Intraocular pressure variation during episodes of pigment dispersion and its relationship with the development of pigmentary glaucoma

Variación de la presión intraocular durante episodios de dispersión pigmentaria y su relación con el desarrollo de glaucoma pigmentario

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Abstract

Objective: To determine the intraocular pressure (IOP) variation during acute attacks of pigment dispersion and its relationship with the development of pigmentary glaucoma (PG). Methods: Retrospective, observational, and descriptive study of patients with pigment dispersion syndrome (PDS). IOP was recorded by Goldman tonometry during acute attacks of pigment dispersion, after cessation, and until last follow-up visit. Results: We analyzed 13 patients: 9 women (69.2%) and 4 men (30.8%), with a mean age of 51.76 years. The minimum follow-up time was 12 months. During the acute phase of pigment dispersion, the mean IOP was 23.3 ± 8.6 mmHg, dropping to 15.2 ± 2.4 mmHg after the event (p < 0.0001). Only 5 (38.4%) patients ended up developing PG. The mean IOP of patients with PDS during the acute event was 22.5 ± 10.6 mmHg, compared to 24.6 ± 4.0 mmHg of those who developed PG (p = 0.0365). Conclusions: We found an elevated IOP in all patients analyzed during acute attacks of pigment dispersion. The IOP variations, along with its persistent elevation, and the appearance of the optic nerve and cup-to-disk ratio should be considered as potential risk indicators for the development of PG in these patients.

Key words: Glaucoma. Optic nerve. Pigment dispersion. Pigmentary glaucoma. Intraocular pressure.

Resumen

Objetivo: Determinar la variación de la presión intraocular durante episodios de dispersión pigmentaria y su relación con el desarrollo de glaucoma pigmentario. Métodos: Estudio retrospectivo, observacional y descriptivo de pacientes con síndrome de dispersión pigmentaria. Se analizaron las presiones intraoculares mediante tonometría de Goldman durante episodios agudos de dispersión y después de estos hasta estabilizarse, y posteriormente hasta su última visita de seguimiento. Resultados: Se incluyeron 13 pacientes: 9 mujeres (69.2%) y 4 hombres (30.8%), con una edad promedio de 51.76 años. Los pacientes fueron evaluados al menos durante un año. La presión intraocular media durante el episodio de dispersión fue de 23.3 ± 8.6 mmHg, reduciéndose a 15.2 ± 2.4 mmHg una vez terminado el mismo (p < 0.0001). Un total de 5 pacientes...
(38.4%) desarrollaron glaucoma pigmentario. La presión intraocular en pacientes con síndrome de dispersión pigmentaria durante el evento agudo de dispersión fue de 22.5 ± 10.6 mmHg comparado con 24.6 ± 4.0 mmHg en pacientes que desarrollaron glaucoma pigmentario (p = 0.0365). Conclusiones: En todos los pacientes estudiados se encontró una elevación de la presión intraocular durante los episodios agudos de dispersión de pigmento. Las variaciones de la presión intraocular, junto con la elevación persistente de la misma, así como la apariencia del nervio óptico y la relación copa-disco deben considerarse como potenciales indicadores de riesgo para el desarrollo de glaucoma pigmentario en estos pacientes.


Introduction

Pigment dispersion syndrome (PDS) is characterized by acute pigment dispersion from iris pigment epithelium and/or ciliary body. Pigment is transported by the aqueous humor into the anterior chamber, where it is deposited in the corneal endothelium, the trabecular meshwork, the iris, and the lens. Patients with PDS usually present transient increases in intraocular pressure (IOP) due to the deposition of pigment in the trabecular meshwork, causing resistance to aqueous drainage and increasing the risk of developing glaucoma. Acute episodes of pigment dispersion may occur after strenuous exercise or spontaneous changes in pupillary diameter. Other theories about pigment release include blinking and the accommodation phenomenon. In some cases, PDS can be inherited in an autosomal dominant pattern, by means of a gene that is located at the end of the telomere of the long arm of chromosome 7 (q35-q36).

These patients may be asymptomatic, but frequently they present extreme photophobia, bilateral red eye, moderate eye pain, and blurred vision. On the contrary, most patients with pigmentary glaucoma (PG) are asymptomatic, although they may present with headaches and transient periods of blurred vision associated with increases in IOP and corneal edema. The signs of PG are very similar to those of PDS, being considered as a clinical spectrum of the same disease. However, the number of patients with PDS who develop glaucoma is not well established.

