Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Ophthalmology

Impact of Hypotonizing Treatment in Patients with Glaucoma on the Ocular Surface: About 52 Patients

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DOI: 10.36347/sjmcr.2021.v09i12.001 | **Received:** 22.10.2021 | **Accepted:** 29.11.2021 | **Published:** 04.12.2021

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Abstract **Original Research Article**

Ocular surface disease (OSD) and glaucoma are common comorbidities in the same patient. Thus, the long-term instillation of topical intraocular pressure lowering drops induces changes in the ocular surface. For this, we have realized a cross-sectional study of 52 patients, collected at the ophthalmology department of the Hassan II University Hospital Center at Fez, Morocco. We have included all patients with glaucoma or ocular hypertonia on hypotonizing treatment for at least 06 months. They have answered the Ocular Surface Disease Index (OSDI) after their consent. All patients have been then examined with a slit lamp by the same ophthalmologist to assess the severity of the OSD. A total of 101 eyes from 52 patients were analyzed. Thirty-six (69%) patients treated with hypotonizing eye drops required multitherapy. Only nine (17%) patients were on preservative-free eye drops. The average OSDI score was 32.4/100 (0—82.5). According to clinical classification, 27 (52%) patients had severe OSD. This study confirms the high frequency of the OSD in patients medically treated for glaucoma or ocular hypertonia. Damage on the ocular surface is responsible for disabling symptoms that can affect both the quality of life of patients and adherence to the treatment. Thus, any ophthalmologist should systematically include the evaluation of the ocular surface in glaucomatous patients.

Keywords: Ocular surface disease, glaucoma, OSDI, quality of life.

INTRODUCTION

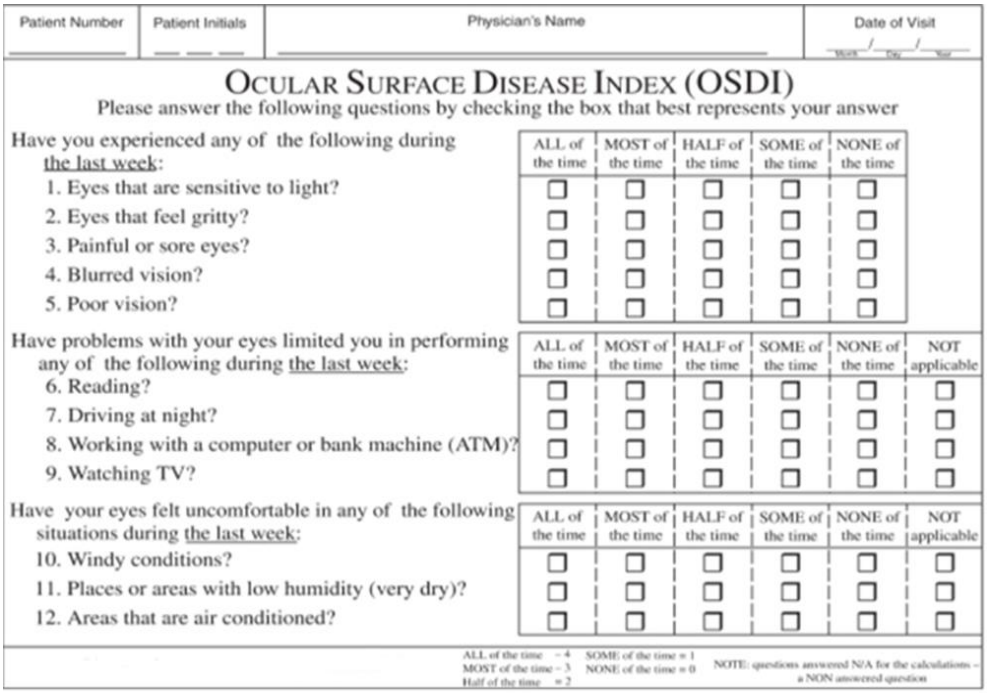
Ocular surface disease (OSD) and glaucoma are common comorbidities in the same patient. Thus, the long-term instillation of topical intraocular pressure (IOP) lowering drops induces changes in the ocular surface. There is an increased prevalence of signs and symptoms of the ocular surface in these glaucomatous patients such as dry eye, chronic blepharitis, conjunctivitis or keratitis [1, 2].

