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Abstract

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THE EFFECT OF LUTEIN INTAKE ON MACULAR PIGMENT DENSITY

By

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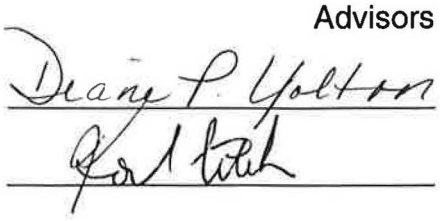
Advisors



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Abstract

Age related macular degeneration (AMD) is a sight-threatening retinal disease found predominately in men and women over 65 years of age. AMD is thought to result from oxidative damage to the retina triggered by UV and blue light. Recent studies have suggested the onset and progression of AMD may be delayed by diet supplementation with antioxidants like lutein and zeaxanthin which are found in the macular area as the macular pigments. The density of the macular pigments can be quantified using heterochromic flicker photometry. In this study, 29 optometry students, between the ages of 22 and 30, were divided into groups. Group one, the control group, experienced no intervention, group two took 4 mg of lutein daily for 30 days and group three ingested 0.75 ounces of spinach daily for 30 days. The macular pigment density was assessed at baseline before any intervention, after 30 days of supplementation and again 30 days after discontinuing supplementation. Neither lutein nor spinach increased the macular pigment density in this study.

Introduction

Age-related macular degeneration (AMD) is a progressive retinal disease. It is the leading cause of blindness in those over 65 years of age in Western countries.(15) AMD has two forms: dry (atrophic) and wet (neovascular). While neovascular AMD can be treated with laser therapy, the atrophic form has no accepted treatment.

AMD is thought to be due to free radical formation. Light entering the eye is focused on the macula. Blue light can cause free radical formation in the photoreceptor outer segments where stacks of membrane discs with unsaturated fatty acids are at risk from these reactive molecules. The radicals damage the membranes in the discs and when the discs are phagocytized by the RPE, these damaged membranes cannot be digested. They accumulate within the RPE cells as lipofuscin and are also deposited on Bruch's membrane as drusen.(2) As more damage occurs, the RPE cells die and, as a consequence, the photoreceptors die.

Many factors are associated with increased risk of developing AMD. Patients who have light irides are at higher risk, as are smokers.(2) Factors such as diabetes, hypertension, age, and atherosclerosis are also thought to contribute to AMD.(6)

Recent research has suggested that nutrition may play a large role in AMD. One nutrient that may have a critical role in macular health is lutein. Lutein gives the macula its characteristic yellow appearance and protects the macular tissue from short wavelength (blue) light by acting as a filter between the incoming light and the photoreceptors. Lutein is a fat-soluble xanthophyll pigment in the carotenoid classification.(15) Humans receive lutein from the diet. It is found in egg yolks, dark green, leafy vegetables, yellow vegetables, and fruit.(16) Kale, amaranth flour, spinach, and green peas are all excellent examples of foods rich in lutein.(19) In addition to being a filter, lutein is an antioxidant. Antioxidants can neutralize free radicals.

The amount of lutein in the diet can be assessed using a food frequency questionnaire. The questionnaire surveys the amount of specific foods consumed and then calculates a daily lutein intake.

Macular pigment density (lutein and zeaxanthin concentration) can be measured using heterochromic flicker photometry. In this technique, blue and green lights are flickered in counter-phase, and the subject is asked to match the brightness of the two lights. Brightness match is determined when the lights are present to the macula and again when they are presented in the perimacular area where the concentration of lutein is low. The match value to the perimacular area provides an indication of the relative absorbances of blue and green lights by the media of the eye exclusive of the macular pigment, and the match for macular stimulation indicates the absorbance of the media plus the macular pigment. The difference in the macular and perimacular match values indicates the macular pigment density.

Recent studies have presented strong evidence that increased dietary lutein intake can increase the amount of lutein in the macula.(10) More lutein concentrated in the macula is thought to decrease the risk or slow the progression of ARM damage. One study documented partial to total reduction in patients' scotomas or metamorphopsia with increased dietary consumption of dark-green leafy vegetables.(17)

Our study evaluated macular pigment density in subjects without ocular disease. We examined the effects of lutein supplementation in the form of a prepared lutein supplement or a food source (raw spinach) on macular pigment density.

Methods

Subjects

Twenty-nine subjects, all optometry students, were involved in this study. Fourteen were females and 15 were males ranging from 22 to 30 years of age. All subjects had good ocular and systemic health.

