Experimental Eye Research 145 (2016) 468–471

Contents lists available at ScienceDirect

Experimental Eye Research

journal homepage: www.elsevier.com/locate/yexer

Evidence of macular pigment in the central macula in albinism

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ARTICLE INFO

Article history:
Received 8 July 2015
Received in revised form
30 August 2015
Accepted in revised form 5 October 2015
Available online 22 October 2015

Keywords:
Albinism
Macular pigment
Foveal hypoplasia
Lutein
Zeaxanthin
Diet supplementation

ABSTRACT

Purpose: Albinism represents a spectrum of disorders with diminished to absent amounts of melanin pigmentation including the posterior segment of the eye. Macular pigment (MP) consists of two main carotenoids, lutein and zeaxanthin, concentrated in the macula. MP serves as blue light absorbent, antioxidant, and may reduce chromatic aberration and glare. It remains unclear if albinos have detectable MP. The purpose was to investigate the distribution of MP in albino patients with psychophysical and imaging techniques.

Methods: MP was measured at the eccentricity of 0.5° by heterochromatic flicker perimetry (QuantifEye®; Tinsley Precision Instruments Ltd.) or by scanning laser ophthalmoscopy (MPOD module, MultiColor Spectralis®, Heidelberg Engineering, Heidelberg, Germany) in four albino patients, who were also investigated with multimodal ophthalmic imaging.

Results: Visual acuity ranged from 20/32 to 20/125, nystagmus was present in three patients, and all patients showed typical foveal hypoplasia on fundus exam and optical coherence tomography. Fundus autofluorescence (FAF) demonstrated various degrees of central FAF signal attenuation. Genetic testing was available in three patients and confirmed the diagnosis. Measurable amounts of MP were detected in all four patients and ranged from 0.05 to 0.24, which is below the normal range.

Conclusions: We conclude that MP can be demonstrated and measured in albinos. Further studies are needed to investigate MP accumulation following carotenoid supplementation and its impact on visual performance.

1. Introduction

Ocular and oculocutaneous albinism represent a spectrum of disorders with absent or significantly diminished amount of melanin either across different body tissues (OCA1 and OCA2), or exclusively in eye tissues (OA1).(Summers, 2009) Clinical findings and visual performance show significant variability without obvious phenotype–genotype correlation (Gargiulo et al., 2011). Typically, the ocular phenotype includes iris transillumination, foveal hypoplasia, nystagmus, reduced best-corrected visual acuity, refractive errors, photosensitivity, and abnormal development of the visual pathways with characteristic abnormal routing of ganglion cell axons in the chiasma, resulting in abnormal pattern visually evoked potentials (Dorey et al., 2003). Current treatment options are limited to low vision aids. Previously a correlation was found between the amount of melanin fundus pigmentation and visual function in albino patients (Summers, 1996).

The macular pigment (MP) consists of two main carotenoids, lutein and zeaxanthin, which are concentrated in the macula (Whitehead et al., 2006). MP is hypothesized to function as a protector by absorbing blue light incident on the retina, thereby reducing photo-oxidative stress to the underlying photoreceptors. It is also thought to improve visual function via reduction of chromatic aberration and glare (Wooten and Hammond, 2002). The only report on macular pigment in albino patients failed to demonstrate any MP (Abadi and Cox, 1992). The MP would be a hypothetical candidate to improve visual performance, simply by increasing pigmentation, reducing light scatter and thus glare sensitivity. MPOD normal range in US population has been estimated to be 0.24–0.45. Even in normal subjects, supplementation and an increase in the macular pigment optical density (MPOD) could be correlated with increased visual performance in randomized, placebo-controlled studies (Nolan et al., 2011; Trieschmann et al., 2007; van den Berg et al., 2009). As this pigment is not produced in the retina, but is absorbed via diet, it can be manipulated by diet and supplementation and thereby

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http://dx.doi.org/10.1016/j.exer.2015.10.006
0014-4835/

providing an opportunity to positively impact visual performance. It needs to be determined if MP is detectable at all in albinism.

In this case series, we evaluated 4 albino patients and performed measurements of MP: in three patients by heterochromatic flicker photometry (HFP), and in one patient with the novel MPOD module of the Heidelberg MultiColor Spectralis®.

2. Methods

Four albino patients were enrolled. Multimodal retinal imaging was performed. MPOD measurements were performed with the QuantifEye® device in 3 albino patients, and an additional patient underwent MPOD evaluation with the new MPOD module of the Heidelberg Multicolor Spectralis®. The study followed the tenets of the Declaration of Helsinki and was approved by the local Ethics Review Board.

The most widely used technique to assess the MPOD is the HFP method: A small (usually about 1°) visual stimulus with alternating blue (wavelength 465 nm, maximally absorbed by MP) and green (wavelength 530 nm, not significantly absorbed by MP) light is presented. We used the QuantifEye® device (QuantifEye®; MPS 9000 series: Tinsley Precision Instruments Ltd., Croydon, Essex, UK) for HFP. The device was first described in 2009 (van der Veen et al., 2009a), and showed good repeatability ($r = 0.97$), and produced similar results to retinal reflectometry (van der Veen et al., 2009b) and MultiColor Spectralis® HRA (Dennison et al., 2013). The device provides the option to either test only the central MPOD (0.5° eccentricity) or perform both the central and the peripheral test of MPOD (performed at 6° eccentricity). In resemblance to the visual field test, during MPOD testing the patient is required to press the button, once noticing the appearance of the flicker at the stimulus spot. While performing the central measurement, the flicker stimulus is presented centrally at the fixation point, and for the peripheral measurement, the flicker is presented at the same central location, however the fixation point is moved to the periphery of the presented field. Peripheral measurement can be challenging due to the required peripheral fixation. If the peripheral measurement is not performed for any reason, the central measurement is estimated based on age-adjusted data, taking into account the “normal yellowing” of the natural human lens. We attempted both, central and peripheral testing in our patients. The measurements were performed with non-dilated pupils, in dim light settings and with habitual correction, based on manufacturer's instructions.

