__Original Research Article__

Relationship of intraocular pressure with environmental factors.

ABSTRACT

Clinical relevance: Intraocular pressure (IOP) has a significant role in glaucoma pathophysiology. There are factors that influence in the IOP value, such as central corneal thickness or the biomechanical properties of the cornea. However, other less studied factors may influence the IOP, such as environmental pollution.

Background: The increase in air pollution is related to acute respiratory pathologies. Regarding the eyes, is related to conjunctivitis or dry eye disease. The purpose was to analyse the correlation of environmental factors (atmospheric pressure, temperature, O_3, NO_2, PM_{10} and $PM_{2.5}$ concentrations) with intraocular pressure in young healthy patients.

Methods: A cross-sectional study was carried out on patients treated at General Optica centres in Spain and Portugal in collaboration with the University of Valladolid. This study included healthy patients (between 18 and 40 years old). IOP measurements were taken with different air tonometers (CT-80, CT-800, NCT-200, NT-510 and NT-530) and correlated with environmental factors. Correlation (Spearman's Rho) analyses were performed between IOP and the different environmental parameters. Moreover, groupings were performed as a function of the values for healthy exposure levels recommended by the WHO. Different comparisons were performed using the Mann–Whitney U test.

Results: Statistically significant correlations were found ($p < .04$) between IOP and temperature ($r = 0.37$), atmospheric pressure ($r = 0.20$), NO_2 ($r = 0.14$), PM_{10} ($r = 0.21$), O_3 ($r = 0.16$) and $PM_{2.5}$ concentrations ($r = 0.16$). Regarding the IOP values of people who were exposed to unhealthy concentrations (AQI > 20) versus those who were not, higher IOP values were only found in people exposed to $PM_{2.5}$.

Conclusion: Slight correlations were found between higher temperature, atmospheric pressure and concentrations of pollutant gases and increased IOP. More clinical studies are needed to understand the role that these environmental factors play in the aqueous humour flow and the value of IOP to know if and to what extent these factors may be risk of glaucoma.

Keywords: intraocular pressure, air pollution, temperature, atmospheric pressure, glaucoma.

INTRODUCTION

Intraocular pressure (IOP) is a very important parameter in the pathophysiology of glaucoma, especially primary open-angle glaucoma.[1] Traditionally, glaucoma is suspected in a patient when their IOP is above 21 mm Hg, although there are a significant number of glaucoma patients with IOP measurements below this value (normotensive glaucoma).[2,3] In any case, regardless of the type of glaucoma, it involves loss of nerve fibres in the optic nerve, causing visual field loss.[2, 3] Glaucoma is the second leading cause of blindness in the world, with an estimated global prevalence of 3.5% in people aged 40-80 years. With the inverted population pyramid, 111.8 million people worldwide are expected to have glaucoma by 2040.[4,5]

In the early stages, glaucoma is a difficult pathology to diagnose because it causes hardly any symptoms, especially in patients who do not have an elevated IOP; for this reason, this clinical sign is not a good diagnostic indicator, making the correct evaluation of the morphology of the optic nerve head essential for the detection of glaucoma.[6] However, IOP has a significant role, and the awareness of some factors that may affect IOP (sex, ethnicity, genetics, etc.) is important.[7] In addition, there are factors that influence the measurement of IOP, such as corneal astigmatism, central corneal thickness (CCT) and the biomechanical properties of the cornea.[8,9]

Nevertheless, there are other less studied factors that may influence the flow of aqueous humour and therefore the IOP value, such as atmospheric pressure, temperature and air pollution concentrations (particulate matter such as $PM_{2.5}$ and PM_{10}, ozone (O_3) and nitrogen dioxide (NO_2), which have been shown to affect the human body in different ways. According to the World Health Organization (WHO), particulate matter (PM) is the most influential air pollutant regarding human health.[10] PM can be classified according to size into particles smaller than 10 microns (PM_{10}) that can be inhaled and enter the respiratory system and particles smaller than 2.5 microns ($PM_{2.5}$ or less). $PM_{2.5}$ can even reach the pulmonary alveoli and transport harmful substances to very sensitive areas of the human body, worsening some respiratory (asthma or bronchiolitis), cardiovascular (coronary arteriosclerosis or myocardial infarction) and brain pathologies (such as Alzheimer's disease).[11] Prenatal exposure to this pollutant can cause damage at the levels mentioned above even before birth.[12]

