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Effect of neodymium:YAG laser iridotomy on number of aqueous melanin granules in primary pigment dispersion syndrome

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Abstract *Purpose:* Increased numbers of aqueous melanin granules have been reproducibly demonstrated in eyes with pigment dispersion syndrome using the cell count mode of the laser flare-cell meter. It was the aim of this study to measure the exact number of aqueous melanin granules in eyes with pigment dispersion syndrome and pigmentary glaucoma before and after Nd:YAG laser iridotomy. *Methods:* Nine eyes of seven patients with a clinical diagnosis of primary pigment dispersion syndrome and secondary open-angle glaucoma (mean age 41.1±10.8 years) were included in this study. Aqueous cells were quantified using the cell count mode of the laser flare-cell meter (Kowa FC-1000) before and 30 min after medical pupillary dilation. Measurements were performed before and 15±7 weeks after Nd:YAG laser iridotomy. The main outcome measure was the number of aqueous melanin granules before and after Nd:YAG laser iridotomy.
Results: The number (mean and quartiles) of aqueous melanin granules/0.075 µl aqueous humor (normal/dilated pupil) before antiglaucoma treatment was 4.5 (4.0, 7.25)/9.0 (5.0, 13.0) and was significantly reduced after iridotomy [1.5 (0.75, 3.25)/4.0 (1.6, 6.25), P=0.016].
Conclusion: Nd:YAG laser iridotomy results in significant (65%) decrease of aqueous melanin granules in eyes with primary pigment dispersion syndrome. This finding appears to confirm the concept of reverse pupillary block in primary pigment dispersion syndrome and may indicate that laser iridotomy is a useful treatment option in this condition.

Introduction

In primary pigment dispersion syndrome (PDS), iridozonular friction causes liberation of melanin granules from the iris pigment epithelium into the aqueous humor [4, 6, 9, 13, 18, 20, 23, 24]. This may lead to decreased aqueous outflow and secondary open-angle glaucoma (pigmentary glaucoma, PG) by deposition of melanin granules in the trabecular meshwork [1, 19, 20]. Previous studies by our group have shown that aqueous melanin granules may be objectively and accurately quantified in patients with PDS by use of the cell count mode of the laser flare-cell meter [12]. Furthermore, it was demonstrated that the number of aqueous melanin granules is significantly increased in eyes with PDS, and that their number correlates with clinical signs of melanin dispersion, with increased intraocular pressure (IOP) and with visual field loss [12, 15]. One treatment option for PDS and PG is laser iridotomy to eliminate reverse pupillary block and reduce the release of melanin granules into the aqueous [10]. It was the aim of this study to investigate whether the objectively quantified number of aqueous melanin granules decreases in eyes with PDS and PG following laser iridotomy.

Methods

Nine eyes of seven patients (six males, one female, mean age 41.1±10.8 years) were included in this study. All patients had the characteristic clinical signs of PDS, including radial defects of the iris pigment epithelium, retrocorneal Krukenberg spindle, marked pigmentation of the trabecular meshwork, melanin granules in the aqueous humor, and deep anterior chamber with a concave anterior iris configuration. Furthermore, all eyes were classified as having manifest PG because of increased IOP, signs of glaucomatous damage to the optic nerve head and visual field defects. None of the patients had a history of previous intraocular surgery, history of uveitis, or other conditions that might be associated with melanin dispersion (pseudoexfoliation syndrome, diabetes mellitus, recent ocular trauma) or increased intraocular pigmentation (melanosis oculi, uveal malignant melanoma, uveal melanocytoma).

In all eyes, Nd:YAG laser iridotomy was performed in the superior peripheral iris to eliminate inverse pupillary block and to reduce further liberation of melanin granules into the aqueous. Before laser surgery, informed consent was obtained from all patients. Laser iridotomy was uncomplicated in all eyes.

