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European real-world data about the use of a new delivery system containing a preservative-free multi-dose glaucoma treatment

Philippe Denis[1], Susana Duch[2], Enping Chen[3], Per Klyve[4], Jesper Skov[5], Païvi Puska[6] and Carl Erb[7]

Abstract

Background: Glaucoma treatments are mostly presented in uni-dose or multi-dose format. A certain number of patients with visual acuity and dexterity problems may have problems in instilling eye drops.

Aim: To assess patient satisfaction and ease of use of a preservative-free glaucoma treatment (dorzolamide/timolol) in a new and innovative patented multi-dose delivery system.

Methods: Retrospective, international, multicentre, non-interventional study in 788 adult patients using a multi-dose delivery system for at least 28 days.

Results: Mean patient age was 68.1 ± 12.1 years. Mean duration of multi-dose delivery system use was 132.1 ± 125.1 days; 66.5% of the patients previously used multi-dose and 33.5% uni-dose delivery systems (n = 734); 78.3% of the patients were satisfied or very satisfied with the multi-dose delivery system. A significant majority (all $p \leq 0.045$) of patients with a QuickDash® score between [0 to 25[(66.4%, n = 211) and [50 to 75[(81.8%, n = 11) rated multi-dose delivery system as easy or very easy to open and significantly more subjects in the [0 to 25[(72%) score group rated multi-dose delivery system as being better or much better than their previous device (n = 211). Significantly (all $p < 0.01$) more subjects with available visual acuity results rated multi-dose delivery system as good, better or much better than their previous dispensing device.

Conclusion: The tested multi-dose delivery system was highly accepted. It is, therefore, suitable for glaucoma patients with decreased visual acuity and/or dexterity problems. Further studies may be necessary to assess the easiness of use of this easy-to-grip delivery system.

Keywords

Preservative-free, multi-dose easy-to-grip delivery system, dorzolamide/timolol, glaucoma, real world, ease of use, patient satisfaction, compliance

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Introduction

Glaucoma is one of the three leading causes of blindness in developed countries along with cataracts and age-related macular degeneration. Primary open-angle Glaucoma (POAG) is characterised by a progressive alteration of the optic nerve. The prevalence of people with glaucoma worldwide will increase to 111.8 million in 2040.[1] Glaucoma can occur at all ages and its prevalence varies between 1% and 4% in people over 40 and increases with age. The prevalence

[1]Service d'Ophtalmologie, Hôpital de la Croix-Rousse, Hospices Civils de Lyon, Lyon, France
[2]Glaucoma Unit, Innova Ocular–ICO Barcelona, Barcelona, Spain
[3]Department of Anterior Segment Disorders, Glaucoma, Neuro-Ophthalmology and Oculoplastics, St. Erik Eye Hospital, Stockholm, Sweden
[4]Department of Ophthalmology, Ullevål Hospital, Oslo, Norway
[5]Eye Clinic, Fredericia, Denmark
[6]Lääkärikeskus Aava Kamppi, Helsinki, Finland
[7]Ophthalmology, Augenklinik am Wittenbergplatz, Berlin, Germany

Corresponding author:
Philippe Denis, Service d'Ophtalmologie, Hôpital de la Croix-Rousse, Bâtiment R, 103, Grande Rue de la Croix-Rousse, 69317 Lyon cedex 04, France.
Email: philippe.denis@chu-lyon.fr

of ocular surface disorders in the aged glaucoma population is estimated between 51% and 59%.[2–4] Intraocular pressure (IOP) is the main risk factor for glaucoma although patients with ocular hypertension (OHT) may not all develop POAG.[5,6]

Managing the condition often involves lifelong daily treatment with, most of the time, eye drops. These treatments have been reported to cause local side effects which are more or less severe and which may cause a deterioration of the patient's Quality of Life (QoL). Some side effects comprising inflammation of the eye surface and conjunctival epithelium dysfunction may be caused by preservatives, such as quaternary ammoniums including benzalkonium chloride (BAK), cetrimide and polyquaternium formulated in these eye drops.[6,7] Consequently, a variety of clinical disorders including dry eye syndrome, conjunctival oedema or blepharitis may be caused in addition to ocular surface disease (OSD). These disorders may also occur after the use of non- or insufficiently adapted instillation systems. As a result, sub-optimal treatment compliance of the patients leading to treatment failure may be observed.[8,9]