There is some evidence that the increase in urban air pollution is related to increased paediatric hospital admissions in one region of Spain (Murcia) due to acute respiratory pathologies, especially asthma and bronchiolitis.[13] This increase can be related to NO_2 above all, a pollutant that mainly comes from the gases emitted by vehicle traffic and can be related to respiratory and cardiovascular diseases.[14] Similarly, PM (especially $PM_{2.5}$) has been linked to risk factors for stroke, heart disease, lung cancer and acute and chronic respiratory diseases.[10] Regarding the eyes, environmental pollution is related to altered ocular surface irrigation, conjunctivitis, and dry eye disease as the most direct results. In addition, environmental pollution is also related to alterations such as chronic inflammation, oxidative stress and cellular toxicity, which could be a risk factor in the development of cataracts, glaucoma, uveitis, retinal layer thinning, macular degeneration and diabetic retinopathy, but in some cases only in vitro research is performed nowadays.[15]

Given this, there are still unknowns in the pathophysiology of glaucoma, especially normotensive glaucoma; it seems necessary to analyse whether any environmental factors that could influence IOP may be involved. Therefore, the aim of this study was to analyse the correlation of environmental factors (atmospheric pressure, temperature, O_3, NO_2, PM_{10} and $PM_{2.5}$ concentrations) with intraocular pressure in young healthy patients.

METHODS

Study design

A multicentric cross-sectional prospective study was carried out on patients treated at General Optica (Optometrist centres in Spain and Portugal) in collaboration with the University of Valladolid. This study included adult patients (between 18 and 40 years old). All patients who showed systemic or eye pathology, underwent ocular surgery or had vision impairment were excluded. All patients underwent three IOP measurements during a single visit, according to the manufacturer's specifications for the tonometer used. The study was approved by the Human Science Ethics Committee (PI 22-2636) of Valladolid East-Area (Hospital Clinic, Castilla y Leon Public Health System-SACYL). All patients were treated in compliance with the Declaration of Helsinki and the European Normative for data protection (2016/679 Regulation of the European Parliament and the Council of the 27th of April in 2016, General Data Protection Regulation).

Materials

In this study, IOP measurements were performed with air tonometers because this technology is widely spread in clinical practice and noninvasive IOP measurements have shown modest agreement with Goldmann applanation tonometry (gold standard) IOP values.[16, 17] Five air tonometers were used: the CT-80 (TopCon, Japan), CT-800 (TopCon, Japan), NCT-200 (Shin nippon, Japan), NT-510 (Nidek, Italy), and NT-530 (Nidek, Italy) tonometers. The protocol followed in all cases was that specified by the manufacturer; three measurements per eye were taken in automatic mode, with the mean of the three measurements and the time of the measurement recorded.

The concentration data for the ambient pollutants collected in this study were obtained using the Air Quality Index (AQI), which includes normalised data that homogenises the concentrations of each factor, analysed on a scale from 0 to 250.[10] An AQI value of 0 to 20 represents low pollution, a value between 21 and 50 indicates moderate pollution, and values above 51 indicate high pollution. This type of index makes it easier to understand measurements, avoiding the need to know the concentration of each gas that has an impact on health but providing the ability to calculate the exact concentrations of these gases by keeping a linear relationship.

These data were collected since the Plume Labs: Air Quality App[18] database provides the average values of the previous 24 h to correlate this value with IOP measurements collected at different points on the Iberian Peninsula.[10] The reference time is 22:00 UTC, which coincides with 00:00 h local time, since the database offers the average of the previous 24 hours; this provides the average value for the day on which the IOP measurement was taken.