Aqueous flare and aqueous "cells" were determined using the laser flare-cell meter (LFCM) FC-1000 (Kowa, Tokyo, Japan) as described in previous studies [12, 15]. Briefly, the instrument measures the scatter of a helium–neon laser beam that is scanned into the anterior chamber. Two consecutive measurements each lasting 0.5 s independently determine aqueous flare (diffuse scatter that is caused by aqueous proteins) and aqueous "cells" (short peaks of scatter of an intensity of more than 4 photon counts/400 ms, counted in 0.075 µl of aqueous humor). For each eye and each condition, five consecutive individual measurements were taken and averaged. Aqueous melanin granules were determined before and 15±7 (median 16, range 8–24) weeks after Nd:YAG laser iridotomy both with normal pupil width and 30 min following pupillary dilation with one drop of phenylephrine hydrochloride 5% (Neosynephrin-POS, Ursapharm Arzneimittel, Saarbrücken, Germany) and one drop of tropicamide 0.5% (Mydriaticum Stulln, Pharma Stulln, Stulln/Nabburg, Germany). Furthermore, IOP was determined in undilated eyes before and after laser iridotomy by Goldmann applanation tonometry.

In order to exclude an effect of the time interval alone on the number of aqueous melanin granules, we also investigated a control group of patients with PG in whom melanin granules were measured several months apart without laser iridotomy. This control group consisted of 11 eyes of 11 patients (9 males, 2 females, mean age 41.6±9.2 years, range 26–56 years) with PDS and PG without previous Nd:YAG laser iridotomy and without miotics. In all patients the number of aqueous melanin granules was quantified twice at a mean interval of 28 weeks (median 24 weeks, range 8–48 weeks). The examination procedures were comparable to those of the patients that underwent Nd:YAG laser iridotomy.

Due to the statistical dependency of left and right eye from the same patient, a subject-related statistical analysis was performed. A subject was classified as "success" if both eyes showed a reduction of aqueous melanin granules following treatment or if one eye showed an improvement and the fellow eye was stable. "Failure" was assigned to the remaining patients. The rate of success was tested statistically using the sign test [2] with a level of significance equal to 0.05 (two-sided).

Results

The number (median and quartiles) of aqueous melanin granules per 0.075 µl aqueous humor in undilated eyes decreased from 4.5 (4.0, 7.25) before to 1.5 (0.75, 3.25) after laser iridotomy, and this difference was statistically significant (P=0.016) (Table 1, Fig. 1). Similarly, following pupil dilation, the number of aqueous melanin granules decreased from 9.0 (5.0, 13.0) before to 4.0 (1.6, 6.25) after laser iridotomy (P=0.016) (Table 1, Fig. 1). All patients were classified as "treatment success" (Table 2). Aqueous flare values were normal and remained virtually unchanged in all conditions (Table 1).

