Prevalence of Low Serum Vitamin A Levels in Young Children With Chalazia in Southwest China

LIN CHEN, XINKE CHEN, QIN XIANG, YUQIANG ZHENG, LIANHONG PI, QIN LIU, JUN XIAO, NING KE, AND JING FANG

• PURPOSE: To detect risk factors that may be related to chalazia in children in southwest China.
• DESIGN: Prospective case-control study.
• METHODS: The case group, 88 children with chalazia, was divided into 2 subgroups. One had 48 children 6 months to 6 years of age (defined as young children), and the other had 40 children 7 to 12 years of age (defined as older children). The control group consisted of 40 young children and 32 older children. Clinical findings for patients were recorded. Serum was tested for concentrations of vitamin A, vitamin D3, and immunoglobulin E.
• RESULTS: World Health Organization definitions were used for vitamin A deficiency (<0.7 μmol/L) and marginal vitamin A deficiency (0.7 to 1.05 μmol/L). The average level of serum vitamin A in the case group was significantly lower than that in the control group (P < .001). Analyses failed to find significant differences in vitamin D3 or immunoglobulin E levels between the case and control groups. The average vitamin A level in young children with multiple chalazia (0.65 ± 0.12 μmol/L) was low. Blepharitis was less prevalent than low serum vitamin A levels in the young child subgroup (odds ratios, 8.5 and 96.9, respectively), but higher than in older children (odds ratios, 17.5 and 9.0, respectively).
• CONCLUSIONS: Low serum vitamin A is associated with a chalazion in young children in southwest China, especially young children with multiple chalazia. (Am J Ophthalmol 2014;157:1103–1108. © 2014 by Elsevier Inc. All rights reserved.)

A chalazion is a localized, lipogranulomatous inflammation and is one of the most common eye diseases affecting the sebaceous glands, particularly the meibomian glands of the eyelids. Chalazia often occur secondary to noninfectious blockage of the sebaceous gland ducts. Previous studies have revealed that several risk factors, including blepharitis, infection of a virus or Demodex brevis, rosacea, gastritis, anxiety, irritable bowel syndrome, and smoking, are associated with chalazia. Hyperimmunoglobulin E syndrome and pulmonary tuberculosis also are reported risk factors. However, most studies have focused on risk factors leading to chalazia in adults and teenagers, and little attention has been paid to the factors that may relate to chalazia in children, especially young children.

In our clinical work, we found that chalazia in young children had different clinical manifestations than chalazia in adults and teenagers. In younger children, chalazia usually featured multiple lesions, increased susceptibility to infection, and higher recurrence than chalazia in older children. In some young children with multiple chalazia, the total number can reach more than 10 lesions in both eyelids. Most children with multiple chalazia also have frequent recurrences. In addition to conservative therapies, such as eyelid hygiene, local hot compresses, topical antibiotic agents, and eyelid massage, surgical methods often are used, including subcutaneous steroid injections and lesion excision. The pain caused by surgical methods and by the disease and the frequent recurrence in young children prompted this examination of other factors that may be involved in the morbidity of chalazia in children.

Vitamin A is a fat-soluble vitamin that plays an important role in reproduction, the visual cycle, and the differentiation and maintenance of epithelial tissues. Evidence is mounting that vitamin A deficiency can lead to metaplasia of the glandular, ciliated, mucus-secreting epithelium and hyperkeratosis of the keratinizing epithelium. Vitamin D is a very important nutrient that influences children’s growth and development. Deficiencies in the final, active metabolite of vitamin D (1,25(OH)2D3) have been reported to result in a set of diseases in children, including rickets and type 1 diabetes. These findings prompted investigation of whether levels of vitamin A, vitamin D3, and immunoglobulin E (IgE) are associated with chalazia in children.

