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ASSESSMENT OF ADHERENCE IN OUTPATIENTS WITH OPEN-ANGLE GLAUCOMA

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Glaucoma is chronic, progressive optic nerve neuropathy that leads to permanent defects of the visual field. Glaucoma still cannot be cured, however, with proper and correct use of prescribed therapy, it can be managed in a way to slow its progression and consequent loss of vision. Thus, having good adherence to recommended medications is of utmost importance for glaucoma patients.

The study aimed to assess the degree of adherence to prescribed therapy for open-angle glaucoma in outpatients.

In February 2019, one-month research was done at the Glaucoma Department of the Eye Clinic, Clinical Center Niši. It was performed on 77 outpatients using an anonymous, volunteer-based questionnaire consisting of 11 questions related to demographic and socioeconomic characteristics, disease duration, as well as adherence to recommended therapy and reasons for possible non-adherence.

Out of the total outpatient number interviewed, 62.34% stated that they took their therapy as recommended, and 37.66% stated doing it not so regularly. Among those who were not taking therapy regularly, more were patients of older age ($p = 0.00001$; $p < 0.05$). No difference related to gender was found. Patients on multidrug glaucoma therapy were less adherent than those who used only one drug ($p = 0.00034$; $p < 0.05$). Better adherence was found in patients without comorbidities (87.5%) compared to those with some concomitant disease (35.14%), there was a statistically relevant correlation between these two parameters ($p = 0.000002$; $p < 0.005$). The most common reasons for non-adherence were adverse drug effects (100%), very long treatment period (89.66%) and patient's forgetfulness.

Relatively high, but not absolutely adequate degree of adherence is present among open-angle outpatients. Improvement of adherence can be achieved with optimal choice of therapeutic regimen, prescription of drugs with milder adverse effects, patient education about the course of disease and its possible consequences, i.e. blindness, as well as with emphasizing the importance of following recommended pharmacotherapeutic measures.

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Key words: *adherence, open-angle glaucoma, outpatients*

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Introduction

Glaucoma is a chronic, progressive neuropathy of the optic nerve leading to changes in the optic nerve and damage to the visual field. Glaucoma is a multifactorial disease, where elevated intraocular pressure (IOP) is a key factor in its development and the only one that can currently be addressed through medication (1). This is a disease with a growing global prevalence, affecting approximately 60 million people worldwide, of whom 4 million are blind. The estimated number of affected individuals in Serbia is around 100,000 (2). It currently ranks as the second leading cause of blindness worldwide but is the leading cause of preventable blindness. Once diagnosed, glaucoma cannot be cured, but proper therapy can prevent further progression of the disease and vision loss.

Adherence represents the extent to which a patient's behavior aligns with the prescribed recommendations of the prescribing authority. Establishing good patient adherence is a constant challenge but is considered a key component of therapy. Several studies have shown that achieving good patient adherence is more likely if the patient has a good understanding of their disease, recognizes the importance of therapy,

and the treatment regimen is straightforward (3). Additionally, the use of eye drops in glaucoma treatment further complicates the proper use of therapy and reduces adherence in these patients (4).

This scientific study aimed to examine the level of adherence among outpatients with open-angle glaucoma.

Material and Methods

The study was conducted at the Glaucoma Department of the Eye Clinic, Clinical Center Niš, in February 2019, through anonymous and voluntary patient surveys. A total of 77 individuals completed the questionnaire. The questionnaire consisted of 11 questions related to the demographic and socioeconomic characteristics of the participants, the duration of the disease, adherence to the prescribed therapy, and reasons for possible non-adherence. Multiple sources were used to compose the questionnaire, and some questions were specifically designed for this research. The survey was conducted in collaboration with the staff of the Eye Clinic, Clinical Center in Niš.

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the Clinical Center Niš, Niš, Serbia (No. 16368/112; approval date: 12 June 2012).

All analyses were performed using the online free calculator Social Science Statistics. Values for continuous variables were presented as the mean with standard deviation, while the frequency was used for categorical variables. Parametric (Student's t-test) and non-parametric (χ^2 test) correlation tests were used to assess the correlations between variables. Statistical significance was determined at the level of $p < 0.05$.

Results

The percentage of adherence in patients with glaucoma is presented in Figure 1. The percentage of patients who regularly used therapy was 62.34%, while the percentage of those who did not regularly use the prescribed therapy was 37.66%.

