TOPICALITIES IN THE SUDDEN UNEXPECTED DEATH SYNDROME IN INFANTS

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(Abstract): Sudden Infant Death Syndrome (SIDS) represents the third cause in postnatal mortality. The pathogenesis is multifactorial. SIDS victims can present sign of preexisting chronic asphyxia, persistent increase in dendritic spine and delayed maturation of synapses in medullary respiratory centers, if a decreased reactivity of 5 hydroxytryptamine 1A (5-HT1A) and 5-HT2A in the dorsal nucleus of the vagus, solitary nucleus and ventrolateral medulla. SIDS is an exclusion diagnosis, so that inexplicable SIDS is the accepted term. The objective of this report is to present current data about the pathogenesis of this syndrome and the medico-legal measures applied in preventive and curative aim. The “face-up” sleeping position has cut in half the SIDS frequency. In conclusion, the infant sleep studies represent an important line for the future research to provide sufficient explanation of the sudden death in these infants. Keywords: SUDDEN DEATH, PATHOGENESIS, CLINICAL EVENTS, MEDICO-LEGAL MEASURES.

The sudden infant death syndrome (SIDS) is the third cause of postneonatal (1 month to 1 year) mortality in industrialized countries (1). The phrase unexpected infant death syndrome (UIDS) is preferred, as it includes all cases of SIDS, defined as the brutal death of a child under 1 year, installed in full health and unexplainable even after the postmortem investigations, including a full and scientific necropsy, extended complementary examinations, full anamnesis and clinical examination and a detailed inquiry at the tragedy scene. SIDS is an exclusion diagnosis, as a series of non-SIDS causes (18.6%) were identified within the UIDS, such as: infections (7.2%), congenital cardiopathy (2.7%), child abuse (2.5%), genetic and metabolic diseases (2.1%) (2). In consequence, SIDS is classified in explainable SIDS (UIDS) and unexplainable SIDS. The SIDS incidence varies between 1.5-2‰ live births in 1994 and 0.45‰ live births in 1999, representing 15% of the pediatric deaths (3). The maximum frequency is recorded between the ages of 2 and 4 months and during the winter months; in 53% of the cases, the infant with SIDS sleeps in the same bed with at least 2 other persons and associates a low social-economic status (4).
ETIOPATHOGENY

Due to the definition from 1970 given by Beckwith (2), SIDS was considered as a causeless death. Subsequently it has been observed that not all the cases of sudden death were normal from the anatopathological point of view, but they associated brain abnormalities original from the intrauterine life, which can determine sudden death in a vulnerable period after birth. In 1972 the hypothesis of the triple risk in SIDS was released, including: general vulnerability, the risk specific to the age and precipitation factors (5). The most important hypotheses in SIDS are the respiratory one (apnea), cardiac one (arrhythmia) or visceral dyskinesia (glottal spasm and/or gastro-esophageal reflux) (6). It has been demonstrated that the autonomous system (respiratory, cardiovascular, upper digestive) participates in all these hypotheses, even if the arrhythmogenic cardiac dyskinesia, as the leading cardiac system is under strictly autonomous control (7).

The subsequent ethiopathogenic concepts assert multifactorial involvement in the SIDS, as follows: genetic factors, infant risk factors, maternal risk factors and environmental factors.

The genetic factors are demonstrated through the new discoveries in the field of molecular genetics and the identification of genetic polymorphism of the victims of sudden death. Almost two thirds of the cases have signs of preexisting chronic asphyxia and higher expression of the vascular endothelium growth factor (VEGF) in the cephalorachidian fluid. Brain abnormalities in infants with SIDS consist of the significant increase of the dendritic extensions and late maturation of synapses in the medullary respiratory centers, as well as the decrease in the immunoreactivity of the receptors of 5 hydroxytryptamine 1A (5HT2A in the vagus nerve, of the solitary nucleus and of the ventrolateral medulla, and increases were discovered in the brain periductal grey matter, along with gliosis (8).

The hypoplasia of the medullary arcuate nucleus, an important cardiorespiratory center was discovered in over 50% of the SIDS cases. This can associate with alterations of other structures of the brain stem, such as hypoplasia of the Kolliker parabrachial area and of the reticular formations of the respiratory system. Rarely cases of SIDS were reported in relation to the neuronal hypoplasia and immaturity of the hypoglossal nucleus responsible for the deglutition alteration (9).

The postmortem genetic studies discovered genetic differences including defects of the sodium channels, serotonin transporters and abnormalities of the genes of the autonomous nervous system, the C4 complements and IL-10. The long QT syndrome is associated with the sodium channels gene (SNC 5A) defect. Over 100 mutations were identified, of which over 30 are associated with the prolonged QT syndrome (10).

