Preliminary Results in Macular Pigment Optical Density Associated with and without Zeaxanthin and Lutein Supplementation

Abstract

Purpose: To determine the change in macular pigment optical density (MPOD) after subjects with low macular pigment decide to either take lutein and zeaxanthin supplementation or forgo supplementation for one year.

Methods: One hundred and ninety eight healthy subjects, 122 women, and 76 men in a clinical setting with low MPOD scores comprised two groups, who either take Lutein (L) and Zeaxanthin (Z) supplements or do not take supplements. All were followed for 12 months.

Results: After 12 months, MPOD had increased by 0.11 AU in the supplement group and decreased to 0.06 AU in subjects who opted not to take supplements. The changes between the two groups were statistically significant (p< 0.0001).

Conclusion: Adding zeaxanthin and lutein, along with other minerals and antioxidants to the diet in subjects with low MPOD resulted in an increase in MPOD scores. Interestingly, in subjects that did not add supplementation to their diet the MPOD scores were reduced. Although diet can play a major role in the increase or decrease of MPOD, our data point to the possibility of enhancement of low MPOD through supplementation.

Factors affecting a patient’s risk for ARMD include exposure to the sun, family history, gender, age, medical history, smoking, poor diet, obesity, and low levels of macular pigment. Individuals that experience excess exposure to sunlight coupled with low serum levels of antioxidants are among the highest at risk. Nolan et al. [8] summarized that any protective effect of MP depends on its ability to guard against chronic and cumulative retinal oxidative damage provoked either by phototoxic blue light or as a result of high oxygen metabolism, will need to be monitored in the young to middle-age.

While the cornea and lens absorb the shorter wavelengths of blue light, longer wavelengths of blue light do pass through to the retina causing cumulative damage over time [9]. One function of the macula pigment is to filter blue light so as not to create an inflammatory response within the retina [10]. Macular pigment is thought to protect against retinal damage by filtering out phototoxic short-wavelength visible light and by defending rod outer segment membranes from oxidative stress [11]. When individuals do not have sufficient macular pigment they are at higher risk of developing ARMD [12-14] because structures posterior to the macular pigment will have a greater exposure to the blue light compared to those of a person with normal to high levels of macular pigment. As a result, we might expect a greater incidence of ARMD among people having a low macular pigment density. In addition to the macular pigment functioning to filter high-energy blue light, it also functions as an antioxidant reducing toxic free radicals. This is important, as the retina is highly susceptible to oxidative stress given its high oxygen consumption and high metabolic turnover.
Macular pigment is a yellow compound, is preferentially distributed in the fovea in the Henle fiber layer which consists of foveal cones’ axons, and in the para fovea; macular pigment is also located in the inner plexiform layers of the retina and RPE (7). It is composed mainly of two carotenoids, lutein, and zeaxanthin which are thought to act as antioxidants and filters of blue light. Zeaxanthin and lutein are not synthesized by the human body and are found in fruits and green leafy vegetables. Their concentration correlates to macular pigment optical density (MPOD) [15]. Meso-zeaxanthin (MZ) is also present in the macula due to the conversion of lutein to MZ. Unlike zeaxanthin and lutein, MZ while not a significant component of a normal diet, can nonetheless be absorbed into the serum [16]. Where as in another study Meso-zeaxanthin is synthesized through a chemical alteration of lutein and not present in serum [17].

MPOD is modified by peak blood serum levels of lutein and zeaxanthin, therefore dietary intake affects MPOD levels. Researchers have increased macular pigment density through dietary intake of foods such as spinach and corn, [18,19] and through lutein/zeaxanthin supplementation [20]. A higher dietary intake of foods rich in lutein and zeaxanthin has been associated with a lower risk of developing advanced exudative ARMD [21].

The value of antioxidant intake on ARMD progression was demonstrated by a reduction in progression of 17% in patients taking only antioxidants, a 21% reduction in progression in patients only taking zinc (Blue MT), and a 25% reduction in progression in patients taking antioxidants and zinc [22]. Richer et al. [23] point out in the Lutein Antioxidant Supplementation Trial (LAST) study that those individuals in greatest need of supplementation, those having the lowest levels of measured macular pigment optical density (MPOD), represent the population with the greatest increase in MPOD.

The purpose of this paper is to investigate whether the intake of carotenoids, lutein and zeaxanthin, can change absorption unit (AU) and thereby change MPOD tested by heterochromatic flicker photometry. This pilot study documented the effects on the MPOD of those subjects without ARMD but suffering from low MPOD levels who decided to accept the therapy of lutein and zeaxanthin and to subjects who decide to forgo the therapy. This pilot evaluation was to compare the change in MPOD in subjects with MPOD scores below 0.30 as a function of supplementation or no supplementation.

Methods

Subjects were eligible for this pilot investigation if they were over the age of 18 and had low MPOD readings. For the purpose of this study, we have defined low MPOD to be 0.30 based upon the average values in normal subjects in the literature [24-28]. The other eligibility criteria were self-identified good health and the ability to return for a second comprehensive eye examination performed 12 months after the initial examination. Subjects were contacted by mail to participate, informed of the nature of the study, and asked to sign an informed consent form approved by the IRB. The study followed the tenets of the Declaration of Helsinki. Each subject recruited into the study was identified as having an annual comprehensive eye examination with a fundus evaluation to ensure that no observable pathologies were present.

Subjects were given the option of adding EyePromise® Restore, a dietary supplement containing Zeaxanthin, Lutein, Omega 3 fatty acids, Tocopherols and antioxidants to their daily intake. Subjects included in this study composed two groups, those who accepted the option of supplementation and those who decided not to add supplementation to their diet. The supplement was a single-dose, containing 4 mg Lutein, 8 mg Zeaxanthin, 120 mg Vitamin C (ascorbic acid), 60 IU Natural Vitamin E (d-alpha tocopherol), 125 mg Omega 3, 10 mg alpha lipoic acid, and 6 mg of mixed tocopherols. Supplemented subjects consumed one soft gel daily for one year and were instructed to take the supplement with a meal that contained at least a small amount of fat providing good bioavailability.

