Changes in macular pigment optical density with age in healthy and in patients with dry age-related macular degeneration: a cross sectional study

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Abstract

Background

To study the changes in macular pigment optical density (MPOD) with age in healthy eyes and in patients with dry age-related macular degeneration (AMD) using the Macular Pigment Screener II (MPSII®).

Methods

One hundred and twenty-six eyes of 126 individuals (51 male, 75 female) were retrospectively evaluated. The MPOD was measured using the MPSII®, which uses a heterochromatic flicker photometry (HFP) method, and the estimated values were reviewed. Spearman's correlation test was used to evaluate the correlations between the MPOD and age. Simple linear regression analysis was performed to obtain determine the association between the MPOD and age and MPOD. The Kruskal-Wallis test was used to compare the MPOD between among the four groups, and the Mann-Whitney U test was utilized to compare the MPOD between the dry AMD group and the elderly controls

Results

Estimated MPOD values decreased significantly with increasing age (Spearman's correlation coefficient, -0.239; p=0.008) in the general population. In the simple regression analysis, a statistically significant linear regression model was observed, and the estimated values of the MPOD decreased by -0.005 as the age increased by one 1 year (p=0.001, Eestimated value of MPOD value = 0.884 – 0.005 ×x Aage). In the healthy population, the estimated MPOD values exhibited a decreasing trend with age, but there were no significant differences according to age, with the exception of patients with dry AMD (p=0.201). The MPOD was significantly lower in patients with dry AMD than in age-matched healthy controls (p=0.001).

Conclusions

Measurement of the MPOD using the MPSII® is feasible in both healthy individuals and in patients with dry AMD. Early detection of AMD and the contributing risk factors may be possible with regular MPOD screening in elderly patients or in patients with a reduced MPOD.

Background

Age-related macular degeneration (AMD) is a leading cause of legal blindness among elderly individuals in industrialized countries.(1, 2) Macular pigment (MP) concentrated at the center of the retina is thought to protect the retinal photoreceptors and retinal pigment epithelium primarily via its antioxidant properties and role as a filter for short wavelength blue light, and is believed to play a beneficial role in visual performance.(3-6) It has been demonstrated that healthy individuals with higher macular pigment optical density (MPOD) experience less disability glare and demonstrate better photo-stress recovery times.(5, 6)

The MP is composed of the hydroxy-carotenoids lutein, zeaxanthin, and meso-zeaxanthin(7) and the level of MP in the central retina is thought to also have an impact on the development of AMD.(8) Previous reports have demonstrated that dietary supplementation of carotenoids can increase(9) and is positively correlated with the MPOD in healthy subjects and also increases the MPOD in AMD patients, and thereby elicits an improvement in visual function including visual acuity, contrast sensitivity, and subject glare recovery.(10, 11)

Thus, measurement of the MPOD may be beneficial in evaluating the risk of AMD and the treatment effects of oral supplementation of carotenoids. The MPOD can be measured clinically using various objective methods and methods requiring subjective response,(12-15) such as Raman resonance spectroscopy,(16, 17) autofluorescence spectrometry,(18) and heterochromatic flicker photometry (HFP).(19)

The macular pigment screener II (MPSII®) (Elektron Eye Technology, Cambridge, UK), which is based on HFP, is now commercially available. To reduce the time required for the examination, the MPSII® proposes obtaining a more simplified value, namely, the estimated MPOD value from the foveal data with consideration of the subject’s age. Previous studies have reported that the estimated MPOD value obtained by the MPSII® is applicable to not only Caucasian individuals(20) but also Asian(21) individuals with or without AMD. Ozawa et al. reported that measurement of the MPOD using the MPSII® may be a crucial method in understanding the role of MP in the pathogenesis of AMD.(21) However, to the best of our knowledge, changes in the MPOD according to age have not yet been investigated and there have been no reports on the differences in MPOD according to the presence

and absence of AMD. In the present study, we aimed to analyze the changes in the MPOD as measured by the MPSII® according to age, and analyze the differences in the MPOD according to the presence or absence of AMD.