This OSD plays a key role - although underestimated - in the management of glaucomatous patients. It is responsible for an alteration of their quality of life and consequently for their therapeutic adherence [3, 4], which will have a negative impact on the control of glaucoma, which is progressive.

MATERIAL AND METHODS

We have realized a cross-sectional study of 52 patients, collected at the ophthalmology department of the Hassan II University Hospital Center at Fez, Morocco. We have included all patients with glaucoma or ocular hypertonia on hypotonizing treatment for at least 06 months.

They have answered the Ocular Surface Disease Index (OSDI) after their consent (*Figure 1*). Note that we have used a translation of the OSDI score adapted to our cultural and social context (*Figure 2 and 3*) where the collection of data can only be done by the doctor himself, while waiting for the elaboration of a questionnaire validated in our context.



Patient Number	Patient Initials	Physician's Name	Date of Visit
			/ /

OCULAR SURFACE DISEASE INDEX (OSDI)

Please answer the following questions by checking the box that best represents your answer

	ALL of the time	MOST of the time	HALF of the time	SOME of the time	NONE of the time	NOT applicable
Have you experienced any of the following during the last week:						
1. Eyes that are sensitive to light?	☐	☐	☐	☐	☐	
2. Eyes that feel gritty?	☐	☐	☐	☐	☐	
3. Painful or sore eyes?	☐	☐	☐	☐	☐	
4. Blurred vision?	☐	☐	☐	☐	☐	
5. Poor vision?	☐	☐	☐	☐	☐	
Have problems with your eyes limited you in performing any of the following during the last week:						
6. Reading?	☐	☐	☐	☐	☐	☐
7. Driving at night?	☐	☐	☐	☐	☐	☐
8. Working with a computer or bank machine (ATM)?	☐	☐	☐	☐	☐	☐
9. Watching TV?	☐	☐	☐	☐	☐	☐
Have your eyes felt uncomfortable in any of the following situations during the last week:						
10. Windy conditions?	☐	☐	☐	☐	☐	☐
11. Places or areas with low humidity (very dry)?	☐	☐	☐	☐	☐	☐
12. Areas that are air conditioned?	☐	☐	☐	☐	☐	☐

ALL of the time = 4 MOST of the time = 3 Half of the time = 2 SOME of the time = 1 NONE of the time = 0 NOTE: questions answered N/A for the calculations = a NON answered question

Figure 1: OSDI (Ocular Surface Disease Index)

خلال الأسبوع الماضي، هل أحسست بشيء من هذا القبيل:

	كل الوقت	أغلبية الوقت	نصف الوقت	بعض الأوقات	أبدا
1) أعينك حساسة من الضوء					
2) إحساس الرمل في عيناك					
3) ألم في العيون					
4) نظرة ضبابية					
5) نقص في النظر					

خلال الأسبوع الماضي، هل أحسست بمشاكل في نظرك أز عجتك للقيام بمهمة من المهام التالية:

	كل الوقت	أغلبية الوقت	نصف الوقت	بعض الأوقات	أبدا	غير مهتم
6) القراءة						
7) سياقة السيارة ليلا						
8) استعمال الحاسوب						
9) مشاهدة التلفاز						

خلال الأسبوع الماضي، هل أحسست بانز عاج في أعينك خلال موقف من المواقف التالية:

	كل الوقت	أغلبية الوقت	نصف الوقت	بعض الأوقات	أبدا	غير مهتم
10) في الرياح						
11) في ظروف جافة جدا						
12) في المكيف الهوائي						