Molecular genetic studies in the SIDS victims identified mutations from the early embryological development of the autonomous nervous system. The relevant genes are MASH 1 (mammalian achaetescute homolog 1), BMP 2 (bone morphogenetic protein 2), PHOX 2b (paired-like homeobox 2b), RET (rearranged transfection factor), ECE 1 (endothelin converting enzyme 1), EDN 1 (endothelin 1), TCLR 3 (T cell leukemia homeobox) and EN (engrailed 1). The mutations of these genes can affect the cardiorespiratory control, but up to the present the genotypic differences between the SIDS victims cannot be related
The risk factors for SIDS specific to the infant are the male gender, age between 4 and 6 months, low weight upon birth and prematurity. The maternal risk factors for SIDS are age under 19 years, active smoking, which doubles the risk for sudden death, the use of illicit drugs, short time between births and limited or delayed prenatal cares (12). The environmental risk factors for SIDS are the ventral position during sleep, passive smoking, high temperature, humidity, the cold season, sleeping in the same bed with someone else and poverty (13).

**FORENSIC MEDICAL MEASURES IN SIDS**

The prior clinical events are determined by the synergy of the changes in the respiratory rhythm on the heart rhythm. Originally, 2–3 days before the fatal event, the infant has tachycardia, profuse sweats, and subsequently bradycardia and low blood pressure. These elements suggest an abnormal sympathetic and parasympathetic activity secondary to the dysfunction of the respiratory rhythm on the heart rate, like the state of shock, when sympathetic excitation (profuse sweats, tachycardia, increase in the blood pressure) happens in the compensatory stage, and sympathetic inhibition (bradycardia, low blood pressure) happens in the decompensating stage, resulting in the loss of tissue perfusion and death. Abnormalities could emerge in the brain structures controlling the variations of the respiratory rhythm, heart rate and the blood pressure values during sleep (cerebellum, medullar central surface, Raphe caudal nucleus, the inferior olive and the fastigial nucleus of the cerebellum). It can be speculated that SIDS is the result of a decrease in the uncompensated blood pressure, because of cerebellum lesion (14).

The forensic medical measures in SIDS are different if applied in curative or preventive purpose.

At the site of a SIDS case firm administrative and medical measures are imposed, which in certain countries are enacted through circular letters of the Ministry of Public Healthcare, mentioning: the direct phone line with the reference regional centers, the manner of urgent transportation of the body of the deceased infant by some medical team or competent personnel in a vehicle authorized by the police to the morgue. The body is transported to the forensics department, after which the police will carry out an investigation, if there are suspicious circumstances of the decease, the clinical examination reveals abuse signs, the refusal of an autopsy, decease after 9 months of age, and if there have been any other deceases of family members in suspicious circumstances.

The main purpose of the medical actions is the detection of the cause of death, possibly in 50–75% of the cases = explainable sudden death (UIDS) and the determination of the risk in siblings, to answer the parents’ question about what would happen to their other children. The etiological medical investigation includes a full physical examination of the deceased infant (weight, height, perimeters, tegument aspect, liver, spleen), X-rays (thorax, skeleton, cranium), biological sampling (intracardiac puncture – blood, suprapubic puncture – urine, lumbar puncture – CRL) for the bacteriological, virological, biochemical and genetic examinations. The anatomopathological
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examination will perform numerous histological sections in all organs (15).

The SIDS relation with the risk of repetition in siblings is like the risk in the general population, the sporadic cases being more frequent than the family ones. Nevertheless, there are families with high risk of repetition of the sudden death, such as: several sudden deaths in the genealogical tree, sudden death after 1 year, the metabolic disease, hereditary vagus hyperreactivity, precarious social-economic conditions, abuse and bronchomalacia in autopsy. The major indications of exploration of the collaterals of a suddenly deceased infant, by means of a 48-hour hospitalization, are the following: clinical signs of gastro-esophageal reflux (GER), uncontrolled fear, family vagus field and congenital prolonged QT syndrome. The twin of a suddenly deceased infant runs a risk 22 times higher for SIDS because of identical infectious and environmental factors, rather than because of genetic factors. Consequently, the twin will be hospitalized urgently with his/her mother, for a clinical examination and paraclinical explorations to exclude infections, GER, vagus hypertonia and congenital prolonged QT syndrome (16).

The prevention of SIDS consists in the elaboration of guides comprising recommendations for a risk-free sleep of infants. The recommended position for sleep in infants is the supine position (“lying on the back face upward”), in a crib with a firm mattress, no pillow or cover, in a room with the temperature between 18 and 20° C. The result of this measure is the decrease in the SIDS frequency by 50% (17).

CONCLUSION
SIDS is a complex multifactorial entity, whose frequency can be decreased by adopting preventive measures for the infant’s sleep. Of the multitude of the physio pathological mechanisms involved, the study of the infant’s sleep if a research line for the future, to find out why some infants die in their sleep, as a functional respiratory and cardiac response to different stimuli in the external environment.

It is of great need to pay attention to the environmental risks factors and the maternal factors as well. Even though no matter how much you prevent it, SIDS still appears to infants, in many cases, the smoking, the drug addiction or alcohol consuming during the pregnancy or after birth can lead to SIDS.

Also, in addition, we consider that infants decease cases should be highly supported and funded by with the great help from pediatricians and other medical specialists.

To get close to the factors and mechanisms of SIDS, and to break down a vicious and pathophysiological circle that also happen to affect infant's siblings.

REFERENCES