

Effects of astaxanthin on accommodation, critical flicker fusion, and pattern visual evoked potential in visual display terminal workers

Yasunori NAGAKI,^{*a)} Seiji HAYASAKA,^{a)} Tetsuya YAMADA,^{a)}
Yoriko HAYASAKA,^{a)} Mari SANADA,^{b)} Takatoshi UONOMI^{b)}

^{a)}Department of Ophthalmology, Faculty of Medicine, Toyama Medical and Pharmaceutical University,
2630 Sugitani, Toyama 930-0194, Japan.

^{b)}Fuji Chemical Industry Co., LTD., 55, Yoko-hoonji, Kamiichi-machi, Nakaniiikawa-gun, Toyama 930-0397, Japan.

(Received July 16, 2002. Accepted September 11, 2002.)

Abstract

We evaluated the effects of astaxanthin, a red carotenoid, on accommodation, critical flicker fusion (CFF), and pattern visual evoked potential (PVEP) in visual display terminal (VDT) workers. As controls, 13 non-VDT workers received no supplementation (Group A). Twenty-six VDT workers were randomized into 2 groups: Group B consisted of 13 subjects who received oral astaxanthin, 5 mg/day, for 4 weeks, and Group C consisted of 13 subjects who received an oral placebo, 5 mg/day, for 4 weeks. No significant difference in age was noted among the 3 groups. A double-masked study was designed in Groups B and C. Accommodation amplitude in Group A was 3.7 ± 1.5 diopters. Accommodation amplitudes (2.3 ± 1.4 and 2.2 ± 1.0 diopters) in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. Accommodation amplitude (2.8 ± 1.6 diopters) in Group B after astaxanthin treatment was significantly ($p < 0.01$) larger than before supplementation, while accommodation amplitude (2.3 ± 1.1 diopters) in Group C after placebo supplementation was unchanged. The CFFs and amplitude and latency of P100 in PVEP in Group A were 45.0 ± 4.2 Hz, 6.5 ± 1.8 μ V, and 101.3 ± 6.5 msec, respectively. The CFFs in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. The CFFs in Groups B and C did not change after supplementation. Amplitudes and latencies of P100 in PVEP in Groups B and C before supplementation were similar to those in Group A and did not change after supplementation. Findings of the present study indicated that accommodation amplitude improved after astaxanthin supplementation in VDT workers.

Key words accommodation, astaxanthin, visual display terminal.

Introduction

Work at visual display terminals (VDT) reportedly induces various visual problems such as eye strain, blurring, and diplopia, and has had adverse effects on the visual system.¹⁻³⁾ Decreased accommodation amplitude, critical flicker fusion (CFF), decreased amplitude and prolonged latency of pattern visual evoked potential (PVEP) were assessed to determine the degree of eye

strain.¹⁻⁴⁾ Astaxanthin (3,3'-dihydroxy- β , β -carotene-4,4'-dione) (Figure 1), a red carotenoid, is present in fruit and sea products and has been used as a source of pigment in aquaculture and food industries.⁵⁻⁶⁾ Carotenoid has an antioxidant activity that may lessen the risk of age-related macular degeneration.⁷⁾ To our knowledge, however, no information has been available about its effect on eye strain. In the present study, we investigated the effects of astaxanthin on the degree of eye strain in VDT workers.

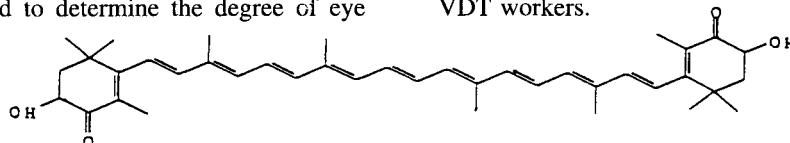


Figure 1. Chemical structure of astaxanthin

*To whom correspondence should be addressed. e-mail : ophthalmol@ms.toyama-mpu.ac.jp