The main objective of this study was to analyze IOP variation during episodes of pigment dispersion and its relationship with the development of PG, that is, the way that IOP behaved before and after acute pigment dispersion events, as well as determining the number of patients who developed PG.

Subjects, materials, and methods

Retrospective, observational, and descriptive study of a series of Mexican patients diagnosed with PDS evaluated during an acute episode of pigment dispersion and followed by a minimum of one year in our clinic (Centro de Salud Integral-Unidad de Oftalmología de la Fundación Santos y de La Garza Evia), located in Santa Catarina, Nuevo León, in the northeast of Mexico. The study was approved by the Ethics and Research Commissions of the Escuela de Medicina y Ciencias de la Salud del Tecnológico de Monterrey, in accordance with the guidelines for the preservation of confidentiality and privacy of personal data, in observance of the Declaration of Helsinki. Information was collected on hereditary and personal ophthalmological history, especially glaucoma, as well as age, gender, main clinical manifestations, ophthalmological findings, and IOP during the acute episode of pigment dispersion, subsequent to it and until the last visit. During an acute episode of pigment dispersion, patients experienced in a variable form, blurred vision, visual halos, eye pain, photophobia, and red eye. In addition, the following findings were evaluated under slit lamp examination: pupil size, corneal edema, and IOP.

The patients underwent gonioscopy, using the 3-prismatic Goldman-type prismatic lens. Furthermore, indirect fundoscopy was performed with a 78D lens under biomicroscopy to assess the morphological characteristics of the optic nerve and macula. The patients who developed PG underwent Humphrey 30-2 campimetry with a size III stimulus. None of the patients had a history of refractive or intraocular surgery. The patients were identified according to the reason for consultation in the acute phase and subsequently in the days following the event. It was considered a resolved event once circulating pigment in the anterior chamber was no longer observed. The follow-up visits had a frequency of every 7 days during an acute attack of pigment dispersion and until its resolution, and every 3 weeks in case of persistence of a high IOP.
or every 4 months in cases of normalization of IOP and until the last follow-up visit at the time of data collection.

The information obtained was recorded in a Microsoft Excel® data processor, version 2007. The statistical and descriptive analysis was carried out using the SPSS v20 software. The nominal or numerical variables were considered with normal or non-normal distribution according to their Gaussian curve. For the comparison of nominal variables, Chi-square test was used and for the comparison of numerical variables, Mann–Whitney test or Student's t-test was used depending on non-normal or normal distribution of the values. p < 0.05 was considered statistically significant.

Results

A total of 18 patients were initially considered, of which 13 (72.2%) patients (24 eyes) who were evaluated during the acute phase of pigment dispersion were included for the study. The other five patients were not included because they were not evaluated during the acute phase of pigment dispersion.

Of the patients analyzed, 4 (30.8%) were male and 9 (69.2%) female, with a male-female ratio of 1:2.2. The average age at diagnosis was 51.7 years (ranging from 27 to 73 years; median 55 years; standard deviation 13.54). The average age of females was 54.5 ± 15.0 years (range 27-73 years; median 58 years; standard deviation of 15.07), and in male, 45.5 ± 7.1 years (range 39-55 years, median of 44 years, standard deviation of 7.18). The disease was bilateral in 11 (84.6%) patients (Table 1). None of the patients reported here-ditary family history of glaucoma or previously known glaucoma diagnosis.

The main signs and symptoms found during the acute episodes of pigment dispersion and that are frequently mentioned as a reason for consultation were extreme photophobia, red eye, moderate eye pain, burning, and blurred vision. On biomicroscopic examination, the most frequent signs were pigment deposition on the trabecular meshwork in 12 (92.3%) patients, pigment in the anterior chamber in 9 (69.2%) patients, and Krukenberg’s spindle in 8 (61.5%) patients (Table 1). None of the patients reported hereditary family history of glaucoma or previously known glaucoma diagnosis.

The predominant refractive error was myopia, found in 11 (84.6%) patients (mean −1.65 ± 2.28 diopters). Only 1 patient (7.7%) had a refractive error higher than 6.00 diopters. One patient was emmetropic and another presented mild hyperopia. All patients had keratometric indexes (41.00-45.00D) and corneal thickness (by ultrasound pachymetry) within normal ranges (500-570 µm of central corneal thickness).

