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Impact of Lutein-Based Food Supplement on Macular Pigment, Glare and Contrast Vision

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Abstract

Purpose: To evaluate the impact of a specially formulated food supplement containing 20 mg free lutein and 2.8 mg zeaxanthin on macular pigment volume (MPV) and visual function. **Methods:** In this prospective non-comparative study healthy subjects were instructed to take one capsule of Eagle Eye Lutein 20 Vision Caps (Innomedis AG) per day with a meal for 6 months. MPV was measured with the MP-Eye system (AzulOptics) after 3 and 6 months of treatment. Mesopic vision (MV), glare sensitivity (GS) and contrast vision threshold (CVT) were measured with the Binoptometer 4P system (OCULUS Optikgeräte). **Results:** Twenty-three healthy subjects between 19 and 56 years were enrolled. A significant increase was observed in MPV ($p < 0.001$), with associated improvements in MV level ($p = 0.042$), GS ($p = 0.009$) and CVT ($p = 0.036$). Mean changes in MPV, MV level, GS and CVT were 2.2 ± 1.7, 0.4 ± 0.8, 0.4 ± 0.7, and −9.3% ± 16.1%, respectively. The change in MV ($r = -0.628$, $p = 0.002$), GS ($r = -0.778$, $p < 0.001$) and CVT ($r = -0.625$, $p = 0.002$) with treatment was found to correlate significantly with their corresponding baseline values. **Conclusions:** The specially formulated food supplement containing lutein and zeaxanthin induced a significant increase in MPV, and consequently an improvement in the visual function after 3 and 6 months in healthy subjects.

Keywords

Macular Pigment, Mesopic Vision, Glare Disability, Contrast Sensitivity, Lutein, Zeaxanthin

1. Introduction

Carotenoids are considered to play an important role in human health due to their powerful antioxidant and anti-inflammatory properties [1]. A lower risk of chronic diseases, including cardiovascular disease and some cancers, has been reported to be associated with an increase in the consumption rate of carotenoids [2]. The role of carotenoids in vision is especially remarkable. In the central area of the retina, an accumulation of three carotenoids can be found, lutein, zeaxanthin and meso-zeaxanthin, being collectively referred to as macular pigment (MP) [3]. Specifically, the dominant carotenoid in the periphery of the macula is the lutein, while zeaxanthin and meso-zeaxanthin can be found predominantly in the mid-periphery and epicenter, respectively, of this area [3]. These carotenoids that compose the MP protect by absorbing short-wavelength light and suppressing oxidative stress [4]. Besides this, lutein and zeaxanthin are also stated that act as anti-inflammatory agents and as modulators of the function of synaptic membranes and enhancers of gap junction communication [5] [6] [7]. For this reason, MP density is significantly correlated with macular thickness and volume, helping to maintain neural health [4]. Furthermore, a link between MP density and visual function has been demonstrated [8] [9] [10], with significant correlations with photo-stress recovery, glare disability, and contrast sensitivity [11]. Richer *et al.* [8] demonstrated that augmenting MP density in individuals with difficulties in night vision led to measurable benefits in several visual functions, crucial for comfortable night vision driving. Stringham and colleagues [9] also found that the increase in MP density was associated with enhanced lateral inhibitory processes, corresponding to improved contrast sensitivity (CS). The landmark study Age-Related Eye Disease Study 2 (AREDS2), which enrolled 6351 eyes of 3882 patients, found a potential beneficial association with further reduction in progression of AMD and late AMD after 10 years of follow-up [12]. In contrast to beta carotene which nearly doubled the development of lung cancer in former smokers, the lutein/zeaxanthin supplement was safe and not associated with lung cancer [12].