Subjects and Methods

Subjects and study design: Thirteen non-VDT workers served as healthy controls (Group A). Most worked outdoors. Twenty-six VDT workers were selected for the present study: Their work at a VDT was over a period of 1 year, 5 days a week (from Monday to Friday), for 4 hours per day. Their visual acuity was better than 20/20. They wore glasses for correction during VDT work. Excluded from the present study were contact lens wearers, workers who had received eyedrops within the past 6 months, and those with severe ocular or systemic disease including diabetes mellitus. Informed consent was obtained from each subject. This study complied with the Declaration of Helsinki. A double-masked study was designed for the VDT workers. They were randomized into either the astaxanthin treatment group (n=13, Group B) or a placebo group (n=13, Group C). No difference in age was noted among the three study groups (Table I). Subjects in Group B were orally administered an astaxanthin capsule (5mg/capsule), once daily, 30 minutes before dinner for 4 weeks. Astaxanthin was prepared from the extract of *Haematococcus pluvialis* (Fuji Chemical Industry Co., LTD, Toyama, Japan). Subjects in Group C were orally administered a placebo (vehicle) capsule, once daily, 30 minutes before dinner for 4 weeks. The subjects in Groups B and C during supplementation continued regular VDT work. Subjects in Group A received no supplementation.

The measurement of accommodation, CFF, and PVEP: All measurements were performed in the right eye of each subject from 9:00 to 12:00 on Saturday morning. Visual acuity was measured at 5 m and at 35

cm using a Landolt ring. To determine the accommodation amplitude, the near and far points were measured. The near point was measured using a D'Acomo instrument (Wac Co., Osaka, Japan), according to the method described by Uozato *et al.*⁸⁾ The far point was measured by the subject's best corrected refraction. The accommodation amplitude (diopters) was calculated by subtracting the far point (in diopters) from the near point (in diopters). CFF was examined by decreasing the frequency of signals at a constant speed with C.F.F Test Apparatus (Yamagi Ltd, Japan). The mean value of 3 measurements was used in each eye. PVEP was recorded with Primus (Mayo Co., Japan), according to the standard set by the International Society for Clinical Electrophysiology of Vision.⁹⁾ The amplitude of one positive peak (P100) and latency (the distance in μ V between the N75 peak and P100 peak) were measured. Before and after VDT works and supplementation, eye strain was inquired in Groups B and C.

Statistical analysis: The paired t test was used for analysis of the data before and after supplementation. Scheffe's procedure was used for multiple comparisons of means in three Groups. A probability value of less than 0.05 was considered significant.

Results

No systemic adverse effects were noted in any subjects in Groups B and C after supplementation. Visual acuity at 5 m and 35 cm did not change in subjects in Groups B and C before or after supplementation. All VDT workers in Groups B and C had complained of eye strain before supplementation. After supplementation, 7 of 13 in Group B did not suffer from eye strain, and 12 of 13 in Group C still complained of eye strain. The improvement of the symptom in Group B was significantly higher ($p<0.05$) than that in Group C. The values of accommodation amplitude, CFF, and PVEP are shown in Table II. Accommodation amplitude in Group A was 3.7 ± 1.5 diopters. In Groups B and C, accommodation amplitudes before supplementation (2.3 ± 1.4 and 2.2 ± 1.0 diopters) were significantly ($p<0.05$) lower than in Group A. No significant difference was found between Groups B and C. Accommodation amplitude (2.8 ± 1.6 diopters) in Group B after astaxanthin was significantly ($p<0.01$) larger than before supplementation. Accommo-

Table I. Characteristics of the study subjects

| | Non-VDT Workers | VDT Workers | |
|-----------------|-----------------|----------------|----------------|
| | Group A | Group B | Group C |
| No. of Subjects | 13 | 13 | 13 |
| Gender | | | |
| Male | 11 | 11 | 10 |
| Female | 2 | 2 | 3 |
| Age(years) | | | |
| Mean \pm SD | 47.6 \pm 4.5 | 47.8 \pm 4.3 | 47.5 \pm 4.8 |
| Range | 39-53 | 40-53 | 38-53 |

Group A; no supplementation. Group B; astaxanthin supplementation. Group C; placebo supplementation.