In order to reduce the impact of OSD and its causes, various preservative-free (PF) treatments contained in different delivery systems such as uni-doses (UDs) and multi-doses (MDs) have been developed.[10,11] Currently, PF eye drops are most often presented in a UD format. However, a study from 2008 reported that elderly patients (aged 80 years and over) had major problems in administering eye drops using UD pipettes or MD bottles. The 43% of the patients using a UD were unable to successfully apply a drop to the surface of the eye, versus 5% of younger patients (50–65 years of age) and 11% using MD had similar problems. Likewise, 27% of the elderly patients were unable to extract a drop of solution from the UD device, versus only 5% and 7%, respectively, of patients in the other control groups. These problems can be partly explained by a lower visual acuity (VA), but also by dexterity problems.[12] Another study confirmed that both age and VA may impact treatment adherence in glaucoma patients.[13] Moreover, poor education on eye-drop instillation technique, missing adequate information or inadequate dispensing systems may worsen treatment adherence.[14–16]

Thus, a specific new multi-dose delivery system (MDDS; Figure 1) was developed and marketed to improve the potential impact of VA and upper extremity disability issues. The system was developed to obtain a calibrated, PF eye drop upon a single push on the pump. The innovative and effective ergonomics with the two grips at the bottom and at the top allows for an easy use by all patients. This novel technology is expected to improve patient compliance and QoL.

The objective of this retrospective survey was to evaluate the patient satisfaction study using a MDDS with two grips (Duokopt®/Dualkopt®, Laboratoires Théa, France) containing a PF fixed combination of dorzolamide/timolol to control increased IOP in patients with open-angle or pseudo-exfoliative glaucoma, when a topical beta-blocker monotherapy treatment is not sufficient.

Methods

This international, multicentre, observational, retrospective and non-interventional study was conducted in real-life settings between 2016 and 2018 in 315 study sites in seven European countries (Denmark, Finland, France, Germany, Norway, Spain and Sweden). The study respected European and local requirements for the conduct of observational studies as well as Good Epidemiological Practices.[17] Prior to participation, patients consented to participate in the study.

The study planned for at least 1000 suitable adult patients with a clinically confirmed diagnosis of open-angle glaucoma, including pseudo-exfoliative glaucoma, uncontrolled with a topical beta-blocker monotherapy treatment. Patients had to be treated and stabilised for at least 28 days using the tested MDDS, be able to instil eye drops by themselves and be instructed by the investigators on how to use the delivery system to instil the drug (Figure 1).

The primary endpoint was the overall proportion of satisfied and very satisfied patients using the tested

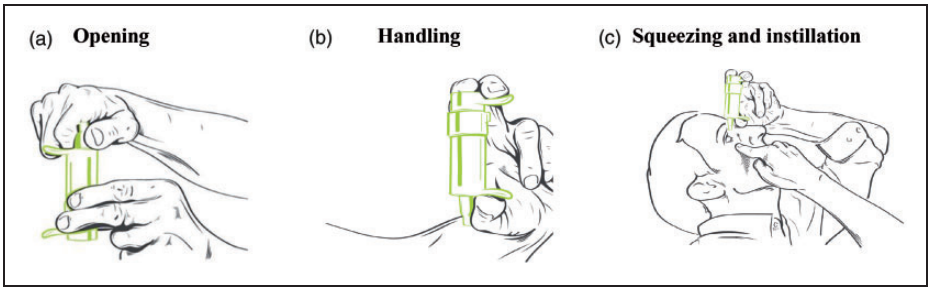

Figure 1. Visual explanation given on how to use the patented multi-dose delivery system.

