Respiratory and arousal responses to hypoxia-hypercapnia; role of inner ear dysfunction and implications for the Sudden Infant Death Syndrome

Dept of Anesthesia, Seattle Children’s Hospital
Center for Integrative Brain Research, Seattle Children’s Research Institute

HIGHLIGHTS

We previously identified an association between newborn hearing loss and SIDS. We established an animal model of inner ear dysfunction with hearing suppression. Animals with inner ear dysfunction displayed significantly suppressed body movement arousal responses to severe hypoxia-hypercapnia compared to controls. The inner ear plays a key role in arousal that has not been previously identified. Inner ear dysfunction may play a key role in the pathophysiology of SIDS.

INTRODUCTION

Sudden Infant Death Syndrome (SIDS) remains the leading cause of infant mortality in Western societies (1). We initially identified an association between a right sided hearing suppression on the newborn hearing test and subsequent death from SIDS (2). Although a research finding, this is the first finding of an abnormality in SIDS cases prior to death by a universally available screening tool. In a following study we identified that inner ear dysfunction precipitates a marked suppression of the hypercapnic ventilatory response (HCVR), (3). Respiratory tracings and abnormalities in brainstem areas involved with cardio-respiratory control support the view that a failure of the infant to arouse from a suffocating hypoxic environment is a key component of the terminal event in SIDS (4,5,6). The objective of the present study was to assess whether inner ear dysfunction not only weakens the hypercapnic response, but also plays a role in suppressing the body movement arousal response to suffocating gas mixtures.

METHODS

Wild type mice (n=28) received intra-tympanic gentamicin (IT-Gent) injections bilaterally or unilaterally to precipitate inner ear hair cell dysfunction. Three control groups (n=22) received intra-tympanic saline (IT-Saline) bilaterally or unilaterally (right or left), or intra-peritoneal gentamicin (IP-Gent). The body movement arousal responses to severe hypoxia-hypercapnia combined (5% CO₂ in nitrogen) were tested under light anesthesia eight days following the administration of gentamicin or saline.

RESULTS

After injections, the bilateral and unilateral IT-Gent treated animals behaved similarly to controls, however the HCVR as well as the arousal movements in response to severe hypoxia-hypercapnia were suppressed in IT-Gent treated animals compared to control animals (P<0.05). Thus the HCVR was significantly decreased in the bilateral (n=9) and unilateral IT-Gent treated mice (n=19) compared to bilateral (n=7) and unilateral IT-Saline (n=9) control groups (P<0.05). Arousal movements were suppressed in the bilateral IT-Gent group (n=9) compared to bilateral IT-Saline controls (n=7, P<0.0001) and in the unilateral IT-Gent group (n=19) compared to unilateral IT-Saline controls (n=10, P<0.0001).

DISCUSSION

Inner ear dysfunction could be relevant in the pathophysiology of SIDS. The inner ear appears to play a key role in arousal from suffocating gas mixtures that has not been previously identified. We are planning a large scale population based study to analyze the hearing difference found in SIDS cases in more detail.

REFERENCES