The MPOD module of Spectralis® uses the MultiColor Spectralis® platform instrument as the basis. In contrast to the BluePeak system used to acquire blue AF images on the (standard) Heidelberg Spectralis®, it is equipped with an additional green laser, resulting in the ability to acquire infrared, green, and blue reflectance images from the retina simultaneously. For the MP measurements, the fluorescence detection is used to measure MP. The built-in software module performs the final MPOD calculation (as described by Trieschmann et al. (Trieschmann et al., 2006)) Once the measurement is performed, the average MPOD can be calculated at any eccentricity covered by the original scan (5°) by the in-built software. In our study we report 0.5 eccentricity measurements, similar to the eccentricity used by the QuantifEye® device. The measurements were performed with dilated pupils, in dim light settings, and with optimal visualization of the anatomical features on the preceding red-free scan, utilizing optimization of focal distance and magnification.

3. Results

The clinical characteristics of the 4 albino patients are summarized below (only positive and disease-specific findings are noted in the descriptions below, while normal finding are omitted):

Patient 1: Forty two-year-old male with sporadic oculocutaneous albinism. His best-corrected visual acuity was 20/63 in the right eye and 20/50 in the left; no nystagmus but mild iris transillumination were noted on ocular exam. On dilated fundus examination a low-pigmented fundus and absence of the foveal reflex were noted. Foveal hypoplasia was confirmed by OCT (Fig. 1B1). Molecular diagnosis is not available for this patient. The macular pigment measured by QuantifEye was 0.05 in the right eye, with reliable central and peripheral measurements, and not measurable in the left eye due to unreliable central and peripheral measurements.

Patient 2: Fifty-year-old male with oculocutaneous albinism. His best-corrected visual acuity on exam was 20/63 in the right and 20/50 in the left eye with hyperopic astigmatic correction. He had pendular nystagmus, moderate iris transillumination and lack of the foveal reflex. OCT scan confirmed foveal hypoplasia in both eyes (Fig. 1B2). Genetic testing was consistent with OCA1 (*TYR* gene *Compound Heterozygous Mutation*: *c.61C > T* (*p.Pro21Ser*) *in exon 1*, *c.1037-7T > A* (*IVS2-7T > A*) *in exon 3*). The macular pigment measured by QuantifEye was 0.14 in the right eye, with reliable central but unreliable peripheral measurements, and not measurable in the left eye due to significant nystagmus.

Patient 3: Sixty five-year-old male with oculocutaneous albinism, with best-corrected visual acuity of 20/80 in the right and 20/50 in the left eye, pendular nystagmus, absence of iris transillumination and foveal hypoplasia in both eyes as detected by dilated fundus examination and confirmed by OCT (Fig. 1B3). Additional clinical findings included bilateral hypermetropia, alternating exotropia, and nuclear sclerosis of the lens in the right eye. He had a positive family history of albinism: two affected siblings, daughter and granddaughter. He reported no history of consanguinity in the family. Genetic testing was consistent with OCA2 (*single heterozygous mutation*: *c.1103C > T (p.Ala368Val) in exon 10*). Macular pigment measured by QuantifEye was 0.12 in the right eye, with reliable central and peripheral measurements, and 0.24 in the left eye with reliable central but unreliable peripheral measurements.

Patient 4: Forty-year-old male with oculocutaneous albinism. He was emmetropic, and his uncorrected visual acuity was 20/40 in the right eye and 20/32 in the left. There was no nystagmus and no iris transillumination on ocular exam. Foveal hypoplasia was detected in both eyes on dilated fundus exam, and confirmed by OCT (Fig. 1B4). Homozygous p.Val443Ile:c.1327G > A mutation was detected, consistent with the diagnosis of OCA2. Macular pigment measured by MultiColor was 0.15 in the right eye, and 0.18 in the left eye (Fig. 2).

Fig. 1 shows retinal images of the right eye of each patient. As can be observed on fundus autofluorescence imaging (Fig. 1C1–C4), different degrees of foveal AF signal attenuation due to absorbance by the MP can be detected: while in patients 1 and 2, there appears to be only a weak, but definite central attenuation of the AF signal, patient 4, and even more so, patient 3 demonstrated quite normal distribution of AF signal with central AF attenuation. OCT scans of all 4 patients demonstrated foveal hypoplasia with complete absence of the foveal pit and presence of all inner retinal layers throughout the fovea (Fig. 1B1–B4).

MP measurements with the QuantifEye® were technically possible in 5 out of 6 eyes of Patients 1, 2 and 3. Central MPOD measurements were possible in all 5 eyes, however appeared unreliable (based on a QuantifEye® software output) in 1 out of 5 eyes (left eye of Patient 1). The peripheral MPOD measurements were technically possible in only 2 out of 4 eyes (right eye of Patient 1 and right eye of Patient 3). In Patient 3, MPOD in the right eye was 0.12, as calculated from central and peripheral measurements. In