Table 1 represents the concentration value for each gas ($\mu g/m^3$) for an AQI value of 20, which is considered by the WHO to be a safe exposure level to these gases. Other AQI values are not detailed because the data were not taken in particularly polluted areas or on days with adverse weather events or other events that would generate abnormally high concentrations of pollutants.

Table 1 – Plume Labs AQI 20 values for each gas concentration. Concentration below these values are considered healthy by the World Health Organization. $PM_{2.5}$: particulate matter inferior to 2.5 micrograms per cubic meter; PM10: particulate matter inferior to 10 micrograms per cubic meter; NO_2: nitrogen dioxide; O_3 (ozone); $\mu g/m^3$: micrograms per cubic meter; h: hour.

AQI 20	**AQI 20**	**AQI 20**	**AQI 20**
$PM_{2,5}$	PM_{10}	NO_2	O_3
10 $\mu g/m^3$	20 $\mu g/m^3$	40 $\mu g/m^3$	20 $\mu g/m^3$

The WHO recommends an atmospheric temperature range between 18 °C and 24 °C for the proper functioning of the human body, and there is evidence that temperatures above 24 °C induce disturbances in sleep, general health, blood pressure, cardiovascular disease, body temperature and mental health.[20] There are no clear recommendations on the range of atmospheric pressure that is considered healthy by the WHO.

Procedure

All participants received information related to the study, and informed consent was obtained prior to any clinical procedure being performed. A complete clinical history was performed to ensure that patients met the inclusion criteria. Clinical data on age, sex, refractive error, and history of diabetes or high blood pressure were collected.

For the environmental data, the geolocation of each General Optica centre involved in the study was sought using the Google Earth tool.[20] Environmental data (atmospheric temperature, pressure) were extracted from publicly available information in the OGIMET database.[18] The geolocation coordinates of each meteorological station closest to the optical centres were determined from the OGIMET database, and the latitude, longitude and altitude of each of the stations were compared with the study centres with the greatest number of data, removing the data from the General Optica centres with an altitude difference from the nearest measuring station of more than 100 m. The atmospheric concentration data ($PM_{2.5}$, PM_{10}, O_3, NO_2) were determined from the Plume Labs: Air Quality App database.

Data analysis

Statistical analysis was performed using the SPSS 23.0 (SPSS, Chicago, IL, USA) statistical package for Windows. The nonparametric distribution of data was verified with the Kolmogorov–Smirnov test ($P < .05$ indicated that the data were nonparametrically distributed). The results are presented as the mean ± standard deviation (SD) and range (minimum-maximum). Correlation (Spearman's Rho) analyses were performed between IOP values and the different environmental parameters. Moreover, groupings were performed as a function of the values for health recommended by the WHO. Different comparisons were performed using the Mann–Whitney U test, and $P < .05$ was considered statistically significant.

RESULTS

IOP values were determined for 594 patients who met the inclusion and exclusion criteria, with a mean age of 29.05 ± 6.23 years; 62.98% of the participants were female and 37.02% were male. The average IOP for the right eye (RE) was 15.72 ± 3.11 mm Hg and that for the left eye (LE) was 15.61 ± 3.15 mm Hg. The data were collected from 30 May to 6 June 2022. The distribution of refractive error was as follows: 9.9% emmetropic, 14.6% hyperopic, 60.3% myopic under 6.00 D, 5.6% myopic under 6.00 D or higher and 9.6% pure astigmatism. The atmospheric temperature ranged from 15.1°C to 31.3°C, and for atmospheric pressure, the range was from 908.6 mB to 1024.9 mB. For gases, the AQI ranges were 0 to 31 for NO_2, 0 to 53 for $PM_{2.5}$, 0 to 44 for PM_{10} and 11 to 41 for O_3.