IOP variation during and after the pigment dispersion event is analyzed in table 3. Mean IOP during the pigment dispersion episode in the overall population (n = 13, 24 eyes) was 23.3 ± 8.6 mmHg (range 10-40 mmHg), and once the acute event finished was 15.2 ± 2.4 mmHg (range 10-21 mmHg), with a statistically significant difference of 8.08 mmHg (p < 0.0001; 95% confidence interval = 4.79-11.38).

A total of 5 (38.4%) patients with PDS developed PG, 2 (40.0%) males and 3 (60.0%) females. The average age of these patients was 56 ± 10 years (range 41-69 years; median 57 years). Follow-up ranged from 1 to 7 years. Mean IOP during the acute episode of pigment dispersion in patients who developed PG is described in table 4. The difference in mean IOP in patients with PDS (22.53 ± 10.6 mmHg) and those who developed PG (24.6 ± 4.0 mmHg) during the pigment dispersion episode was 2.07 mmHg (p = 0.0365).

On examination of the optic nerve in patients who developed PG, an average cup-to-disk ratio of 0.5 ± 0.2

Table 1. Patient’s demography by gender and age

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (30.8%)</td>
<td>9 (69.2%)</td>
</tr>
<tr>
<td>45.5 ± 7.1 years (39-55)</td>
<td>54.5 ± 15.0 years (27-73)</td>
</tr>
</tbody>
</table>

Table 2. Main signs of patients with pigment dispersion syndrome

<table>
<thead>
<tr>
<th>Clinical signs</th>
<th>Number of eyes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigment in the trabecular meshwork</td>
<td>24 (92.3)</td>
</tr>
<tr>
<td>Pigment in the anterior chamber</td>
<td>18 (69.2)</td>
</tr>
<tr>
<td>Krukenberg’s spindle</td>
<td>16 (61.5)</td>
</tr>
<tr>
<td>Iris transillumination defects</td>
<td>10 (38.5)</td>
</tr>
<tr>
<td>Iris heterochromia</td>
<td>7 (26.9)</td>
</tr>
<tr>
<td>Triad: Krukenberg’s spindle, iris transillumination defects, pigment in the trabecular meshwork</td>
<td>3 (23.0)</td>
</tr>
</tbody>
</table>
(range 0.3 to 0.9; median 0.6) was found. The vast majority (n = 4, 8 eyes) of patients with PG had some kind of visual field defect, with a DM of −6.5 ± 3.0 dB (range from −2.6 to −11.2 dB; median –6.1 dB) and media DSM of 5.3 ± 3.6 dB (range from 1.6 to 12.5 dB; median 4.7 dB).

**Discussion**

The true prevalence of PDS is unknown. This is due, in large part to the fact that the vast majority of these patients, as mentioned before, have asymptomatic or subclinical disease, making detection difficult. In some

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**Table 3. IOP comparison in patients with pigment dispersion syndrome**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of eyes (patients)</th>
<th>IOP (mmHg) during an acute PD episode (range)</th>
<th>IOP (mmHg) after the PD episode (range)</th>
<th>IOP difference p value (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>17 (N = 9)</td>
<td>23.6 ± 8.5 (10-40)</td>
<td>15.2 ± 2.6 (10-21)</td>
<td>8.3 p = 0.0001* (4.7-11.9)</td>
</tr>
<tr>
<td>Male</td>
<td>7 (N = 4)</td>
<td>22.5 ± 9.7 (14-43)</td>
<td>15.1 ± 1.8 (12-18)</td>
<td>7.4 p = 0.1† (-1.9-16.8)</td>
</tr>
<tr>
<td>Total population</td>
<td>24 (N = 13)</td>
<td>23.3 ± 8.6 (10-40)</td>
<td>15.2 ± 2.4 (10-21)</td>
<td>8.08 p &lt; 0.0001* (4.79-11.38)</td>
</tr>
</tbody>
</table>

DP: pigment dispersion; CI: confidence interval; IOP: intraocular pressure.

*Statistically significant. †Insufficient number to conclude statistical significance.
patients, several years may pass before developing PG without having previously presented known events of pigment dispersion with IOP increase. Due to this fact, it has been considered that PDS is much more common than originally reported. Ritch found 18% of iris concavity in patients with PG. Karickhoff biomicroscopy studies have demonstrated the existence of pigment dispersion with IOP increase. Due to this fact, without having previously presented known events of patients, several years may pass before developing PG ultimately develop PG.