Considering the biological selectivity of the central retina capturing the three mentioned types of carotenoids, intense research has been performed on the potential of dietary supplements with such carotenoids, in order to optimize the vision of healthy subjects [8] [9] [13]-[19] and subjects with ocular pathologies [20]-[25]. The impact on visual performance of different combinations of lutein, zeaxanthin and meso-zeaxanthin as dietary supplementation has been tested and showed positive effects [8] [9] [13]-[25]. Likewise, the supplementation of lutein only has been shown to be beneficial for visual function [14] [16] [17], although doses of more than 6 mg are recommended to obtain a relevant positive impact. 14 The therapeutic effect of the specific combination of lutein and zeaxanthin has been investigated in previous studies [8] [13] [18] [22] [24]. The current study aimed at evaluating the impact of a specially formulated food supplement containing 20 mg free lutein (L) and 2.8 mg zeaxanthin (Z) on macular pigment volume, glare and contrast vision.

2. Material and Methods

2.1. Study Design and Patients

This monocentric prospective non-comparative study enrolled healthy adult subjects. Eligibility criteria included: 18 years or older, a corrected distance visual acuity (CDVA) of 20/20 or better, no more than 5 D of the spherical equivalent of refraction, no diabetes mellitus, no ocular pathology, and no previous consumption of supplements containing L and/or Z. Prior to enrolment, all patients were informed about the nature of the study and signed a written informed consent according to the tenets of the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of the Hospital.

All subjects enrolled were instructed to take one capsule of Eagle Eye Lutein 20 Vision Caps (20 mg·L + 2.8 mg·Z) (Innomedis AG, Köln, Germany) per day with a meal for 2 months. Besides L and Z, it contains vitamin B-complex, selenium, copper, zinc, coenzyme Q10 and pantothenic acid. The specific formulation of this food supplement is based on a combination of L and Z which has been shown to be associated with several benefits, including increases in MP volume, and improvement in glare and contrast vision [8] [13] [18] [22] [24].

Study visits took place at baseline and at 3 and 6 months.

2.2. Measurement of the Visual Function

The measurement of several aspects of the visual function before and after using the nutritional supplement was performed with the Binoptometer 4P system (OCULUS Optikgeräte GmbH, Wetzlar, Germany). The Binoptometer is a screening instrument for visual function, including tests on contrast sensitivity, mesopic vision and glare sensitivity. In the current study, the following parameters were evaluated:

- Measurement of photopic corrected distance (5 m) visual acuity (CDVA): Tumbling E charts were used, with five E letters generally displayed per visual acuity level, of which at least three had to be identified in order to pass that visual acuity level.
- Photopic contrast vision: The contrast of E letters was changed to examine the patients' contrast vision. This testing was done under normal daylight conditions (photopic). To pass a certain contrast level, patients had to correctly identify at least three out of the five visual targets. This device provided the value of the contrast threshold and therefore lower values of this parameter represent better contrast sensitivity.
- Mesopic vision: The luminance conditions were adapted to simulate the traffic situations at night: the optotype was presented at a brightness of 0.032 cd/m^2. In contrast to the visual acuity test, the size of the optotype character was not reduced in this test, but rather its contrast compared to the surroundings. The size of the Landolt rings corresponded to a visual acuity of 20/200. Four contrast levels were available (1:23, 1:5, 1:2.7, and 1:2), with 1:23 representing the highest contrast which was the easiest to identify. Specifically, a contrast of 1:23 indicates the ratio of the luminosity of the optotype character to the luminance of the surrounding area.
- Glare sensitivity was measured with a similar method as described for measuring mesopic vision, but with a test field brightness of 0.1 cd/m^2.

2.3. Macular Pigment Measurement

The MP measurement was done with the MP-Eye system (AzulOptics, Bristol, UK). It is based on the polarization-dependent absorption of blue light by MPs, which results in the entoptic phenomenon called Haidinger's brushes [26]. How well a person can perceive Haidinger's brushes is a function of the density of their macular pigments, which is the underlying principle used by the MP-eye. [26]. The Haidinger's brushes effect is subtle, so the MP-eye uses a special lighting environment to optimize conditions for seeing the effect. Haidinger's brushes would normally disappear within 2 - 5 seconds as the brain quickly adapts to static images (Troxler effect), so the MP-eye uses a rotating polarizer to maintain the effect indefinitely. Specifically, subjects were asked to identify the direction of rotation of the brushes while observing a screen through a visor with a circular illumination stimulus of even intensity of polarized white light, in which the electric field vector was rotating either clockwise or counterclockwise. The polarization threshold was determined by reducing the degree of polarization of the stimulus light until the patient reported that no brushes could be detected. This threshold has been shown to correlate to MP optical density assessed with dual-wavelength fund us autofluorescence [26].

