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RESEARCH ARTICLE

IMPACT ON THE OCULAR SURFACE OF SOME GLAUCOMA DRUGS

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ABSTRACT

Purpose: To compare the impact on the ocular surface of glaucomatous patients under monotherapy by latanoprost, tafluprost, bimatoprost and bimatoprost/timolol 0.50% fixed combination. **Patients and Methods:** This is a single center, clinical and epidemiological study. Fourty glaucomatous patients (20 males; 20 females), age and sex-matched were divided in four groups according to monotherapy (latanoprost 0.005%, tafluprost 0.0015%, bimatoprost 0.03% and bimatoprost 0.03%/timolol 0.50% fixed combination). All of these patients had at least three months follow-up and were under tonometric control. All of these patients were categorized according to a new algorithm to classify the clinical and familiar risk factors. All of them received OSDI and NEI-VFQ-25 questionnaires to evaluate their quality of life under monotherapy. The statistical analysis was performed by Student's t-test as for demographical data and one-way ANOVA as for the questionnaires results. $P<0.05$ was considered statistically significant. **Results:** All the glaucomatous patients answered their questionnaires. According to the different groups, latanoprost group had a p=0.302, tafluprost group p=0.381, bimatoprost/timolol 0.50% fixed combination p=0.141 and bimatoprost group p=0.000. **Conclusions:** All the glaucomatous patients completed this study. The Author hypothesizes that the bimatoprost group is the only statistical significant because bimatoprost is a drug usually prescribed in advanced glaucomatous patients, where the clinical picture and the ocular surface are usually more damaged than in the early stage of glaucoma disease.

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INTRODUCTION

Glaucoma is a chronic, progressive optic neuropathy, involving around 60.5 millions of people worldwide in 2010 and 80 millions cases estimated to ensue in 2020 (1). Ocular surface disease (OSD) and dry eye disease (DED) are very common diseases in the elderly and they can decrease vision-related quality of life (2, 3, 4, 5). Hollo' termed this disease as glaucoma therapy-related ocular surface disease. In glaucoma drugs benzalkonium chloride (BAK), used as a preservative, has a dose-dependent toxic effect, induction of apoptosis and destruction the tear film lipid layer, increasing tear film evaporation. That's why long term use of preservatives in topical glaucoma drugs may induce OSD and worsenes OSD in eyes with OSD or DED. Preservative-free (PF) topical glaucoma drugs have been available worldwide. When OSD is detected, it is strongly recommended to introduce PF artificial tears. However these efforts are not always sufficient. As OSD may suffer our glaucomatous patients, it is advisable to use PF glaucoma medications. A new questionnaire (F.A.S.T Fast Assessment of ocular Surface Trouble) was recently presented as poster at the 13th European Congress of Glaucoma E.G.S. (Florence, May 19th-22nd 2018) by Misiuk-Hojlo M. et al. (6). Prostaglandin analogs (PGAs) are, nowadays, the first-line therapeutic class for medical treatment of glaucoma worldwide (7, 8, 9, 10, 11, 12). They are used as monotherapy and they have a well-tolerated systemic safety profile. A part of these side-effects are caused by the preservatives used in conjunction with the PGA molecule. The impact of preservatives on the ocular surface became more and more important in the last years in the international Literature and novel preservative-free PGA have been developed. In this clinical and epidemiological study we used: latanoprost 0.005% (with BAK 0.02%) Xalatan®Pfizer, tafluprost 0.0015% (preservative-free) Saflutan®Santen, bimatoprost 0.03% (with BAK 0.02%) Lumigan 0.3®Allergan and bimatoprost 0.03%/timolol 0.50% (preservative-free) Ganfort®Allergan.

