

Sudden unexpected post-natal collapse (SUPC) during skin-to-skin care (SSC): where is the trouble?

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Summary

Skin-to-skin care (SSC) consists in the early and prolonged skin-to-skin contact between the newborn and the mother. This practice brings several benefits to infants, such as cardiorespiratory stability, breastfeeding, thermoregulation and crying reduction; therefore, SSC application represents the best practice in the birth points around the world. However, it is not risk free; in fact, the occurrence of a sudden unexpected post-natal collapse (SUPC) has been reported many times in literature. SUPC can be defined as a sudden and unexpected postnatal collapse affecting term or near term infant, who appears well at birth, but who unexpectedly collapses within the first week of life, in such a way as to require intensive care or to develop encephalopathy or to die. New research acquisitions suggest that the hypoplasia of the rostral pontine Kölliker-Fuse nucleus, notoriously deputy to regulate the breathing rate, may represent the cause of death for SUPC during SSC.

Key words: Skin-to-skin care (SSC); Kangaroo mother care; Sudden unexpected post-natal collapse (SUPC); Sudden infant death syndrome (SIDS); Kölliker-Fuse nucleus; Immunohistochemistry.

Skin-to-skin care (SSC), also known as kangaroo care or kangaroo mother care for the similarity to how certain marsupials carry their young, consists in the early and prolonged skin-to-skin contact between the newborn and a family member, typically the mother [1]. At first, this practice was introduced in Bogotá, Colombia, in 1970s, as an alternative method to incubators for high-risk preterm infants, in order to reduce both mortality and hospital-acquired infection in a socio-economic context where the incubators were either unavailable or unreliable [2]. Afterwards, SSC had many supporters, who have led to its widespread dissemination, given the numerous benefits for newborns, such as cardiorespiratory stability, breastfeeding, thermoregulation, and crying reduction [3].

In 2016 a Cochrane review collected data from 21 studies including 3,042 low birth-weight babies (less than 1,500 grams at birth), highlighting that newborns provided with SSC have a reduced risk of death, hospital-acquired infection or hypothermia and a gain in terms of weight and breastfeeding rates [4]. A further 2016 Cochrane review provides clinical support for the scientific rationale, but looks at evidence for early SSC for healthy infants.

The available evidence shows that early SSC is associated with increased rates of breastfeeding, and some evidence of improved physiological outcomes, such as stability of the heart rate and breathing [5]. Today, the SSC application in the first hours of life represents the best practice in the birth points, also for healthy full-term newborns, and the International Kangaroo Care Awareness Day is cel-

ebrated on May 15 since 2011 (Figure 1). However, SSC is not risk-free for newborns; in fact, the occurrence of a sudden unexpected post-natal collapse (SUPC) has been reported many times in literature, while the newborn is lying in a prone position on the mother's bare chest and the mother is alone or maybe distracted or exhausted after childbirth [6]. According to the *British Association of Perinatal Medicine*, SUPC can be defined as a sudden and unexpected postnatal collapse affecting term or near term infants (> 35 gestational weeks), who appears well at birth (normal 5-minute Apgar score), but who unexpectedly collapses within the first week of life, in such a way as to require intensive care or to develop encephalopathy or to die [7]. Therefore, SUPC can manifest itself with varying severity, from episodes of apnea and/or bradycardia to sudden infant death, also called "early" sudden infant death syndrome (SIDS). SUPC occurs in 0.03-0.08/1000 live-births with an incidence in the first 12 hours of 1 in 20,000 live births within the United Kingdom [7].

The prone position of the infant, with the face pressed against the mother's chest during SSC, seems to be a clear risk factor, which contradicts the universal recommendation to keep infants on their sides or backs [8]. Moreover, the prone position is one of the components of the internationally recognized triple-risk model for SIDS, which defines the sudden death of an infant as a result of three events occurring simultaneously: 1) a vulnerable infant, 2) a critical developmental period in homeostatic control, and 3) an exogenous stressor [9-12].

All these events are present in infants who die during

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Figure 1. — The logo of the International Kangaroo Care Awareness Day is for free use without modification and it serves to celebrate, share, encourage skin-to-skin care globally.

