The Role of the QT Interval in the Sudden Infant Death Syndrome

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SUMMARY To evaluate the role of QT interval prolongation in the genesis of the sudden infant death syndrome (SIDS), the postresuscitation electrocardiograms of 21 aborted SIDS infants were reviewed. The infants had been found apneic, cyanotic, limp and unresponsive during sleep and required vigorous physical stimulation and mouth-to-mouth resuscitation. Three subsequently experienced repeat similar episodes from which they could not be resuscitated.

Extensive studies eliminated all “known” etiologies for death. The QT intervals of these infants were compared to age and sex matched normal infants as well as to established normal values in the literature; in both the aborted and the subsequent actual SIDS infants, the QT intervals were not significantly different from those of the normal population. Thus, we conclude that QT interval prolongation does not play a major role in the genesis of the aborted SIDS.

The SUDDEN INFANT DEATH SYNDROME (SIDS) is the leading cause of infant death between the ages of 1 and 12 months, and claims approximately 10,000 lives in the United States each year.1-4 Because these deaths are sudden, usually occur outside of the hospital, are observed only rarely by physicians, and have few associated autopsy findings,4-6 we still know very little about their etiology. Explanations for these deaths include apnea, laryngomalacia, bronchospasms, infection, occult endocarditis, neurologic or renal disease, apnea, and autonomic dysfunction.4-11 In addition, QT interval prolongation with fatal ventricular arrhythmia has been proposed as a cause for SIDS.12-17 However, because SIDS victims themselves rarely have electrocardiographic evaluation before death, recent workers have examined relatives of SIDS infants because it is known that QT prolongation in some families is genetically transmitted.18-20 Based on this indirect approach, these studies suggest a causal relationship between QT prolongation and the SIDS.21,22 In this report, we examine the postresuscitation QT intervals of aborted SIDS infants, including three who subsequently died from actual SIDS.

Methods
Between 1974 and 1976, 21 survivors of the aborted SIDS were referred to the Massachusetts General Hospital.
(MGH) for evaluation and treatment. These infants were found apneic, cyanotic, limp, and unresponsive during sleep, and required vigorous physical stimulation and mouth-to-mouth resuscitation. No infant required electrical defibrillation. All infants had complete history and physical examination as well as laboratory evaluation including complete blood count, urinalysis, measurement of serum calcium, phosphate, magnesium, glucose, and amino acids, evaluation of urinary amino acids, chest and skull radiography, electroencephalograms, and continuous twelve-hour pneumogram recordings to evaluate respirations and heart rate. All known causes of sudden death were ruled out.

The 21 aborted SIDS infants included three infants who subsequently experienced similar episodes from which they could not be resuscitated. These three became actual SIDS babies. At autopsy, no cause of death was found in them. In six of the 21 aborted SIDS infants, the aborted episode was so severe that transient hypoxic damage following resuscitation was present, and 10 resuscitated infants had subsequent prolonged monitored apneic episodes lasting longer than 20 seconds which required bag and mask resuscitation and vigorous physical stimulation. Forty-six normal control infants matched for sex and age were selected from our ambulatory clinic population, and normal values for the QT interval were selected from the literature. All infants had standard 12 lead electrocardiograms taken within 48 hours of the aborted SIDS episode. These electrocardiograms were recorded while the infants were resting quietly using Marquette series 2,000 electrocardiographic recorders at 25 mm/sec paper speed. QT intervals were determined by averaging six complexes in lead II. Care was taken to avoid including U or P waves, and the QT intervals were measured from the onset of the Q wave (or the R wave if no Q wave was present) to the end of the T wave (junction with the isoelectric baseline). Only complexes with normal QRS and T waves were evaluated and no patient was taking medication which is known to alter the QT interval at the time of recording. Heart rate was calculated from the same complexes in which QT intervals were measured by averaging six R-R intervals in lead II. All QT intervals were corrected for heart rate (QTc) by dividing the QT by the square root of the R-R interval. Measurements were made on four separate occasions by two observers without knowledge of whether the patient was an aborted SIDS or a normal control. The QTc intervals of the aborted patients were plotted on the nomogram of QTc intervals derived by Alimurung et al.

Results

The general characteristics of these infants are shown in table 1. Physical and neurologic examinations were normal except in the six patients with transient postresuscitation hypoxia, and laboratory data and chest and skull radiographs were also normal. The mean serum calcium level was 9.9 mm/100 ml (range 9.0 to 10.9). Electroencephalograms were normal except in two of the infants who had transient hypoxic changes. Pneumogram recordings in ten infants demonstrated episodes of prolonged sleep apnea (greater than 20 seconds).