Of the 594 IOP values, 564 could be correlated with atmospheric pressure values, 583 could be correlated with atmospheric temperature values, 420 could be correlated with NO_2 values, 403 could be correlated with $PM_{2.5}$ values, 420 could be correlated with PM10 values and 402 could be correlated with O_3 values.
No statistically significant correlations (Spearman's Rho) were found between the IOPs of both eyes and atmospheric pressure ($P > .14$), neither with the values of $PM_{2.5}$ ($P > .14$) or PM_{10} ($P > .11$), nor with that of O_3 ($P > .47$), considering that the values of atmospheric pressure and ozone recorded on the days in which the study was carried out did not exceed the limits that are considered healthy. However, statistically significant correlations were found between the IOPs of both eyes and atmospheric temperature ($r = 0.12$; $P < .01$ for RE and $r = 0.11$; $P = .01$ for LE) and NO_2 ($r = 0.10$; $P = .04$ for RE and $r = 0.11$; $P < .03$ for LE). Given the controversy in the agreement studies between air tonometry and goldman tonometry, the data will be analyzed by tonometer.

Analysis of the variables according to the tonometer used

Performing the same analysis with the 5 tonometers used, it is necessary to consider that 127 patients had measurements taken with the NT-510 tonometer (Nidek, Italy), 30 patients had measurements taken with the NT-530 tonometer (Nidek, Italy), 175 patients had measurements taken with the NCT-200 tonometer (Shin Nippon, Japan), 46 patients had measurements taken with the CT-80 tonometer (Topcon, Japan) and 216 patients had measurements taken with the CT-800 tonometer (Topcon, Japan), as shown in Table 2. The results comparing the age (to find out if the groups are different) and IOP data of the patients with measurements taken with the different tonometers are shown in the Table 3 and correlation with environmental factor in table 4.

Analysis of the variables in relation to ametropia

The data were analysed considering the refractive error (Table 2) of the patients and by comparing both the mean IOP values and mean age to determine whether the differences in IOP could be attributed to the difference in age of the groups compared, as shown in Table 3 and correlations depend on the refractive error as shown in Table 4.

The analysis according to the WHO-recommended healthy values (AQI < 20) showed different areas where the AQI exceeded the recommended healthy values, with 259 IOP measurements associated with data exceeding the recommended values for O_3 exposure (AQI: 23.01 ± 6.05). For PM_{10}, there were 102 measurements with an AQI above healthy values (AQI: 14.45 ± 9.11). For $PM_{2.5}$ (AQI: 18.02 ± 11.03), there were 133 IOP measurements that were taken at locations where the $PM_{2.5}$ concentration was above the WHO-recommended value on that day (AQI > 20). However, in the case of NO_2 (AQI: 4.59 ± 3.73), only two data points were above the value recommended by the WHO as healthy. The variations in atmospheric pressure were very slight and did not seem to be related to the variations in IOP.

Comparing the IOP measurements taken at healthy $PM_{2.5}$ values (267 measurements) versus those taken at sites where the $PM_{2.5}$ concentration exceeded the recommended value for health, statistically significant differences were obtained for IOP values for both eyes (P = .03 for the RE and P = .01 for the LE) but not for the mean age (P = .87) of the groups studied (28.76 ± 6.10 years old versus 28.74 ± 6.86 years old in the group with $PM_{2.5} \geq 20$). The IOP was higher in the group exposed to $PM_{2.5}$ values above healthy levels (IOP for the RE: 15.55 ± 3.17 mm Hg versus 16.43 ± 3.19 mm Hg in the group with AQI $PM_{2.5} \geq 20$ and IOP for the LE: 15.36 ± 3.09 mm Hg versus 16.47 ± 3.43 mm Hg, respectively). In the case of PM_{10} and O_3, no statistically significant differences were found between IOP values (RE: P > .15 and LE: P > .07) and age (P > .84) in the patients exposed to unhealthy concentrations (AQI > 20).