2.4. Statistical Analysis

The statistical data analysis was performed using the software SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov normality test was performed, and all data variables were found to be not normally distributed. Nonparametric statistical tests were then applied for the data analysis. Specifically, the Wilcoxon test was used to analyze the significance of differences in the parameters evaluated between consecutive visits. The Spearman correlation coefficient was calculated to evaluate the level of correlation between the changes experienced in MP and in visual function parameters.

3. Results

This prospective case series included 23 subjects with ages ranging from 19 to 56 years (mean: 39.1; standard deviation, SD: 13.1; median: 45.0 years), 52% were females. All subjects had a monocular CDVA of 0.00 logMAR or better. **Table 1** shows a summary of the results at baseline and for the follow-up visits. As shown, a significant change was observed in macular pigment volume (MPV) ($p < 0.001$) (**Figure 1**), mesopic vision ($p = 0.042$) (**Figure 2**), glare sensitivity ($p = 0.009$) (**Figure 3**) and contrast vision threshold ($p = 0.036$) (**Figure 4**) after 3 months of treatment. Specifically, there was an increase in MPV and mesopic vision and glare sensitivity levels, whereas there was a decrease in contrast vision threshold. Between month 3 and month 6 of treatment, significant changes were not observed in any of the evaluated parameters, although the change in MPV was close to the limit of statistical significance ($p = 0.062$), with a trend to increase as found during the 3 months of treatment.

Table 1. Summary of the main outcomes in the evaluated sample.

Mean (SD) median (range)	Baseline (a)	1 month follow-up (b)	2 months follow-up (c)	p-values
MPV	2.74 (1.68) 3.00 (0.00 to 5.00)	4.43 (1.93) 4.00 (0.00 to 8.00)	4.96 (2.08) 5.00 (1.00 to 9.00)	(a)-(b) < 0.001 (b)-(c) 0.062
Mesopic vision level	2.82 (1.14) 3.00 (1.00 to 4.00)	3.18 (0.96) 3.00 (1.00 to 4.00)	3.23 (0.81) 3.00 (1.00 to 4.00)	(a)-(b) 0.042 (b)-(c) 0.715
Glare sensitivity level	3.26 (1.01) 4.00 (1.00 to 4.00)	3.70 (0.76) 4.00 (1.00 to 4.00)	3.70 (0.76) 4.00 (1.00 to 4.00)	(a)-(b) 0.009 (b)-(c) 1.000
Contrast vision threshold (%)	21.14 (20.93) 12.50 (10.00 to 80.00)	14.77 (15.39) 10.00 (5.00 to 80.00)	11.82 (7.64) 10.00 (5.00 to 40.00)	(a)-(b) 0.036 (b)-(c) 0.131

Abbreviations: MPV, macular pigment volume; mesopic vision and glare sensitivity levels: 1:23, 1:5, 1:27, and 1:2.

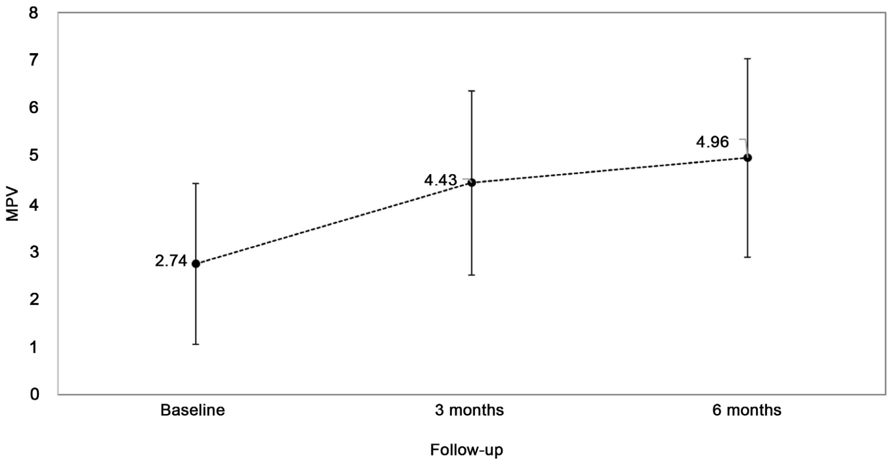

Figure 1. Changes in macular pigment volume (MPV) during the follow-up.