Methods

Subjects

This retrospective medical records review was performed in the Department of Ophthalmology of Busan Paik Hospital (Busan, Republic of Korea) with the data collected from November 2018 to January 2019. Approval for data collection and analysis was obtained from the institutional review board at Busan Paik Hospital, Inje University. This study was performed in adherence with the tenets of the Declaration of Helsinki.

The subjects were divided into four groups according to age: Group 1, 30-40 years; Group 2, 40-50 years; Group 3, 50-60 years; and Group 4, 60-70 years. In addition, subjects aged >55 years were further divided into two subgroups according to the presence or absence of dry AMD. Each group was further used for statistical analysis.

The inclusion criteria were subjects with no history of glaucoma, uveitis, diabetic retinopathy (more severe than moderate non-proliferative diabetic retinopathy), or neovascular AMD. The exclusion criteria were the presence of media opacity that would prevent the examination of the retina and optical coherence tomography (OCT) imaging, and a history of prior laser treatment or vitrectomy surgery. The individuals with high myopia (>-6.00 diopter) were also excluded.

A detailed ophthalmologic examination including measurement of the best-corrected visual acuity (BCVA), slit-lamp examination, and fundus examination was performed. All subjects underwent additional examinations using a retinal camera (Topcon TRC 50DX, Topcon Corporation, Tokyo, Japan), Optos California® (Optos PLC, Dunfermline, Scotland, UK), and OCT using a Zeiss OCT system (Cirrus HD-OCT 5000, Carl Zeiss Meditec Inc., Dublin, CA, USA) to evaluate the retinal status.

MP Screening

The MPOD was measured using the MPSII® (Elektron Eye Technology, Cambridge, UK), which uses an HFP technique. Two MPOD parameters were automatically calculated: the absolute value and the

estivated value. The measurement was performed before pupil dilation.

Statistical Analysis

The data were analyzed using SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA) and all results are expressed as the mean ± standard deviation. Spearman's correlation test was used to evaluate the correlations between the MPOD and age. Simple linear regression analysis was performed to determine the association between the MPOD and age. The Kruskal-Wallis test was used to compare the MPOD among the four groups, and the Mann-Whitney U test was utilized to compare the MPOD between the dry AMD group and the elderly controls. A p-value of <0.05 was accepted as statistically significant.

Results

A total of 126 eyes of 126 individuals (51 male, 75 female; aged 31-79 years, mean age, 56.15±12.33 years) were included. Among the subjects, 19 eyes (15%) were included in Group 1 (30-40 years of age), 17 eyes (13%) were included in Group 2 (41-50 years of age), 41 eyes (33%) were included in Group 3 (51-60 years of age), and 49 eyes (39%) were included in Group 4 (61-79 years of age). There were no statistically significant differences in the mean BCVA among the groups (p=0.032). The baseline characteristics of the individuals are summarized in Table 1.

The mean estimated MPOD values as measured by the MPSII® were 0.72±0.08 in Group 1, 0.70±0.09 in Group 2, 0.60±0.17 in Group 3, and 0.57±0.23 in Group 4. Groups 1 and 2 exhibited higher estimated values than did Groups 3 and 4 (Kruskal-Wallis test, p=0.002). There were no significant differences between Group 1 and Group 2 (Mann-Whitney U test, p=0.528), or between Group 3 and Group 4 (Mann-Whitney U test, p=0.641). The details of each group are described in Table 2.

According to Spearman's correlation analysis, the MPOD significantly decreased with increasing age (Spearman's correlation coefficient, -0.239; p=0.008). In the simple regression analysis, a statistically significant linear regression was observed, and the estimated values of the MPOD decreased by 0.005 as the age increased by 1 year (p=0.001, estimated MPOD value = 0.884 – 0.005 × age) (Figures 1,2).