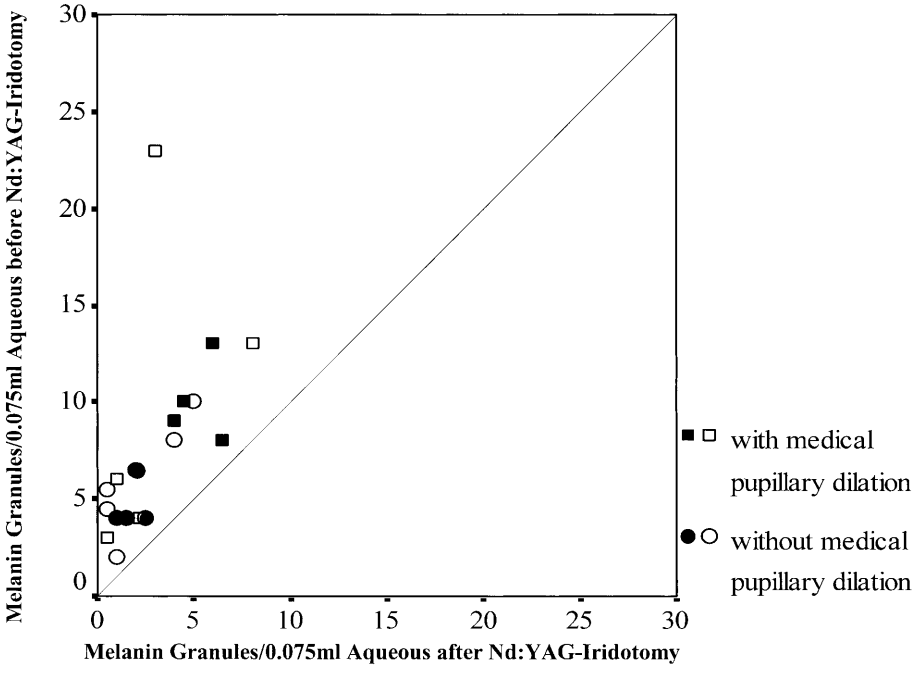

Fig. 1 Scatterplot depicting number of aqueous melanin granules in nine eyes of seven patients with primary pigment dispersion syndrome and secondary open-angle glaucoma before and after Nd:YAG iridotomy. *Circles* Examination without dilated pupils, *squares* examination following pupillary dilation

Table 1 Number of aqueous melanin granules and aqueous flare values (median, quartiles, range) in nine eyes of seven patients with pigment dispersion syndrome and pigmentary glaucoma. Measurements were performed before and after laser iridotomy and with and without medical pupillary dilation

Patient group	No. of melanin granules/0.075 µl	Aqueous flare (photon counts/ms)
Undilated, before iridotomy	4.5 (4.0, 7.25; 2.0–10.0)	5.0 (3.6, 6.25; 2.9–7.0)
Undilated, after iridotomy	1.5 (0.75, 3.25; 0–5.0)	5.15 (3.85, 5.9; 3.0–6.5)
Dilated, before iridotomy	9.0 (5.0, 13.0; 3.0–23.0)	5.2 (4.2, 5.95; 3.2–7.7)
Dilated, after iridotomy	4.0 (1.6, 6.25; 0.5–8.0)	4.3 (3.45, 5.55; 2.7–6.5)

Table 2 Data of seven patients (nine eyes) with pigmentary glaucoma undergoing neodymium:YAG iridotomy. The number of melanin granules indicated was taken after medical pupillary dilation in all patients

Patient no.	Gender	Age (years)	Eye	Before iridotomy			After iridotomy			Time interval (weeks)
				IOP (mmHg)	Antiglaucoma medication	Aqueous melanin granules/0.075 µl	IOP (mmHg)	Antiglaucoma medication	Aqueous melanin granules/0.075 µl	
1	M	27	OD	21	Pilocarpine	3.0	16	Pilocarpine	0.5	24
2	M	39	OS	25	Pilocarpine, ß-blocker, clonidine	4.0	14	Aceclidine	2.0	16
3	M	58	OD	22	Pilocarpine, clonidine	13.0	16	Clonidine	6.0	8
3	M	58	OS	20	Pilocarpine, clonidine	9.0	12	–	4.0	8
4	M	32	OS	23	Aceclidine, ß-blocker	6.0	20	Aceclidine	1.0	24
5	M	36	OD	21	Aceclidine	13.0	12	–	8.0	24
6	F	50	OD	20	Pilocarpine, ß-blocker	8.0	14	–	6.5	8
6	F	50	OS	21	Pilocarpine, ß-blocker	10.0	14	–	4.5	8
7	M	46	OD	22	Pilocarpine	23.0	16	–	3.0	16

Table 3 Number of aqueous melanin values (median, quartiles, range) measured at two different times 6–48 weeks apart in 11 eyes with pigment dispersion syndrome and pigmentary glaucoma without laser iridotomy (“control group”). Measurements were performed before and after medical pupillary dilation

Patient group	No. of melanin granules/0.075 µl
Undilated, first measurement	3.0 (1.0, 5.0; 0–6.0)
Undilated, second measurement	3.0 (1.0, 4.6; 0–4.6)
Dilated, first measurement	7.0 (3.0, 9.0; 0–11.0)
Dilated, second measurement	5.0 (3.0, 8.0; 0–10.0)

Mean IOP without pupillary dilation was 21.7± 1.6 mmHg before and 14.0±3.2 mmHg after Nd:YAG laser iridotomy with a mean number of antiglaucoma drugs of 1.7 before and 0.4 after iridotomy (Table 2).

In the control group without Nd:YAG iridotomy, the number of aqueous melanin granules (median and quartiles) was similar at the first and second measurements [without pupillary dilation 3.0 (1.0, 5.0) and 3.0 (1.0, 4.6) granules per 0.075 µl, after pupillary dilation 7.0 (3.0, 9.0) versus 5.0 (3.0, 8.0); statistical difference between the two measurements not significant (P=0.5 for nondilated pupils and 1.0 for dilated pupils)] (Table 3).