Table II. Accommodation amplitude, CFF, and PVEP in workers

| | Non-VDT Workers | VDT Workers | | | |
|-----------------------------|---------------------|---------------------|-------------------|---------------------|---------------|
| | Group A (N=13 eyes) | Group B (N=13 eyes) | | Group C (N=13 eyes) | |
| | no supplementation | before astaxanthin | after astaxanthin | before placebo | after placebo |
| Accommodation amplitude (D) | 3.7±1.5 | 2.3±1.4* | 2.8±1.6# | 2.2±1.0* | 2.3±1.1 |
| CFF (Hz) | 45.0±4.2 | 39.9±5.3* | 38.4±4.8 | 39.9±5.5* | 38.4±3.9 |
| PVEP | | | | | |
| amplitude of P100 (μV) | 6.5±1.8 | 5.8±1.7 | 5.6±1.6 | 5.7±2.3 | 5.5±1.3 |
| latency of P100 (msec) | 101.3±6.5 | 102.5±6.9 | 104.8±7.4 | 104.4±5.7 | 105.2±5.7 |

Mean±Standard Deviation. #, $p<0.01$, compared with the value before supplementation.

*, $p<0.05$, compared with the value in Group A. CFF; critical flicker fusion. PVEP; pattern visual evoked potential.

dation amplitudes (2.3 ± 1.1 diopters) in Group C after placebo was unchanged. CFF in Group A was 45.0 ± 4.2 Hz. Measurements in Groups B and C before supplementation (39.9 ± 5.3 and 39.9 ± 5.5 Hz) were significantly ($p<0.05$) smaller than observed in Group A. CFFs in Groups B and C did not change after supplementation. The amplitude of P100 in PVEP in Group A was $6.5 \pm 1.8 \mu\text{V}$. In Groups B and C before supplementation, amplitudes (5.8 ± 1.7 and $5.7 \pm 2.3 \mu\text{V}$) were similar to that in Group A. No significant differences were found between Groups B and C. Amplitudes (5.6 ± 1.6 and $5.5 \pm 1.3 \mu\text{V}$) in Groups B and C after supplementation were similar to those before supplementation. Latency of P100 in PVEP in Group A was 101.3 ± 6.5 msec. Latencies (102.5 ± 6.9 and 104.4 ± 5.7 ms) in Groups B and C before supplementation were similar to that in Group A. No significant differences were noted between Groups B and C. Latencies (104.8 ± 7.4 and 105.2 ± 5.7 ms) in Groups B and C after supplementation were similar to those before supplementation.

Discussion

Accommodative amplitude varies with age. In the present study, therefore, ages were matched in all three groups. Also, diabetes mellitus is a risk factor for reduced accommodative amplitude.¹⁰⁾ Therefore, diabetic patients were excluded from the present study. Our findings showed that accommodation amplitude improved after astaxanthin supplementation in VDT workers. Increase in near point and decrease in accommodation have been reported in VDT workers by Murata *et al.*^{3,4)}

The authors have suggested that chronic stress of VDT use may induce hypofunction of the ciliary body, resulting in decreased accommodation. Astaxanthin has antioxidant activity.^{11,12)} Yang *et al.*¹³⁾ have reported that astaxanthin has a protective effect on the promotion of cancer metastasis in mice treated with restraint-stress. Tso and Lam⁷⁾ have reported that astaxanthin reduces the risk of age-related macular degeneration. Koide and Ueda¹⁴⁾ examined the effects of extract of Whortleberry (*Vaccinium myrtillus* anthocyanosides, VMA), which had antioxidative activity,¹⁵⁾ in VDT workers, and found that the VMA group showed improvement in accommodation, as compared with the placebo group. Their result was similar to our present findings. Although the exact mechanism remains unclear, it is likely that antioxidant activity of astaxanthin may be involved in improvement in accommodation amplitude in VDT workers. Decreased CFF and lowered amplitude and prolonged latency of P100 in PVEP have been reported in VDT workers.^{2,4)} In the present study, decreased CFFs were found in VDT workers. However, the CFF levels did not improve after astaxanthin supplementation. In the present study, decreased amplitude of P100 in PVEP was not found in VDT workers.

