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The QT Interval in Aborted Sudden Infant Death Syndrome Infants

GABRIEL G. HADDAD,[27] MARY ANNE F. EPSTEIN, RALPH A. EPSTEIN, NORMAN M. MAZZA, ROBERT B. MELLINS, AND EHUD KRONGRAD

Departments of Pediatrics, Chemical Engineering and Applied Chemistry, and Anesthesiology, Columbia University and Babies Hospital, New York, USA

Summary

The QT interval was measured in 12 normal and 7 aborted sudden infant death syndrome (SIDS) infants in rapid eye movement (REM) and quiet sleep at monthly intervals through the age of 4 months. An accuracy of better than 2 msec was assured by high resolution of the digitized signal and calibration of each QT measurement with an accurately generated time code. In contrast to current speculations, the QT index was significantly smaller in the infants with aborted SIDS than in the normal infants in both REM and quiet sleep ($P < 0.05$). In addition, as in normal infants, the QT_c was smaller in REM than in quiet sleep ($P < 0.01$). Although these results offer no support for the hypothesis that SIDS results from prolongation of the QT interval, they suggest that aborted SIDS infants have a functional abnormality in the autonomic nervous system.

Speculation

We suggest that 1) the shortening of the QT interval in the aborted SIDS infants results from a uniform increase in the sympathetic outflow to the cardiac ventricles or an increase in circulating levels of catecholamines; and 2) an imbalance between the left and the right sympathetic outflow to the ventricles of aborted SIDS infants, as has been previously hypothesized, is not likely since the QT_c was not larger in REM sleep, a sleep state in which an increase in sympathetic activity occurs.

Experimentally induced imbalance in the sympathetic outflow to the ventricles causes prolongation of the QT interval (24, 25). Such a prolongation of the QT interval is associated with increased vulnerability to ventricular arrhythmias and sudden death. The clinical counterpart of these experimental observations is the long QT syndrome in which infants, as well as adults, die suddenly and unexpectedly after physical or emotional stress (8, 16, 17). Recently, it has been postulated that infants dying in the first few months of life of the SIDS might have an asymmetrical development of the sympathetic innervation of the ventricles, causing an imbalance in the ventricular sympathetic tone (18). This asymmetric innervation could then lead, especially during the increase in sympathetic activity accompanying REM sleep, to prolongation of the QT interval, ventricular fibrillation, and sudden death (12, 18, 25). In this paper, we report studies of the QT index in REM and quiet sleep in infants with aborted or near-miss SIDS and normal infants studied in the first 4 months of life.

MATERIALS AND METHODS

INFANT POPULATION

Seven infants with aborted episodes of SIDS were included in this study. We defined an aborted episode of SIDS as one characterized by apnea, cyanosis or pallor, and unresponsiveness requiring vigorous physical stimulation for resuscitation; mouth-to-mouth resuscitation was required in five. At the time of the episode, four of the seven infants were clearly asleep; the level of consciousness was not known in the remaining three infants. Detailed clinical and laboratory assessment failed to reveal an explanation for the aborted SIDS episode. The laboratory evaluation included hematologic profile, serum glucose, calcium, magnesium, sodium, potassium, and chloride, acid-base and blood gas analysis, a chest x-ray, a conventional 12-lead electrocardiogram, an electroencephalogram, and a roentgenographic study of the upper gastrointestinal tract after swallowing barium. Although the precise relationship between massive gastroesophageal reflux and the cardiorespiratory collapse of the aborted SIDS episode is not well understood, we excluded four infants with massive gastroesophageal reflux because their recurrent aborted SIDS episodes were eliminated by thickening the feedings and placing the infants in the upright position.

All aborted SIDS infants were full-term and their birth weights were appropriate for their gestational age. The mean birth weight of this group was 3.31 kg (SD = 0.30) as compared with 3.48 kg (SD = 0.44) in the normal group. There was no significant difference in the weights of the two groups either at birth or at any of the ages studied ($P > 0.1$). There were two males and five females. Three had siblings, and one had a cousin who died of SIDS. They were first studied during their initial hospitalization, generally within 1 week after the aborted SIDS episode. Subsequently, they were studied at approximately their monthly "birthdays" through the age of 4 months. There was no family history of deafness (7). No infant was on any medications. Informed written consent was obtained from the parents of all infants.