Subjects were divided into 3 groups: a control group who received no intervention, a group who took one lutein supplement (4 mg) a day for 30 days and a group who ingested 0.75 ounces of spinach per day for 30 days.

Supplementation

The lutein supplements that we used were FloraGlo lutein capsules containing 4 mg of lutein extracted form marigold flowers, as lutein esters, enzymatically hydrolyzed, and purified to crystalline form.(7,13) Subjects in this group took one capsule per day. Our other subject group was required to eat 0.75 ounces of spinach per day. This amount has been shown to contain approximately 3.8 mg of lutein.(10)

Dietary Assessment

Before the onset of the experiment, dietary intake of lutein and other nutritional factors was gathered from all subjects using a Food Frequency Questionnaire from Block Data Dietary Systems. This questionnaire surveyed specific foods: the frequency of ingestion, the amount ingested and the number of servings. This data was then analyzed by Block Data Dietary Systems to give the daily intake of various nutrients. The dietary survey was administered two times about a year apart to determine if the lutein intake of the subjects changed over that period of time.

Measurement of Macular Pigment Density

Macular pigment density was measured using heterochromic flicker photometry. The optical system for this technique is illustrated in Figure 1. A

xenon arc source was divided into three beams by a beam splitter and front surface mirror. Neutral density filters control the amount of light passing through the system. Interference filters produce the desired wavelength of 460 nm for the measuring field and background field, and 550 nm for the reference field. Apertures were used to concentrate both the reference field and measuring field to subtend one degree, and the background field to subtend ten degrees. A rotating sectored wheel produces the flickering test stimulus by alternating the transmission of the measuring field and reference field. The subject's eye position was monitored using a low powered telescope. The three fields were combined into one field through the use of beam splitters and a front surface mirror, and the combined image of all three apertures was placed at the subject's pupil by an achromatizing lens.

Minimal flicker was achieved at 5.5 degrees from the macula, where macular pigment is optically undetectable, by adjusting the luminance of the measuring field. The target was then presented at the macula and subjects re-adjusted the luminance of the measuring field with a variable density beam splitter to achieve minimum flicker. Macular pigment measures were based on the difference in neutral density filter used in the periphery to the neutral density filter used at the macula when minimal flicker was achieved. Multiple measures were taken on each eye for both macular and perimacular positions. Macular pigment measures are expressed in equivalent terms of neutral density filters.