SSC. In fact, at birth, the newborn is particularly vulnerable to the external world and sensitive to stress factors, including the prone position that reduces the amount of oxygen supplied to the still immature brain [13]. At this point one question spontaneously arises: why do only some newborns inexplicably suffer of SUPC during SSC in a form so severe as to encounter death? The ‘Lino Rossi’ Research Center of the Milan University (Italy) for the study and prevention of SIDS and of unexpected perinatal death, in collaboration with the Institute of Pathology, *Santa Maria del Carmine Hospital*, Rovereto (Trento, Italy), examining in depth the autonomic nervous system and, in particular, the brain stem, where the main centers that coordinate the respiratory activity are localized, has described a possible pathogenic mechanism of these deaths in a recent study [14]. From a large series of sudden neonatal deaths, collected thanks to the application of the Italian law n. 31, 2 February 2006, ‘Discipline of the diagnostic check on the victims of SIDS and of the unexpected death of the fetus’ [15], 22 cases of sudden death in the first hours of life, 12 of which occurred during SSC, and a group of 10 control cases of the same age, died from known causes (congenital heart disease, myocarditis, severe bronchopneumonia, pulmonary dysplasia) have been selected.

The histological and immunohistochemical study on serial sections of the brain stem have revealed the presence of development abnormalities in the rostral pontine Kölliker-Fuse nucleus, also known as diffuse reticular nucleus, in 11 out of 12 cases subjected to SSC (92%). This alter-

ation was found in only two of the remaining ten cases, in which the SSC had not been practiced, and in no control case (0%). These results suggest that the hypoplasia of the Kölliker-Fuse nucleus may represent the cause of death for SUPC during SSC [14]. The Kölliker-Fuse nucleus is one of the three parabrachial nuclei between the midbrain and the pons and it regulates the breathing rate.

It receives signals from the caudal cardio-respiratory part of the solitary nucleus and sends signals to the lower medulla oblongata, the spinal cord, the amygdala, and the lateral hypothalamus [16]. A thorough neuropathological examination in case of sudden and unexpected neonatal death is therefore essential, especially if this occurs during SSC, following a specific protocol, well-developed by the ‘Lino Rossi’ Research Center, which provides, in addition to the histological examination by serial sections of the brain stem to search for morphological alterations, the application of immunohistochemistry, in order to highlight life-treating dysfunctions [17-19].

The most important immunohistochemical investigations are those specific for:

- *Brain derived neurotrophic factor (BDNF)*: an essential growth factor for the development of the respiratory nuclei, in particular the Kölliker-Fuse [20].

- *Neuronal nuclear (NeuN) antigen*: normally expressed in vital neurons, its alteration is indicative of neuronal degeneration [21].

- *Nicotinic receptors*: essential for the brain development, since they control the acetylcholine-mediated transmission [22].

- *Orexin*: a neuropeptide involved in the regulation of sleep-wake status in newborns, as well as other autonomous functions [23].

- *Somatostatin*: a neuromodulator that participates in neurotrophic processes, in particular during the brain development [24];

- *Serotonin*: a neuromodulator produced by the rafe nuclei, which regulates the main neuronal circuits [25].

Although the current trend is to encourage SSC, clinicians should be informed regarding the possible presence in neonates of developmental alterations in neuronal centers that play an important role in the respiration control, particularly the hypoplasia of the Kölliker-Fuse nucleus. This defect can compromise vital functions, especially in situations of oxygen deficiency caused by the positioning of the newborn during SSC. Therefore, in the first hours of life, it is important to carefully monitor the child’s condition during SSC, ensuring that the nose and mouth are not occluded. However, when a component of the respiratory neural circuit is seriously damaged at birth, the chances of survival remain very poor, despite a constant monitoring. In conclusion, SSC can be considered a new risk factor for sudden neonatal death in case of defective development of one or more brainstem vital nuclei, in particular the Kölliker-Fuse. Any directives for the prevention of SUPC must

provide for a continuous monitoring during SSC. In case of death, the autopsy should be performed according to the aforementioned illustrated guidelines, in order to protect physicians from medicolegal sequelae and to obtain reliable epidemiological data on a larger scale.

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