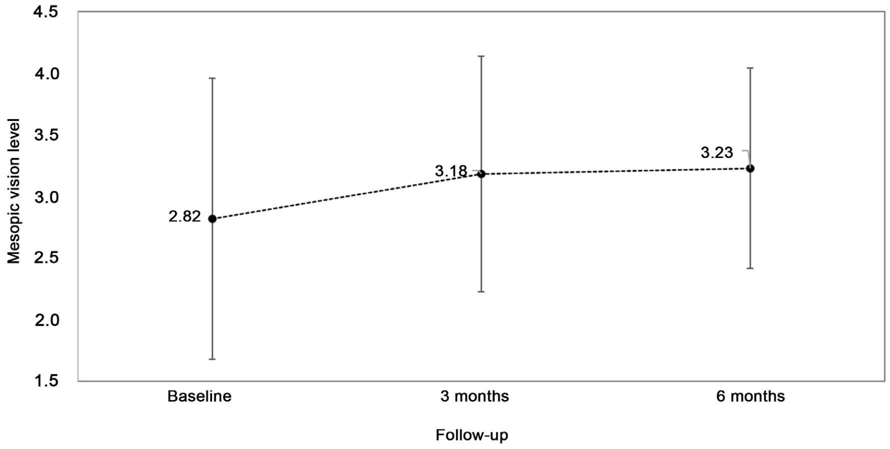

Figure 2. Changes in mesopic vision level during the follow-up.

Mean changes with the treatment in MPV, mesopic vision level, glare sensitivity level and contrast vision threshold were 2.2 (SD: 1.7; median: 2.0; range: 0.0 to 5.0), 0.4 (SD: 0.8; median: 0.0; range: −1.0 to 2.0), 0.4 (SD: 0.7; median: 0.0; range: 0.0 to 2.0), and −9.3 (SD: 16.1; median: −5.0; range: −65.0 to 0.0), respectively. An inverse significant correlation was found between the changes in MPV

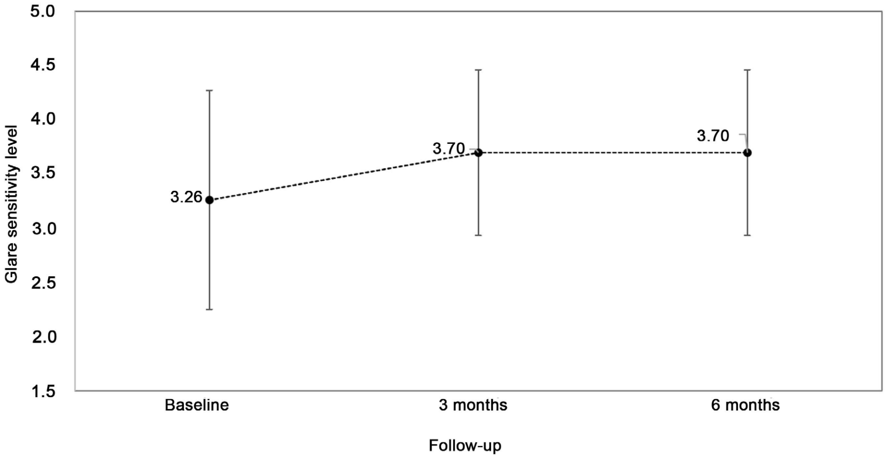

Figure 3. Changes in glare sensitivity level during the follow-up (higher value means better outcome).

