Impact of Photochemical Reactions Induced by UV Light in Pterygium Lesions

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Pterygium is a frequent ocular disease whose etiopathology is not completely known. Several factors are considered involved in pterygium formation and progression, among which light exposure, age, dry eyes condition, bacterial infections or genetic predisposition. The purpose of our study was to perform a partial evaluation of the social history of 118 patients with pterygium. All of them presented lesions of various sizes, unilateral or bilateral, and underwent surgical removal. We have analysed potential correlations between the degree of progression (lesion size expressed in mm, measured before removal) and several factors: age, sex, residence, sun exposure, presence of chemical burns, smoking habits. According to our results, UV radiation was identified as an important factor, as patients with prolonged exposure exhibited larger lesions. Other factors presented less significant correlations with the size of pterygium lesions.

Keywords: pterygium, ultraviolet radiation, sun exposure

Human vision, expressed in scientific terms, is simple chemistry – an ensemble of reactions enchained one after another, based on the light that enters the eye through the pupil and reaches a focusing point on the retina. Around 100 years ago, scientists have proven that light has a dual nature, being able to act both as a wave, as well as a particle. Over the past decades, doctors have also proven that, from a medical point of view, light is both beneficial and harmful. The visible spectrum, with wavelengths greater than 400-500 nm, is considered safe, while the non-invisible one, composed by ultraviolet light (UVA / UVB / UVC) is considered responsible for damages at skin and eyes level [1, 2], through photochemical reactions and photoimmuno-suppression [3].

Pterygium is recently considered a consequence of UV exposure [4, 5] and represents one of the most frequent diseases of the eye [6]. It is a fibro-vascular growth of subepithelial tissue, originating on bulbar conjunctiva and evolving on the cornea [7]. Nemet describes it as a common, benign, wing-shaped excessive tissue on bulbar conjunctiva [8], with a predilection for nasal location (inner or medial section of the eye), often bilateral. However, Livezeanu et al. considers pterygium to be an invasive disease [9], defined by angiogenesis and chronic inflammation, involving connective tissue remodelling.

Next to light exposure, several other risk factors have been studied before for this lesion, among which irritating environmental conditions (wind, dust, micro-trauma) [10], occupational and hereditary factors (sun exposure, DNA alterations, smoking), bacterial infections [11, 10], etc.

A critical factor however seems to be low spectrum radiation; UV that reaches the Earth's surface is composed by 95% UVA and around 5% UVB. Both types of radiation are involved in the formation of pterygium, but also in the continuous development of these lesions, by altering limbal stem cells and various chemical mechanisms affecting growth factors and angiogenesis [10]. Radiation, no matter its type, determines DNA damage, but also the activation of receptors located on cells' surface. UVB radiation induces oxidative stress, activating intracellular signalling pathways.

On the other hand, UVA radiation generates reactive oxygen species (ROS), which produce an indirect damage of cellular DNA. It is also a source of oxidative stress that initiates the activation of intracellular signalling pathways and transcript factors for multiple targeted genes [12, 13]. Tsai et al. have proven that Ku70 gene, which is, in fact, directly responsible for DNA repairing, indicates a genetic predisposition to develop pterygium [14].

The aim of this study is to partially analyse patients' social history, to assess the role of sex, gender, residence, as well as chemical burns, smoking, previous UV exposure, and determine potential correlations with the length of pterygium lesions, measured before surgical removal.

Experimental part

Materials and method

The research was conducted on a group of 4269 patients which were admitted for different diseases in the Ophthalmology Clinic of the Emergency Hospital Craiova, between 01.03.2017-01.03.2019. From these patients, we selected those with a confirmed pterygium diagnosis, which underwent surgical treatment. The approval for this study was obtained from the Ethic Committee of the Medicine and Pharmacy University of Craiova. An informed consent was obtained from each participant in this study, regarding the treatment and data analysis. A total of 118 patients admitted for pterygium surgery were reviewed.

In order to centralize and study data statistically, the quantitative variables analysed were divided into categories. Lesions have been clinically classified, according to their size, in four categories: stage I (1-2 mm), stage II (3-4 mm), stage III (5-6 mm), stage IV (7-8 mm). Furthermore, the participants were divided into age groups (by decades).

This study included data regarding the following general variables: age, sex, area of residence, chronic UV exposure, smoking, unilateral or bilateral lesion. Each subject underwent a complete eye examination including visual acuity and slit-lamp examination. Other collected data taken into consideration were the presence of ocular burn in the clinical history, side of lesion (right / left) surgically

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treated during the current hospital admission, the lesion location (nasal / temporal / double), variables that could induce a local predisposition or variables that determined the patient to ask for medical advice.

All statistical analyses of the collected data were performed using Microsoft Office Excel (San Francisco, USA). The Chi-square test and T-student were used to evaluate the studied groups distributions and to compare different results (a p value <0.05 was considered statistically significant).