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PATIENTS AND METHODS

It is a single center clinical and epidemiological study. We enrolled 40 glaucoma patients (20 males, 20 females), who were under therapy since at least 3 months. According to their topical glaucoma therapy, these patients were divided in 4 groups: latanoprost (L), tafluprost (T), bimatoprost 0.3 (B) and

Table 1. Evaluation algorithm of risk progression in glaucoma patients

	<14 mmHg	14-18 mmHg	19-24 mmHg	25-30 mmHg	>30 mmHg
No risk factor	A1	A2	A3	A4	A5
Life expectancy > 15 y	B1	B2	B3	B4	B5
Vascular risk	C1	C2	C3	C4	C5
Additional vascular risk	D1	D2	D3	D4	D5
Any perimetric damage	E1	E2	E3	E4	E5
Central perimetric Damage	F1	F2	F3	F4	F5
PEX	G1	G2	G3	G4	G5
Perimetric progression speed > 1db/y	H1	H2	H3	H4	H5

Table 2. Results

Latanoprost (l)	P=0.302
Tafluprost (t)	P=0.381
Bimatoprost (b)	P=0.000
Bimatoprost/timolol (bt)	P=0.141

Ocular Surface Disease Index© (OSDI©)[2]

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

Have you experienced any of the following *duringthe last week?*	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light? . .	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

Have problems with your eyes limited you in performing any of the following *duringthe last week?*	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
6. Reading?.	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?.	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

Have your eyes felt uncomfortable in any of the following situations *duringthe last week?*	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
10. Windy conditions?.	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?. . .	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

Add subtotals A, B, and Cto obtain D (D= sum of scores for all questions answered) (D)

Total number of questions answered (do not include questions answered N/A) (E)

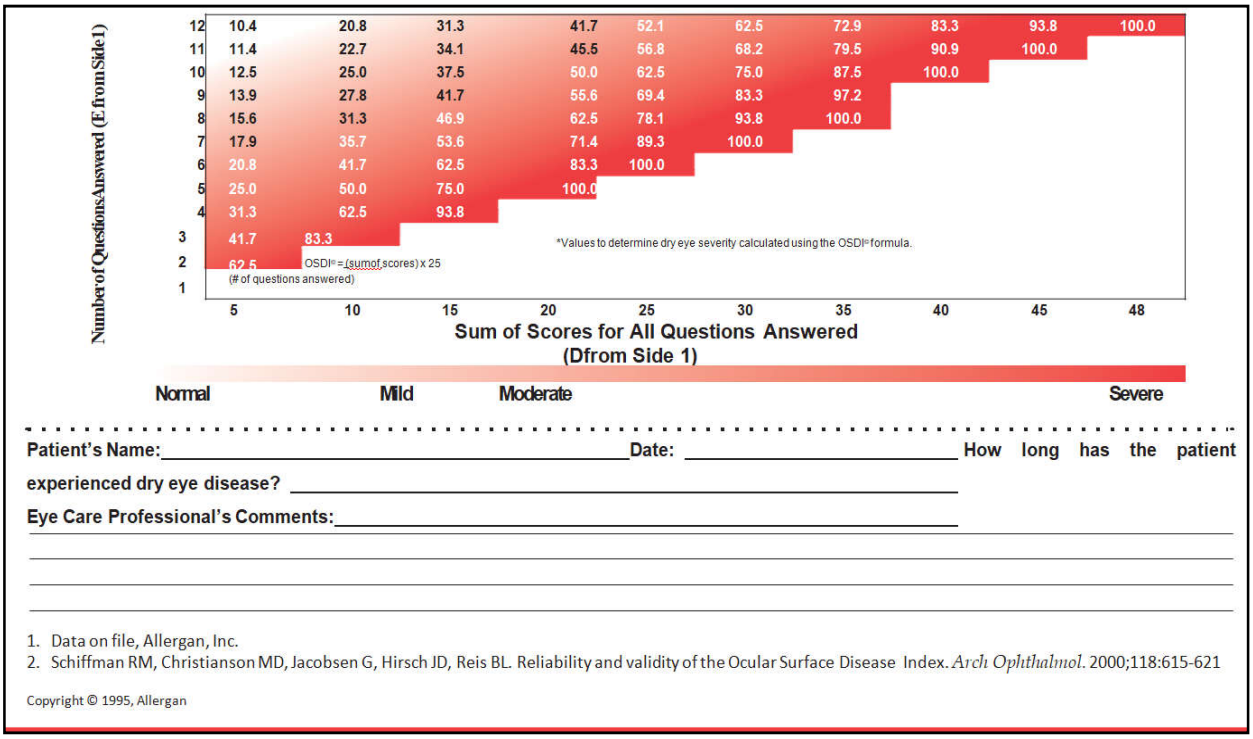
Please turn over the questionnaire to calculate the patient's final OSDI© score.