MDDS. Secondary endpoints were the evaluation of the impact of VA or dexterity problems on the patient satisfaction using a dedicated questionnaire (Quick DASH®).[18]

The study consisted of a single visit to be performed at the same time as the scheduled routine visit. During this visit, the ophthalmologist completed the first part of the questionnaire about patient demographic and disease information (including age, gender, visit date, glaucoma stage), medical history (including year of diagnosis, previous glaucoma treatment(s) with the type of the delivery system in MD or UD, date of initiation of therapy with the MDDS), IOP, measurements since start of use of the MDDS, VA using the Snellen scale, if performed during the routine visit, and the use of tear substitutes.

Following this, the patient completed independently the second part of the questionnaire. This part included questions about satisfaction regarding the tested delivery system (easiness to open, handle, squeeze and instil a drop; global satisfaction vs the previous delivery system; if the patient was satisfied enough to carry on using the treatment; compliance and if he or she had the impression of using the treatment more regularly).

Since monocular vision determines the ease with which the patient is able to instil eye drops, results were associated, whenever available, with three levels of VA: Normal VA ranged from [0.8 to 1.0], mild vision loss from [0.3 to 0.8[and moderate/severe vision loss from [0 to 0.3[.

Moreover, in selected centres, patients completed the modified QuickDASH® self-questionnaire. It is comprised of 11 questions regarding daily tasks, housework, leisure, work, pain in shoulder-arm-hand, symptoms and quality of sleep. The calculated score allowed to classify patients into four equal subgroups from [0 to 100]; 0 corresponded to a high dexterity and 100 to a very low dexterity; impairment categories were associated with the easiness of use of the tested MDDS. At sites where the QuickDASH® questionnaire was used, some patients with score over 50 were considered heavily impaired concerning their dexterity that may impact their capacity to instil their eye drops themselves.

Any adverse events, as well as ocular signs or symptoms that were considered to be related to the device or the contained treatment, were to be recorded by the ophthalmologist according to the current local procedures for reporting adverse drug reactions for marketed treatments.

Quantitative variables were described in terms of mean, standard deviation, median and extreme values. Qualitative variables were described in terms of absolute frequency and percentage by category. For both qualitative and quantitative endpoints, 95% confidence intervals (CIs) were calculated. Demography and risk factors only were described. The association between patient-reported symptoms between glaucoma treatment instillations and the ophthalmologist's assessment of patients' ocular signs, demography and risks factors was assessed using a univariate statistical analysis (logistic regression and ordinal logistic regression). Results were presented, when appropriate, by means of odds ratio with 95% CIs and corresponding p values. Mean IOP values were calculated based on IOP measurements recorded since the start of use of the MDDS.

Results

From the 1032 collected questionnaires, 788 were suitable for statistical analysis and were considered as the Full Analysis Set (FAS) (Table 1). In all, 241 questionnaires were excluded from the statistical analysis because the delivery system was used for less than 28 days and 3 questionnaires for other reasons.

For accuracy reasons, and as this was a retrospective and non-interventional study conducted in real-life settings, investigators might not have reported all information for all patients as requested by the questionnaires. Thus, for each item, percentages and number of patients are based on the number of available replies.

Patient and disease characteristics

The overall mean age of patients was 68.1 ± 12.1 years. Mean time since diagnosis of glaucoma or OHT was 8.5 ± 7.7 years and mean duration of use of the tested MDDS was 132.1 ± 125.1 days. The majority (43.8%) had an early (<6 dB) glaucoma. In total, 66.5% had used previously MD and 33.5% patients UD delivery systems.

Table 1. Inclusion by country.

Country	Germany	Denmark	Spain	Finland	France	Norway	Sweden	Total
n	267	23	189	8	240	26	35	788
%	33.9%	2.9%	24.0%	1.0%	30.5%	3.3%	4.4%	100.0%

Table 2. Overall patient satisfaction.

Question	Answer	Total
Overall, how would you rate the delivery system compared to your previous eye drop?	n	762
	Same, better or much better	598 (78.4%)
	Less or much less	164 (21.5%)
Overall, are you satisfied with the delivery system bottle?	n	784
	Satisfied or very satisfied	614 (78.3 %)
	Unsatisfied or very unsatisfied	170 (21.7%)
Based on your satisfaction, are you going to carry on using the delivery system?	n	783
	Yes or probably yes	648 (82.8%)
	No or probably no	135 (17.2%)

Table 3. Patient satisfaction of use.