METHODS
• STUDY POPULATION: This was a prospective case-control study of 88 children with chalazia. The Ethics Committee of the Children’s Hospital of Chongqing Medical University, Chongqing, China, approved the study.
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and tenderness in the acute phase and a persistent,
enlarging eyelid nodules manifesting pain, inflammation,
patients’ medical histories of presenting with gradually
(defined as older children). Chalazia was identified by the
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Chinese Clinical Trial Registry. The registration number
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Helsinki were followed in all procedures. Written informed
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enlarging eyelid nodules manifesting pain, inflammation,
and tenderness in the acute phase and a persistent,
nontender mass in the chronic phase.12 Blepharitis, diag-
nosed with the standard lid examination technique and
quantified by changes in the lid condition, was defined as
an inflammation in the palpebral margin involving the
skin, lashes, and meibomian glands.13,14 Table 1 shows
clinical findings for the children with chalazia, including
age, gender, and symptoms. During the same period, an
age- and gender-matched control group was recruited
from Children’s Hospital of Chongqing Medical University.
The control group consisted of 40 young children and
32 older children. Individuals in the control group
had undergone surgery for strabismus, congenital ptosis,
congenital cataract, or ocular trauma. Blood from the indi-
viduals in the control group was drawn before surgery.
Because infants 0 to 6 months of age have lower serum
vitamin A levels than older children, children younger
than 6 months were excluded from the study.

<table>
<thead>
<tr>
<th>Case Group (n = 88), No. (%)</th>
<th>Control Group (n = 72), No. (%)</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Male-to-female gender</td>
<td>47:41</td>
<td>37:35</td>
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<tr>
<td>Age (mean ± SD), y</td>
<td>5.24 ± 3.64</td>
<td>5.17 ± 3.65</td>
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<tr>
<td>Patients with a chalazion, no. (%)</td>
<td>48 (54.5)</td>
<td></td>
</tr>
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<td>Patients with blepharitis, no. (%)</td>
<td>42 (47.7%)</td>
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<td>Vitamin A level, mean ± SD (μmol/L)</td>
<td>0.84 ± 0.24</td>
<td>1.08 ± 0.31</td>
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<tr>
<td>Vitamin A level in patients with multiple chalazia, mean ± SD (μmol/L)</td>
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<td>IgE level in patients with multiple chalazia, mean ± SD (IU/mL)</td>
<td>10.88 ± 16.51</td>
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SD = standard deviation.

• **CLINICAL LABORATORY ANALYSES:** The blood samples
were collected at similar months of the year for the case
and control groups. Serum was tested for levels of vitamin
A, vitamin D3, and IgE in the clinical laboratory of the
Children’s Hospital of Chongqing Medical University
using a high-performance liquid chromatograph (Shimadzu,
Kyoto, Japan) and a chemiluminescence immune assay sys-
tem (ADVIA Centaur, Pittsburgh, Pennsylvania, USA).
World Health Organization definitions were used for
vitamin A deficiency (< 0.7 μmol/L) and marginal vitamin
A deficiency (0.7 to 1.05 μmol/L).15 Vitamin D3 deficiency
and hyperimmunoglobulin E were considered to be present if
concentrations were less than 17.25 nmol/L and more than
150 IU/mL, respectively.

• **STATISTICAL ANALYSIS:** Data on the serum levels
of vitamin A, vitamin D3, and IgE are shown as mean ±
standard deviation. One-way analyses of variance,
independent-samples tests, and Nemenyi tests were
performed to analyze levels of serum vitamin A, vitamin
D3, and IgE using SPSS software version 13.0 (SPSS, Inc,
Chicago, Illinois, USA). Logistic regression analysis was
applied to adjust for simultaneous effects of low serum
vitamin A levels and blepharitis in children with chalazia.
An χ² test was used to compare patients with a chalazion or
multiple chalazia lesions, relapsing patients, patients with
infected chalazia, and blepharitis in various groups. P
values less than .05 were considered statistically significant.

### RESULTS

• **CLINICAL FINDINGS FOR CHILDREN WITH CHALAZIA:**
Table 1 summarizes the vitamin A, vitamin D3, and IgE
levels and clinical characteristics of the study subjects as

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**TABLE 1. Clinical Findings for Children with Chalazia**

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assessed at diagnosis. In the case group, the average vitamin A level, in all patients (0.84 ± 0.24 μmol/L) and patients with multiple chalazia (0.70 ± 0.15 μmol/L) were marginally deficient. The average vitamin A level in all patients with chalazia or patients with multiple chalazia in the case group were significantly lower than those in the control group (P < .001 and P < .001, respectively). Analyses failed to find significant differences in the average levels of vitamin D3 and IgE in the case and control groups.

