Sudden Infant Death Syndrome: Plasma Vitamin E Levels and Dietary Factors*

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ABSTRACT

Vitamin E and selenium deficiency have previously been suggested to be responsible for the Sudden Infant Death Syndrome (SIDS). New experimental data reveal that this is not the case since vitamin E as well as plasma selenium levels of SID infants are approximately equal to those of normal controls. Although breast feeding was believed to have a protective effect against SIDS, a statistical study of groups of SID- and control infants in San Diego County indicate no such correlation. Totally or partially breast-fed SID infants actually died at an earlier age than those fed by formula only (p = 0.02). Compared to matched normal controls, SID infants appear to have received a less varied diet with a lower incidence of extradietary vitamin supplementation (p = 0.02). There is also a somewhat greater prevalence of mothers smoking during pregnancy in the SID group (one-tail p = 0.05).

Introduction

Extensive investigations on the etiology of the Sudden Infant Death Syndrome (SIDS) have thus far failed to indicate a single causal factor. Inadequacy in the respiratory reflexes, sleep apnea, airway obstruction, viral infections, allergy to cow's milk, or hypoglycemia do not appear to be solely responsible for the etiology of SIDS.2,4,8 Recently, increased attention has been given to dietary factors; a prominent suggestion is due to Money11 who, on the basis of observations with pigs, suggested that selenium and/or vitamin E deficiency may cause sudden death in human infants. In addition, some authors have stressed the importance of breast feeding and indicated that mother's milk may protect against SIDS.6 It has been shown by us that the blood selenium levels of SID cases are essentially identical to those of normal controls.13 The vitamin E plasma levels of SID infants appeared to be slightly low, but our initial studies were performed on only a small number of samples and thus did not permit a clear conclusion regarding this point. The results of additional determina-

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tions of vitamin E levels in SIDS and normal infant blood are reported in this paper as well as the feeding histories and other data accumulated by sending a questionnaire to parents of confirmed SIDS cases and to comparable groups of demographically matched and unmatched control infants. San Diego County provides an interesting location for this type of investigation inasmuch as monthly temperature variations are small, and the overall climate is subtropical. Since drastic seasonal changes are absent, infants in San Diego County are not exposed to extreme cold or large temperature variations as compared to infants in other geographic areas where earlier epidemiological studies on SIDS were conducted.²⁴⁸

Methods and Materials

Plasma Vitamin E Levels

Diagnosis of SIDS. All infants dying unexpectedly in San Diego County are coroner's cases and are autopsied by the pathology staff of Sharp Memorial Hospital, San Diego. Intrathoracic petechiae are observed frequently and histologic sections of all major organ systems are examined microscopically. The diagnosis of SIDS is made when the post mortem examination does not demonstrate an adequate cause for death.²

Collection of SIDS and Control Plasma Samples and Determination of Vitamin E Levels

Blood samples were received from 18 SIDS victims* and from 17 normal control infants, ages one to seven months.† Unhemolysed cord blood samples from 18 normal newborn infants were obtained‡ after storage for several hours at 4°. All plasma samples were deep frozen immediately after separation and stored for future analysis. Total vitamin E levels in plasma were determined by a spectrophotometric technique, with sample volumes of 0.5 to 1.0 ml.³⁵. The reported plasma vitamin E levels of control infants and SIDS victims are approximately 8 to 10 and 15 to 20 percent lower than their true values, respectively, owing to vitamin E losses during storage and handling.§ Vitamin E losses are assumed to be negligible during storage of the plasma at −10°.⁵

Dietary History Questionnaire

Form of the Questionnaire

The questionnaire was four pages long, was self-administered and was based in part on a questionnaire used in a British study,⁶ but contained more extensive questions pertaining to dietary factors.

Distribution of Questionnaires to Parents of SIDS Victims, and Matched and Unmatched Control Infants

The addresses of the parents of all San Diego County SIDS victims in the last 2.5 years were obtained from the county coroner. Questionnaires, accompanied by a letter explaining the aims of the authors, were mailed to the parents. Of the 108 questionnaires mailed, 46 (43 percent) were returned completed, 23 (21 percent) were returned undelivered and 39 (36 percent) were never returned. In a few cases, questionnaire responses were supplemented by interviews. Addresses of parents of selected control infants were also obtained. Control infants were selected from the birth records on the basis of the informations.