Question	Answer	Total
Is the delivery system bottle easy to open?	n	782
	Very easy or easy	590 (75.5%)
	Difficult or very difficult	192 (24.5%)
How do you consider the handling of the delivery system?	n	783
	Very easy or easy	599 (76.5%)
	Difficult or very difficult	184 (23.5%)
Is it easy to squeeze and obtain the drop?	n	784
	Very easy or easy	550 (70.2%)
	Difficult or very difficult	234 (29.8%)
Is it easy to instil a drop with the delivery system	n	784
	Very easy or easy	576 (73.5%)
	Difficult or very difficult	208 (26.5%)

The modified QuickDASH® questionnaire was completed by 268 patients: 79.1% had a score of [0 to 25[, 16.8% a score of [25 to 50[, 4.1% had a score of [50 to 75[, and none of the patients had a score of [75 to 100].

VA data were available for 685 patients, of those 47.9% had normal vision ($\geq$0.8), 33.3% had mild vision loss (0.3–0.8) and 18.9% had moderate to severe vision loss (<0.3) in the worse eye.

Patient satisfaction

Overall satisfaction.

In total, 78.4% of the patients rated the tested MDDS as good, better or much better than their previous delivery system, 78.3% were satisfied or very satisfied with the tested delivery system and 82.8% stated that they would continue or probably continue using the tested delivery system (Table 2).

Overall satisfaction of use.

When asked, 75.5% of the patients declared being satisfied or very satisfied with the easiness of opening and 76.5% stated that the tested MDDS was easy or very easy to handle. Overall, 70.2% indicated that squeezing and obtaining a drop with the tested MDDS was the same as or easier compared to previous glaucoma treatments, and 73.5% reported that the drop was easy or very easy to instil (Table 3).

Satisfaction of patients having previously used UD or MD delivery systems.

A total of 84.5% of the patients having previously used UD and 71.3% having previously used MD delivery systems rated the tested MDDS as easy or very easy to open. Overall, 81.6% having previously used UD and 74.4% having previously used MD eye drops assessed the test delivery system as easy to very easy to handle. Squeezing and obtaining a drop was the same or was easier compared to their previous UD treatment for 79.3% and for 58.5% who previously used MD delivery systems (Table 4).

The univariate logistic regression model showed that both age-related disease such as dexterity issues and type of previously used delivery systems impacted patient satisfaction (both $p \leq 0.05$) significantly.

Impact of dexterity on patient satisfaction

There were more patients with a QuickDASH® (n = 211), score between [0 to 25[(66.4%) and [50 to 75[(81.8%), that rated the tested delivery system easy or very easy to open ($p \leq 0.05$), and significantly more subjects in the [0 to 25[(72%) score group rated the tested delivery system as the same, better or much better than their previous device ($p \leq 0.05$). Even though there was no statistically significant difference for handling, squeezing, obtaining a drop and instillation, all patients except those in the group [25 to 50[for squeezing and obtaining a drop stated that the tested MDDS was easier or much easier to use (Table 5).

Impact of level of VA on patient satisfaction

Overall 78.3% of patients (614, all $p < 0.01$) rated the tested MDDS as same, better or much better than their previous dispensing device. Even though not

Table 4. Patient perception of easiness of use according to the previous type of eye-drop device.

Question	Answer	Multi-dose (N = 488)	Uni-dose (N = 246)	p value Chi-square test
Is the delivery system easy to open?	n	484	245	**<0.001***
	Very easy or easy	345 (71.3%)	207 (84.5%)	
	Difficult or Very difficult	139 (28.7%)	38 (15.5%)	
How do you consider the handling of the delivery system?	n	484	245	**0.028***
	Very easy or easy	360 (74.4%)	200 (81.6%)	
	Difficult or very difficult	124 (25.6%)	45 (18.4%)	
Is it easy to squeeze and obtain the drop?	n	335	164	**<0.001***
	Same or easier	196 (58.5%)	130 (79.3%)	
	Less easy	139 (41.5%)	34 (20.7%)	
Is it easy to instil a drop with the delivery system?	n	485	245	0.363
	Very easy or easy	353 (72.8%)	186 (75.9%)	
	Difficult or very difficult	132 (27.2%)	59 (24.1%)	

*Differences were significantly in favour of multi-dose delivery system compared to uni-dose.