Another of the poorly studied aspects of PDS are the risk factors that favor the development of PG. Knowing these factors would allow the ophthalmologist to recommend patients a correct frequency of monitoring as a preventive measure for the potential visual loss caused by glaucoma. In a study conducted by Siddiqui et al., it was found that the risk for developing PG after PDS is low, but not negligible, of around 10% at 5 years, increasing up to 15% at 15 years of follow-up. The predictor for conversion to PG found in this study was an IOP > 21 mmHg registered during the initial diagnosis of PDS.

These authors conclude that considering this value as a reference; there is a significant risk with each acute episode of pigment dispersion of developing PG if IOP is not adequately controlled. In this study, the patients with PDS who did not develop PG had a mean IOP during the acute episode of pigment dispersion of developing PG if IOP is not adequately controlled. In this study, the patients with PDS who did not develop PG had a mean IOP during the acute episode of pigment dispersion of 22.5 versus 24.6 mmHg in those who finally developed glaucoma. After the dispersion event, IOP in patients with PG was 14.7 mmHg, while in those who developed PG was 16.1 mmHg. Comparing IOP during and after the acute episode in both groups of patients, there was a statistically significant difference (p = 0.0069 and p = 0.0002, respectively). The results of this study suggest that in addition to considering the IOP level during the acute event of pigment dispersion as a predictor of PG risk, variations in IOP during and after the dispersion event should be taken into account as potential risk indicators for the development of PG.

Another factor that we consider important is the appearance of the optic nerve. In patients who developed PG, the evaluation of the cup-to-disk ratio showed a mean of 0.58. With Humphrey Field Analyzer, of 4 (80%) patients with PG, visual field defects were found in 3 (75%) patients.

### Table 4. IOP comparison among patients with pigment dispersion syndrome versus those who developed pigmentary glaucoma

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of eyes (patients)</th>
<th>IOP (mmHg) during an acute PD episode (range)</th>
<th>IOP (mmHg) after the PD episode (range)</th>
<th>IOP difference (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigmentary glaucoma</td>
<td>9 (N = 5)</td>
<td>24.6 ± 4.0 (20-32)</td>
<td>16.1 ± 1.5 (12-18)</td>
<td>8.5 p = 0.0002*</td>
</tr>
<tr>
<td>Pigment dispersion</td>
<td>15 (N = 8)</td>
<td>22.53 ± 10.64 (10-40)</td>
<td>14.73 ± 2.71 (10-21)</td>
<td>7.8 p = 0.0099*</td>
</tr>
<tr>
<td>IOP difference between PG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>versus PDS p value</td>
<td></td>
<td>2.07 p = 0.0395*</td>
<td>1.37 p = 0.0603</td>
<td>0.58 p = 0.703</td>
</tr>
</tbody>
</table>

*Statistically significant.

DP: pigment dispersion; GP: pigmentary glaucoma; IOP: intraocular pressure; PDS: pigment dispersion syndrome.
patients, and the fourth was considered as an unlikely case. The mean DM of these patients was −6.55 dB.

One of the limitations of this study, in addition to its retrospective nature, is the total number of eyes analyzed. Detecting and evaluating patients with PDS during an acute event of pigment dispersion is not an easy task since most patients seek consultation late when the dispersion event has ended, and we can only detect the syndrome due to the existing findings in the anterior segment. Another limitation of this type of analysis is the lack of an extensive clinical follow-up since many patients do not return to consultation over time. However, despite this, we believe that the information presented in this research is valuable since it contributes to the knowledge of IOP behavior in patients with PDS during pigment dispersion events and their potential for PG development. Prospective, multicenter, and controlled studies are required to study a greater number of patients with PDS during and after an acute event of pigment dispersion, and especially in the long term, to know the prevalence of conversion to PG and its repercussions.

**Conclusion**

PDS is an underdiagnosed, complex disease with a wide spectrum of clinical manifestations, in which the greatest concern is the development of PG. In all patients studied, mean IOP during the acute episode of pigment dispersion was ≥23 mmHg, which implies a risk for developing glaucoma. In addition, IOP variations during and after the dispersion event should be considered as potential risk indicators for the development of PG, as well as the appearance of the optic nerve and the cup-to-disc ratio.

**Ethical responsibilities**

**Protection of human or animal subjects.** The authors declare that no experiments have been conducted in humans or animals for this research.

**Data confidentiality.** The authors declare that they have followed the protocols of their institution on the publication of patient data.

**Privacy rights and informed consent.** The authors declare that patient data are not included in this article.

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**Conflicts of interest**

The authors declare no conflicts of interest.

**References**