlin, which was found in a sample consisting of 68 SIDS cases in the proportion amounting to 100%, i.e. in all SIDS victims, so infection is considered to be significant [16].

Siblings of a child who died of SIDS have five to six times increased risk of SIDS, identical twins two times, and the risk of another child dying (in the same family) is lower than 1% [16], while in our material positive heredity was found in four cases. It may appear during either day and night, anywhere, and causes cannot be confirmed with certainty. It has been noticed and accepted that socioeconomic status does not play a role in SIDS occurrence [2,4,25], and in our material more than a half of families of children who died of SIDS had middle class status.

As far back as in 1992 The American Academy of Pediatrics (AAP) launched the Back To Sleep campaign, i.e. set up recommendations for SIDS prevention, especially regarding the child sleeping in prone position, which resulted in reducing the number of SIDS cases in the USA, but also globally, by almost 50% [26]. In the last couple of years this SIDS occurrence drop stagnates, while on the other hand there is an increased number of SUID cases (sudden unexpected infant death*)* that occur during sleep and involve asphyxiation, suffocation, being trapped (e.g. within the crib fence), as well as certain pathological states or other undetermined death causes (infections, ingestions, metabolic diseases, cardiac channelopathies related to arrhythmias, intentional or accidental trauma…). Authors believe that the drop in SIDS occurrence appeared due to the successful campaign of AAP – Back To Sleep, which provided a sequence of recommendations regarding SIDS prevention, including sleeping in lateral and supine position, as well as due to anti-smoking campaigns, while others think that it is due to more precise diagnoses of death causes.

However, it seems that further intensive experimental, clinical and public health studies and programs are needed, which will act in the area of reducing the incidence of this tragic syndrome. Therefore, this paper is aimed at presenting epidemiological movements according to known etiological prenatal and postnatal factors for SIDS in the Bjelovar-Bilogora County.

References

[1] Willinger M, James LS, Catz C. Defining the sudden infant death syndrome (SIDS): deliberations of an expert panel convened by the National Institute of Child Health and Human Development. Pediatr Pathol 1991;11:677–684

[2] Corwin MJ. Sudden infant death syndrome: risk factors and risk reduction strategies. UpTo Date, Jun 12, 2012

[3] Habek D, Habek JC, Jugović D, Salihagić A. Intrauterine hypoxia and sudden infant death syndrome. Acta Med Croatica 2002;56:109-118

[4] Thach BT. The role of respiratory control disorders in SIDS. Respir Physiol Neurobiol 2005;149:343–353

[5] Habek D, Živko M, Selthofer , Kulaš T. Sudden infant death syndrome and perinatal risk. J Perinat Med 2005;33 (Suppl 1):261

[6] Hunt CE. Gene-environment interactions: implications for sudden unexpected deaths in infancy. Arch Dis Child 2005; 90:48–53

[7] Guntheroth WG, Spiers PS. The triple risk hypotheses in sudden infant death syndrome. Pediatrics 2002;110:64

[8] Scott CB, Nickerson BG, Sargent CW, Dennies PC, Platzker AC, Keens TG. Diaphragm strength in near-miss sudden infant death syndrome. Pediatrics 1982;69:782–784

[9] Highet AR, Berry AM, Bettelheim KA, Goldwater PN. The frequency of molecular detection of virulence genes encoding cytolysin A, high-pathogenicity island and cytolethal distending toxin of Escherichia coli in cases of sudden infant death syndrome does not differ from that in other infant deaths and healthy infants. J Med Microbiol 2009;58:285–289

[10] Supinski GS, Callahan LA. Hemin prevents cardiac and diaphragm mitochondrial dysfunction in sepsis. Free Radic Biol Med 2006;40:127–137

[11] Remmers JE, deGroot WJ, Sauerland EK, Anch AM. Pathogenesis of upper airway occlusion during sleep. J Appl Physiol 1978;44:931–938

[12] Kinney HC, Feliano JJ. Brain stem research in sudden infant death syndrome. Pediatrician 1988; 15: 240-243

[13] Del Bigio MR, Becker LE. Microglial aggregation in the dentate gyrus: a marker of mild

hypoxic-ischemic brain insult in human infants. Neuropathol Appl Neurobiol 1994;20:144–151
[14] Storm H,Nylander G,Saugstad OD.The amount of brainstem gliosis in sudden infant death syndrome victims correlates with maternal cigarette smoking during pregnancy.Acta Paed 1999;1:13-18
[15] Valdes Dapnea M. The sudden infant death syndrome: pathologic findings. Clin Perinatol 1992;19:757-772
[16] Goldwater PN. Sudden infant death syndrome: a critical review of approaches to research, Arch Dis Child 2003;88:1095–1100
[17] Jones RE. Dysfunctional development of the diaphragm in SIDS and the prone sleeping position. Clin Pediatr 1996;35:173–174
[18] Rehan VK, Nakashima JM, Gutman A, Rubin LP, McCool FD. Effects of the supine and prone position on diaphragm thickness in healthy term infants. Arch Dis Child 2000;83:234–238
[19] Paluszynska DA, Harris KA, Thach BT. Influence of sleep position experience on ability of prone-sleeping infants to escape from asphyxiating microenvironments by changing head position. Pediatrics 2004;114:1634-1639
[20] Kinney HC, Thach BT. The sudden infant death syndrome. N Engl J Med 2009;361:795–805
[21] Valdés-Dapena M, Gilbert-Barness E. Cardiovascular causes for sudden infant death. Padiatr Pathol Mol Med 2002;21:195-211
[22] Tester DJ, Ackerman MJ. Sudden infant death syndrome: how significant are the cardiac channelopathies? Cardiovasc Res 2005;67:388–396
[23] Tester DJ, Dura M, Carturan E, et al. A mechanism for sudden infant death syndrome (SIDS): stress induced leak via ryanodine receptors. Heart Rhythmol 2007;4:733–739
[24] Schwartz PJ, Stramba-Badiale M, Segantini A, et al. Prolongation of the QT interval and the sudden infant death syndrome. N Engl J Med 1998;338:1709–1714
[25] Haas JE, Taylor JA, Bergman AB, et al. Relationship between epidemiologic risk factors and clinicopathologic findings in SIDS. Pediatrics 1993;91:106–112
[26] Mathews, TJ, Menacker, F, MacDorman, MF. Infant mortality statistics from the 2002 period: linked birth/infant death data set. Natl Vital Stat Rep 2004;53:1