The QT intervals in aborted SIDS ranged from 0.20 to 0.33 seconds with a mean of 0.26 seconds compared to our normal infants in whom QT intervals ranged from 0.20 to 0.31 seconds with a mean of 0.25 seconds. The QTc for the aborted SIDS ranged from 0.35 to 0.42 seconds with a mean of 0.39 seconds compared to the QTc for normal controls which ranged from 0.34 to 0.43 seconds with a mean of 0.39 seconds. The QT intervals of our three infants who subsequently died from actual SIDS were 0.27, 0.28 and 0.28 and their calculated mean QTc was 0.39 seconds. Reports in the literature of 861 normal infants reveal a mean QTc of 0.39 seconds. The differences among the QTc in the aborted SIDS patients, the actual SIDS, our normal control infants, and reported normals in the literature were not statistically significant; and the QTc intervals in the aborted and actual patients were within the normal range when plotted on Alimurung's nomogram. To rule out possible age related QT variations, we compared our study and control populations by age as shown in table 2 and did not find significant differences in QTc intervals between these groups.

Discussion

While the etiology for SIDS is still unclear, review of our infants with aborted SIDS as well as three infants who subsequently were actual SIDS, reveals that QT interval prolongation is not present in these infants following resuscitation. Thus, unlike previous reports which demonstrated QT prolongation in relatives of SIDS and thus suggested that QT prolongation is related to SIDS, we could not demonstrate QT prolongation in the aborted or actual SIDS infants themselves. In addition, as shown in table 2, we could find no age subgroup in which the QTc intervals differed from controls. Further strong evidence against involvement of QT prolongation in SIDS derives from the fact that the presumed mechanism for death in QT prolongation is ventricular fibrillation which in nearly all patients requires defibrillation; in none of our resuscitations was defibrillation needed. It has been suggested that QT prolongation may be related to sleep or activity, and it is therefore possible that our single ECG samples did not detect intermittent QT prolongation; however, evaluation of this requires continuous long-term ECG recordings.

While it is conceivable that aborted SIDS is not the same

### Table 1. Characterization of Aborted SIDS and Normal Control Infants

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Mean age (months)</th>
<th>Mean weight (kg)</th>
<th>Sex</th>
<th>Mean gestational age (weeks)</th>
<th>Mean birth weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aborted SIDS</td>
<td>21</td>
<td>4.6</td>
<td>6.2</td>
<td>M/F</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subsequent actual SIDS</td>
<td>3</td>
<td>10.0*</td>
<td>8.2</td>
<td>2/1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal control infants MGH</td>
<td>46</td>
<td>4.5</td>
<td>6.2</td>
<td>25/21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal controls literature</td>
<td>861</td>
<td>5.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Means ages at the initial aborted SIDS episodes were 1, 3, and 7 months and at the actual SIDS episodes were 10, 8 and 12 months.
entity as actual SIDS and therefore that our study infants are not representative of the actual SIDS population, we believe this is not so because three of our study infants subsequently died of actual SIDS, six had significant clinical hypoxia demonstrating the severity of their aborted episodes, and ten infants had pneumogram documentation of prolonged, severe, and clinically significant apnea, which we believe could have precipitated actual SIDS.

We conclude from our data that demonstrable QT prolongation is not present in resuscitated aborted SIDS, and therefore is unlikely to be a major cause for the sudden infant death syndrome.

Acknowledgment

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References


| Table 2. QTc Intervals in Aborted SIDS and Normal Control Infants by Age |
|-----------------|-----------------|-----------------|-----------------|
| Age             | Aborted SIDS    | Normal control infants (MGH) | Normal controls literaturea,b,c |
|                 | No. | QTc | Range | No. | QTc | Range | No. | QTc | Range |
| 1 mo            | 5   | .39 | .35-.42 | 13 | .39 | .34-.43 | 107 | .39 | .32-.46 |
| 2 mos           | 6   | .40 | .38-.42 | 10 | .38 | .34-.42 | 98  | .40 | .34-.47 |
| 3 mos           | 2   | .39 | .38-.40 | 2  | .40 | .39-.40 | 94  | .40 | .34-.47 |
| 4-6 mos         | 3   | .40 | .39-.40 | 10 | .39 | .36-.43 | 184 | .40 | .33-.49 |
| 7-9 mos         | 2   | .38 | .38-.40 | 3  | .38 | .35-.40 | 107 | .39 | .32-.45 |
| 10 + mos        | 3   | .38 | .35-.42 | 8  | .39 | .35-.42 | 107 | .39 | .32-.45 |
| Total           | 21  | .39 | .35-.42 | 46 | .39 | .34-.43 | 693 | .40 | .32-.49 |
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