Table 5. Patient perception of easiness of use based on QuickDASH® questionnaire scoring.

		Score [0, 25[(N = 212)	Score [25, 50[(N = 45)	Score [50, 75[(N = 11)	p value
Is the delivery system bottle easy to open?	n	211	45	11	**0.045***
	Very easy or easy	140 (66.4%)	22 (48.9%)	9 (81.8%)	
	Difficult or very difficult	71 (33.6%)	23 (51.1%)	2 (18.2%)	
How do you consider the handling of the delivery system?	n	211	45	11	0.232
	Very easy or easy	145 (68.7%)	25 (55.6%)	7 (63.6%)	
	Difficult or very difficult	66 (31.3%)	20 (44.4%)	4 (36.4%)	
Is it easy to squeeze and obtain the drop?	n	212	45	11	0.122
	Same or easier	123 (58.0%)	20 (44.0%)	7 (63.6%)	
	Less easy	89 (42.0%)	25 (55.6%)	4 (36.4%)	
Is it easy to instil a drop with the delivery system?	n	212	45	11	0.647
	Very easy or easy	134 (63.2%)	26 (57.8%)	6 (54.5%)	
	Difficult or very difficult	78 (36.8%)	19 (42.2%)	5 (45.5%)	
Overall, how would you rate the delivery system compared to your previous eye drop?	n	211	44	11	**0.043***
	Same or better or much better	152 (72.0%)	26 (59.1%)	6 (54.5%)	
	Less or much less	59 (28.0%)	18 (40.9%)	5 (45.5%)	
Based on your satisfaction, will you continue using the new delivery system?	n	212	45	11	0.148
	Yes or probably yes	163 (76.9%)	29 (64.4%)	7 (63.6%)	
	Probably no or no	49 (23.1%)	16 (35.6%)	4 (36.4%)	

*Differences were significantly different between disability levels.

significant, more patients stated that, based on their satisfaction, they would carry on using the tested MDDS (Table 6).

Ophthalmologists' satisfaction

Overall, 97.2% of the ophthalmologists were satisfied or very satisfied with the tested MDDS.

Compliance

According to the ophthalmologists (n = 786), 51.1% of the patients and 60.2% according to the patients themselves never forgot to use the delivery system, 20.2% forgot to use the MDDS up to two times per month and 19.6% forgot for more than twice per month their treatment. A total of 39% of patients declared using

Table 6. Patient satisfaction with the tested delivery system based on assessed Visual Acuity.

Question	Answer	Severe vision loss (N = 112)	Moderate vision loss (N = 17)	Mild vision loss (N = 228)	Normal vision (N = 328)	p value
Overall, how would you rate the delivery system compared to your previous eye drop?	n	100	15	222	324	**<0.001***
	Same or better or much better	74 (74.0%)	10 (66.7%)	172 (77.5%)	272 (84.0%)	
	Less or much less	26 (26.0%)	5 (33.3%)	50 (22.5%)	52 (16.0%)	
Based on your satisfaction, will you continue using the new delivery system?	n	112	17	225	327	0.120
	Yes or probably yes	93 (83.0%)	13 (76.5%)	181 (80.4%)	285 (87.2%)	
	Probably no or no	19 (17.0%)	4 (23.5%)	44 (19.6%)	42 (12.8%)	

*The difference was significantly different between multi-dose delivery system and uni-dose.

their eye drops more regularly, since having switched to the tested MDDS system.

Concomitant use of tear substitutes

According to the patients (n = 770), 57.0% used tear substitutes, of those 31.4% stopped or decreased their concomitant use since having switched to the tested MDDS.

IOP

The mean IOP remained unchanged during the study (Supplementary Table 1).