Figure 2: OSDI in Arabic

كيفية حساب مؤشر OSDI

كل الوقت	أغلبية الوقت	نصف الوقت	بعض الأوقات	أبدا
4 نقاط	3نقاط	2 نقاط	1 نقطة	0 نقطة

مجموع النقاط = X

مجموع الأسئلة المجاب عنها = Y

مؤشر OSDI = (X*25) / Y

Figure 3: Calculation of the OSDI score in Arabic

Each item was associated with a score. The entire questionnaire, once completed, gave a total score on 100 points. Patients were thus classified into several groups (5):

- Group 1 (score from 0 to 12): no symptoms of damage on the ocular surface.
- Group 2 (score from 13 to 22): slight damage on the ocular surface.
- Group 3 (score from 23 to 32): moderate damage on the ocular surface.
- Group 4 (score from 33 to 100): severe damage on the ocular surface.

All patients have been then examined with a slit lamp by the same ophthalmologist to assess the severity of the OSD. This was classified into three groups (A: no OSD, B: moderate OSD, C: severe OSD) (Table 1).

Table 1: Evaluation of the ocular surface disease

Group A	Absence of staining on the ocular surface by the fluorescein test despite the possible presence of minimal blepharitis on at least one eye.
Group B	Presence of moderate blepharitis (inflammation of the free edge of the eyelids with abnormal, viscous, or absent Meibomian secretion) associated with a BUT < 5s and or superficial punctate keratitis (SPK) < 30% of the ocular surface on at least one eye.
Group C	Presence of a SPK > 30% and/or presence of chronic non-infectious ulceration on at least one eye.

N.B.: the most affected eye was considered during the clinical analysis.

The statistical analysis has been carried out by Excel software. Statistical comparisons have been made using SPSS software, a $p < 0.05$ was considered significant.

RESULTS

A total of 101 eyes from 52 patients were analyzed. There were 30 women and 22 men with an average age of 59.53 ± 14.57. The mean visual acuity was 0.4 LogMar, or 4/10 after conversion to decimal visual acuity. The mean pachymetry was 542.2 µm (431 - 620). The average IOP was 17.2 mmHg (8 - 42). Glaucoma had been known for 5.2 years (0.5 – 15) (Table 2).

Table 2: Profile of patients in the study, average (min-max)

Parameters	Average
Number of patients	52
Number of eyes	101
Age (years)	59.53 (26 - 91)
Sex ratio (M/W)	0.73
Visual acuity (logarithmic scale)	0.4 (no light perception - 0)
Visual acuity (decimal scale)	0.4 (no light perception - 1)
Intraocular pressure (mmHg)	17.2 (8 - 42)
Pachymetry (µm)	542.2 (431 - 620)
Age of glaucoma (years)	5.2 (0.5 -15)

Thirty-six (69%) patients treated with hypotonizing eye drops required multitherapy (two active substances or more), compared to sixteen (31%) patients who were on monotherapy. Of these, only nine (17%) patients were on preservative-free eye drops, while thirty-two (62%) were on preservative-containing hypotonizing eye drops, and the rest (21%) were on eye drops containing two or more preservatives. It should be noted that only eight (15%) patients used artificial tears at the time of the study.

Based on the results of the questionnaire from the OSDI, we divided patients into four groups according to the intensity of symptoms of ocular surface involvement. Eight patients (15%) had no significant symptoms of ocular surface involvement (group 1). The second group included nine patients (18%). The third group had 10 patients (19%) and the fourth group had twenty-five patients (48%). The average OSDI score was 32.4/100 (0—82.5).

Patients were assigned according to clinical classification A, B and C. Group A (no OSD), group B (moderate OSD) and group C (severe OSD) had 15 (28%), 10 (20%) and 27 (52%) patients, respectively.

