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Marija Božić[1,2,♣], Milica Knežević[1], Miroslav Stamenković[3,4]

Patient-reported behavior and problems related to topical glaucoma medication

Понашање пацијената и проблеми повезани са локалном медикаментном терапијом глаукома

[1]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[2]Unversity Clinical Center of Serbia, Eye Clinic, Belgrade, Serbia;
[3]Zvezdara University Medical Center, Clinic for Eye Disease, Belgrade, Serbia;
[4]University of Belgrade, Faculty of Special Education and Rehabilitation, Belgrade, Serbia

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♣**Correspondence to:**
Marija BOŽIĆ
Pasterova 2, 11000 Belgrade, Serbia
marija.bozic@med.bg.ac.rs

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Понашање пацијената и проблеми повезани са локалном медикаментном терапијом глаукома

SUMMARY

Introduction Compliance to medicamentous therapy in glaucoma patients if of great importance since it has great effect on clinical outcome.

Methods The descriptive cross-sectional study included patients (303) referred for diagnostic procedures and follow up examinations at the glaucoma outpatient clinic of the University Clinical Center of Serbia University Eye Hospital, in the period from January 2023 to January 2024. The study included glaucoma patients older than 18 years, who have been taking therapy for more than a month. Patients were asked questions about the use of topical antiglaucoma medications. Statistical analysis was performed in SPSS 18 using t test. A p value of less than 0.05 was considered statistically significant.

Results 303 glaucoma patients were included in the study, of which 120 (39.6%) were men, and 183 (60.4%) women. The average age was 67.4 ± 12.6 years (19–92). The average duration of therapy was 7.1 ± 5.8 years (one month to 30 years). The largest number of patients, 177 of them (58.4%) stated that they regularly use the prescribed therapy.

Conclusion Our study showed a high degree of reported compliance of the tested patients, which is significant for the correct choice of therapeutic modalities in the future, which would slow down the progression of this incurable disease.

Keywords: compliance; topical antiglaucoma therapy; drop instillation technique

САЖЕТАК

Увод Придржавање медикаментне терапије код пацијената са глаукомом је важно јер има велики утицај на клинички исход лечења.

Методе У дескриптивну студију пресека укључени су пацијенти (303) упућени на лечење у амбуланту за глауком Клинике за очне болести УКЦС, у периоду од јануара 2023. године до јануара 2024. године. У студију су укључени пацијенти старији од 18 година, који узимају терапију дуже од месец дана. Испитаницима су постављана питања везана за примену топикалне антиглаукомне терапије. Добијени подаци су обрађени у СПСС 18 статистичком програму помоћу т теста. Статистички значајном је сматрана п вредност мања од 0,05.

Резултати Од 303 испитаника 120 (39,6%) су били мушкараци, а 183 (60,4%) жене. Просечна старост износила је 67,4 ± 12,6 година (19–92). Просечно трајање терапије је 7,1 ± 5,8 година (месец дана до 30 година). Највећи број пацијената, њих 177 (58,4%) наводи да редовно укапава прописану терапију.

Закључак Наша студија показала је висок степен пријављене комплијансе тестираних пацијената, што је значајно за правилан избор терапијских модалитета у будућности којима би се прогресија ове неизлечиве болести успорила.

Кључне речи: комплијанса; топикална антиглаукомна терапија; техника укапавања капи

INTRODUCTION

Chronic diseases require long-term and persistent use of medications [1]. The course of the disease, in addition to choosing the optimal therapeutic protocol, is also decisively influenced by compliance – which is defined as "whether the patient uses the drug as prescribed by the doctor" or "the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency„ [2]. In chronic ophthalmological diseases, for which there are different therapeutic modalities, such as glaucoma, topical drug therapy is often the first choice. It has been proven an effective and

non-invasive solution, available to everyone and relatively simple to use [3, 4]. Whenever medical therapy for chronic diseases is discussed, the concept of compliance is inevitably mentioned.

The aim of this study is to assess glaucoma patients' compliance and to evaluate and point out the most common errors when applying eye drops.

METHODS

The prospective cross-sectional study included 303 patients referred for diagnostic procedures and follow up examinations at the glaucoma outpatient clinic of the University Clinical Center of Serbia University Eye Hospital, in the period from January 2023 to January 2024.

