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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

# Effect of Different Doses of Lutein and Zeaxanthin on Macular Pigment Optical Density

## Maküler Pigment Optik Yoğunluğuna Farklı Doz Lutein Ve Zeaksantinin Etkisi

Osman Sayin[1], Hasan Altinkaynak[1]

[1]Health Sciences University, Konya City Hospital, Department of Ophthalmology, Konya, Türkiye

**ÖZET**

**Amaç:** Sağlıklı bireylerde, iki farklı lutein ve zeaksantin dozunun maküler pigment optik yoğunluk (MPOY) üzerindeki etkilerini heterokromatik fliker fotometre (MPS II) yöntemi ile değerlendirmek.

**Gereçler ve Yöntemler:** 20 sağlıklı bireyin 20 sağ gözü çalışma kapsamına alındı. Olgular eşit sayıda olmak üzere randomize iki gruba ayrıldı. Grup 1'deki olgular 5 mg lutein ve 1 mg zeaksantin takviyesi alırken Grup 2'deki olgular 10 mg lutein ve 2 mg zeaksantin takviyesi aldı. Grup 1 ve Grup 2 olgularda takviye öncesi ve takviye sonrası 1.ay MPOY değerleri karşılaştırıldı.

**Bulgular:** Olguların yaş ortalaması grup 1'de 34.0±6.9 iken grup 2'de 33.4±6.8 idi. Grup 1'deki olguların sağ gözlerinin destek tedavisi öncesi ve destek tedavisi sonrası 1.ay MPOY değerleri sırasıyla ortalama 0.41±0.09 ve 0.41±0.10 olarak ölçüldü. Sol gözlerinin destek tedavisi öncesi ve destek tedavisi sonrası 1.ay MPOY değerleri ise sırasıyla ortalama 0.44±0.14 ve 0.42±0.12 olarak ölçüldü. Grup 2'deki olguların sağ gözlerinin destek tedavisi öncesi ve destek tedavisi sonrası 1.ay MPOY değerleri sırasıyla ortalama 0.39±0.10 ve 0.37±0.11 olarak ölçüldü. Sol gözlerinin destek tedavisi öncesi ve destek tedavisi sonrası 1.ay MPOY değerleri ise sırasıyla ortalama 0.41±0.12 ve 0.39±0.11 olarak ölçüldü. Değerler istatistiksel olarak anlamlı bulunmadı (p>0.05).

**Sonuç:** Sağlıklı bireylerde, 5 mg lutein ve 1 mg zeaksantin takviyesinin (Grup 1) ve 10 mg lutein ve 2 mg zeaksantin takviyesinin (Grup 2) MPOY üzerine 1.ayda istatistiksel olarak anlamlı etkisi bulunmamıştır.

**Anahtar Kelimeler:** Hetereokromatik fliker fotometre, lütein, maküler pigment optik yoğunluk, zeaksantin

**ABSTRACT**

**Aim:** To evaluate the effects of two different doses of lutein and zeaxanthin on macular pigment optical density (MPOD) in healthy subjects using heterochromatic flicker photometer (MPS II) method.

**Materials and Methods:** 20 right eyes of 20 healthy subjects were included in the study. The subjects were randomly divided into two groups with equal numbers. Group 1 received 5 mg lutein and 1 mg zeaxanthin supplements, while Group 2 received 10 mg lutein and 2 mg zeaxanthin supplements. MPOD values before and 1 month after supplementation were compared in Group 1 and Group 2 subjects.

**Results:** The mean age was 34.0±6.9 years in group 1 and 33.4±6.8 years in group 2. The mean MPOD values of the right eyes of the subjects in group 1 before and 1 month after supplement treatment were 0.41±0.09 and 0.41±0.10, respectively. The mean MPOD values of the left eyes of the subjects in group 1 before and 1 month after supplement treatment were 0.44±0.14 and 0.42±0.12, respectively. The mean MPOD values of the right eyes of the subjects in group 2 before and 1 month after supplement treatment were 0.39±0.10 and 0.37±0.11, respectively. The mean MPOD values of the left eyes of the subjects in group 2 before and 1 month after supplement treatment were 0.41±0.12 and 0.39±0.11, respectively. The values were not statistically significant (p>0.05).

**Conclusion:** In healthy subjects, 5 mg lutein and 1 mg zeaxanthin supplementation (Group 1) and 10 mg lutein and 2 mg zeaxanthin supplementation (Group 2) had no statistically significant effect on MPOD at 1 month.