DISCUSSION

Patients treated for glaucoma or ocular hypertonia often have OSD due to the long-term administration of hypotonizing eye drops. The toxic effect of eye drops is time-dependent, so it often takes several years to be able to highlight clinical damage on the ocular surface. However, glaucoma patients may also have eye surface involvement pre-existing local treatment. Indeed, Moss *et al.*, determined the frequency of dry ocular syndromes on a sample of 3722

patients whose average age was equal to 65 years (48 to 91 years), age corresponding to that of glaucomatous patients. The prevalence of recovered dry syndrome was equal to 14.4% [6].

Studies have focused specifically on this damage of the ocular surface in patients treated for glaucoma or ocular hypertonia. Van Went et al. thus showed a particularly high frequency of symptoms and clinical signs. In this study of 88 patients, 82% of patients had an abnormal OSDI score (groups 2, 3 and 4), and 76% of patients had slit lamp visible OSD (B+C). This study also showed a lower frequency of symptoms of OSD in patients treated with eye drops without preservatives [7]. Fechtner *et al*., conducted a similar study in the United States. In 630 glaucomatous or hypertonic patients treated with eye drops, the incidence of symptoms of OSD was 48.4% [8]. In another study, Rossi *et al.*, reported that 45.1% of medically treated glaucoma or hypertonic patients had symptoms of OSD [9]. Saade *et al*., from Canada, showed on a sample of 31 patients, that 68% had a symptomatology consistent with OSD.

In our study, 44 patients (85%) had significant symptomatology (abnormal OSDI), and 72% of patients had OSD visible to the slit lamp (B+C). The frequency of damage on the ocular surface was high. Because, our study was carried out within a university department, the profile of the patients brought to consult was therefore particular. Glaucoma was very often advanced and more or less well controlled by local hypotonizing treatment.

Nowadays, we are seeing the rise of new ocular surface imaging platforms, combining several tools for assessing the ocular surface. Among the latter, we find infrared meibography which makes it possible to study the morphology of the Meibomian glands. The interferometry of the tear film which allows an indirect measurement of the thickness of the lipid layer of the tear film between the blinks. Some platforms also allow automated measurement of break-up time (BUT) with fluorescein (FBUT), or even without fluorescein or NIBUT (non-invasive break up time) based on an analysis of the stability of the reflections of placido's disc sights. Finally, some devices also allow an automated measurement of the height of the lacrimal meniscus, or a semi-quantitative evaluation of conjunctival hyperemia. These new platforms thus allow an objective assessment of the ocular surface, compared to the subjective analysis made in our study as in most studies on OSDI. So why not integrate these paraclinical platforms into future studies on ocular surface?

One of the major problems with the medical treatment of glaucoma, as with other insidious chronic diseases, is adherence to treatment [4]. After forgetfulness and administration errors, side effects related to glaucoma treatment are believed to be the third leading cause of poor adherence [10]. Nordmann *et al*., analyzed quality of life in 204 patients treated for glaucoma or ocular hypertonia. Nearly 93% of patients experienced at least one side effect. These local side effects were associated with a poorer quality of life, with a greater risk of poor adherence and therefore loss of therapeutic efficacy [3].

A recent literature review (ASIEDU 2018) points out that symptoms of dry eye are more common in glaucoma patients, compared to the general population. This is related -among other things- to the presence of preservatives in hypotonizing eye drops. The main preservative implicated is BAK (benzalkonium chloride), although the other preservatives are also implicated [11]. Thus, these therapeutics are therefore involved in the occurrence of dry syndrome in glaucoma. For this, ophthalmologists must anticipate the management of pathologies of the ocular surface in case of glaucoma.

CONCLUSION

Glaucoma is a potentially blinding progressive chronic anterior optic neuropathy that evolves in an insidious way. For this, it requires a lifetime treatment; and on the front line, medical treatment is used. This study confirms the high frequency of the OSD in patients medically treated for glaucoma or ocular hypertonia. Damage on the ocular surface is responsible for disabling symptoms that can affect both the quality of life of patients and adherence to the treatment. Thus, any ophthalmologist should systematically include the evaluation of the ocular surface in glaucomatous patients, in the same way as the measurement of intraocular pressure in them.

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