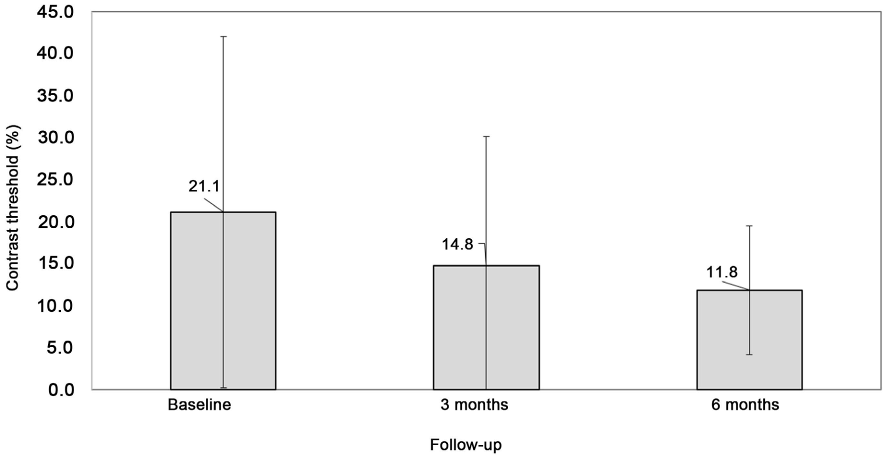

Figure 4. Changes in contrast vision threshold during the follow-up (lower value means better outcome).

with treatment and age (r = −0.433, p = 0.039) (**Figure 1**). However, this change did not correlate significantly with baseline MPV (r = −0.260, p = 0.232). The change in mesopic vision levels with treatment was found to correlate significantly with the baseline level of mesopic vision (r = −0.628, p = 0.002), but not with age (r = 0.174, p = 0.440). Similarly, the change in glare sensitivity level correlated significantly with the baseline sensitivity (r = −0.778, p < 0.001) and not with age (r = 0.272, p = 0.209). The change in contrast vision threshold during the follow-up also correlated with the baseline threshold (r = −0.625, p = 0.002). Age did not correlate with the change in contrast vision during the nutritional supplement intake (r = 0.301, p = 0.173).

4. Discussion

In the current study, the impact on the visual function of a specially formulated food supplement containing L and Z has been investigated in healthy subjects. The consumption of one capsule per day of the supplement containing 20 mg of

L and 2.8 mg of Z was associated with an increase in MPV, evaluated with a device based on the perception of Hadinger brushes. Different studies have investigated the benefit of using carotenoid-based nutritional supplements in pathological eyes, such as age-related macular degeneration (AMD) [21] [22] [23] [24] [25] or glaucoma, reporting significant changes in MP density [20]. Likewise, significant changes in MP density have been reported in healthy subjects using L-based nutritional supplements, as in the current study [8] [9] [11] [13]-[18]. Only Sasamoto *et al.* [20] found that daily supplementation with 6 mg of L did not affect the MP optical density level for 1 year, suggesting that 6 mg of L may be insufficient to increase MP density. In our series, a nutritional supplement containing higher levels of L combined with Z has been used and therefore the results are consistent with those obtained recently with other capsules also containing more than 6 mg of L. Concerning the differences to previous studies in terms of the magnitude of MPV changes, it should be considered that different devices, based on different physical concepts, have been used for measuring this parameter. Therefore, numerical comparisons are not accurate as devices for analyzing MP distribution are not exactly measuring the same variable. Indeed, to this date, this is the first series reporting MPV changes after the intake of a nutritional supplement using the MP-Eye device. Akuffo *et al.* [27] demonstrated in a comparative study that the MP measures obtained with customized heterochromatic flicker photometry (Macular Metrics Densitometer) and dual- wavelength fundus autofluorescence (Heidelberg Spectralis HRA + OCT MultiColor) were not comparable and should not be used interchangeably in any clinical or research setting. These authors showed that both devices could detect significant increases in MP following 6 months of supplementation with macular carotenoids in early AMD [27].