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§W. Rhead, M.D., unpublished results.
*Courtesy of J. B. Askew, M.D., Director, San Diego County Department of Public Health.
tion given on the birth certificate. At least three control infants were preliminarily matched with each SIDS victim for date and hospital of birth, sex, race, birth order and parents’ age and occupation; questionnaires were mailed to the parents of 137 matched control infants with a letter explaining the aims of the authors' study. Of the 137 control questionnaires mailed, 48 (35 percent) were returned completed, 30 (22 percent) were returned undelivered and 59 (43 percent) were never returned. Questionnaires were distributed in person to the parents of 39 randomly selected infants at the Pediatrics Clinic, S.E. San Diego Health Center, San Diego, CA. This study was retrospective and was conducted in an area with a highly mobile population, contributing to our low response rate. Repeated attempts to contact the non-respondents in both SID and control groups by phone and mail have been consistently unsuccessful.

**Statistical Analysis of Questionnaire Responses**

After summarizing the answers of all three groups, the responses of the SIDS parents were compared to those of both the matched and unmatched control groups using either the t-test, binomial distribution, X²-test, or ordered contingency tables; all probabilities (P) are two-tailed. After the 48 matched controls were compared with the 46 SIDS victims, 10 of them were removed from the control group without reference to their dietary histories to guarantee demographic and socioeconomic identity between the two groups, leaving 38 rigorously matched controls.

**Results**

**Plasma Vitamin E Levels**

All infants evidently received an adequate supply of vitamin E from the beginning of postnatal life. Human milk contains approximately 7 to 8 IU of vitamin E per liter and all the infant formulas fed to both SID and control infants contain 4.3 to 7.9 IU of vitamin E per liter. Some infant multivitamin preparations are supplemented with 5 IU of vitamin E per ml, and these were administered to equal proportions of both SID and control infants. The plasma vitamin E levels and ages of 18 SID infants, 17 normal control infants and 18 normal neonates are shown in table I. The observed vitamin E levels of neonatal plasma, while lower than those noted by Nitowsky, et al, are similar to more recently published values. The neonates have lower plasma vitamin E levels than do either the SID infants or the normal controls (P = 0.01). In our earlier study, the plasma vitamin E levels of the SID infants were 25 percent lower than those

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean Age (Months)</th>
<th>Range (Months)</th>
<th>± S.D.</th>
<th>Mean Plasma Vitamin E (mg per dl)</th>
<th>Range (mg per dl)</th>
<th>± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates (Cord blood)</td>
<td>18</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>0.28</td>
<td>0.04-0.54</td>
<td>0.11</td>
</tr>
<tr>
<td>SIDS Infants</td>
<td>18</td>
<td>2.33</td>
<td>0.3-12.0</td>
<td>± 2.85</td>
<td>0.49</td>
<td>0-1.28</td>
<td>0.45</td>
</tr>
<tr>
<td>Control Infants</td>
<td>17</td>
<td>4.28</td>
<td>1.5-9.0</td>
<td>± 1.97</td>
<td>0.72</td>
<td>0.26-1.12</td>
<td>0.26</td>
</tr>
</tbody>
</table>

SIDS = Sudden Infant Death Syndrome
shown in table I\textsuperscript{3} owing to losses from extended storage of the plasma samples at 4°C. The SID infants, although younger than the controls (p = 0.01), do not have significantly lower plasma vitamin E levels than the controls (p = 0.05) (figure 1). Adjusting for the losses of vitamin E during handling and storage would raise the SID plasma vitamin E levels relative to those of the controls (Materials and Methods on page 32). Accordingly, it appears unlikely that any significant differences exist between the vitamin E contents of normal and SID infant plasma.