**Keywords:** Hetereochromatic flicker photometer, lutein, macular pigment optical density, zeaxanthin

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**Sorumlu Yazar/Corresponding Author:** Osman Sayin, Sağlık Bilimleri Üniversitesi, Konya Şehir Hastanesi, Göz Hastalıkları Kliniği, Konya, Türkiye
**e-mail:** drosmansayin@gmail.com

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## INTRODUCTION

Lutein and zeaxanthin (L/Z) are two fat-soluble antioxidants belonging to the carotenoids class (1, 2). Together with their isomer meso-zeaxanthin, they are the primary components of macular pigment (MP). Among the more than 1000 carotenoids found in nature, only L/Z and their metabolites are found in the human macula (3). Humans can not synthesize L/Z and must obtain them through dietary sources (4). These carotenoids are more concentrated in the macular region of the retina and are responsible for maintaining central vision (1). MP helps to protect the macula from the phototoxicity of blue light with its 460 nm absorption spectrum (5). Additionally, it acts as a free radical scavenger, protecting the macula from photochemical damage and serving an antioxidant function (5). Studies indicate that low MP levels are a risk factor for age-related macular degeneration (AMD), the leading cause of blindness in developed countries (6). Macular pigment optical density (MPOD) is a measure of L/Z concentrations in the macula (7). A relationship has been demonstrated between MPOD and visual function, contrast sensitivity, and photostress recovery (8). Dietary L/Z intake has been shown to support visual function by increasing MPOD and reduce the risk of developing AMD (9, 10). Ma et al. concluded that L/Z supplements could increase MPOD in patients with AMD and healthy subjects and reported a dose-response relationship (11). One of the first comprehensive studies on carotenoids, Eye Disease Case-Control Study, which compared nutrition with the risk of developing AMD, demonstrated that individuals with higher serum L/Z levels had a significantly lower risk of developing eye diseases (12). Furthermore, those consuming a diet containing 5.8 mg L/Z daily had a lower risk of AMD compared to those consuming a diet containing 1.2 mg L/Z daily (12).

Following the recognition of L/Z's effects on eye health, supplementation through dietary means or commercially available preparations has been considered. There is no consensus on the appropriate daily dose for L/Z supplementation. Toxicology studies have shown that L/Z does not pose health risks even at high doses (4, 40 and 400 mg/kg body weight) (13). The ocular effects of dietary L/Z intake at doses <5 mg/day are not fully evident (4). Studies have shown that total L/Z intake of <5 mg/day does not result in a statistically significant change in MPOD (4).

Further research is necessary to determine the minimum L/Z dose and duration required to elicit clinically significant effects on MPOD and visual function. The aim of this study is to determine whether there is a minimum concentration of L/Z intake that causes a statistically significant and/or clinically important change in MPOD over a 1-month period, and to evaluate the dose-response relationship between L/Z intake and MPOD.

## MATERIALS AND METHODS

The entire study protocol was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (date/number: 05.06.2023/18362). Patients who visited the ophthalmology clinic of Konya City Hospital between January 2021 and December 2021, underwent MPOD measurements following routine ophthalmologic examination, and were prescribed L/Z supplementation were analyzed. Patients with visual acuity of 10/10 on the Snellen chart and refractive error with a spherical equivalent value below ±2.0 D were included in the study. Patients with any eye disease or media opacity, intraocular surgery history, pregnancy, smoking history or systemic disease were excluded. After applying these criteria, 20 eyes of 20 healthy individuals were included in the study. The subjects were randomly divided into two groups with equal numbers. Group 1 consisted of patients who received 5 mg lutein and 1 mg zeaxanthin supplementation, while Group 2 consisted of patients who received 10 mg lutein and 2 mg zeaxanthin supplementation. MPOD values before and 1 month after supplementation were compared in both groups.

### *Examination protocol*

MPOD measurements were taken using a device employing the heterochromatic flicker photometry (HFP) technique (MPSII®, Elektron Technology, Switzerland). The device measures the amount of blue light absorbed by the MP in the patient's retina layer. A small stimulus alternating between green (530 nm) and blue (465 nm) is seen on a white background. If the brightness of blue and green light is not equal or the frequency of alternation is too high, the stimulus appears to flicker. Initially, the blue brightness is set to a relatively high value and the frequency is reduced until flicker is detected. Blue light is absorbed by the MP while green light is not. Patients are handed a device with a button and instructed to look at the target in the center. The device starts to display the alternating lights and the patients are instructedto press the button when a flicker is noticed. The MPOD value is automatically calculated by the MPSII device's software based on the graph generated from the patient's button presses during each flicker event. Normal MPOD values are between 0.00 and 1.00, with higher MPOD values indicating higher MP levels.