Table 2- Descriptive analysis (mean ± standard deviation and range) of the variables grouped by tonometer and refractive error. Some environmental values were not available for data collection and for this reason the sample size varies. n: sample size; RE IOP: right eye intraocular pressure; LE IOP: left eye intraocular pressure; P: atmosferic pressure; T: temperature; AQI: Air Quality Index.

TONOMETER GROUPING									
Tonometer	Age (years)	RE IOP (mmHg)	LE IOP (mmHg)	P (hPa)	T (ºC)	AQI NO_2	AQI $PM_{2.5}$	AQI PM_{10}	AQI O_3
n	127	127	127	127	124	74	69	74	71
NT-510	30.24±6.27 (18 to 40)	14.73±2.98 (8.3 to 28.0)	14.69±2.99 (8.7 to 28.0)	1007.81±21.53 (909 to 1020)	21.06±2.83 (15 to 26)	4.80±4.50 (0 to 31)	19.06±10.74 (0 to 44)	19.99±9.67 (0 to 36)	26.46±6.25 (11 to 41)
n	30	30	30	28	28	15	15	15	15
NT-530	30.24±6.27 (18 to 40)	15.10±273 (10 to 21.3)	14.86±2.63 (9 to 19.5)	1013.23±1.68 (1008 to 1015)	20.61±1.99 (17 to 23)	2.27±1.22 (1 to 4)	11,05±3.71 (8 to 22)	8.83±3.54 (5 to 16)	22.07±5.67 (14 to 33)
n	175	175	175	158	171	116	116	116	111
NCT-200	28.83±6.34 (18 to 40)	16.36±3.46 (7 to 31)	16.32±3.70 (6 to 28)	1013.11±3.14 (1008 to 1025)	20.10±2.27 (15 to 31)	6.05±3.46 (1 to 15)	23.49±10.73 (5 to 51)	18.09±9.25 (4 to 40)	21.78±5.68 (13 to 33)
n	46	46	46	46	46	26	26	26	26
CT-80	28.13±5.65 (18 to 40)	14.85±3.15 (10 to 21)	14.78±3.15 (9 to 22)	1011.95±2.32 (1008 to 1019)	21.5±1.78 (17 to 26)	4.38±4.22 (0 to 16)	14.42±8.16 (0 to 31)	9.92±4.86 (0 to 19)	23.38±5.72 (13 to 31)
n	216	215	215	205	214	189	177	189	179
CT-800	28.74±6.36 (18 to 40)	16.10±2.66 (4 to 23)	15.89±2.56 (10 to 23)	994.93±37.22 (906 to 1019)	20.86±2.72 (15 to 31)	3.83±3.31 (1 to 16)	15.15±10.64 (5 to 53)	11.88±8.20 (4 to 44)	22.41±5.84 (14 to 40)
REFRACTIVE ERROR GROUPING									
Refractive error	Age (years)	RE IOP (mmHg)	LE IOP (mmHg)	P (hPa)	T (ºC)	AQI NO_2	AQI $PM_{2.5}$	AQI PM_{10}	AQI O_3
n	57	57	57	53	55	43	43	43	41
Astigmatism	29.17±5.79 (18 to 40)	14.77±3.23 (7 to 21)	14.91±3.36 (6 to 21)	1011.15±14.15 (912 to 1023)	20.64±2.46 (15 to 27)	5.21±3.58 (1 to 15)	19.26±9.73 (7 to 53)	15.77±8.78 (4 to 40)	22.95±7.17 (13 to 41)
n	86	86	86	85	85	65	65	65	63
hyperopia	31.10±6,38 (18 to 40)	15.86±3.32 (10 to 24.7)	15.76±3.62 (10 to 28)	1004.95±26.80 (906 to 1004.95)	20.73±2.59 (16 to 31)	4.57±3.75 (1 to 15)	18.52±11.49 (5 to 53)	14.54±9.36 (4 to 44)	23.14±5.66 (13 to 34)
n	358	358	358	339	352	246	234	246	235
Myopia <6	28.72±6,21 (18 to 40)	15.87±2.92 (4 to 31)	15.73±2.90 (9 to 28)	1033.33±28.65 (907 to 1025)	20.64±2.51 (15 to 31)	4.39±3.77 (0 to 31)	17.46±11.23 (0 to 53)	14.11±9.29 (0 to 40)	22.88±5.97 (11 to 39)
n	33	33	33	30	32	27	23	27	25
Myopia ≥6	28,72±5,93 (19 to 40)	16.09±3.59 (11 to 26.7)	16.12±3.53 (10 to 25.7)	1008.73±18.99 (909 to 1018)	21.59±3.22 (15 to 31)	5.15±3.67 (1 to 16)	20.52±12.38 (0 to 51)	15.74±9.01 (0 to 39)	23.92±5.80 (15 to 37)
n	60	59	59	57	59	39	38	39	38
Emmetropia	28,13±6,24 (18 to 40)	15.48±3.24 (8.3 to 28)	15.11±3.25 (8.7 to 28.0)	1009.46±16.86 (922 to 1022)	20.77±2.46 (15 to 27)	4.82±3.67 (1 to 14)	17.71±9.70 (6 to 53)	14.05±8.13 (5 to 40)	23.03±6.34 (15 to 40)