Results and discussions

This retrospective study revealed that between 01.03.2017-01.03.2019, a total of 4269 patients were admitted to the Ophthalmology Clinic of the Emergency County Hospital Craiova, among which 118 (2.74%) were diagnosed with pterygium and underwent surgical treatment, being eligible subjects for our study.

Age of the participants included in the study ranged from 35 to 91 years, with a mean age of 65.38 ± 11.6. Furthermore, they were divided in 6 groups, according to age decades, starting with 35-44 years (first decade) and finishing with 85-94 (sixth decade). Most affected age group was 65-74 years (41 patients, 34.75%) followed by 75-84 years (28 patients, 23.73%), 55-64 years (24 patients, 20.34%), 45-54 years (17 patients, 14.41%), 35-44 years (6 patients, 5.08%) and the last group 85-94 years (2 patients, 1.69%). The age of urban area residents was mostly included in decades 2-5 (excepting one patient, 44 years old), in comparison with the rural area residents, which were found in every age group.

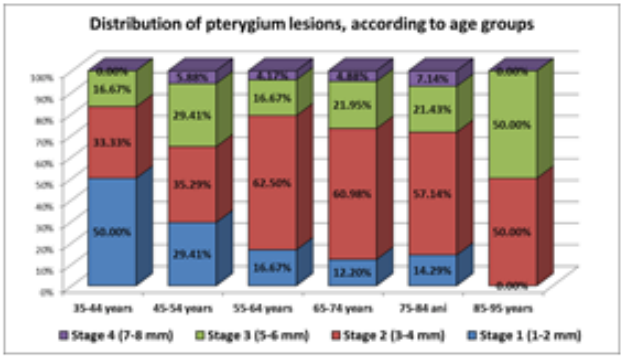

Fig. 1. Distribution of patients in age groups, according to stage of pterygium lesion

Regarding the affected eye, a total of 78 patients had unilateral pterygium, from which 48 patients presented the lesion in the right eye, 30 patients in the left eye. Bilateral lesions were found in 40 patients. There are no statistically significant differences in pterygium size variation depending on the affected side ($p=0.94$). There are significant differences regarding the unilateral / bilateral disease ($p<0.05$); in unilateral disease the mean extent was 3.41 mm compared with a mean extent of 4.65 mm described in bilateral disease.

As far as grading is concerned, stage II was the most common. Out of the 118 patients included in the analysis, 65 subjects were classified as stage II (3-4 mm), representing 55.08%, followed by stage III (26 subjects, 22.03%), stage I (21 subjects, 17.80%) and stage IV (6 subjects, 5.08%). The distribution of patients from out study group according to age and stages is shown in figure 1.

Analysing the progression of pterygium lesions within every age decade, we observed that stage I had a similar number of patients for all 6 decades (3-5 patients); however, the percentage corresponding to these values decreased from 50% in the first decade to 0% in the last decade. Stage II had a normal distribution, with an increase in the first three decades, a maximal value in the 55-64 years decade, and a decrease in the last three decades. Grades III and IV have shown small variations between successive decades (maximum 12.7%), being constantly represented throughout the age groups included in the research.

As for the size of the pterygium lesions, there was no linear correlation with the age of the patients (an increasing age trend doesn't imply a similar size trend). The largest lesions were described in 3 patients belonging to different age groups (51, 71, 73 years).

There were no significant differences between gender groups, 58 participants were female, representing 49.15%, the rest of 60 participants being male, representing 50.85% of the total. Moreover, the differences regarding the size of the lesion between male and female were not statistically significant ($p=0.17$) (table 1).

As far as the residence area is concerned, the presence of pterygium was associated mostly with rural residents – 92 patients, representing 77.97 %, in comparison with 24 patients from urban area (22.03%). In the rural area, the sex distribution shows a slight female predominance, with 52 female participants compared to 40 male participants. There are no statistically significant differences between lesion sizes in correlation with the area of residence (rural / urban) ($p=0.22$), nor between male and female from rural area ($p=0.51$) or urban area ($p=0.18$) (table 1).