### *Statistical analysis*

Statistical analysis was performed using SPSS 22 (SPSS Inc., Chicago, Illinois, USA). The Kolmogorov Smirnov test was used to determine whether the data conformed the normal distribution. Parametric tests were preferred due to normal distribution. The Independent Samples Test was used to compare the parameters between the groups. The Mixed ANOVA test was used to compare the parameters before and after supplementation and to compare values between right and left eyes. P values <0.05 were considered statistically significant.

## RESULTS

Group 1 and Group 2 each comprised 5 males (50%) and 5 females (50%). The mean age of the patients was 34.0±6.9 years (min:29, max:40 years) in Group 1 and 33.4±6.8 years (min:30, max:39 years) in Group 2. In Group 1, mean MPOD values for right eyes of the patients before and 1 month after supplemenatation were 0.41±0.09 and 0.41±0.10, respectively

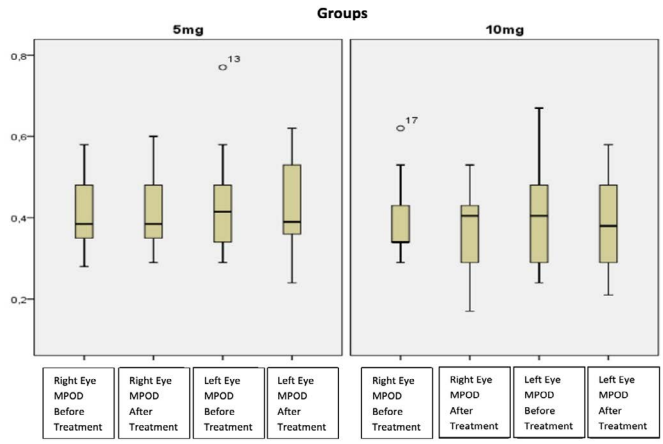


**Figure 1.** Box-plots of the groups before and after supplement treatment

(Figure 1). For left eyes, the values were 0.44±0.14 and 0.42±0.12, respectively. In Group 2, mean MPOD values for right eyes of the subjects before and 1 month after supplementation were 0.39±0.10 and 0.37±0.11, respectively. The mean MPOD values for left eyes before and 1 month after supplement treatment were 0.41±0.12 and 0.39±0.11, respectively.

The changes in MPOD values for right eyes of the subjects in Group 1 before and 1 month after the supplementation were not statistically significant (p=0.768) (Table 1). The changes in MPOD values for right eyes of the subjects in Group 2 before and 1 month after the supplementation were not statistically significant (p=0.559). The changes in MPOD values for left eyes of the subjects in Group 1 before and 1 month after the supplementation were not statistically significant (p=0.494). The changes in MPOD values for left eyes of the subjects in Group 2 before and 1 month after the supplementation were not statistically significant (p=0.349).

The mean spherical equivalent values for patients in Group 1 and Group 2 were -0.67±0.22D and -0.62±0.19D, respectively (p=0.802). There was no significant correlation between spherical equivalent value and MPOD (p=0.873, r=0.32 for male, p=0.914, r=0.37 for female). When right and left eyes of the patients in Group 1 were compared, mean MPOD values were 0.41±0.09 and 0.44±0.14 (p=0.303), respectively. When the right and left eyes of the patients in Group 2 were compared, the mean MPOD values were 0.41±0.10 and 0.42±0.12 (p=0.716), respectively.

## DISCUSSION

AMD is a multifactorial disease and oxidative stress caused by short wavelength blue light is considered to be an important factor in the disease (1). Numerous studies have investigated the relationship between MP and AMD, as MP protects against blue light hazards (1). Some studies have found significantly lower MPOD levels in AMD patients compared to normal eyes (6). Supplementation with macular xanthophyll carotenoids and antioxidants has been associated with delaying progressive macular diseases such as AMD (1). The large-scale clinical study investigating the effects of lutein and zeaxanthin supplements on preventing AMD (Age-Related Eye Disease Study 2 Research Group 2013) recommended antioxidant supplements containing L/Z (14). These AMD-preventive effects of carotenoids are due to their biochemical (anti-oxidant) and photochemical (blue light filtration) properties (5).