**Epidemiology of SIDS in San Diego County**

The epidemiology of SIDS is well elucidated: Deaths from SIDS display a peak in the winter months in infants from two to four months of age and an increased incidence in male children as well as in lower socioeconomic groups.\textsuperscript{2,4,5} The group of 46 SID infants investigated in our study have similar characteristics. For the years 1970 to 1972 the incidence of SIDS in San Diego County is 1.87 per 1,000 live births and accounts for 39 percent of the total infant mortality (one month to one year). SIDS is the third leading cause of death in the first year of life in San Diego County, following perinatal deaths and deaths owing to cogenital defects.\textsuperscript{1}

**Dietary History Study**

The demographic and socioeconomic variables of all three groups of subjects were summarized and compared statistically. The rigorously selected matched controls did not differ significantly from the SID infants in length of pregnancy, date and hospital of birth, birth order, birth weight, sex and race of infant, parental age, education, occupation and total family income (p = 0.05). Thus, this group of control infants is identical to the SIDS infants in all important respects. The randomly selected unmatched controls have a higher proportion of black and Mexican-
American infants, of first-born children and of a lower total family income than do the SID infants (p = 0.05). A higher proportion of the fathers of the unmatched controls are employed in manual trades than are those of the SID infants (p = 0.01). The unmatched control group sociologically resembles a population segment that experiences a higher incidence of SIDS and was included in our study to compensate for the low response rate from minority SID parents.

The SID infants showed significant differences from both the matched and unmatched control groups in certain variables; these factors are shown in Table II. Fewer SID infants received extradietary multivitamin supplementation and the SID infants were breast-fed for shorter periods than the controls (p = 0.02). The proportion of infants from all three groups partially and/or totally breast-fed is plotted against the age in months in Figure 2. Thirty-nine percent of the SID infants in our study were at least partially breast-fed, compared to 34 percent in King County, Washington. However, the apparent decreased length of breast feeding among SID infants is a consequence of the early death of the partially or totally breast-fed infants, as evidenced from the data in table II (p = 0.02). The SID infants also re-
received baby food and vitamin supplements earlier than the controls (p = 0.05), and smoking during pregnancy was more frequent among the mothers of SID infants than in the controls (one-tail p = 0.05). Although these differences may be secondary to some factor primarily related to SIDS, i.e. poverty and/or poor maternal care, there was no indication that the SID mothers in our study group provided less maternal care than those of the control infants.

The SID infants demonstrated insignificant differences from the control groups in a number of dietary variables. These factors include the incidence of breast and bottle feeding in the hospital and at home, and brands of infant formula and vitamin supplements fed to the infants. In contrast to an earlier study suggesting more frequent use of soft pillows among SIDS victims, it was found by us that the type of pillow used in the crib (soft, hard, or none at all), did not influence the incidence of SIDS (p = 0.84). Drug intake of the mothers during pregnancy was not remarkable, comprising mainly of aspirin, cold remedies and diuretics, which were taken by both groups of mothers without any preference. None of the mothers of SID infants reported significant observations on the behavior of their infants in the weeks or days preceding their death.

**Conclusions**

SIDS is not due to vitamin E deficiency, as evidenced from a comparison of the plasma vitamin E levels of SID infants at death with those of normal controls. There also is no evidence for insufficient dietary supply of vitamin E among breast-fed or formula fed infants at any time during early postnatal life, as suggested by Money. However, the present investigation suggests that SIDS may be directly or indirectly associated with certain dietary factors. Perhaps the most surprising result of our study is that breast feeding does not protect against SIDS, in contrast to previous claims. In fact, the totally or partially breast-fed SID infants actually died sooner than the exclusively formula fed infants (p = 0.02). Compared to the controls, the number of fully or partially breast-fed SID infants was not different. However, more normal control infants received extradietary multivitamin supplements than did SID infants (p = 0.02). Finally, a larger proportion of SID-infant mothers smoked during pregnancy (one-tail p = 0.05), in agreement with earlier studies; other reports also indicate increased mortality in the first year of life in infants whose mothers smoked during pregnancy. It thus appears that the diet of the SID infants of this study was less varied and less vitamin-supplemented than that of the normal controls. On the basis of these findings, the authors feel that more attention should perhaps be given to the relation of dietary factors to the etiology of SIDS, although our work also demonstrates that neither selenium nor vitamin E deficiency is re-
sponsible. Since the present study dealt with SID infants from a relatively small area of the U.S., it would also be of interest to establish whether or not similar trends are noticeable in other states or countries.

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References