Regarding the distribution of patients according to pterygium location, we observed that 110 patients (representing 93.22% from the study group) exhibited nasal location, among which 76 had unilateral lesions (46 patients with the right eye, 30 patients with the left eye), and 17 had bilateral lesions. Seven patients (5.93%) presented a double location – both nasal and temporal, among which 2 patients (1.69%) with unilateral lesions,

Table 1

DISTRIBUTION OF PATIENTS ACCORDING TO SEX, RESIDENCE, AND THE MAIN VARIABLES ANALYSED IN OUR STUDY

	Urban		Rural		
	Males	Females	Males	Females	*P*
Sex / residence	20	6	40	52	0.17 / 0.22
Right eye / Left eye	13 / 7	2 / 4	19 / 21	34 / 18	0.94
Unilateral / Bilateral	15 / 5	3 / 3	23 / 17	37 / 15	**<0.05**
Nasal location / Nasal and temporal location	19 / 1	6 / 0	35 / 5	51 / 1	0.31
UV exposure	6 / 14	1 / 5	37 / 3	50 / 2	**<0.05**
Chemical burns	1	0	4	0	0.76
Smoking	11	0	30	0	0.07

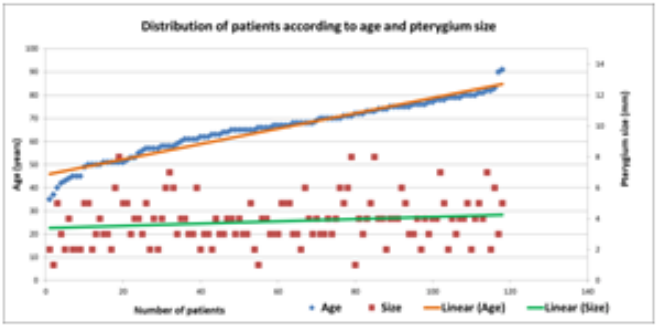

Fig. 2 Distribution of patients according to age and pterygium size

both for the right eye, and 5 (4.23%) with bilateral lesions, 2 patients with the right eye, 3 patients with the left eye. One patient (a 45 years old male, rural residence, pterygium lesion size 2 mm) exhibited an asymmetrical location: nasal for the right eye, temporal for the left eye.

Our statistical analysis upon the study lot performed so far was completed with the study of possible correlations between lesions' size and other observed parameters: sun exposure, chemical burns and smoking habit.

When we centralized our data regarding the UV exposure, we observed that patients with urban residence declared UV exposure, but in a smaller ratio compared with patients with rural residence (5.93% compared with 73.73% from the entire study group) (table 1). These differences regarding the degree of sun exposure may justify the large number of patients with rural residence and pterygium lesions (due to specific outdoor activities, mostly agricultural, the UV exposure level is higher).

The impact of UV exposure upon the pterygium length, measured before the surgical removal, was statistically significant, since we observed significant differences regarding the lesions' size for the group of patients with a high degree of sun exposure and the group with less sun exposure. From the same point of view, there are no significant differences between males and females, or patients with urban and rural residence, or patients with unilateral and bilateral lesions, all from the group of patients with a high degree of UV exposure ($p > 0.05$) (table 1). We can thus assume that the longer the sun exposure, the greater the lesion will be (if left untreated).

Five patients (4.23% from the total study group) presented chemical burns; they were all males, 4 with rural residence and 1 with urban residence, all with ages between 49 and 60 years old (patients included in decades 2 and 3) and with pterygium lengths varying from 2 to 5 mm. There is no correlation between the lesion size measured before the admittance in the Ophthalmology Clinic, and the presence of chemical burns (table 1).

In what concerns smoking habit, we observed that 34.75% from all patients in the study group (all males) presented this addiction. Most of the 41 smokers had ages included in the decades 2, 3 and 4, being distributed according to residence as follows: 30 patients (25.42%) with rural residence and 11 patients (9.32%) with urban residence. Eleven patients (26.83%) had lesions in the first stage (2 mm), almost all the rest had lesions in stages 2 and 3 (70.73%), and only one patient had a lesion in stage 4. Pterygium length and smoking do not seem to be correlated, yet the computation of Pearson's coefficient lead to a value quite close to the threshold value ($p = 0.07$), which means however that there are no significant differences between the two series of patients (table 1).

Earth's atmosphere is a natural barrier for UV light, especially below 280 nm. However, recent studies have indicated that the ozone layer has decreased, leading thus to a higher amount of UV radiation reaching the surface [1, 15]. According to K. Walsh, almost 95% of the general population associates prolonged UV exposure to skin problems, varying from minor sun burns to melanoma [16]. But the impact of UV radiation upon the eyes is hardly known, thus most people are unaware of the need to protect their eyes with sun glasses or hats with large brims, especially when they perform outdoor activities. This explains why the prevalence of pterygium varies from 2.2% in China (mostly persons older than 40 years), where the population lives at high altitudes [17], up to 41.8% in Ethiopia [18], a country located in the Equatorial region. Bikbov studied a Russian population in 2019, reporting a prevalence of 2.3% for pterygium [19].

This current report issued from our research does not define the prevalence of pterygium in Romania, but the ratio among the ocular pathology of patients admitted in the Ophthalmology Clinic, Emergency County Hospital of Craiova (2.74%).