The study included glaucoma patients older than 18 years, who have been taking topical antiglaucoma therapy for more than three months, which was inclusion criteria. The exclusion criteria were - persons under 18 years of age and those who are not being treated for glaucoma. Respondents were asked questions about the use of topical antiglaucoma medications. The questionnaire consisted of questions related to the patient disease (length of treatment), therapy (number of drugs, regularity of use) and technique of applying eye drops. The questions asked are recommended by the European Glaucoma Society for assessing compliance with glaucoma medication therapy (https://www.eugs.org/educational_materials/6). Descriptive statistics of participant demographics were computed, including means, standard deviations (SD), frequencies, and percentages and for three independent variables (age, gender, number of drops). Multiple logistic regression analysis was then used to examine how the preselected variables were associated with compliance. The obtained data were processed in the SPSS 18 statistical program. A p value of less than 0.05 was considered statistically significant.

Ethics: This study was undertaken according to the tenets of the Helsinki Declaration, and approved by the Ethics Committee of the University Clinical Center of Serbia (278/22). All participants received oral and written study-related information, and each participant provided written informed consent.

RESULTS

303 glaucoma patients were included in the study, of which 120 (39.6%) were men, and 183 (60.4%) women. The results are presented in Table 1. The majority of patients (40.3%), were on monotherapy, and the fewest tested patients had four drugs in their glaucoma therapy (10.2%). Of all patients tested, 177 (58.4%) stated that they regularly use the prescribed therapy. As many as 224 (73.9%) patients stated that they take the therapy themselves, 42 of them (13.9%) require the help of another person, while 37 patients (12.2%) stated that they apply it both by themselves and with the help of others. As for the position in which patients administer drops, it is most often the sitting position (45.5%), and the least common is the standing position (23.5%). 225 patients (74.3%) instill one drop in the eye, 65 (21.4%) instill two drops on average during application, while 13 patients (4.3%) instill three or more drops in each eye. Less than half of the respondents were given a demonstration of instillation by an ophthalmologist or nurse (132 patients or 43.6%). Most patients wash their hands before instilling eye drops (85.2%), but also most of them do not have the habit of pressing the lacrimal ducts after instilling the drops (78.5%). Our results show no statistically significant difference in compliance in relation to age ($p = 0.627$) and gender ($p = 0.512$) in our study group. In addition, the number of medications did not affect the regularity of administration ($p = 0.514$), nor did the demonstration of the technique of applying the drops. No relationship between tested independent variables and reported compliance was found. Results shown in Table 2.

DISCUSSION

Mutual trust between doctor and patient is very important for all diseases, but the concept of trust in the case of glaucoma has a multifaceted meaning. Glaucoma is a chronic neurodegenerative disease in which responsibility for the disease outcome is shared between the doctor and the patient. The responsibility for timely diagnosis and adequate therapy rests with the doctor, but responsibility related to treatment equals regular instillation of eye drops, and is practically exclusively a matter of the patient. Glaucomatologists must be convinced that their patients take seriously the need to be treated, that is, to instill their eye drops multiple times every day. Also, very often it is necessary to reassure that proper treatment is on. It is precisely from there that the issues of compliance and adherence in glaucoma arise.

Concepts of compliance and adherence first emerged in early 70's of XX century [5]. In glaucoma, these terms became more visible with the appearance of newer types of topical antiglaucoma medications [6]. Adherence is a term that describes the prevalence of the use of the prescribed medicine at different points in time and directly depends on the active role of the subject – the patient must understand what disease he is suffering from, how it should be treated and believe in the effectiveness of the therapy. According to current definitions, compliance is the degree to which the patient „complies", or obeys the instructions related to his treatment. In the very name of this term, passivity is expressed, and the joint fight of doctor and patient against chronic disease is neglected, which bothers many physicians. That is why lately the active role that the patient must take in the treatment of his chronic disease is more often pointed out. The responsibility for increasing the degree of compliance and adherence lies largely with the prescribing physician. The problem of compliance in glaucoma is complex for various reasons [7]. First, it is difficult for patients to recognize the importance of regular application of therapy for slowly progressing diseases because they do not disturb the quality