Table 3. Comparison between intraocular pressure in different grouping, by tonometer or refractive error. Differences in age are only found reported between NT-510 versus CT-800 (p=0.04) and betweem emmetropic and hyperopic patients (p<0.01).

GROUPINGS BY TONOMETER	
Tonometer pair	P-value
Tonometers with statistically significant differences in IOP values measurement	
NT-510 versus NCT-200	p<0.01
NT-510 versus CT-800:	p<0.04.
NT-530 versus NCT-200:	p<0.04
NCT-200 versus CT-80:	p<0.01
CT-80 versus CT-800:	p<0.01
Tonometer without statistically significant differences in IOP values measurement	
NT-510 versus NT-530	p>0.38
NT-510 versus CT-80	p>0.06
NT-530 versus CT-80	p>0.58
NT-530 versus CT-800	p>0.05
NCT-200 versus CT-800	p>0.30
GROUPINGS BY REFRACTIVE ERROR	
Refractive error	P-value
Refractive error with statistically significant differences in IOP values measurement	
Emmetropic (n=60) versus hyperopic (n=86)	p<0.01
Hyperopia (n=86) versus myopia under 6 D (n=358;)	p<0.01
Astigmatism (n=57) versus myopia under 6 D (n=358) in the LE	p=0.04
Refractive error without statistically significant differences in IOP values measurement	
Emmetropic patients (n=60) versus pure astigmatism patients (n=57)	p>0.22
Emmetropic patients (n=60) versus with myopia under 6 D patients (n=358;)	p>0.06
Emmetropic patients (n=60) versus myopia over 6 D patients (n=33;)	p>0.18
Astigmatism patients (n=57) versus hyperopia patients (n=86;)	p>0.07
Astigmatism patients (n=57) versus patients with myopia over 6 D (n=33;)	p>0.22
Hyperopia patients (n=86) versus patients with myopia over 6 D (n=33;)	p>0.06
Myopia over 6 D (n=33) versus myopia under 6 D (n=358)	p>0.81

Table 4. Statistically significant correlations between intraocular pressure and environmental factors calculated in the different groupings, by tonometer and by refractive error.

