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Visual function and vitamin A/zinc nutriture in patients with complaints of night blindness

Abstract
Eighteen adults with night vision complaints showed significantly increased final rod thresholds as compared to their age and sex-matched controls, but vitamin A and zinc levels did not differ between the two groups. Vitamin A supplementation of three subjects produced changes in final rod thresholds and serum vitamin A levels, but these changes did not produce subjective improvements in night vision. It is concluded that patients with complaints about night vision often have increased final rod thresholds, but that actual vitamin A or zinc deficiencies are not common in these patients. Supplementation of selected patients may not improve night vision function to a degree noticeable by the patients and may produce unwanted side effects.

Degree Type
Thesis

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Visual Function and Vitamin A/Zinc

Nutriture in Patients

with Complaints of Night Blindness

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ABSTRACT

Eighteen adults with night vision complaints showed significantly increased final rod thresholds as compared to their age- and sex-matched controls, but vitamin A and zinc levels did not differ between the two groups.

Vitamin A supplementation of three subjects produced changes in final rod thresholds and serum vitamin A levels, but these changes did not produce subjective improvements in night vision.

It is concluded that patients with complaints about night vision often have increased final rod thresholds, but that actual vitamin A or zinc deficiencies are not common in these patients. Supplementation of selected patients may not improve night vision function to a degree noticeable by the patients and may produce unwanted side effects.
KEY WORDS

Vitamin A, zinc, photopigment, nutrition, dark adaptation, supplementation, night blindness.
ACKNOWLEDGEMENTS

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INTRODUCTION

Occasionally, patients present to the optometrist with a constellation of symptoms including an inability to see objects well at dusk, slow adaptation when entering dark rooms, and prolonged dazzle after passing a car with bright headlights. Usually these complaints are expressed in rather vague terms, and it is often difficult to decide if the patient has a "real" problem associated with dark adaptation or if the complaints are simply associated with aging (or perhaps changes in the weather or season) that might make night vision more difficult.

If it can be determined that the patient's symptoms are "real" and that she is suffering from a form of night blindness*, the optometrist's first concern is to rule out frank genetic or acquired retinopathies. If this has been done, nutritional deficiencies should be considered. Traditionally, night blindness has been associated with inadequate vitamin A levels which can occur either because of insufficient dietary intake of the vitamin (primary deficiency) (1) or because the metabolism of vitamin A has been altered, possibly due to a zinc deficiency (secondary vitamin A deficiency). (2)

In the body, vitamin A is stored in the liver and is delivered to the retina via the blood. In the photoreceptors, it is metabolized to its aldehyde form (retinal) which is used for the formation of rhodopsin.

*The term "night blindness" will be used in this paper to indicate a condition in which the patient has reduced ability to function in dim environments. Of course the patient is not "blind" at night just as a "color-blind" patient is not usually "blind" to all colors.
of the visual pigments. During light detection, quanta trigger the breakdown of the visual pigments into vitamin A and opsin. Most of the vitamin A is recycled, but, some is lost so a continuous dietary replacement is necessary for maintenance of proper blood and retinal levels. When dietary and blood levels of vitamin A are low, the amount of available pigment decreases causing, first, a change in rod function seen clinically as night blindness, and second, a change in cone function (3,4) if the vitamin A level declines even further.

In addition to the need for vitamin A, sufficient zinc must also be available or night blindness can result (2). Zinc has two functions in the maintenance of proper vision. First, it is required to produce and mobilize retinol binding protein from the liver, and this protein is necessary to release vitamin A into the blood (5). Thus, without sufficient zinc, the vitamin A level in the blood may be too low to support proper retinal function. Second, zinc is a required component of the enzyme retinol dehydrogenase which converts retinol from the blood to retinal needed to make the visual pigments. Low zinc levels can cause reduced activity of this enzyme (6), and thus cause night blindness by decreasing the amount of available visual pigment in the retina.

Although supplementation with vitamin A and/or zinc is useful in cases of gross nutrient deficiencies (7,8), little is known about treatment in cases of marginal deficiencies. Thus, it is difficult for the optometrist to know whether nutritional testing, counseling and treatment are appropriate for her patients who have night vision complaints. To investigate vitamin A and zinc nutriture
in such patients and to evaluate vitamin A supplementation therapy for selected patients, the following study was designed. Three specific questions were asked:

1. Can the night vision complaints of patients who do not have frank pathologies typically be verified by using standard clinical testing procedures?

2. Do patients with verifiable night blindness complaints (and no frank pathologies) typically have abnormal vitamin A or zinc nutriture?