In the current study, MPV changed significantly from a baseline value of 2.74 ± 1.68 to 4.96 ± 2.08 after 6 months of nutritional supplement intake in a sample of 23 subjects in an age range from 19 to 56 years. Obana *et al.* [13] found in a previous study, evaluating the impact in 16 healthy subjects aged between 26 and 57 years, which the total volume of MP optical density measured by autofluorescence within 9˚ eccentricity significantly increased after 8 weeks of taking a high dose of L/Z supplement. Similarly, Richer *et al.* [8] reported a significant increase of MP optical density in 33 subjects taking a 14 mg Z/7 mg L-based supplement during 6 months: 0.41 ± 0.05 and 0.35 ± 0.04 density units in the right and left eyes, respectively. Machida *et al.* [14] also found improvements in MP optical density after administration of 12 mg L for 16 weeks in 59 healthy male and female adults aged 20 - 69 years. Therefore, our results are in line with previous research, demonstrating the benefit of this type of carotenoid-based supplements in terms of MP.

In our series, the increase in MP was associated with significant changes in mesopic vision, glare sensitivity and contrast vision threshold. This finding was coherent, considering that a consistent relationship has been found between MP and visual function in other studies [4] [8] [9] [14] [15] [17] [18]. Furthermore, MP density has been suggested as an indirect indicator of neural health [3]. Specifically, Nagai *et al.* [4] found that MP optical density was correlated with the retinal neural volume of the ganglion cell layer, inner plexiform layer, and outer nuclear layer of the retina. Considering this, it may be expected that the oral supplementation of carotenoids that complement the MP in healthy subjects is associated with potential improvements in some visual functions, as reported previously by a great variety of authors [8] [9] [14] [15] [17] [18]. Richer *et al.* [8] demonstrated that the intake of a 14 mg Z/7 mg L-based supplement in healthy subjects led to significant improvements in contrast sensitivity (CS) with glare and glare recovery time as well as a decreased preferred luminance required to complete visual tasks. Likewise, these authors also found that the increase in MP with the supplement was also associated with improvements in useful field of view (UFOV) scores of divided attention and improved composite crash risk score, which are important factors for night driving [8]. Stringham *et al.* [9] found that increases in MP optical density with carotenoid-based supplementation led to enhanced lateral inhibitory processes in healthy young subjects, which corresponded to improved CS. Obana *et al.* [17] found in 36 healthy volunteers that the consumption of L-based supplements was associated with glare sensitivity improvement in a subgroup of retinal responders (increasing of both MP optical density levels and serum L concentrations), but no remarkable changes in CS were detected. Nolan *et al.* [14] showed that healthy subjects consuming a formulation containing 10 mg L, 2 mg Z, and 10 mg MZ daily experienced statistically significant improvements in CS at 6 and 1.2 cycles/degree. Therefore, the results of the current series are consistent with the previous scientific evidence on visual function changes with MP increases due to carotenoid-based supplementation.

Finally, the relationship between changes in MPV, mesopic vision, glare disability and contrast vision and the baseline magnitude of these parameters were investigated. An inverse correlation was found between the change in MPV and age which means that more improvement can be obtained in MPV in younger subjects. It should be considered that MP optical density levels were found to decline by more than 10% each decade [28]. Furthermore, correlations were found between changes in mesopic vision level, glare sensitivity and contrast threshold and their corresponding baseline values. These results indicate that a higher improvement can be achieved in those subjects with a worse baseline visual function, which makes sense as there is more room for improvement in such cases.

This study has some limitations: First, no control group was included and consequently no comparison can be done with the use of other components or the absence of dietary supplement use. Second, the sample size is limited and for this reason current results should be confirmed in future studies with larger samples, including not only healthy eye, but also pathological eyes. In any case, dietary supplementations based on L and Z has been previously demonstrated, as mentioned before, to be useful for increasing MPV measured with other device. Therefore, our results are consistent with previous scientific evidence.

In conclusion, the specially formulated food supplement Eagle Eye Lutein 20 Vision Caps, containing 20 mg L and 2.8 mg Z, taken for 2 months by healthy subjects induced a significant increase in macular pigment volume, and consequently an improvement in mesopic vision, glare sensitivity and contrast sensitivity. More improvement can be achieved in younger subjects with worse visual function at baseline, suggesting that this treatment might be an interesting option to prevent further MP decrease and visual deterioration in younger subjects. This should be investigated further in future studies.

Conflicts of Interest

The author declares no conflict of interest.

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