The QT index in 7 aborted SIDS infants were compared with those of 13 normal infants, previously reported (6) and studied by identical methods at 1, 2, 3, and 4 months of age. All subjects, including aborted SIDS infants, were under observation for 6 to 24 months and were neurologically normal.

TECHNIQUE

Detailed description of the technique used for the study of the QT interval has been previously reported (6). In brief, all infants were studied during sleep for 2–3 hr after their midmorning feed. Sleep staging was performed utilizing electroencephalogram, electrooculogram, electromyogram, and behavioral criteria (2). In both groups of infants, one electrocardiogram electrode was placed to the left of the manubrium and the other, lateral and 1 to 5 cm inferior to the first electrode. The electrocardiogram was recorded on analog tape, and played on polygraph paper at a paper speed of 100 mm/sec. Twenty QT intervals were selected at random (5) from the first REM and quiet sleep cycle of each sleep study. The measurement system included a precision potentiometer mounted on a pair of calipers and an A/D converter. The output of this potentiometer was digitized, linearized, and averaged by a minicomputer. An accurate, electronically generated, 1-sec interval

Table 1. *QT index in 7 infants with aborted SIDS (17 studies) and 12 normal infants (31 studies) in REM and quiet sleep*

Sleep state	Normal	Aborted SIDS
REM	0.436 ± 0.015[1]	0.416 ± 0.017
	(0.384–0.466)	(0.377–0.435)
Quiet	0.433 ± 0.017	0.422 ± 0.022
	(0.402–0.479)	(0.363–0.450)

[1] Mean ± SD; ranges in parentheses.

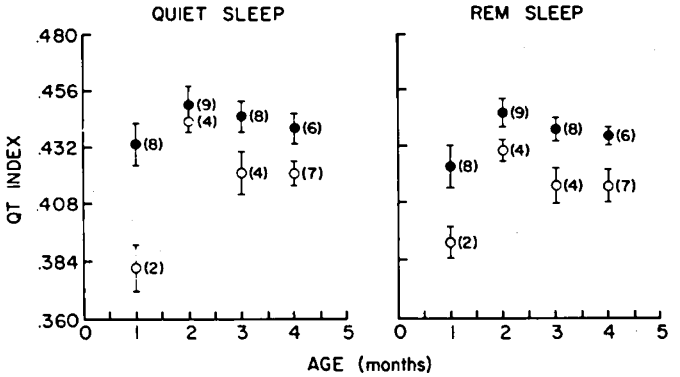

Fig. 1. The QT index of aborted SIDS (*open circles*) and normal infants (*solid circles*) in REM (*right panel*) and quiet sleep (*left panel*). The QT index was smaller in the aborted SIDS than in normal infants in both sleep states and at all ages. This difference was significant at 3 and 4 months of age ($P < 0.05$, Wilcoxon rank sum test). Means, standard deviations, and number of infants are shown at each age for both groups of infants.

was used for calibration of each QT and corresponding RR measurement. Error analysis disclosed a total potential error of 2 msec or less. To normalize for the heart rate, the QT index of QT_c was calculated using Bazett's formula $QT_c = QT/\sqrt{RR}$ (3). Paired and unpaired *t* tests and Wilcoxon's rank sum test were utilized for statistical analysis.

RESULTS

Table 1 summarized the data of 17 sleep studies in 7 aborted SIDS infants and 31 sleep studies in 12 normal infants in both REM and quiet sleep. Although there was an overlap between the normal and aborted SIDS groups, the mean QT index was significantly smaller in the aborted SIDS than in the normal infants in both sleep states ($P < 0.05$, unpaired *t* test). In spite of the relatively small number of infants, the mean QT_c was smaller in the aborted SIDS than in the normal infants in both sleep states at each age (Fig. 1) and this was significant at 3 and 4 months of age ($P < 0.025$, Wilcoxon rank sum test). As in normal infants, the mean QT index in the aborted SIDS infants was significantly smaller in REM than in quiet sleep ($P < 0.01$, paired *t* test) (Table 1). These differences in the QT_c means in REM and quiet sleep were also significant at each age, except in our youngest infants where the number of subjects was smallest ($n = 2$) ($P < 0.01$, paired *t* test).