Studies have demonstrated that dietary L/Z intake is associated with the amount of MPOD (15, 16). However, the precise dosage required to increase MPOD remains unclear. Randomized, placebo-controlled studies investigating the effects of dietary L/Z intake of <5 mg/day on MPOD, have not shown statistically significant increases in MPOD (17, 18). In these studies, dietary L/Z intake was between 0.5 and 4.5 mg/day and participants were followed up for 3 to 6 months (17, 18). Whereas, studies using L/Z supplements between 5-20 mg/day for 3-12 months have shown statistically significant increases in MPOD (19, 20). Similarly, a statistically significant increase in MPOD value was also observed in studies in which L/Z supplementation was higher than 20 mg/day (21, 22).

MPOD is expected to increase by 0.003 optical density units (95% CI: 0.001 to 0.006) for every 1 mg increase in total daily L/Z intake (4). The increase in MPOD value was significantly higher in studies with ≥5 mg/day L/Z supplementation compared to those using <5 mg/day L/Z supplementation (4). There is a lack of literature evaluating MPOD effects using total daily L/Z doses between 5 and 10 mg. Comparing studies where L/Z was provided through dietary sources with those using L/Z-containing supplements, it is evident that patients can achieve higher L/Z doses with supplements (4). The total daily L/Z dose in dietary intervention studies typically remains <5 mg,

**Table 1.** Macular Pigment Optical Density Changes Before and After Supplement Treatment

| | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|
| | **Before Treatment** | **After Treatment** | **p*** | **Before Treatment** | **After Treatment** | **p*** |
| MPOD right | 0.41±0.09 | 0.41±0.10 | 0.768 | 0.39±0.10 | 0.37±0.11 | 0.559 |
| MPOD left | 0.44±0.14 | 0.42±0.12 | 0.494 | 0.41±0.12 | 0.39±0.11 | 0.349 |
| | | **Group 1** | | | **Group 2** | |
| SE | | -0.67±0.22D | | | -0.62±0.19D | 0.802# |

MPOD, Macular Pigment Optical Density; SE, Spherical Equvalan; *Mixed ANOVA #Independent samples test

while studies using supplements often reach levels ≥12 mg (4). When comparing studies using supplements containing only L/Z with those using preparations that include L/Z along with vitamin C, vitamin E, zinc, copper, and ω-3 fatty acids, no significant difference was observed in their effects on MPOD (20, 23).

Cardinault et al. (24) investigated MPOD changes in two groups aged 20-35 years and 60-75 years by giving 9 mg lutein and 0.45 mg zeaxanthin daily for 5 weeks and found no significant change in both groups. Similarly, our study showed no significant changes in MPOD levels in the right eye at either doses (p=0.168 for Group 1, p=0.559 for Group 2). This may be due to the relatively low additional L/Z dose and short supplementation period. A review of 46 studies suggested that L/Z intake for ≥3 months and at doses above 5 mg/day could increase MPOD concentrations by 0.04 to 0.11 optical density units in healthy adults (4). It has been observed that L/Z intake increases the MPOD value in healthy adults, especially at doses >10 mg/day. In our study, an increase in MPOD may not have been observed because low doses of L/Z were given. There seems to be a dose-response relationship in which higher doses of L/Z have a greater effect on MPOD. Since most studies of low doses of L/Z have evaluated dietary supplementation, it is difficult to determine the dose of L/Z, the effect of the dose of L/Z given and other effects of the dietary source.

## CONCLUSION

Our study found no statistically significant change in the amount of MPOD after 1 month in patients taking 5 mg lutein 1 mg zeaxanthin supplementation and 10 mg lutein 2 mg zeaxanthin supplementation. With the expected increase in AMD incidence due to global population aging, the optimal L/Z dosage and its relationship with MPOD remain unclear. Our study contributes to preventing unnecessary L/Z supplementation and ensuring adequate dosing. Future research is needed to determine the L/Z dose and duration that causes clinically significant increases in MPOD.

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***Address correspondence to:*** *Osman Sayin, Sağlık Bilimleri Üniversitesi, Konya Şehir Hastanesi, Göz Hastalıkları Kliniği, Konya, Türkiye*
***e-mail:*** *drosmansayin@gmail.com*

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