3. Will vitamin A supplementation alleviate the complaints and problems of these patients?

SUBJECTS

Information regarding this research project was placed in several local newspapers, and persons who felt that they could not see well at night were asked to contact the experimenters. From the approximately 30 people who responded, 18 experimental subjects were selected. Fifteen were females and 3 were males (mean age 32, range 24 to 46 years). Selection of subjects was based on the following series of evaluations which were intended to rule out patients with psychological, pathological or night myopia problems:

1. Each potential subject was interviewed to assess the level of her/his night vision complaints. Specific questions involved situations in which the subject and another person were standing next to each other in a dim environment and viewing identical objects such as road signs. Each potential subject had to strongly indicate that in comparison situations such as these, their night vision was much worse than that of peers.
2. During the interview, it was also determined that each potential subject was in good physical health and that there was no known family history of eye disease or night blindness.

3. To insure clear media and to rule out ocular pathology, each subject was required to have best correctable visual acuity of 20/20, ophthalmoscopy had to reveal clear media and normal ocular structures, and no subject could be more than 50 years of age.

4. Since night myopia may cause complaints similar to night blindness, potential subjects with night myopia were eliminated by use of a bichrome test in which a dim 20/40 line was projected in a darkened room. To be used in the experiment, the subject's red/green balance under these conditions had to be within 0.25D of the best subjective refraction obtained under normal testing conditions.

The 18 subjects who met these requirements were age-and sex-matched to normal control subjects who had no complaints of night vision problems and who were free from pathologies.

METHODS

Dark adaptometry

To verify the subject's complaints of night blindness, a Goldmann-Weekers Adaptometer was used to measure final rod and cone thresholds and the time to the shift from cone to rod vision.

Each of the subjects was prepared for adaptometry by using 0.5% tropicamide to dilate one pupil to a diameter of at least 7 mm. The non-dilated eye was patched, and the subject was preadapted in the adaptometer for 5 minutes using a diffuse white 200 millilambert light. The subject was then asked to fixate a small red spot
displaced 20° superior from the center of the ganzfeld, and a
flashing 11.0 degree white spot was used to determine the threshold
at one minute intervals following the start of the adaptation
cycle. Threshold changes were monitored for 35 minutes or until a
stable final rod threshold had been reached. For each of the
experimental and control subjects, log thresholds were plotted
against time, and these curves were used to determine the final
thresholds and the time to the rod-cone breaks.

Vitamin A Assessment

Dietary intake and blood serum levels were used to determine
each subject's vitamin A nutriture. Dietary intake of vitamin A
was assessed by using a computerized analysis in which each subject
was asked to complete a food frequency questionnaire on their
daily, weekly, and/or monthly consumption of specific food types.
The subjects were also asked to include reports on any nutritional
supplements that they were currently taking.

To determine serum levels of vitamin A, blood samples were
drawn from each subject and analyzed by the use of fluorometric (9)
or spectrophotometric procedures (10,11).

Zinc Assessment

Zinc nutriture was assessed using dietary and hair analyses.
The dietary analysis was the same one used for the vitamin A assess­
ment with special care taken to insure that all mineral supplements
were reported. Since the level of zinc in the hair is a good in­
dicator of the averaged intracellular zinc level (12), one gram of
recent hair growth was cut from the suboccipital region of the
head, washed, digested in acid, and the zinc level determined by atomic absorption spectrophotometry (12).

RESULTS

Figure 1 presents the results from the dark adaptometry, vitamin A, and zinc tests. Dark adaptometry data do not reveal any significant differences between the control and experimental subjects in final cone thresholds or rod-cone break times, but there is a significant difference in final rod thresholds. Subjects who had complaints of an inability to see well at night had a mean threshold 0.4 log unit higher than their age-and sex-matched controls. This finding substantiates the subjects' complaints of night vision problems.**

The results of the vitamin A and zinc analyses indicate that both experimental and control subjects consumed more than the recommended daily allowance of both vitamin A and zinc and that their serum and hair levels were within normal ranges. Thus, while the experimental subjects did have a verifiable increase in final rod threshold, they did not differ from their matched controls in vitamin A or zinc nutriture.