和文抄録

赤色カロテノイドの一種であるアスタキサンチンの visual display terminal (VDT) 作業者の調節力, 中心フリッカー値, パターン視覚誘発電位に及ぼす影響を調べた。VDT 作業を行わない13人をコントロールとした (Group A)。26人のVDT作業者を2群に無作為に分け

た。Group Bはアスタキサンチン一日5 mg 4週間内服した13人で、Group Cはアスタキサンチンを含むカプセルを4週間内服した13人とした。外見上同じカプセルでの内服投与を行った。

結果：Group AはGroup B及びGroup Cと比較して、調節力、中心フリッカー値は有意に高い値であったが、パターン視覚誘発電位検査結果は、Group B, Cと有意差はなかった。Group Bでは、アスタキサンチンの投与前後で有意な調節力の改善がみられた ($p < 0.01$)。しかし、中心フリッカー値、パターン視覚誘発電位に変化はみられなかった。Group Cでは、投与前後で、調節力、中心フリッカー値、パターン視覚誘発電位に変化はみられなかった。

考察：VDT作業では、非作業者と比べ調節力、中心フリッカー値が低下していることは以前より報告されており、今回の我々の研究でも同様の結果であった。VDT作業で、アスタキサンチン非内服群では、調節力は投与前後で変化がなかったが、アスタキサンチンの内服群で、有意に調節力が改善した。VDT作業の調節力の改善には、アスタキサンチンの内服が有効と考えられた。

*〒930-0194 富山市杉谷 2630

富山医科薬科大学眼科 長木康典

References

- Misawa, T., Yoshino, K., Shigeta, S.: An experimental study on the duration of a single spell of work on VDT performance. *Jpn. J. Industr. Health* **26**, 296-302, 1984.
- Iwasaki, T.: Eye-strain and changes in accommodation of the eye and in visual evoked potential following quantified visual load. *Ergonomics* **31**, 1743-1751, 1988.
- Murata, K., Araki, S., Kawakami, N., Saito, Y., Hino, E.: Central nervous system effects and visual fatigue in VDT workers. *Int. Arch. Occup. Environ. Health* **63**, 109-113, 1991.
- Murata, K., Araki, S., Yokoyama, K., Yamashita, K., Okamatsu, T., Sakou, S.: Accumulation of VDT work-related visual fatigue assessed by visual evoked potential, near point distance and critical flicker fusion. *Industr. Health* **34**, 61-69, 1996.
- Johnson, EA., An, GH.: Astaxanthin from microbial sources. *Crit. Rev. Biotechnol.* **11**, 297-326, 1991.
- Kobayashi, M., Kakizono, T., Nishio, N., Nagai, S., Kurimura, Y., Tsuji, Y.: Antioxidant role of astaxanthin in the green alga *Haematococcus pluvialis*. *Appl. Microbiol. Biotechnol.* **48**, 351-356, 1997.
- Tso, MOM., Lam, TT.: Method of retarding and ameliorating central nervous system and eye damage. *U.S. Patent*, 5527533, 1996.
- Uozato, H., Nakagawa, A., Hirai, H., Saishin, M.: A new near-point ruler using constant dioptric stimulus. *Folia Ophthalmol. Jpn.* (Nippon Ganka Kyo) **39**, 1247-1248, 1988.
- Harding, GFA., Odom, JV., Spileers, W., Spekreijse, H.: Standard for visual evoked potentials 1995. *Vision Res.* **36**, 3567-3572, 1996.
- Braun, CI., Benson, WE., Remaley, NA., Chew, EY., Ferris, FLIII., The Early Treatment Diabetic Retinopathy Study group.: Accommodative amplitudes in the early treatment diabetic retinopathy study. EDTRS report number 21. *Retina* **15**, 275-281, 1995.
- Oshima, S., Ojima, F., Sakamoto, H., Ishiguro, Y., Terao, J.: Inhibitory effect of β -carotene and astaxanthin on photosensitized oxidation of phospholipid bilayers. *J. Nutr. Sci. Vitaminol.* **39**, 607-615, 1993.
- Naguib, YMA.: Antioxidant activities of astaxanthin and related carotenoids. *J. Agric. Food Chem.* **48**, 1150-1154, 2000.
- Yang, ZB., Asami, S., Toyoda, Y., Fujii, W., Suwa, Y., Tanaka, T.: Protective effect of astaxanthin on the promotion of cancer metastases in mice treated with restraint-stress. *J. Jpn. Soc. Nutr. Food Sci.* **50**, 423-428, 1997.
- Koide, R., Ueda, T.: Effects of Whortleberry extract on ocular function. *J. Eye (Atarashii Ganka)* **11**, 117-121, 1994.
- Tsuda, T., Horio, F., Osawa, T.: The role of anthocyanins as an antioxidant under oxidative stress in rats. *Bio Factors* **13**, 133-139, 2000.