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Clinical Pearl: A New Potential Biomarker for Sudden Infant Death Syndrome (SIDS): Butyrylcholinesterase

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A new, engaging, and potentially clinically relevant article by Harrington, Hafid, and Waters, investigators in New South Wales, Australia, was just published in *eBioMedicine part of Lancet Discovery Science* about a case-control study in which samples from dried blood spots were used to measure levels of butyrylcholinesterase in a group of infants who died of SIDS. These levels were compared with normal controls and infants who died of what the investigators termed "non-SIDS," or children who died at age 12-24 months of age of Sudden Unexplained Death of Infancy (SUDI) (1). They found significantly lower butyrylcholinesterase levels in the blood of SIDS infants (1).

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The feedback from SIDS families to members of the board of SIDS of Illinois was discussed at our meeting on Monday, May 16, 2022. "A cure for SIDS" came from some families (personal communication, Nancy Maruyama).

As you already know, a biomarker is an indicator that the infant is at higher risk for SIDS (1,2). Other abnormalities, including cardiac arrhythmias, inborn errors of metabolism, brain stem abnormalities, and genetic abnormalities, have been identified in SIDS infants (1,2). The problem is that these abnormalities have been identified after the fact, and these infants no longer died of SIDS but of prolonged corrected QTc syndrome or medium-chain COA dehydrogenase deficiency (2). As a result, the percentage of infants who die of SIDS is getting smaller.

We now know that lower Butyrlcholinesterase, a cholinergic enzyme with acetylcholinesterase, is active in the parasympathetic nervous system (1). The fact that Butyrlcholinesterase levels are low suggests an abnormality in the cholinergic nervous system, which also works with the serotonergic nervous system, and abnormalities in the serotonergic nuclei in SIDS infants have been demonstrated by Hannah Kinney and coinvestigators (2).

The problem may be a lack of arousal in the triple risk model in an infant at risk for SIDS(1,2). However, the biomarker suggests a mechanism or abnormality but not a solution. Even with this new information, in an at-risk infant with lower Butyrlcholinesterase levels, until investigators find a way to increase the levels, SIDS cannot be prevented.

"The problem may be a lack of arousal in the triple risk model in an infant at risk for SIDS(1,2). However, the biomarker suggests a mechanism or abnormality but not a solution. Even with this new information, in an at-risk infant with lower Butyrlcholinesterase levels, until investigators find a way to increase the levels, SIDS cannot be prevented."

References:

1. *Harrington CT, Hafid NA,Waters KA. Butyrylcholinesterase is a potential biomarker for Sudden Infant Death Syndrome. EBioMedicine 2022; 80, 104041.*
2. *Hayes RL. Serotonin abnormalities in the brain stem of Sudden Infant Death Syndrome. Investigation of Sudden Infant Death Syndrome. Ed. Cohen, MC, Schiemberg 1B*

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