bimatoprost 0.3/timolol 0.50 (BT) fixed combination. The demographic characteristic of the group L are: 10 glaucoma patients (5 M, 5F), mean age 57 years S.D. 14.73, range 48-74 years. The T group included 10 glaucoma patients (5M, 5F), mean age 67.5 years S.D. 5.802, range 59-72 years. The B group included 10 glaucoma patients (5M, 5F), mean age 76.67 years S.D. 10.9, range 59-88 years. The BT group included 10 glaucoma patients (5M, 5F), mean age 59.6 years S.D. 6.189, range 53-69 years. All the patients included in this study were stratified in an algorithm by the same observer. This algorithm evaluates the risk of glaucoma patients in low, moderate, high and very high. Table 1 shows this algorithm: on x-axys the level of the intraocular pressure (IOP) <14 mmHg, 14-18 mmHg, 19-24 mmHg, 25-30 mmHg and > 30 mmHg; on y-axis the risk factors. They are divided in: life expectancy > 15 years; vascular risks such as diastolic perfusion pressure < 55 mmHg, hypertension treated with more than 2 drugs, cerebrovascular accidents, Raynaud syndrome and optic disk hemorrhages (Table I). Further vascular risks are at least 2 among: older than 65 years; Afro-Caraibic descent; first degree glaucoma blind; corneal thickness < 500 µm; myopia > 6 diopters; only one eye patient (Table I). Other risk factors

The OSDI© is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI© is a valid and reliable instrument for measuring dry eye disease (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease[1, 2]

Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.* Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



1. Data on file, Allergan, Inc.
2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621

mentioned are: mean deviation > 12 dB; any central perimetric damage; pseudoexfoliation (PEX) and perimetric progression rate > 1 dB/year. All these data were matched and classified from A1= 1 point = early glaucoma till H5 = 40 points = advanced glaucoma (Table I, 13 Gandolfi S. et al. unpublished data presented as poster at the 13th European Glaucoma Congress E.G.S. Florence May 19th-22nd 2018). Indeed, all the patients had an Ocular Surface Disease Index (O.S.D.I.) score (Fig. 1) and a NEI-VFQ-25 score. Both of these questionnaires may be downloaded for free. The statistical analysis was performed by Student's t-test as for demographical data and by one-way ANOVA as for the questionnaires scores. $P<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

All the 40 patients (20 males; 20 females) were stratified according to their risk factors (Table I). They were divided in 4 groups, based on their medical therapy: L, T, B and BT (see Patients and Methods section). In the same ophthalmological assessment they answered the two questionnaires: O.S.D.I. (Fig. 1) and NEI-VFQ-25. In each group the figures obtained were statistically analyzed by one-way ANOVA. The Results are summarized in Table II: L P=0.302; T P= 0.381; B P=0.000 and BT P=0.141. As all the patients were under complete tonometric control and there was no statistically significant difference in their IOP, during tonometric curve, we can hypothesize that only bimatoprost 0.3% group was statistically significant because this drug is usually prescribed in advanced glaucoma, not in early stage glaucoma patients. In any case, this is a preliminary report on patient compliance versus glaucoma risk factors and further studies are needed because the sample of patients is quite poor.

The Author declares no financial interest in any drug cited in this paper

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