To find a statistically significant reduction in the MPOD in patients aged >50 years, the patients were

re-analyzed after excluding patients with dry AMD. After excluding these patients, Groups 3 and 4 were renamed Healthy Group 3 and Healthy Group 4, respectively. In Group 1 and Group 2, there was no significant lesion of the macula. The estimated values then exhibited a decreasing trend with increasing age, but there were no statistically significant differences among the four groups (Table 3). Analysis using Spearman's correlation test and simple regression analysis was also performed. As a result of Spearman's correlation analysis in healthy subjects, there was no statistically significant correlation between MPOD and age ($p=0.201$).

To compare the MPOD in patients with dry AMD and in healthy controls, subjects aged >55 years were divided into dry AMD patients and healthy controls. The mean estimated MPOD values that were measured by the MPSII® were 0.69±0.18 in the healthy controls and 0.55±0.17 in the dry AMD patients. The estimated MPOD values in the patients with dry AMD were significantly lower than those in the healthy controls (Mann-Whitney U test, $p=0.001$).

Discussion

The MPSII® is an HFP device that is approved for commercial use in Republic of Korea. HFP uses different light wavelengths; the blue light is absorbed by the MP and the green light is not absorbed. The MPSII® has two modes: standard mode and detail mode. With the detail mode, evaluation of the MPOD using HFP is performed at the fovea and parafovea, wherein the MP is negligible. The values obtained using the detail mode are described as absolute values. Because obtaining both foveal and parafoveal data to calculate the absolute MPOD value is a time-consuming process, skipping the parafoveal examination reduces the time. In the standard mode, standard values previously recorded at the parafovea are used for reference, and the values obtained with the standard mode are termed estimated values. The estimated values were previously validated in a Caucasian population(22) and in Asian individuals.(21) Ozawa et al(21) reported that the absolute value was correlated with the estimated value in both young and aged Asian populations with or without AMD.

For the precision of the test using the MPSII®, the interclass correlation coefficients (ICCs) and coefficients of variation were previously reported. Van der Veen et al. reported high ICCs of 0.97 ($p<0.001$), but they repeated the measurement only twice.(22) Obana et al. reported that the ICCs of

both the absolute and estimated values were almost perfect (absolute values: 0.80; estimated values: 0.87).(23) Thus, in the present study, we used estimated values to evaluated the MPOD in all subjects.

In the current study, significantly lower MPODs were observed in the population aged >50 years of age than in the population aged <50 years of age, and a negative correlation was indicated by Spearman's correlation analysis. However, Ozawa et al(21) reported that there were no statistically significant differences between young and aged healthy populations. Therefore, only the healthy subjects were analyzed. There were no statistically significant differences among all groups, and no correlation with age was observed. The estimated MPOD value is determined only by the foveal value and is modified by age, according to the manufacture's empirical algorithm based on the deduced age-related increase in cataracts.(20, 24) These findings are consistent with those of previous studies reporting that the magnitude and spatial arrangement of MPOD was remarkably stable over time in elderly eyes, as reported by Westrup et al.(25)

Additionally, we compared the MPOD between dry AMD patients and healthy controls aged >55 years to evaluate the changes in MP in the AMD patients. The patients with dry AMD exhibited significantly lower MPOD than did healthy controls. Based on the results of this study, a lower MPOD may be the risk factor for dry AMD. Because MP protects the macula from photooxidation via its light-screening capacity and antioxidant activity,(26) there is growing interest in the potential role of dietary lutein and zeaxanthin to prevent the development and progression of AMD. The Age-Related Eye Study-2 (27) and several other studies have reported that lutein and zeaxanthin supplements are associated with a lower risk of AMD development,(28) and Fujimura et al. reported that the foveal MPOD was increased by dietary supplementation of lutein, zeaxanthin, and docosahexaenoic acid.(29)

Risk factors for dry AMD include age, smoking, exposure to ultraviolet rays, race, and decreased MP. (30) Among the risk factors, MPOD is one of the modifiable risks, and MPOD measurement may be a potential method for evaluating the treatment efficacy of oral supplementation of carotenoids and for detection of early AMD or identification of risk factors for the development of dry AMD.