Safety

Overall, 10 out of the 1032 patients (0.97%) who tested the MDDS reported 17 related, non-serious adverse events; 3 patients reported more than one event, and 3 patients withdrew from the trial due to adverse events. Eleven adverse events had resolved; the information was missing for 6 adverse events. No adverse events were reported with the use of the bottle.

Eye discomfort (five events) and decreased lacrimation (three events), foreign body sensation, irritation, pruritus, hypersensitivity, hyperaemia, dry eye, oedema and erythema were the most often reported adverse events.

Discussion

This retrospective, international and non-interventional study assessed for the first time the easiness of use of a specifically developed patented and ergonomic MDDS, in considering VA, dexterity and global satisfaction of patients with glaucoma.

While safe and effective topical treatments for glaucoma exist, insufficient treatment compliance may impact on the treatment success.[15] Patients with instilling problems of their topical glaucoma medication due to vision or dexterity problems are acknowledged to be at higher risk for poor compliance, frequent medication switching and, ultimately, surgery.[13] Several clinical studies evaluating patient satisfaction with their glaucoma treatment have been conducted in the past.[19–21] However, all of these studies only focused on the patient's satisfaction regarding the clinical safety through reported symptoms and adverse events. Patient satisfaction and treatment compliance in glaucoma patients is not only related to experienced symptoms of treatment but also to the type of drug delivery system.[12,16] Glaucoma occurs at any age, and in real-world conditions, glaucoma patients suffer from often vision problems and sometimes, if aged, from upper extremity disabilities, especially of their hands and fingers, thereby making the use of MD or UD dispensing devices difficult.[12,22–24] These physical disabilities may lead to decreased treatment compliance and thus to a lower clinical efficacy. Therefore, proposing a specifically developed delivery system was expected to improve patient satisfaction, treatment compliance and treatment outcome.

The present patient questionnaire reports satisfaction results for opening, using, handling, squeezing and obtaining a drop, as well as for instilling eye drops using a specific delivery system. Overall, high satisfaction of use compared to previously used MD or UD delivery systems was observed. The univariate logistic regression model showed that age and type of previously used device systems significantly impact patient satisfaction (both $p \leq 0.05$). However, the comparison to the previous dropper with different levels of VA and dexterity problems impacted patients' satisfaction. The reason for the overserved dissatisfaction may potentially reside in the incapacity of certain patients to use any instillation device themselves despite the fact

that the study required the inclusion of patients being able to instil themselves their treatment which obviously was not respected for a certain number. We could have excluded these patients from the statistical analyses; however, for accuracy reasons, we preferred presenting these data. Despite this, results confirm that the tested MDDS may be suitable for most of the patients, providing high patient satisfaction and high treatment adherence.

Patient-reported treatment compliance with the tested MDDS was high (60.2%); 31.4% of patients having used tear substitutes decreased or even stopped their use after the switch to the tested MDDS, which may result in an improved QoL. The patients' capability to correctly use their MD eye-drop delivery system is key to treatment adherence and ultimately to treatment efficacy. Results from this study confirm that specifically adapted MDDS, such as the patented one, increases the patient's satisfaction of use, leads to improved treatment compliance, and reduces or stops the use of tear substitutes, thus potentially improving efficacy.

In conclusion, the tested MDDS is highly accepted in the studied population and is a suitable choice for a fixed-combination glaucoma therapy. Further studies may be necessary to assess the easiness of use of this easy-to-grip delivery system in patients with greater disability to instil or having severe problems in instilling their eye drops themselves.

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Supplemental material

Supplemental material for this article is available online.