of life for a long period of time. Another reason is that after receiving therapy, there may be no subjective improvement of the clinical symptoms. Non-compliance with therapeutic protocols leads to further progression of the disease, change of the previously prescribed therapy, and even recommendations of unnecessary surgical procedures, all of which burdens the healthcare system [8]. Studies show that the percentage of non-compliant behavior in glaucoma is 5–80%. Ha et al came to conclusion that 50% of patients stop using drops during the first six months of use, and after a year that percentage drops to 33% [9]. We investigated self reported glaucoma medication compliance in our study, and the results on limited sample size show that 58.4% of glaucoma patients use antiglaucoma medications on regular bases. There are several ways to check our patient's compliance and adherence. For quick orientation in everyday clinic work, one of the indicators is whether the patient knows the names of the drugs he instills, whether he knows the instillation regime and whether he instilled the drops on the day he comes for the check-up. Besides patient self-reporting, other traditional and least expensive methods of monitoring medication adherence is analyzing health insurance claims data or pharmacy claims data [10]. However, it is clear that there is potential inaccuracy in traditional compliance and adherence monitoring methods, so more objective methods such as digital sensor monitoring systems have been developed, and are considered the "gold standard" for assessing medication adherence. One of the first, more modern and precise way of monitoring adherence was designed in the 90s of the last century, when the eye drop bottle with a C cap was designed [11]. The shortcoming of this compliance monitoring model was that it could only be applied to one type of antiglaucoma drug and that it was not implemented among ophthalmologists, nor among glaucoma patients. However, this attempt to improve compliance led to its increase from 54 to 73%, as determined in studies conducted on this issue. Recent advances in electronic adherence monitoring include E-Novelia, Kali Drop, Eye drop bottle motion sensor system which are all used with variable implementation among patients [12–16]. Unfortunately, each

of these systems entails a significant increase in glaucoma treatment costs, making it financially difficult to implement, so it is necessary to reorient to the more affordable systems and methods. In addition to financial obstacles for the implementation of modern electronic models for monitoring the compliance and adherence of glaucoma patients, there are also a number of ethical issues that arise on this topic, especially concerns about patient privacy and data sharing.

When discussing the technique of instilling eye drops, it is important to demonstrate the patients the correct way how to do it, even several times. These data vary by region and depend on the organization of the ophthalmology service [18]. We tried to emphasize the training of patients, i.e. the fact that it is important to point out to every patient, at the beginning of glaucoma treatment, the importance of regular eye drops usage and to show them in a practical way how to do it correctly. Almost half of our respondents (43.6%) stated that they were shown how to put in their eye drops- in 72% of cases it was shown by a doctor, and in 28% by a nurse. A way to indirectly evaluate patient compliance is to estimate how many drops are actually instilled into the eye in each instillation, and 225 of our tested subjects self-report that they (74.3%) instill 1 drop in the eye, 65 (21.4%) instill two drops on average during application, while 13 patients (4.3%) instill three or more drops in each eye. In other studies, these data vary from 48.1% to 51% of patients who dispensed more than one necessary drop for single application.

Due to the prevalence and complexity of the compliance problem, intensive work is being done to develop methods that would objectively determine its degree. This is possible through questionnaires, interviews or diary keeping, video analysis of the drip procedure or direct observation of the pouring technique [19]. In theory, electronic dosage monitoring represents the most objective method. However, it does not provide information on whether the drop of the medicine actually got into the eye, so it must be supplemented with a video recording or

supervision of the examinee during instillation. On the other hand, the measurement of intraocular pressure is also not reliable because even a couple of doses before the scheduled control will show values within the reference range [20]. Since it is difficult to find an objective method, which will provide an objective assessment of compliance, and it is even more demanding to implement it, questionnaires are often used. They are based on the self-assessment of the respondents and therefore, in 9–14% of cases, they show a deviation from the results of the objective parameters. Nevertheless, they are considered sufficiently informative and are today the most widespread way of evaluating compliance [21, 22].

Our strong belief is that the most important way to fight for greater compliance and adherence is to educate patients. Knowledge about the chronic disease, its course, methods of treatment and consequences of non-treatment can lead to increase of compliance. Although some authors believe that the patient who is familiar with the disease is the one who better adheres to therapy, others emphasize discipline and the help of family and environment [17, 18]. Other strategies are - the use of as few drugs as possible - monotherapy or the use of fixed combinations of drugs [19, 20, 21]. When it comes to ophthalmological diseases, eye drop instillation technique is of crucial importance in successful treatment, since the delivery of medicine is different than just swallowing a pill [22, 23]. Studies have shown that less than 10% are able to do all the steps adequately. We were particularly interested in data on the technique of instillation of drops in our respondents, and our results show that majority of patients instill the drops themselves (73.9%), most of them in sitting position (31%), and almost half of them (56.1%) have the habit of closing their eyes after putting eye drops in. Our results show no statistically significant difference in compliance in relation to age ($p = 0.627$) and gender ($p = 0.512$) in our study group. In addition, the number of medications did not affect the regularity of administration ($p = 0.514$), nor did the demonstration of the technique of applying the drops.