- **CLINICAL FINDINGS FOR PATIENTS IN BOTH SUBGROUPS:** Table 2 summarizes the vitamin A, vitamin D3, and IgE levels and clinical characteristics of both case subgroups. The distribution of patients with a chalazion or multiple chalazia, the number of relapsing patients (defined as patients who demonstrated a new chalazion near the location of a chalazion within 3 months after recovery from the excision and curettage for the chalazion), and the number of patients with infected chalazia were significantly different in the young child subgroup and the older child subgroup (P < .001, P < .001, and P = .02, respectively). The rates of all 3 phenomena in the young child subgroup (62.5%, 52.5%, and 62.5%, respectively) were markedly higher than in the older child subgroup (25%, 15%, and 37.5%, respectively). The average vitamin A levels in the young child subgroup (0.77 ± 0.25 μmol/L) were marginally low and were low for young children with multiple chalazia (0.65 ± 0.12 μmol/L). Meanwhile, the average vitamin A level of the patients in the older child subgroup and older children with multiple chalazia (0.94 ± 0.20 μmol/L and 0.84 ± 0.15 μmol/L, respectively) were marginally low. The average vitamin A levels in patients in the young child subgroup or patients with multiple chalazia in the young child subgroup were significant lower than those in the older child subgroup (P < .001 and P = .002, respectively). We did not find a significant difference in the average levels of vitamin D3 or IgE in these subgroups.

- **COMPARISON OF VITAMIN A LEVELS IN CASE SUBGROUPS AND CONTROL SUBGROUPS:** The results indicate that the average vitamin A levels in the case group were significantly lower than in the control group. To minimize bias, we compared the average vitamin A levels only between the young child case and control subgroups and the older child case and control subgroups, respectively (Table 3). The average vitamin A levels in the young child case subgroup (0.77 ± 0.25 μmol/L) were markedly lower than in the young child control subgroup (1.08 ± 0.32 μmol/L; P < .001).


**TABLE 4. Comparison of Vitamin A Levels in Case Group Patients with a Chalazion or Multiple Chalazia**

<table>
<thead>
<tr>
<th>Vitamin A Level (μmol/L)</th>
<th>Patients with a Chalazion</th>
<th>Patients with Multiple Chalazia</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case group</td>
<td>0.96 ± 0.23</td>
<td>0.70 ± 0.15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Young child case subgroup</td>
<td>0.95 ± 0.29</td>
<td>0.65 ± 0.12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Older child case subgroup</td>
<td>0.96 ± 0.19</td>
<td>0.84 ± 0.15</td>
<td>.08</td>
</tr>
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</table>

Data are mean ± standard deviation unless otherwise indicated.

**TABLE 5. Simultaneous Effects of Low Vitamin A Levels and Blepharitis in Children with Chalazia**

<table>
<thead>
<tr>
<th></th>
<th>P Value</th>
<th>Odds Ratio (95% Confidence Interval)</th>
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<tbody>
<tr>
<td>Low vitamin A in the case group</td>
<td>&lt;.001</td>
<td>37.7 (6.5 to 220.2)</td>
</tr>
<tr>
<td>Blepharitis in the case group</td>
<td>&lt;.001</td>
<td>12.2 (4.1 to 35.9)</td>
</tr>
<tr>
<td>Low vitamin A in young child case subgroup</td>
<td>&lt;.001</td>
<td>96.9 (7.9 to 1187.2)</td>
</tr>
<tr>
<td>Blepharitis in young child case subgroup</td>
<td>.007</td>
<td>8.5 (1.8 to 40.0)</td>
</tr>
<tr>
<td>Low vitamin A in older child case subgroup</td>
<td>.12</td>
<td>9.0 (0.6 to 140.5)</td>
</tr>
<tr>
<td>Blepharitis in older child case subgroup</td>
<td>&lt;.001</td>
<td>17.5 (3.6 to 84.6)</td>
</tr>
</tbody>
</table>

Similarly, the average vitamin A levels in the older child case subgroup (0.94 ± 0.20 μmol/L) were lower than in the older child control subgroup (1.09 ± 0.30 μmol/L; P = .01).

**COMPARISON OF VITAMIN A LEVELS IN CASE GROUP PATIENTS WITH A CHALAZION OR MULTIPLE CHALAZIA:**

Table 4 shows the vitamin A levels of the case group patients with a chalazion or multiple chalazia. The vitamin A levels of the patients with multiple chalazia were significantly lower than those of patients with a single lesion in the case group or the young child case subgroup (P < .001 and P < .001, respectively). In the older child case subgroup, no significant difference was found between the vitamin A levels of patients with multiple chalazia and patients with a single lesion.

