ABSTRACT

Objective: To assess whether there are variations in the intraocular pressure (IOP) between the morning and afternoon in healthy subjects.

Methods: This study was carried out in a Primary Care Health Center among usual patients of general practitioners. Two measurements of the intraocular pressure were assessed on the same day (between 8 and 9 a.m. and between 5 and 6 p.m.) using a Perkins applanation tonometer. The subjects (119 females and 101 males) had a mean age of 46.3 years, with ages ranging between 14 and 83 years. They were proportionally distributed among 4 age groups (14-24, 25-44, 45-64 and >65 years).

Results: The IOP mean values were: right eye, morning time and afternoon, 13.29 and 11.81 mm Hg, respectively (p<0.001); left eye, morning time and afternoon, 13.48 and 12.04 mm Hg (p<0.001). The IOP was significantly higher in males than in females, and showed a weak association with age.

Conclusions: We found a diurnal variation of IOP of approximately 1.5 mm Hg. The time of day when the IOP is measured needs to be considered as a variable in research in ocular hypertension and glaucoma (Arch Soc Esp Oftalmol 2007; 82: 675-680).

Key words: Intraocular pressure, glaucoma, variability, tonometry, Primary Care.
INTRODUCTION

Intraocular pressure (IOP) may be defined as the resulting balance between aqueous humor production and removal (1). By means of mechanisms that are not yet well known, its increase is considered to be one of the main risk factors leading to the development of glaucoma (2). Although 21 mmHg is commonly accepted as the maximum arbitrary value for normalcy (3), one should bear in mind, as with many other biological parameters, that this is a variable value determined by multiple factors: age (4), gender (5), race (6), tobacco consumption (7), local ocular problems (8), obesity (9), hormonal changes (10), physical exercise (11), etc.

Furthermore, it seems to follow a circadian rhythm, although this has not clearly been established among humans, with a maximum peak in the morning and the lowest point by late evening; the even more confusing changes occurring during the night have not been taken into account (12-15).

Understanding this cyclical changes in IOP, as well as their scope and potential factors inducing change, is very significant not only from a research viewpoint but also from a clinical perspective in terms of diagnosis and management of patients suffering from ocular hypertension and glaucoma. For instance, in a study on the prevalence of ocular hypertension and glaucoma performed by our team five years ago during the evening schedule, the existence of IOP average values considerably lower than those described in similar papers came to our attention (16).

The purpose of the present study was to check whether there were differences in the intraocular pressure values of a certain population during those times in the day when measurements were taken and to quantify the resulting differences.

SUBJECTS, MATERIAL AND METHODS

This is a descriptive and cross-sectional study performed at a healthcare center in the city of Toledo. Residents in this area were included and distributed proportionately in four age groups (14-24 years, 25-44, 45-64 and ≥ 65), not previously diagnosed with glaucoma or ocular hypertension and belonging to the population assigned to the healthcare center. Patients chosen among those visiting the doctor’s office for any reason between 8 and 9 am were informed of the study and once their consent was obtained, they were subjected to an IOP measurement and given an appointment for the next measurement that same day between 5 and 6 pm.

IOP measurement was performed resorting to two IOP serial samples for both eyes (first the right eye and then the left one) after instilling one anesthetic drop and fluorescein (0.25% sodium fluorescein solution and 0.4% oxibuprocaine hydrochloride); patients sat upright, using a Perkins applanation tonometer (MK2 model, Clement Clarke Ltd., England) and choosing for each eye the highest value resulting from both measurements. All measurements were performed using one single examiner with ample experience in this technique.

The data obtained were added to the SPSS 9.0 database for Windows (SPSS for Windows, SPSS Inc, Chicago, USA) for statistical purposes. The results were described using the standard parameters (average, standard deviation, percentage) and 95% confidence intervals. The statistical analysis, once IOP non-normalcy was checked by means of the Kolmogorov-Smirnov test, resorted to the Mann-Whitney (U), Kruskall-Wallis ($\chi^2$) and Wilcoxon (Z) tests, the former aimed at comparing matched data. The Spearman Rho ($\rho$) correlation was also estimated.

RESULTS

The final sample consisted of 220 individuals, 119 females (54.1 percent) and 101 males (45.9 percent). The average age was 46.3 years, ranging from 14 to 83. Age among males was higher than among females (49.3 versus 43.7; $p<.05$).

Figure 1 illustrates IOP values obtained for each eye in the morning and evening. IOP values are slightly higher in the left eye when compared to the right, and are also higher in the morning than in the evening ($p<.001$). The difference between IOP in the morning and in the evening was +1.48 mmHg (95% CI 1.24-1.72) for the right eye and +1.44 mmHg (95% CI 1.21-1.67) for the left eye.