DISCUSSION

Our finding of a shorter QT interval in aborted SIDS infants contrasts with previously published results showing a prolonged QT interval (4) or a QT interval that is no different from the normal (10). Three possible factors may contribute to the difference between our results and those of previous studies. First, previous studies of aborted SIDS infants did not control for the level of consciousness by appropriate neurophysiologic recordings including electroencephalography and electrooculography. Second, different criteria were used to define these aborted episodes of SIDS. We defined an aborted SIDS episode as a severe apneic episode requiring vigorous resuscitation and excluded infants with massive gastroesophageal reflux. In previous reports (4, 10), studies of gastroesophageal reflux were not described. Finally, our method of measuring the QT interval has greater accuracy than previous methods because of the higher frequency response of the system, higher polygraph paper speed, and calibration of each measurement using an accurate time code. In fact, the differences we observed between aborted SIDS and normal infants could not have been detected using conventional techniques for measuring the QT interval.

With a smaller QT index in aborted SIDS than in normal infants, one might ask whether the differences in the QT index can be attributed to differences in the heart rate of the two groups. We used Bazett's method of correcting the QT interval for heart rate which is adequate when the RR intervals are in a range similar to ours and when differences in heart rate between the two groups is small (22). Indeed, the heart rate in the aborted SIDS was only 5 to 10% higher than in normal infants (11). Since the RR interval was shorter in the aborted SIDS groups, correction for heart rate by Bazett's formula increases the QT_c; this adds significance to our finding of a smaller QT_c in this group.

Although ventricular tachycardia and fibrillation are rare in infants with no myocardial disease (23), several investigators have suggested that the sudden infant death syndrome might result from sudden ventricular arrhythmia and fibrillation, presumably from a prolonged QT interval (4, 12, 18). It has also been postulated that a delay in the development of the right sympathetic nerves during early infancy might lead to further prolongation of the QT interval and ventricular fibrillation, especially in the presence of an increased cardiac sympathetic activity as in REM sleep (18). Experimental work has shown that an imbalance in the ventricular sympathetic activity, from either a decrease in the right sympathetic activity, as would be expected from the postulated developmental delay, or an increase in the left sympathetic activity, produces a prolonged QT interval and lowers the ventricular fibrillation threshold (19, 21). Patients suffering from Jervel-Lange-Nielson and Romano-Ward syndromes presumably have a congenital imbalance in their cardiac sympathetic activity and die suddenly when challenged with emotional or physical upsets (8, 9, 16). Although our studies offer no support for the hypothesis that a prolonged QT interval is at the basis of SIDS, they do not exclude the possibility that sudden and unexpected deaths in infancy are caused by paroxysmal prolongation of the QT interval as in the long QT syndrome (20).

The smaller QT_c found in our aborted SIDS infants in both sleep states may be a reflection of a uniform increase in the sympathetic outflow to the ventricles or an increase in circulating levels of catecholamines (1). Indeed an increase in the thickness of the chromaffin cell layer in the adrenal medulla has been described in victims of SIDS (15). Also supporting this hypothesis is the fact that the heart rate was higher in aborted SIDS than in normal infants at each age and in both REM and quiet sleep (11). We speculate that this increase in the activity of the sympathetic nervous system in aborted SIDS infants might result from chronic hypoxemia, evidence for which exists on postmortem examinations in many cases of SIDS (13, 14). In addition, an imbalance or a developmental delay in the ventricular sympathetic innervation seems unlikely since the QT interval in aborted SIDS infants (as in normal infants) is shorter in REM sleep, a state characterized by an increase in sympathetic activity.

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27. Requests for reprints should be addressed to: G. G. Haddad, M.D., Pediatric Pulmonary Division, Columbia-Presbyterian Medical Center, 622 West 168th Street, New York, NY 10032 (USA).
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