References

1. Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 2014; 121(11): 2081–2090.
2. Barnebey HS and Robin AL. Adherence to fixed-combination versus unfixed travoprost 0.004%/timolol 0.5% for glaucoma or ocular hypertension: a randomized trial. *Am J Ophthalmol* 2017; 176: 61–69.
3. Nordmann JP, Baudouin C, Bron A, et al. Xal-Ease: impact of an ocular hypotensive delivery device on ease of eyedrop administration, patient compliance, and satisfaction. *Eur J Ophthalmol* 2009; 19(6): 949–956.
4. Davis SA, Sleath B, Carpenter DM, et al. Drop instillation and glaucoma. *Curr Opin Ophthalmol* 2018; 29(2): 171–177.
5. Weinreb RN and Khaw PT. Primary open-angle glaucoma. *Lancet* 2004; 363(9422): 1711–1720.
6. Nordmann JP, Auzanneau N, Ricard S, et al. Vision related quality of life and topical glaucoma treatment side effects. *Health Qual Life Outcomes* 2003; 1: 75.
7. Baudouin C, Renard JP, Nordmann JP, et al. Prevalence and risk factors for ocular surface disease among patients treated over the long term for glaucoma or ocular hypertension. *Eur J Ophthalmol* 2013; 23(1): 47–54.
8. Leung EW, Medeiros FA and Weinreb RN. Prevalence of ocular surface disease in glaucoma patients. *J Glaucoma* 2008; 17(5): 350–355.
9. Stewart WC, Stewart JA and Nelson LA. Ocular surface disease in patients with ocular hypertension and glaucoma. *Curr Eye Res* 2011; 36(5): 391–398.
10. Goldberg I, Graham SL, Crowston JG, et al. Clinical audit examining the impact of benzalkonium chloride-free anti-glaucoma medications on patients with symptoms of ocular surface disease. *Clin Exp Ophthalmol* 2015; 43(3): 214–220.
11. Aptel F, Labbe A, Baudouin C, et al. Glaucoma medications, preservatives and the ocular surface. *J Fr Ophtalmol* 2014; 37(9): 728–736.
12. Dietlein TS, Jordan JF, Luke C, et al. Self-application of single-use eyedrop containers in an elderly population: comparisons with standard eyedrop bottle and with younger patients. *Acta Ophthalmol* 2008; 86(8): 856–859.
13. Gao X, Yang Q, Huang W, et al. Evaluating eye drop instillation technique and its determinants in glaucoma patients. *J Ophthalmol* 2018; 2018: 1376020.
14. Nordmann JP and Akesbi J. Improve adherence in glaucoma patients: a doctor's duty. *J Fr Ophtalmol* 2011; 34(6): 403–408.
15. Atey TM, Shibeshi WT, Giorgis A, et al. The impact of adherence and instillation proficiency of topical glaucoma medications on intraocular pressure. *J Ophthalmol* 2017; 2017: 1683430.
16. Gabisson P, Briat B, Le Foll J, et al. Handiness and acceptability of the new Abak bottle in chronically treated patients. *Ann Pharm Fr* 2011; 69(1): 22–29.
17. Recommendations for professional standards good epidemiological practices (version France 2007).

Rev Epidemiol Sante Publique 2008; 56(Spec No 1): S121–S175.
18. Beaton DE, Wright JG and Katz JN. Development of the QuickDASH: comparison of three item-reduction approaches. *J Bone Joint Surg Am* 2005; 87(5): 1038–1046.
19. Lemij HG, Hoevenaars JG, van der Windt C, et al. Patient satisfaction with glaucoma therapy: reality or myth? *Clin Ophthalmol* 2015; 9: 785–793.
20. Munoz Negrete FJ, Lemij HG and Erb C. Switching to preservative-free latanoprost: impact on tolerability and patient satisfaction. *Clin Ophthalmol* 2017; 11: 557–566.
21. Sun X, Lin M, Duan X, et al. Patient satisfaction with fixed-combination bimatoprost/timolol ophthalmic solution: a survey study in patients with glaucoma in China. *Patient Prefer Adherence* 2017; 11: 845–852.
22. Unterlauft JD and Bohm MRR. Role of the aging visual system in glaucoma. *Ophthalmologe* 2017; 114(2): 108–113.
23. Klein R and Klein BE. The prevalence of age-related eye diseases and visual impairment in aging: current estimates. *Invest Ophthalmol Vis Sci* 2013; 54(14): ORSF5–ORSF13.
24. Chou CF, Frances Cotch M, Vitale S, et al. Age-related eye diseases and visual impairment among U.S. *Am J Prev Med* 2013; 45(1): 29–35.