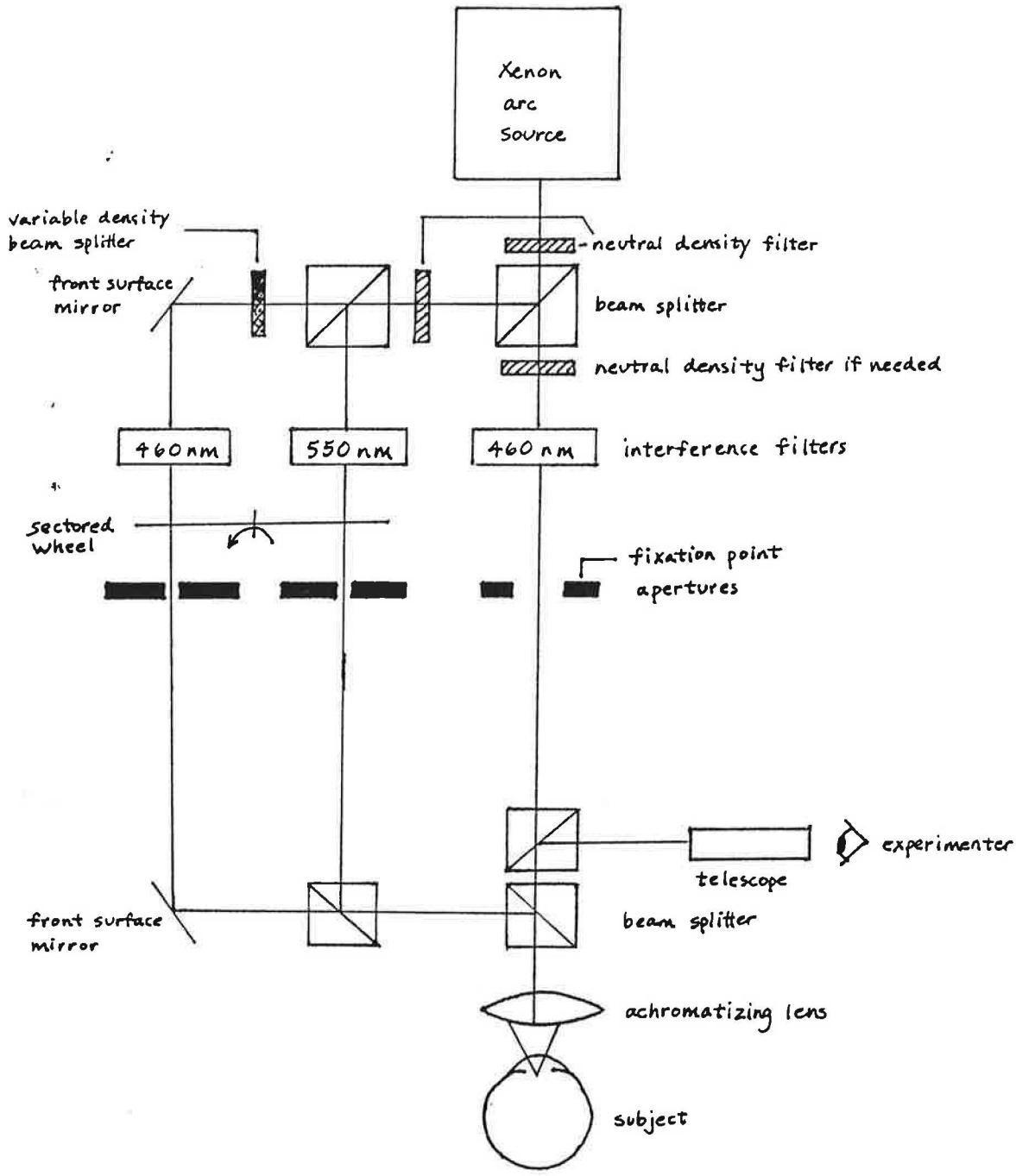

Figure 1.
Optical system for measuring macular pigment density

Results

Macular pigment density values for the three groups at baseline, after one-month supplementation and again after a one-month washout are shown in Table 1. Macular pigment density did not increase following lutein or spinach supplementation for one month.

The lutein intake as determined by the Block food frequency questionnaire is also shown in Table 1. There was no significant difference between the lutein intake values measured about a year apart.

Table 1. Daily Intake of Lutein and Macular Pigment Density

ID #	M/F	Age	Lutein (ug/day) Diet Intake	Lutein (ug/day) Diet Intake	Macular Pigment Density	Macular Pigment Density	Macular Pigment Density
			1st msrmt	2nd msrmt	Baseline	Intervention	Washout
Control							
16	F	22	640.66	212.43	0.025	1.38	0.44
17	F	27	2877.65	2812.16	0.44	1.37	0.75
32	F	24	1296.54	1117.08	0.56	0.06	1.06
38	F	27	405.03	574.71	0.19	1.31	0.44
41	F	24	1086.3	356.94	0.19	0.06	1.56
20	M	23	944.27	571.81	0.88	-0.94	1.13
24	M	23	1660.05	2234.42	0.19	1.06	0.5
27	M	23	1316.67	713.68	0.25	0.43	0.44
35	M	29	870.91	1871.49	0.63	0.63	0.5
n			9	9	9	9	9
Mean			1233.12	1162.75	0.373	0.596	0.758
S.D.					0.274	0.783	0.405

Table 1 continued.

Lutein							
1	F	22	825.95	52.5	0.5	0.19	0.38
31	F	23	388.01	326.43	0.13	0.63	0.56
33	F	27	503.1	474.46	0.69	0.75	1.06
39	F	27	1116.01	849.4	1.13	0.62	0.88
40	F	22	583.67	590.86	1.63	0	0.69
6	M	23	531.66	802.51	0.06	0.56	1
7	M	27	1947.36	4015.67	1.19	0.94	0.06
13	M	25	1343.64	614.74	2.06	1.81	0.88
19	M	28	805.38	639.49	0	0.69	0.56
n			9	9	9	9	9
Mean			893.86	929.56	0.821	0.688	0.674
S.D.					0.731	0.509	0.322
Spinach							
11	F	23	461.85	877.69	0.31	0.068	0.5
14	F	22	4056.47	493.46	0	0.06	0.31
26	F	24	4755.09	2940.66	0.75	0.62	0.44
42	F	23	248.56	708.37	0.81	0.25	1.38
10	M	23	644.08	508.66	0.94	0.5	1.63
12	M	22	745.13	775.32	-0.31	-0.93	0.13
15	M	22	248.65	618.14	1.31	1.63	0.25
25	M	24	1825.92	2683.11	0	0	0.19
30	M	22	943.43	928.97	0.5	0.88	0.13
34	M	27	751.52	1329.95	0.56	1.07	0.44
37	M	24	522.82	636.46	1.13	0.44	0.88
n			11	11	11	11	11