The correlation between age and IOP is very weak ($\rho= +0.15$ and $+0.13$ for the right and left eye, respectively). Table I shows IOP based on the defined age brackets, usually observing slight increases in IOP when augmenting the age range, although differences were not significant.
As illustrated in Figure 2, IOP was higher among males than females. This observation was confirmed in three out of four age groups.

**DISCUSSION**

Our paper confirmed the differences between IOP figures recorded in the early hours of the morning and afternoon in the same population group and measurements taken on the very same day.

The mean IOPs found are similar to those recorded in a previous study on prevalence covering the same health area (16) and using similar methods, although the age group was over 40 years of age. In the latter, no IOP differences were found based on age nor gender, whereas the present study does reveal gender-based differences. The impact of age and gender on IOP values is usually positive, although not all studies assessing such impact confirm this statement. Thus, focusing on the Spanish population, there are two recent papers that point at such an impact in one case (17) while the other does not (18). Likely, the reasons for these discrepancies are the different methods used and the different populations targeted by the study.

IOP differences between both eyes have already been described in the past (19,20) and may be due to the fact that IOP is measured first in one eye and then in the other; moving or massaging one eye is known to cause changes in the IOP of the other eye (21). In any case, this difference is scarcely relevant in clinical terms, since it stands at approximately .2 mmHg.

Although it still remains unclear, IOP values, just as other biological parameters and variables, are known to follow a circadian rhythm, values chan-

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**Table I. Intraocular pressure (IOP) values based on age ranges, eye and time of measurement**

<table>
<thead>
<tr>
<th>Eye and time</th>
<th>Age group</th>
<th>N</th>
<th>Mean IOP</th>
<th>Typical deviation</th>
<th>Statistic significance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>14-24</td>
<td>41</td>
<td>12.65</td>
<td>2.684</td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>25-44</td>
<td>59</td>
<td>13.17</td>
<td>2.919</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-64</td>
<td>63</td>
<td>13.25</td>
<td>2.967</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>57</td>
<td>14.00</td>
<td>3.454</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>14-24</td>
<td>41</td>
<td>12.63</td>
<td>2.817</td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>25-44</td>
<td>59</td>
<td>13.20</td>
<td>2.815</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-64</td>
<td>63</td>
<td>13.90</td>
<td>3.031</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>57</td>
<td>13.89</td>
<td>3.534</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>14-24</td>
<td>41</td>
<td>11.54</td>
<td>2.550</td>
<td></td>
</tr>
<tr>
<td>Evening</td>
<td>25-44</td>
<td>59</td>
<td>11.76</td>
<td>2.445</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-64</td>
<td>63</td>
<td>11.81</td>
<td>2.923</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>57</td>
<td>12.05</td>
<td>3.061</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>14-24</td>
<td>41</td>
<td>11.54</td>
<td>2.675</td>
<td></td>
</tr>
<tr>
<td>Evening</td>
<td>25-44</td>
<td>59</td>
<td>11.92</td>
<td>2.548</td>
<td></td>
</tr>
<tr>
<td></td>
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<td>3.019</td>
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<tr>
<td></td>
<td>&gt;65</td>
<td>57</td>
<td>12.23</td>
<td>3.301</td>
<td></td>
</tr>
</tbody>
</table>

* Kruskall-Wallis’ test.
ging throughout the day. Usually, although not continuously, healthy subjects yield the highest IOP values at the beginning of the day, upon waking up, slowly decreasing during the day until bedtime and gradually increasing again during the night. Differences between maximum and minimum values may amount to 8 mmHg (22). This cycle may be altered or be different in glaucoma patients (20).

As far as we know, the study of daytime IOP variation has been scarcely addressed in Spanish population, finding only one paper published in this respect (23) targeting the population attending an ophthalmology unit.

Our study shows that in the target population (general population attending one healthcare center) IOP is lower (approximately 1.5 mmHg) in the early afternoon than in the morning, both in men and women. Saccá et al (14) find in non-glaucomatous subjects similar differences between measurements taken at 8 am and 4 pm.

The first consequence, as reported by other authors, is that those patients exhibiting limit IOPs in the early afternoon should be reassessed in the morning schedule. Confirming this variable also requires caution when interpreting intraocular pressure values detected in both healthy and glaucomatous populations and in terms of both diagnostics and treatment control and related to the time of day when measurements are performed, backing up the well-known fact that isolated IOP measurements provide little information on maximum values, variation range and variability (20). In fact, this element (the time of IOP measurement) should be taken into consideration as an additional variable in epidemiological studies related to ocul hypertension and glaucoma.

REFERENCES