According to our study, most patients with pterygium had ages between 65 and 75 years, followed by those with ages included in 55-65 years old interval, and those with ages between 75-85 years old. Basically, our study group was mostly composed by elderly persons. In 2013, Nangia V [20] reported that in India, the patients with ages within the interval 70-79 years old were predominant. H Hashemi, in 2017, reported similar values for a population in Iran, only that, this time, the predominant age interval was 61-70 years old. Other studies [6, 19, 21, 22] have identified significant correlations between pterygium and patients' higher age. On the other hand, Zhao L [23] had conducted a study over a 10-years period of a population divided in age intervals, and concluded that age does not seem to have an impact on pterygium prevalence. Similar results are presented in [24, 25].

When it comes to sex distribution, the debate is still active à there are authors that indicate females as most likely to develop pterygium [26, 27], while others state that males are more affected [28,17]. Our study emphasized that both sexes are almost equally impacted, with a slightly larger number of males. Differences between results are based on outdoor activities performed by the patients included in the study lots, which are specific for every region / country, climatological context, as well as the habit to use protective measures during UV exposure (sunglasses, large brim hats).

Similar differences also justify the association between residence and sun exposure (UV radiation) - our study reported a clear correlation between these variables and pterygium: most patients lived in rural regions, and presented sun exposure, most likely in the context of performing daily agricultural activities. Other studies have reported similar correlations with the rural residence [17-20] or light exposure [29, 10].

Regarding lesion localisation, patients from our study group exhibited mostly nasal pterygium (93.22%), and only rarely was it double – both nasal and temporal location (5.93%). Our results are similar to those obtained by F. Duman [30], based on a study group of 158 patients, who presented double pterygium in 5% of the cases, and also by M. Bikbov who studied a group of 138 patients [19]. Other studies conducted by Ribeiro and Bikbov also confirm the preference of this lesion for the nasal aspect [19, 31]. This is mainly due to two different factors: environmental context that influences the distribution of UV radiation

along the palpebral fissure, and Peripheral Light Focusing (PLF). The first factor is related to how uniform is the distribution of incident UV across the lid border, based on clear or cloudy skies, and solar zenith angle (SZA) (which represents the angle between the position of the sun and the zenith). PLF takes place when radiation strikes the cornea at temporally oblique angles; these angles may determine a maximum intensity of solar rays at the nasal limbus, hence predominant pterygium location [32, 4].

Pterygium is rarely double, but it is more often bilateral. From our study lot, a number of 40 patients (representing 34% of the total number of patients) presented bilateral lesions. Bikbov reported a similar value – 32.6% patients with bilateral pterygium [18], while two more studies on sample populations from Brazil [31] and Myanman [33] reported more extreme values: 75.6%, respectively 8%.

Pterygium size was measured before the surgical removal. This value was recorded at that specific moment of time. We did not perform a study of lesions' progression over a certain period of time. For our study, we report a variation of pterygium lesions' dimension between 1 mm to 8 mm, with an average of 3.83 ± 1.47, a very high value compared to a study conducted by Mohammad-Salih PA in 2008 [34], where the lesion size varied between 0.25 and 6.50, as well as another study managed by LAM Ribeiro in 2011 [31], where 93% of all patients had lesions smaller than 2 mm. We observed a probability of pterygium formation similar for all age groups, indicating thus an independence degree for this parameter. Also, we report a slightly increasing trend towards the average lesions' size, correlated with age progression, especially for the first decades.

Most of our patients presented lesions of stage II, which indicates either a potential stabilisation of dimension around the average value (up to 4 mm) [23], or the reach of a certain border value beyond which the discomfort is serious enough for the patient and thus surgical removal of pterygium is required. The largest lesions were reported mostly for patients with rural residence (stages III and IV), associated with a late request for surgery, despite the size of the lesion and the presence of some associated symptoms. Pterygium size is important due to its consequences (astigmatism) [35, 31, 34], but also by its associations with tearing, feeling of foreign body or blurred vision.

According to [36, 37], smoking is not associated with pterygium, and our study seems to confirm this hypotheses. However, smoking is a controversial variable, as there are also studies which confirm the association [17] or, moreover, state that it is a protective factor [38, 39].

The only variable that basically represents, without a doubt, the most significant risk factor for pterygium is the exposure to UV radiation [13, 18, 19, 29, 40]. This is also confirmed by our study, both as a variable whose status was declared by every patient, as well as a potential consequence of the residence context and outdoor activities involved by this reason[41-55].

Conclusions

Pterygium affects mainly elder persons, with rural residence and a prolonged sun exposure. Within our study, the patients presented mostly nasal location, with similar distributions for both eyes. Pterygium length varied from 1 mm to 8 mm – value which was recorded only once, in the moment of admittance in the clinic, prior to surgery. Analysing the average size of lesions, we observed that patients who were more exposed to UV radiation presented bigger lesions than patients with less sun exposure, indicating a potential correlation between these two variables.

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Manuscript received 19.10.2018