Our study has some limitations. First, the study sample was relatively small, and further research with

a larger sample is required. Second, a general investigation of risk factors for macular degeneration, other than MPOD, has not been conducted. However, to the best of our knowledge, this study was the first to demonstrate the changes in MPOD according to age in Korean populations. Additionally, through the results of this study, the need for dietary supplementation related to MPOD in patients with dry AMD was identified.

Conclusions

The MPOD measured with the MPSII® reflects the MP density in healthy individuals and in patients with dry AMD. Early detection of risk factors for AMD and early detection of dry AMD may be possible with regular MPOD screening in patients aged >50 years or when the MPOD is decreased. Future studies are needed to provide information regarding the dosage of supplementation according to the MPOD if the degree of MPOD changes in patients receiving low doses of MPOD is known.

Abbreviations

MP: Macular pigment; MPDO: macular pigment optical density; MPSII®: Macular Pigment Screener II; AMD: age-related macular degeneration; HFP: heterochromatic flicker photometry; ICC: interclass correlation coefficient; BCVA: best-corrected visual acuity; OCT: optical coherence tomography

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Busan Paik Hospital and the requirement for individual consent was waived.

Consent for publication

Not applicable.

Availability of data and material

The datasets obtained and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors’ contributions

Conception and design of the study: I.B.C, H.D.K., K.S.K.

Acquisition of data : W.H.J., J.H.L., J.H.B.

Analysis and interpretation of data: W.H.J., I.B.C.

Drafting of the manuscript: I.B.C., H.D.K.

Critically revision of the manuscript: W.H.J., J.H.L., N.H.P., J.H.L., I.B.C, H.D.K.

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Tables

Table 1. Baseline characteristics of all subjects.

Groups	No. of eyes	Age	BCVA (LogMAR)
Group 1	19 (15%)	34.80 ± 2.60	0.00 ± 0.00
Group 2	17 (13%)	46.44 ± 2.45	0.00 ± 0.00
Group 3	41 (33%)	56.63 ± 2.69	0.10 ± 0.02
Group 4	49 (39%)	67.90 ± 4.73	0.22 ± 0.07

BCVA, best-corrected visual acuity; Group 1, 30-40 years of age; Group 2, 41-50 years of age; Group 3, 51-60 years of age; Group 4, 61-79 years of age.

Table 2. The differences of the estimated values of the MPOD. Group 1 and 2 showed higher estimated values than Group 3 or Group 4 (Kruskal-Wallis test, p=0.002). Statistical comparisons by Mann-Whitney U test were described for each group in the below.

	Group 1	Group 2	Group 3	Group 4
Estimated MPOD values	0.72 ± 0.08	0.70 ± 0.09	0.60 ± 0.17	0.57 ± 0.23
Intergroup differences	Group 1	Group 2	Group 3	Group 4
Group 1	N/A	0.528	0.004*	0.011*
Group 2	0.528	N/A	0.023*	0.039*
Group 3	0.004*	0.023*	N/A	0.641
Group 4	0.011*	0.039*	0.641	N/A

*Statistically significant difference among the groups.

MPOD, macular pigment optical density; Group 1, 30-40 years of age; Group 2, 41-50 years of age; Group 3, 51-60 years of age; Group 4, 61-79 years of age.

Table 3. The differences of the estimated values of the MPOD in the group1, 2, healthy group 3 and healthy group 4. There were no statistically differences among the four groups (Kruskal-Wallis test, p=0.379). Statistical comparisons by Mann-Whitney U test were described for each group in the below.

	Group 1	Group 2	Healthy group 3	Healthy group 4
Estimated value of the MPOD	0.72 ± 0.08	0.70 ± 0.09	0.64 ± 0.16	0.61 ± 0.25

Intergroup differences	Group 1	Group 2	Group 3	Group 4
Group 1	N/A	0.528	0.083	0.298
Group 2	0.528	N/A	0.195	0.412
Group 3	0.083	0.195	N/A	0.738
Group 4	0.298	0.412	0.738	N/A

MPOD, macular pigment optical density; Group 1, 30-40 years of age; Group 2, 41-50 years of age; Group 3, 51-60 years of age; Group 4, 61-79 years of age.