**SIMULTANEOUS EFFECTS OF LOW VITAMIN A LEVELS AND BLEPHARITIS IN CHILDREN WITH CHALAZIA:**

According to previous research and the results of this study, blepharitis and low levels of vitamin A are associated with chalazia in children. Table 5 shows the prevalence of these 2 factors in children with chalazia versus the matched controls. Blepharitis was less prevalent than low levels of vitamin A in all child groups (P < .001; odds ratio [OR], 12.2; 95% confidence interval [CI], 4.1 to 35.9; and P < .001; OR, 37.7; 95% CI, 6.5 to 220.2, respectively). Blepharitis was less prevalent than low levels of vitamin A in the young child subgroup (P = .007; OR, 8.5; 95% CI, 1.8 to 40.0; and P < .001; OR, 96.9; 95% CI, 7.9 to 1187.2, respectively), but higher in the older child subgroup (P < .001; OR, 17.5; 95% CI, 3.6 to 84.6; and P = .12; OR, 9.0; 95% CI, 0.6 to 140.5, respectively).

**DISCUSSION**

This study investigated the factors that may be related to chalazia in children in southwest China. We found that the average serum vitamin A levels of patients with chalazia and patients with multiple chalazia in the case group were significantly lower than the average for the control group. In addition, in the case group, the average serum vitamin A levels of 6-month-old to 6-year-old children (young children) were lower than those of 7- to 12-year-old children (older children). The percentage of patients with multiple chalazia, the relapse rate, and the rate of infected chalazia in young children were markedly higher than those in older children. Furthermore, the average vitamin A levels in the case group were marginally low, and in young children with multiple chalazia, the average level was low. As to the simultaneous effects of factors associated with chalazia in children, blepharitis was less prevalent than low levels of vitamin A in young children, but higher than low levels of vitamin A in older children. No significant difference was found in the IgE and vitamin D3 levels between the cases and the controls.

Chalazia, which are characterized by foci of granulomatous inflammation (epitheliotic cells and multinucleated giant cells) surrounding lipids, are a chronic inflammatory response to meibomian gland inspissation. Recently, studies on the risk factors for chalazia have been published. Blepharitis and the use of makeup are believed to mainly contribute to chalazia. Other factors reported are rosacea, infection of a virus or Demodex brevis, gastritis, anxiety, irritable bowel syndrome, smoking, hyperimmunoglobulin E syndrome, and pulmonary tuberculosis. However, previous studies have focused on adults or teenagers with chalazia and have paid little attention to the factors that may relate to chalazia in children, especially young children.

In this study, we found that low vitamin A levels were associated with chalazia in children. The average vitamin A levels in the case group were lower than those in the control group. Furthermore, average vitamin A levels in the young child case subgroup were lower than they were in the older child case subgroup. However, no significant difference was found between children of different ages in the control group. More than half of the young children in the case group did not have blepharitis. Parents of patients who...
sought treatment with recurrent chalazia several times paid more attention to their children’s ocular hygiene, but the recurrence rate was not reduced appreciably by this attention. This study’s findings suggest that low vitamin A levels may play a key role in the morbidity of chalazia in young children.

We found that the average vitamin A levels in the case group were marginally low, and for young children with multiple chalazia, the levels were low. This finding suggests that low vitamin A may play an important role in the pathogenesis of chalazia in children, especially young children. Vitamin A deficiency may cause keratinization of the epithelial cells of the ducts of the meibomian glands, which would lead to obstruction of the ducts and accumulation of secretions. This may worsen to a chronic inflammatory process with phagocytosis, a key finding described as chronic, inflammatory granuloma in the meibomian gland. In this case, infection by bacteria, virus, or demodexis plays a secondary role in young children with chalazia. Because the meibomian gland ducts in young children are thinner than in older children, abnormal keratinization of the epithelial cells of these ducts in young children can lead more easily to obstruction than in older children. Moreover, the lower the vitamin A levels, the more serious the abnormal keratinization. This could explain why multiple chalazia and relapses were more common in young children than in older children. Several previous studies have shown similar results: patients of both genders with chalazia in every age group had markedly lower blood serum vitamin A levels than the corresponding control groups. In addition, a higher incidence of chalazia has been noted among pregnant and lactating mothers.