Discussion

Numerous investigators have found that patients with higher concentrations of the carotenoids, lutein and zeaxanthin, have lower rates of AMD.(5,7,12,20) Biochemical analyses have shown that dark, green leafy vegetables, such as spinach and collard greens, and egg yolk are particularly rich sources of lutein and zeaxanthin.(5,7,8,10,12) Of utmost importance is lutein however, because lutein is also converted to zeaxanthin in the retina, therefore being the more essential carotenoid.(5,7)

It has been noted that a typical diet high in fruits and vegetables would be expected to contain about 2.3 mg/day of lutein.(10) The average daily diet, however, only contains 0.6-0.8 mg/day of lutein.(7) In our study, for example, lutein in our subjects's diets range from 0.25 mg/day to 4.7 mg/day. (Table 1) On average, these values are not enough to make a significant difference in macular pigment density.(10) It has also been shown that macular pigment density remains elevated for some time after discontinuing supplements, possibly for up to 8 weeks.(7,10) This protection can be explained by the fact that these carotenoids are accumulated in the macular region of the retina in high concentration.(5,7,18) Although the FDA has not yet set a Recommended Daily Allowance (RDA) for lutein, it seems that there is enough evidence to suggest that more than the average intake of lutein would be protective.(7)

There are also suggestions throughout the literature that show an accelerated loss of macular pigment density with age.(12) Thus, it is especially critical for elderly patients to be taking supplements to maintain high levels of carotenoids in their system.(20) Unfortunately, diet surveys in the United States have shown that older people have a low intake of lutein.(20)

Numerous studies have explored that role of nutrition in eye health. We wanted to be sure to use a reliable, well-accepted method for evaluating the nutritional value of our subject's diets. The Food Frequency Questionnaire (FFQ), from Block Data Dietary Systems, seems to be a valid, yet simple

assessment of the daily diet.(3) The intake of lutein in two food frequency questionnaires evaluated about one year apart show the diets of the subjects were stable with regard to lutein .

Several problems in the methods used in this study can be suggested. Assessing the density of macular pigment is difficult. All subjects reported difficulty in observing the light flicker. In another study, Bone and Sparrock also using an apparatus with the flicker technique, concluded that this technique for measurement is difficult.(4) A simpler technique for measuring macular pigment density may give more accurate results.

Studies have suggested that there may also be methodological errors in measuring the macular pigment density such as accommodation, retinal illuminance (depending on pupil size), accuracy of fixation and age variations. However, it should be noted that Werner, et al. (21) has done a study showing that accommodation differences were not associated with a change on macular pigment density; and that neither miosis nor mydriasis had any effect. As for age variations, their study used subjects with a much wider distribution of ages, 10-90 years old, than ours, which was 22-30 years old, and still showed that there was not a statistically significant difference related to age.(7,21) As well, their data showed that the stimulus could be enlarged to 3° without altering the macular pigment density estimates, and no subjects varied their fixation greater that ±1.00°, therefore, showing no changes due to fixational accuracy.(21) Another study also backs this up by an analysis of the atrophic area in AMD, implying that the region out to 4° is particularly vulnerable to damage, so measurements into this area are still useful.(11)

It should also be noted that there have been studies to show that interocular differences in macular pigment density may exist, as well as day-to-day differences in measurements, even in the same eye.(9) This may suggest that results that vary just slightly in their measurement may not accurately portray changes in macular pigment density due to supplementation alone. After reading numerous other studies, it seems that our lutein dosage and length of time on the

supplements, was not long enough to see results. These other studies have suggested that changes in macular pigment density are only seen when dosages of lutein supplements were from 20-40 mg/day (7), or when 60g of spinach per day was used (10.8 mg of lutein).(10) It has also been suggested that the supplement needs to be taken for more than 30 days to start to see increases in pigment density, and the pigment density plateaus in 6-14 weeks after starting the supplements.(7,10) Since our subjects were only required to take their supplements over a 30 day period, lutein was not sustained in the system long enough to have any effect.

Although our study showed no significant results, we have reviewed numerous studies that do show significant effects of dietary supplements on macular pigment density. Therefore, we would suggest that until further conclusions are drawn, all patients at risk for AMD should take vitamin supplements containing carotenoids such as lutein. Several manufacturers have already introduced many products directed toward eye health, which we believe would be beneficial.(20)

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