Figures

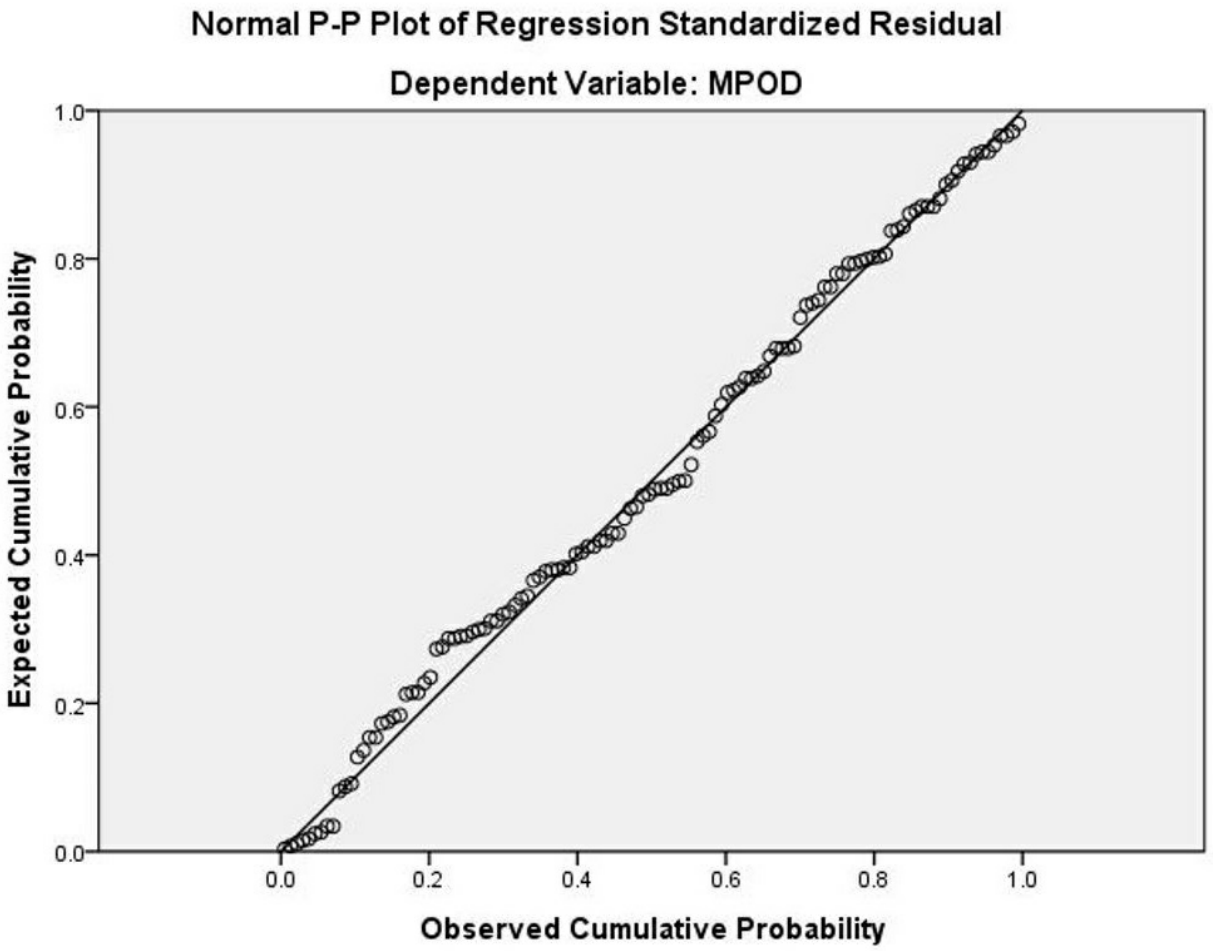

Figure 1

In the simple regression analysis, a statistically significant linear regression was observed, and the estimated values of the MPOD decreased by 0.005 as the age increased by 1 year (p=0.001, estimated MPOD value = 0.884 – 0.005 × age)