**The effects of such a loss can be demonstrated by placing a 0.4 ND Wratten filter in front of one completely dark-adapted eye. A comparison can then be made between scenes viewed with and without the filter.
Table 1

Results of Dark Adaptometry and Nutritional Assessment for Subjects With and Without Complaints of Night Blindness

<table>
<thead>
<tr>
<th></th>
<th>Normal Range</th>
<th>Subjects With Complaints</th>
<th>Subjects Without Complaints</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CONE THRESHOLD (log cd/m²)</strong></td>
<td>-2.04 -2.60(a)</td>
<td>-2.2 (.3)(b)</td>
<td>-2.2 (.3)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>BREAK TIME (seconds)</strong></td>
<td>6-8 (c)</td>
<td>6.6 (2)</td>
<td>6.8 (3)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>FINAL ROD THRESHOLD (log cd/m²)</strong></td>
<td>-5.17 -5.37(a)</td>
<td>-4.8 (.3)</td>
<td>-5.2 (.2)</td>
<td>( p .05 )</td>
</tr>
</tbody>
</table>

**VITAMIN A**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>INTAKE (IU/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4000-females(d)</td>
<td>12152 (6340)</td>
<td>11141 (8871)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>5000-males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BLOOD SERUM (ug/dl)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-80 (e)</td>
<td>57 (24)</td>
<td>68 (33)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

**ZINC**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>INTAKE (mg/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 (d)</td>
<td>16 (8)</td>
<td>18 (19)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>HAIR (mg%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-24 (e)</td>
<td>23 (11)</td>
<td>22 (9)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

(a) (Reference 4)
(b) The first value is the mean; the value in parenthesis is the standard deviation.
(c) (Reference 13)
(d) Recommended Daily Allowance established by National Academy of Sciences
(e) Established by laboratory performing analysis
VITAMIN A SUPPLEMENTATION

Even though the experimental subjects did not have "abnormal" levels of vitamin A or zinc, the possibility still remained that these subjects required higher than "normal" levels of these substances for proper retinal function. To evaluate the possibility that the experimental subjects could benefit from taking large doses of vitamin A, they were asked to participate in an additional experiment involving vitamin A supplementation. Five of the subjects agreed to participate.

The supplementation and testing schedule for these subjects is outlined in Figure 2. A serum biochemical screen was used to rule out any contraindications to vitamin A supplementation (14), and, later in the experiment, it was used to insure that the vitamin A supplementation was not producing any unwanted changes in blood chemistry.

The supplementation experiment used a single-blind design in which subjects received a daily placebo dose of 200 mg of vitamin C for one month prior to receiving vitamin A supplementation.*** Following this month, subjects received a "high" daily dose of 40,000 IU of vitamin A for one month after which they received 10,000 IU daily for a two month maintenance period. The subjects were examined at the end of each supplementation phase as shown in Figure 2. During each examination, dark adaptometry was

***Subjects were aware that they might be receiving a placebo for part of the experimental period, but were not aware of when in the experiment this might occur. At no point were they told whether they were receiving vitamin A or vitamin C, and the tablets were disguised so as to make it impossible for them to make this determination on their own.


<table>
<thead>
<tr>
<th>Visit number</th>
<th>Total Time Elapsed</th>
<th>Tests Performed</th>
<th>Supplementation Started</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0 months</td>
<td>Dark adaptometry</td>
<td>Vitamin C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum biochemical screen</td>
<td>200 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>for 1 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionnaire on symptoms</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 month</td>
<td>Dark adaptometry</td>
<td>Vitamin A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum biochemical screen</td>
<td>40,000 IU/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum vitamin A level</td>
<td>for 1 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionnaire on symptoms</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 months</td>
<td>Dark adaptometry</td>
<td>Vitamin A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum biochemical screen</td>
<td>10,000 IU/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum vitamin A level</td>
<td>for 2 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionnaire on symptoms</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4 months</td>
<td>Dark adaptometry</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum vitamin A level</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionnaire on symptoms</td>
<td></td>
</tr>
</tbody>
</table>
performed and the subjects completed a rating scale questionnaire regarding their ability to perform common tasks in dim light. There were fourteen items on the questionnaire. Twelve items were questions involving specific situations, and two items were questions about the general performance of the subject in dim illumination. Subjects responded to each item using ten point rating scales with appropriate verbal anchors provided at both ends and the midpoint of the scales. Results of the questionnaire were evaluated by comparing subjects' ratings before, during and after supplementation.

Of the 5 subjects who began the supplementation phase of the study, three completed it. One subject (SK) dropped out because of a skin rash that developed after she began taking the high dose of vitamin A (14) and another (SL) was concerned about a possible increase in intracranial pressure that occurred while she was taking the vitamin C placebo. Her physician suggested that she should not take the high doses of vitamin A since a toxic side effect of such supplementation can be increased intracranial pressure (14). The results of vitamin A supplementation for the remaining three subjects are summarized in the following case reports:

Case 1 - TJ was a normal 41 year old female with specific complaints of difficulty when walking at night and slow adaptation to large luminance decreases (e.g. when entering a movie theatre). Her initial vitamin A and zinc levels were normal (Figure 3) but
Figure 3

Final rod thresholds and vitamin A serum levels for subjects participating in the supplementation study. Note that there are only small changes in the final rod thresholds measured before and after the vitamin C placebo. This indicates good repeat-measure reliability for the adaptometry. Arrows placed next to the threshold curves represent mean final rod thresholds for the experimental and control groups. Initials in parenthesis next to each curve represent the subjects referred to in the text.
her final rod threshold was 0.3 log unit above that for her age and sex matched control.