Discussion

PDS is a relatively common cause of secondary open-angle glaucoma and is usually seen in mildly myopic males in their third or fourth decade.

Melanin granules derived from the iris pigment epithelium and dispersed in aqueous humor are the major diagnostic and pathogenetic feature of PDS. Therefore, we believe that the potential of exactly, objectively and reproducibly counting aqueous melanin granules, as is possible by use of the non-invasive LFCM [12], is an important new diagnostic method with great potential to significantly improve evaluation of patients with this condition. In previous studies we applied this method to patients with PDS and PG with a number of interesting findings: It was possible to reproducibly quantify aqueous melanin granules in vivo [12], the number of aqueous melanin granules was increased significantly (more than tenfold in comparison with normal control eyes) in

PDS [12], medical pupil dilation caused an additional, more than twofold increase of aqueous melanin granules in PDS [12], and the number of aqueous melanin granules in eyes with PDS was strongly associated with increased IOP and also with glaucomatous visual field loss [15].

In understanding the pathogenesis of PDS, the concept of reverse pupillary block has gained wide acceptance [4, 6, 10, 18]: A pressure gradient from the anterior to the posterior chamber causes the iris to bow posteriorly, thus inducing iridozonular friction with release of melanin granules. This concept has been confirmed by ultrasound biomicroscopic findings [17, 22].

Laser iridotomy has been proposed as a therapeutic option to eliminate reverse pupillary block in eyes with PDS [10]. A number of studies have used ultrasound biomicroscopy to investigate the effect of Nd:YAG laser iridotomy on the configuration of the anterior segment in PDS and have found that iridotomy decreases iris-lens contact [3]; restores normal iris shape [5]; increases the depth of the posterior chamber [14]; prevents iris concavity with accommodation [16]; andcauses iris configuration to remain plain after exercise [11]. Furthermore, a traumatic defect of the peripheral iris appears to protect against development of PDS and PG [21].

With availability of the LFCM allowing exact quantification of aqueous melanin granules, there is now the possibility to objectively investigate and possibly prove the hypothesis that, by eliminating reverse pupillary block, laser iridotomy reduces continuous release of melanin granules into the aqueous. In fact, the results of this small pilot study clearly show that Nd:YAG laser iridotomy significantly reduces the release of melanin granules both in undilated and in dilated eyes with PDS, whereas no such reduction was observed in a control group not undergoing iridotomy. This is further proof of the concept of reverse pupillary block and indicates that laser iridotomy has the potential to eliminate reverse pupillary block and reduce release of melanin granules in PDS. However, in contrast to the effect of laser iridotomy in eyes with acute pupillary block angle-closure glaucoma, it is logical that iridotomy in PG will not result in immediate normalization of IOP, but may be expected to slowly progressively lead to stabilization and reduction of IOP by continuously reduced liberation of melanin granules, allowing the trabecular meshwork to slowly clear from melanin deposition. Thus, in this context it is understandable, and not contradictory, that some authors who analysed the short- and intermediate-term effect of Nd:YAG laser iridotomy in eyes with PDS and PG reported only mild or no reduction of IOP [8,14], although they may have drawn inaccurate conclusions from their findings. Accordingly, it has been shown that Nd:YAG laser iridotomy reduces the incidence of IOP increase in eyes with PDS after 2 years [7], and in our study, both mean IOP and number of antiglaucomatous drugs were reduced 15±7 weeks following laser iridotomy. We ourselves were surprised by the good effect of Nd:YAG laser iridotomy on IOP. However, as the analysis of IOP was not a major aim of this study, our results with regard to IOP have to be regarded somewhat cautiously. In addition, more detailed studies for evaluation of long-term effects of Nd:YAG laser iridotomy on IOP in patients with PG are certainly necessary.

In conclusion, we were able to show that Nd:YAG laser iridotomy results in significant decrease of aqueous melanin granules in eyes with PDS. This finding appears to confirm the concept of reverse pupillary block in PDS and may indicate that laser iridotomy is a useful treatment option in this condition.

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