As for the definition of a compliant patient, there is no standardized questionnaire to determine it, so there are differences among authors regarding this issue. Some authors consider that a patient who misses one dose during the month or week is already non-compliant, while Wolfram et al include in this category those who miss 2 or more doses per week [24]. Although in many studies the subject is either compliant or not, McClelland and the authors divided compliance into three categories: low, medium and complete [17]. All this further complicates the interpretation of data and the comparison of the results of different studies.

Compliance is largely determined by factors related to the patient (age, gender, education), by socioeconomic conditions, the health system, the disease itself, and the type of therapy [26, 27]. The results of our study did not show a relationship between compliance and age and gender of the patient, which is confirmed by previous research [22, 24]. Such results are due to the fact that the elderly population makes up the majority of patients on antiglaucoma therapy, which is also the case in this study. However, when looking only at patients on prostaglandin analogues, Erras et al. [10] concluded that a lower degree of compliance is present in patients under 50 and over 80 years of age. The conclusions of some studies suggest that a larger number of prescribed drops doubles the chance that the patient will miss to administer the therapy [7]. In our sample, the number of medications did not influence the compliance, which is also confirmed by the study by Kang JM et al. [27].

The economic or financial aspect of glaucoma treatment cannot be ignored, i.e. the impact that high compliance and adherence have on the price of glaucoma treatment. The conclusions of several studies on chronic disease management are that there are strong economic arguments for investing in multidisciplinary interventions that improve patient compliance and adherence [28]. Precise data on how much glaucoma treatment "costs", are unknown for Serbia, but

certainly the entire price of "successful" treatment is much lower than the price we would have to pay for a person who is legally blind due to glaucoma [29].

Another confirmation of the thesis that our patients suffering from glaucoma require not only timely diagnosis and treatment, but also continuous support in terms of maintaining adherence and compliance is obtained from the results of the study published by Killeen and colleagues (in which a significant drop in adherence and compliance was obtained after the cessation of a motivational glaucoma coaching intervention [30]. So, in order to achieve the best outcome of glaucoma treatment, it is necessary for our patients to be constantly in some sort of support program. This may mean the need to discuss the use of eye drops with our patients at each check-up and constantly emphasize the importance of good compliance and adherence.

CONCLUSION

Our results show that the majority of our patients adhere to the ophthalmologist's advice regarding regular instillation of anti-glaucoma drops. For a better insight into this problem, it needs to be processed on a much larger sample. We consider our study as an excellent opportunity to point out again the importance of compliance in glaucoma and the need to spend more time with our patients, in order to explain to them in detail, and even more than once, the nature of their disease and the method of treatment.

Conflict of interest: None declared.

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Table 1. Characteristics of the study population

Gender	**n (%)**
Male	120 (39.6%)
Female	183 (60.4%)
Regular usage of eye drops	
Yes	177 (58.4%)
No	126 (41.6%)
Number of topical medications	
1	122 (40.3%)
2	88 (29%)
3	62 (20.5%)
4	31 (10.2%)
Drop instillation technique	
By themselves	224 (73.9%)
With assistance	42 (13.9%)
By themselves and with assistance	37 (12.2%)
Position	
Sitting	138 (45.5%)
Lying	94 (31%)
Standing	71 (23.5%)
Demonstrated technique	
Yes	132 (43.6%)
No	171 (56.4%)
Closing eyes	
Yes	170 (56.1%)
No	133 (43.9%)
Press lacrimal duct area	
Yes	65 (21.5%)
No	238 (78.5%)
Washing hands	
Yes	258 (85.2%)
No	45 (14.8%)
Tip contamination	
Yes	39 (12.8%)
No	264 (87.2%)
Instilling drop straight to the eye	
Yes	241 (79.5%)
No	62 (20.5%)
Number of drops per one instillation	
1	225 (74.3%)
2	65 (21.4%)
3	13 (4.3%)
Total	303 (100%)

Table 2. Results

Independent variables	**Age**	**p-value**
Age	Above 40 years	0.78
	Above 50 years	0.64
	Above 60 years	0.72
	Above 70 years	0.45
	Above 80 years	0.57
Gender: female		0.51
N of glaucoma medications		0.88