GROUPINGS BY TONOMETER			
Intraocular correlation with:	Eye	r	p
Atmospheric pressure in IOP values measured with CT-800	RE	0.20	<0.01
	LE	0.22	<0.01
Temperature in IOP values measured with NCT-200	RE	0.23	<0.01
	LE	0.21	<0.01
Temperature in IOP values measured with CT-800	RE	0.19	<0.01
	LE	0.20	<0.01
$PM_{2.5}$ concentration in IOP values measured with CT-800	RE	0.21	<0.01
PM_{10} concentration in IOP values measured with CT-800	RE	0.21	<0.01
	LE	0.15	0.04
PM_{10} concentration in IOP values measured with NCT-200	LE	0.20	0.04
O_3 concentration in IOP values measured with CT-800	LE	0.16	0.03
GROUPINGS BY REFRACTIVE ERROR			
Intraocular pressure correlation with:	Eye	r	p
Atmospheric temperature in patients with myopiaover 6D	RE	-0.43	0.01
	LE	-0.50	<0.01
Atmospheric temperature in patients with myopia under 6D	RE	0.18	<0.01
	LE	0.17	<0.01
Atmospheric temperature and IOP values in patients with emmetropia	RE	0.37	<0.01
	LE	0.36	<0.01
$PM_{2.5}$ AQI in patients with myopia below 6 D	RE	0.13	0.04
	LE	0.16	0.01
PM_{10} AQI in patients with myopia below 6 D	RE	0.14	0.03
	LE	0.16	0.01
NO_2 AQI in patients with myopia below 6 D	LE	0.14	0.03

IOP: intraocular pressure

DISCUSSION

IOP is an important parameter in ocular physiology, especially in the pathophysiology of glaucoma. Environmental factors are little studied in this field, but there is scientific evidence linking these factors to ocular pathologies, especially of the ocular surface.[15] There is also evidence that $PM_{2.5}$ and PM_{10} are associated with adverse pathological processes, particularly in the respiratory system, and are dependent on the level of exposure.[13,14]. Furthermore, given that $PM_{2.5}$ can penetrate internal anatomical structures, it seems interesting to know whether there is a relationship between these factors and the physiology of IOP and therefore the IOP value in a healthy population that could produce changes such as vascular disorders that would affect glaucoma development.[22] It has already been shown that retinal vascular disorders and poor blood flow in the optic nerve head are related to an increased resistance index. However, in their study of patients with diabetes mellitus, Yu-Wei Chiang et al.[22] found an association between $PM_{2.5}$ exposure and central retinal artery occlusion due to structural changes that also occur in the process of glaucoma development.

The findings of this study show an asymmetric distribution in both refractive error and the number of IOP measurements with each tonometer that could affect the results. For this reason, the results were analysed globally and according to the tonometer and ametropia. There is evidence that air tonometers measure IOP with reasonable agreement to the Goldmann applanation tonometry, but there are no studies comparing the models of tonometers used.[16,17] The results of this work indicate a possible difference among tonometers, although it could not be determined in this study whether the difference was associated with the tonometer or the heterogeneity of the groups. However, in some cases, fluctuations in IOP values were not accompanied by other factors, such as the age difference between the groups.

For the analysis in relation to ametropia, it was necessary to take into account that myopia over 6 D is a risk factor for glaucoma; for this reason, it was relevant to perform an analysis based on refractive error, as environmental factors can aggravate the problem. A curious finding was found in these patients, because the correlation with temperature is both strong and negative and it is the only case in which it occurs, as if temperature had a significant influence on the IOP of myopic patients with more than 6 diopters. To the best our knowledge, there are no similar findings, being it an interesting finding for future studies. Again, there was asymmetry in the study groups, as there is a refractive error distribution in the general population. However, Table 2 shows that the group with myopia over 6 D was the group with the highest IOP, with no difference in age compared to the group with low myopia or emmetropia. Environmental factors in other studies along these lines were based on exposure to much higher concentrations of pollutant gases (O_3, NO_2) and particles ($PM_{2.5,}$ PM_{10}), such as that of 106.2 $\mu g/m^3$ for $PM_{2.5}$ in Saudi Arabia or 157 $\mu g/m^3$ for $PM_{2.5}$ in China, which are incomparable to those recorded in the Iberian Peninsula on the study days.[13,21] Likewise, the variation in atmospheric pressure was much smaller than that in other studies, which found variations of more than 1000 mB.[23] Even with low levels of exposure to these gases and slight variations in atmospheric pressure and temperature, correlations have been found that may be of interest, although more limited studies are needed to corroborate these associations, as well as to identify whether a causal relationship exists. Statistically significant correlations were found ($P < .04$) between IOP values and atmospheric temperature ($r = 0.37$), atmospheric pressure ($r = 0.20$), and NO_2 ($r = 0.14$), PM_{10}, ($r = 0.21$), O_3, ($r = 0.16$) and $PM_{2.5}$ concentrations ($r = 0.16$).