The current study found that the percentage of patients with multiple chalazia, the relapse rate, and the rate of infected chalazia in young children were markedly higher than those in older children. Young children with chalazia had incidences of multiple lesions, more easily infected with bacteria, and had higher recurrence rates. These characteristics of young children with chalazia were different from those of older children or adults. Interestingly, children with multiple chalazia had lower average serum vitamin A levels than case group children with a chalazion in the case group, the young child subgroup, and the older child subgroup. Low vitamin A levels may be involved in the pathogenesis of multiple chalazia in children. Further studies investigating the role of vitamin A in multiple chalazia in children may shed more light on this hypothesis.

Based on the conclusions of previous studies and the data obtained in this study, simultaneous effects of blepharitis and low serum vitamin A were hypothesized in children with chalazia. The data showed that blepharitis was less prevalent than low vitamin A in the young child case subgroup, but higher than low vitamin A in the older child case subgroup. This suggests that blepharitis is one of the main factors contributing to chalazia in older children. This finding is in line with those of previous studies, which have reported that blepharitis is the main factor in chalazia. However, low vitamin A may play a more important role than blepharitis in the onset of chalazia in young children. More data are needed to support this hypothesis.

The current study did not find high serum IgE levels. This may be the reason that hyperimmunoglobulin E syndrome was not a common risk factor, and the study included no patients with hyperimmunoglobulin E syndrome. More studies on the role of IgE in children with chalazia are needed to support this hypothesis. In addition, no significant difference was found in the levels of vitamin D in the cases and the controls. This result suggests that vitamin D has no relation to chalazia in children. The fact that vitamin D and IgE were not different in both groups suggests that this is neither a global nutritional deficiency nor an inflammatory condition and that the association with vitamin A is real.

The current study has certain limitations. First, the patients were recruited from southwest China, which may lead to a selected population of patients. Because average serum vitamin levels in children vary geographically, studies are needed on whether low serum vitamin A pays a key role in chalazia in young children in other areas of the world. Second, few children with chalazia observed in the study had a history of taking oral vitamins, especially children with multiple chalazia, although this is very common in the developed world. This study did not address the therapeutic effects of vitamin supplements on chalazia. On the contrary, the development of chalazia is likely to cause a decrease in serum vitamin A. The results of the current study showed an association between low serum vitamin A levels and chalazia, and we were unable to determine causation. Further studies are needed to clarify that issue. Third, because this study did not have a large number of subjects, the data obtained may deviate from real conditions. Data from larger samples are needed to minimize this deviation. Fourth, patients with severe blepharitis may be at higher risk of a chalazion than those with milder cases of blepharitis. Because blepharitis was taken as an integral risk factor for a chalazion in previous reports, we did not classify blepharitis as severe or mild while we collected the clinical findings for patients with chalazia. Further studies are needed to investigate the roles of different types of blepharitis in patients with chalazia. Finally, the control group subjects were children undergoing surgery for strabismus, congenital ptosis, congenital cataract, or ocular trauma. The conditions of these children may not be exactly the same as those of normal controls. Studies with normal controls are needed to support the data in this study. This study reports for the first time that low serum vitamin A is associated with a chalazion in young children in southwest China, especially young children with multiple chalazia.
REFERENCES

Biosketch

Lin Chen, Medical Master, graduated from the Second Affiliated Hospital of Chongqing Medical University, Chongqing, China. Since graduation with Medical Master’ degree, she had been a pediatric ophthalmologist for eight years in Department of Ophthalmology, Children’s Hospital, Chongqing Medical University, Chongqing, China. Her research interests are in children’s ocular surface diseases, refractive errors and oblique amblyopia.
Biosketch

Jing Fang, MD, graduated from the First Affiliated Hospital of Chongqing Medical University, Chongqing Key Laboratory of Ophthalmology and Chongqing Eye Institute, Chongqing, China. He had been an ophthalmologist for 15 years, especially a pediatric ophthalmologist for 10 years in Department of Ophthalmology, Children's Hospital, Chongqing Medical University, Chongqing, China. His research interests are in ophthalmic genetics, ocular surface diseases and optometry.
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