Following high dose vitamin A supplementation, her serum level increased and her final rod threshold decreased to a value equal to that of her control. During the maintenance period, her vitamin A serum level continued to increase, but her final rod threshold increased slightly.

Contrary to expectation, her responses on the rating scale questionnaire did not reflect the improved vitamin A and threshold levels. In fact, TJ indicated that her night vision difficulties became slightly worse during the vitamin A supplementation. Prior to supplementation she rated her overall ability to see in dim light as 5 on the 10 point scale (1 equals "not difficult", 10 equals "extremely difficult"), but following supplementation, her rating rose to 8.

Case 2 - The second subject, MA, was a normal 29 year old female with complaints associated with night driving. At the time of her initial evaluation, zinc and vitamin A levels were within the normal range. Her final rod threshold was, however, 0.2 log units above the threshold for her matched control subject.

Supplementation with the high dose of vitamin A produced the expected increase in the serum level and a 0.1 log unit decrease in threshold. MA's threshold continued to decrease during the two month maintenance period until it reached -5.3 log cd/m^2.

Just as with subject TJ, MA did not notice differences in her night vision corresponding to the decrease in final rod threshold or the increase in serum vitamin A level. From the beginning
of the study to the end neither her overall night vision rating
nor her night driving rating changed.

Case 3 - Subject HL was a normal 26 year old female who indicated
that she had problems performing almost any task in dim light.
Initially, her vitamin A levels and her dietary intake of zinc were
normal, but she had a zinc hair level of 31 mg% which suggested a
systemic zinc deficiency. The normal range of the hair zinc level
is 16-24 mg% with both higher and lower values indicating systemic
deficiency (12). Prior to starting vitamin A supplementation, her
final rod threshold was -4.9 log cd/m² which was 0.3 log unit above
the comparable level for her control subject. After one month of
high dose vitamin A supplementation, her final rod threshold had
increased to -4.6 log cd/m² indicating that her night vision had
worsened. This occurred even though HL's vitamin A serum level
had increased as a result of supplementation. Following the two
month maintenance period, HL's final rod threshold was -4.7 log
cd/m² and her vitamin A serum level remained at 85 ug/dl, but
she reported that her night vision had become worse during the
course of the study. Her overall night vision rating was 4 on the
initial visit but on the final visit she rated her ability to see
in dim light as 9. (A rating of 1 equals "not difficult" and 10
equals "extremely difficult").

In summary, these case reports suggest that vitamin A supple-
mentation for subjects who have normal vitamin A levels may not
produce noticeable improvements in night vision. While it is
possible to increase the level of vitamin A in the blood serum,
one of the three subjects reported corresponding increases in
vision, and two of them actually felt that their vision had deteriorated during the vitamin A supplementation.

DISCUSSION

We studied a group of subjects who complained that their night vision was worse than that of their peers. The severity of their symptoms was not extreme enough to debilitate any of the subjects, and only a few had sought professional help prior to participation in the study. Thus, these subjects represent a group of patients who might complain of night vision problems in an optometric examination, but who probably would not make it the major reason for coming to the optometrist.

The experimental subjects did, however, have real night vision problems as demonstrated by the fact that their mean final rod threshold was 0.4 log unit worse than the comparable threshold for the age- and sex-matched controls. This suggests that "normal" patients who present with vague night vision complaints may have "real" problems which should be evaluated. Whether such an evaluation should include the expensive vitamin A and zinc nutriture tests used in this study is questionable since the majority of patients with reduced final rod thresholds were not found to have abnormal vitamin A or zinc levels.

The question of whether nutritional supplementation of otherwise normal patients with night complaints is beneficial also remains open. Of the five subjects who received vitamin A supplementation, at least one experienced an adverse (but easily reversible) reaction to the high vitamin A doses and none of the subjects
reported a decrease in their night vision complaints during supplementation.

In conclusion, we feel that vague patient complaints of night vision difficulties should be regarded as "real" by the optometrist, but that the universal use of vitamin A supplementation for such patients is questionable; the risks of high dose vitamin A supplementation must be weighed against any possible benefits. Based on our limited number of subjects, we suggest that such risks may outweigh the benefits for patients who have normal vitamin A levels prior to supplementation.
REFERENCES