Regarding the IOP values of people who were exposed to unhealthy concentrations (AQI > 20) versus those who were not, higher IOP values were only found in people exposed to $PM_{2.5}$. Several studies showed variations in IOP values when measurements were taken at different seasons of the year or when the population was permanently exposed to higher levels of $PM_{2.5}$ or PM_{10}.[1,23,24] An analysis of data collected from hospitals in Shanghai found a link between increased IOP values and atmospheric factors that can cause harm to human health. The results showed a significant association between exposure to air pollutants and visits for acute angle-closure glaucoma.[24] In this line, several studies with a mouse animal model exposed these animals to normal concentrations of gases (control) and to high concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO and O_3 in air. After months of exposure, the visual function of the mice was assessed by electroretinography, and a decreased response to light stimuli was observed in mice in the experimental group compared to the response of mice in the control group. In addition, histological analysis of the retina showed thinning and death of ganglion cells consistent with acute angle-closure glaucoma.[25,26]. In this case, there seems to be a relationship between systematic exposure to pollutant gases in mice and the deterioration of their visual function and neuronal degeneration of the retina by triggering oxidative stress that activates pyroptosis in the cells of the trabecular meshwork (TM) mediated by the NLRP3 inflammasome. However, this may be far from a real situation, first because it is an animal model and second because exposure to high concentrations of these gases occurs occasionally.[26]

Other studies have also shown some evidence that $PM_{2.5}$ has a toxic effect on intraocular tissues and may contribute to the development of ocular hypertension and glaucoma. Topical application of fluorescent mock $PM_{2.5}$ to the eye caused deposition in the outflow tissues, including the iris, ciliary body, and TM.[26] In addition, the work of Chua et al.[21] stated that air pollution may contribute to glaucoma by constricting blood vessels and having a direct toxic effect on the nervous system. The study found that environmental pollution can cause migraine-like reactions where spasms occurred in the blood vessels and around the optic nerve. It also stated that people living in more polluted areas were more likely (18%) to suffer from glaucoma than people living in less polluted areas.[21]

In summary, there appears to be some scientific evidence that levels of gaseous pollutants have some relationship with increased IOP through the different mechanisms of action described above. Exposure to gaseous pollutants could therefore be a risk factor for the development of glaucoma that has not been considered thus far. Although there is still not enough evidence to know its scope and importance in the process, this line of research needs to be explored further, especially in patients with glaucoma and real situations, since pollution levels could be related to a worse prognosis of glaucoma, given that this study found correlations with IOP values in healthy subjects.[24,26,27] Analysis of the scientific evidence indicates the possibility that contamination may have some association with altered aqueous humour flow or inflammatory processes and may be related to the development of glaucoma or even be implicated in normotensive glaucoma.

Study limitations
The main limitations of this study are that the environmental data were collected from two different sources due to the difficulty of finding environmental records a few days after data collection, so not all IOP data could be correlated with environmental data. On the other hand, the IOP data were obtained using five models of air tonometers, technology that has been shown to be reliable in normal IOP ranges; however, in analysing the differences among the tonometers, they may not be interchangeable devices (as some studies suggest), although this study had neither the design nor the analysis to confirm this.[16,28]

Conclusion : there are slight correlations between increased atmospheric temperature, atmospheric pressure, and concentration of gaseous pollutants and increased IOP values in young healthy subjects. Further clinical studies are needed to determine the role of these environmental factors on the aqueous humour flow and thus on the IOP value to determine whether and to what extent they may be risk factors for glaucoma.

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