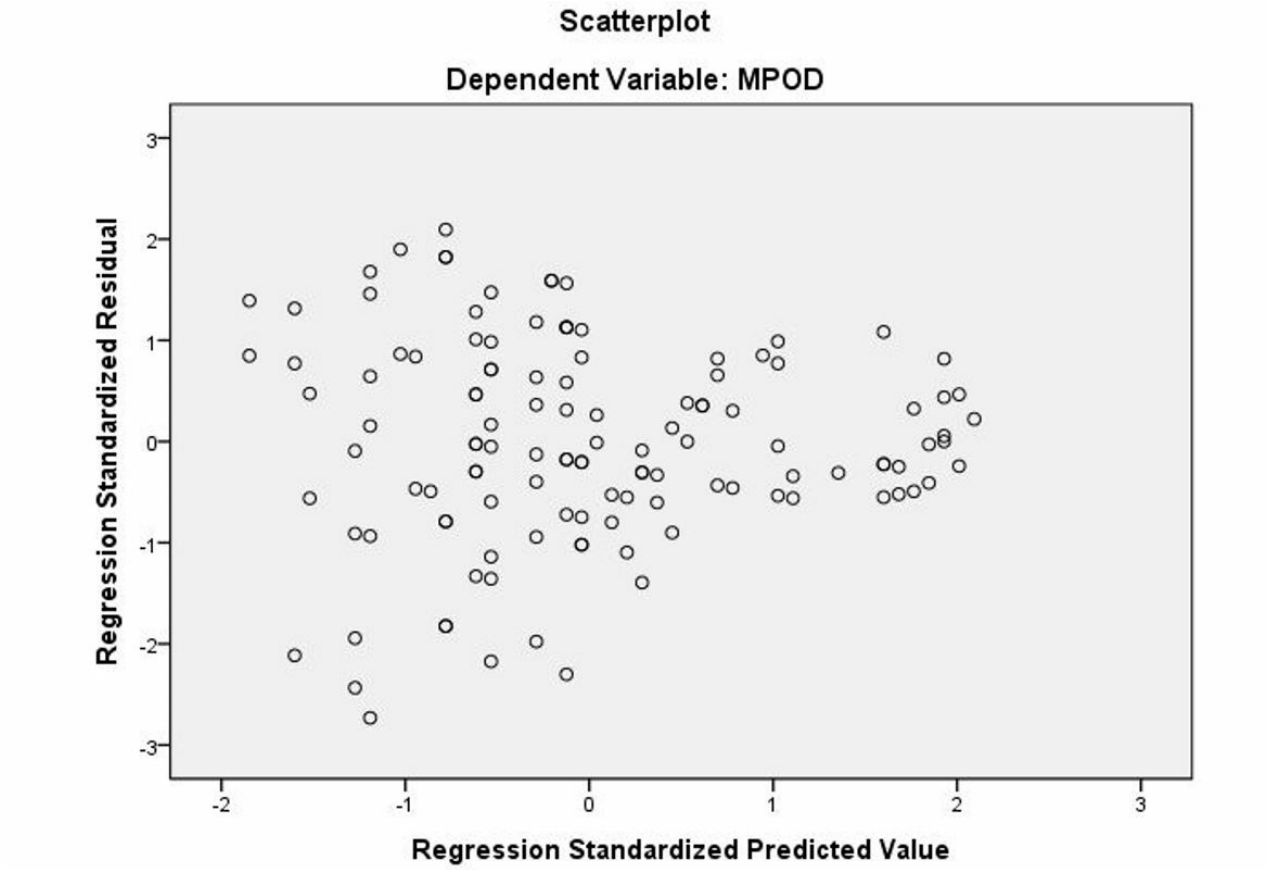

Figure 2

Scatterplot showing the correlation between the expected changes in MPOD and the age by simple regression analysis.