MPOD was measured by the QuantifEye® instrument, distributed by Zeavision. The QuantifEye® uses heterochromatic flicker photometry to determine the level of filtering properties of the macular pigment which provides diagnostic information about MPOD. The MPOD measurement is defined as absorbance which is the same as optical density unit ODU or absorbance unit AU. This is a logarithmic unit used to measure optical density, the absorbance of light transmitted through a partially absorbing substance. If T is the percentage of light transmitted, then the absorbance is defined to be \(-\log_{10} T\) absorbance units. No other data were collected.

Kinkelder determined the QuantifiEye device, MPS 9000 series: Tinsley Precision Instruments Ltd., Croydon, Essex, had good correlation with a fundus reflectance method. They found high agreement between test and retest measurements of QuantifEye (0.02±0.18) and the fundus reflectance method. Kinkelder [29] suggested the Macuscope (MacuVision Europe Ltd., Lapworth, Solihull, UK, was not a repeatable and reliable test because of low agreement with test and retest measurements. They also found the macuscope had poor agreement with fundus reflectance measurements. Others have found similar results and is the reason why we determine the QuantifiEye was the best test for our investigation [30-37]. At each visit patients were tested twice using the technique of heterochromatic flicker photometry (HFP).

Means were calculated for MPOD at the baseline and twelve-month visit. Comparisons were made between the two groups at baseline using a t-test to determine similarity at baseline. Changes over time between the two groups were also completed using a t-test, a chi-square test was used to compare categorical variables, and an analysis of variance that controlled for the baseline amount of MPOD was done.

Results

One hundred and ninety eight healthy subjects (n=198) in total, 122 women, and 76 men equally were divided into two groups: one group (n=100) opted to take the supplement and the other group (n=98), opted not to take the supplementation both group patients were followed up with ocular exams at 12 month
Preliminary Results in Macular Pigment Optical Density Associated with and without Zeaxanthin and Lutein Supplementation

Table 1 presents the MPOD data for the subjects for the two visits. Baseline MPOD for the subjects who supplemented was 0.27 AU ± 0.13, while those who did not supplement had a baseline MPOD of 0.25 AU ± 0.13. The two groups did not differ significantly at baseline (p-value = 0.21). After 12 months, the MPOD had increased to 0.38 AU ± 0.15 in the supplement group and had decreased to 0.19 AU ± 0.07 in those who chose not to supplement. The changes between the two groups were statistically significant (p< 0.0001) (Figure 1), even after controlling for baseline MPOD in an analysis of variance.

Table 2 categorizes subjects by their change in MPOD (no change, increase, or decrease) over the year of supplementation. Seventy-eight percent (78%) of subjects had an increase in their MPOD scores after one year of supplementation. Three-quarters (3/4) of the subjects who did not take supplements had a decrease or remained the same in their MPOD scores after one year (chi square p-value <0.0001).

Discussion

This pilot study was designed to investigate the change in MPOD measurement for a group of subjects without ARMD but who did have low MPOD levels taking lutein/zeaxanthin supplement and for a group who did not take the supplement. This study questioned the modifiability of MPOD scores by changing subject’s ingestion of antioxidant supplements. At the end of the study, those subjects who agreed to take supplements had an average MPOD of 0.39 AU. This is similar to a report from Van der Veen who studied the US population and found that MPOD scores averaged 0.33 AU, although no investigation has studied the optimal range of acceptable MPOD [38]. Additionally those subjects who did not add supplementation to their diet not only failed to show increase in macular pigment on average but in the majority of cases showed a decrease from baseline levels. MPOD is a variable measurement dependent on renewal, ingestion, absorption, metabolism, and utilization. This study only looked at the ingestion aspect of lutein and zeaxanthin.

A reduced macular pigment layer allows blue light through to the photoreceptors and reduces its protective nature. Maintaining high levels of both zeaxanthin and lutein either by supplementation or the ingestion of foods containing these carotenoids to increase the macular pigment layer may reduce this one risk factor of ARMD. While no study has evaluated subjects with low MPOD prior to the onset of ARMD, the Blue Mountain Study, Beaver Dam Study and Aged-Related Eye Disease Study have shown that a higher dietary intake of lutein and zeaxanthin is associated with a reduced risk of developing advanced ARMD [39-41]. The LAST study demonstrated that lutein in combination with other antioxidants significantly increased MPOD and glare recovery, near visual acuity, and contrast sensitivity [42]. The outcomes of the LAST study supported the notion that subtle signs of photoreceptor and retinal pigment epithelium disturbances characteristic of ARMD, such as glare recovery difficulties, degraded contrast sensitivity, scotomas, and metamorphopsia often occur long before the appearance of obvious fundus signs, when up to 80% of photoreceptors and retinal pigment epithelium complexes are already gone. The conclusion of the study raised the possibility that antioxidant intervention may be useful in patients without macular degeneration to protect the retina.

“The Zeaxanthin and Visual Function (ZVF) Study in AMD” concluded that zeaxanthin increased estimated Macular Pigment in AMD patients similar to lutein at 1 year. Researchers determined that adding zeaxanthin supplementation to an ARMD patients’ vitamin regimen is logical based on the Zeaxanthin’s
Preliminary Results in Macular Pigment Optical Density Associated with and without Zeaxanthin and Lutein Supplementation

Acknowledgment

The authors thank Natalie Cogswell and Lisa A. Jones-Jordan, PhD, for assistance with statistics.

References

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