The distribution of participants by gender did not show a statistically significant difference between male and female genders, although the number of female participants was higher (46 males, 31 females). The average age of the participants was 62.7 ± 12.73 years. Ten patients (12.99%) completed primary school, 41 patients (53.25%) completed high school, and 26 patients (33.77%) had higher education. The correlation between demographic and socioeconomic characteristics and the degree of adherence is shown in Table 1. We proved that there was no statistically significant correlation between genders and the degree of adherence ($p = 0.32$; $p < 0.05$). The average age of participants who regularly used therapy was 57.4 ± 12.29 years, while the average age of participants who did not regularly take therapy was 71.4 ± 7.52 years. There was a statistically significant correlation between the average age and the degree of adherence ($p = 0.00001$; $p < 0.05$), as well as between the level of education and the degree of adherence ($p = 0.00012$; $p < 0.05$).

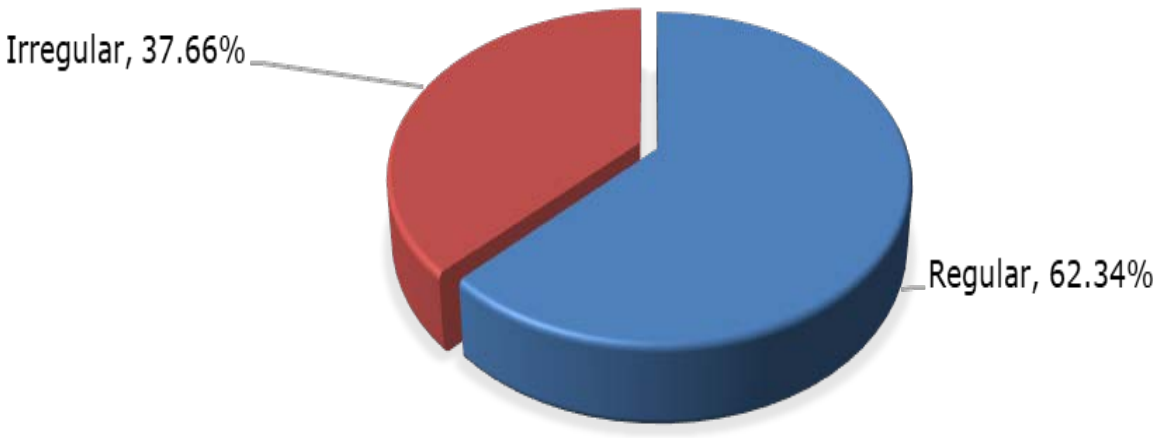

Figure 1: Percentage of patients who regularly use therapy

Table 1. Correlation between demographic and socioeconomic characteristics and degree of adherence

	Sex male/female N (%)	Average age (years)	Education ps/hs/he N (%)
Regular use of therapy	26/21 (56.52/67.74)	57.4 ± 12.29	2/24/22 (20/58.54/84.62)
Irregular use of therapy	20/10 (43.48/32.26)	71.4 ± 7.52	8/17/4 (80/41.46/15.38)
	p = 0.32; p < 0.05	p = 0.00001; p < 0.05	p = 0.00012; p < 0.05

We also showed that there was a statistically significant correlation between regular follow-up visits and regular medication intake (p = 0.01; p < 0.05). All patients who regularly took medication also reported regularly attending follow-up examinations.

Figure 2 shows the reasons for patient non-adherence. The largest number of non-adherent patients cited discomfort and unwanted effects during therapy (100%) as the reasons for their non-adherence, followed by the long duration of therapy (89.66%) and forgetfulness (62.01%). Just over half of the patients said they only used therapy when they experienced symptoms (58.62%), while about half of the patients expressed uncertainty about how long they should continue the therapy (51.72%). Patients less frequently mentioned not understanding how to use therapy (44.83%), thinking that the therapy would not help them (44.83%), not seeing the importantance of regular use was (27.59%), not considering glaucoma a serious disease (24.14%), and not having anyone to help them with the application of therapy (24.14%). The least common reason mentioned by respondents was the belief that the therapy could do more harm than good (3.45%).

Table 2 shows the correlation between the duration of the disease and the degree of adherence. The average duration of the disease in participants who regularly took therapy was 6.71 ± 3.63 years, while the average duration of the disease in participants who did not regularly take therapy was 10.97 ± 4.54 years. There was a statistically significant correlation between the duration of the disease and the degree of adherence (p = 0.000014; p < 0.05).

Table 3 presents the correlation between associated diseases and the degree of adherence. Patients with associated diseases, whether ophthalmological or systemic, had a significantly lower degree of adherence (35.14%) compared to patients without associated diseases (87.5%). There was a statistically significant correlation between these two parameters (p = 0.000002; p < 0.005).

Table 4 displays the correlation between the number of medications used in therapy and the degree of adherence. Patients who used three or four drugs in therapy had a significantly lower degree of adherence (three drugs—42.86%, four drugs—30.77%) compared to patients who used one or two drugs in therapy (one drug—81.81%, two drugs—88%). There was a statistically significant correlation between the number of drugs used in therapy and adherence (p = 0.00034; p < 0.05).

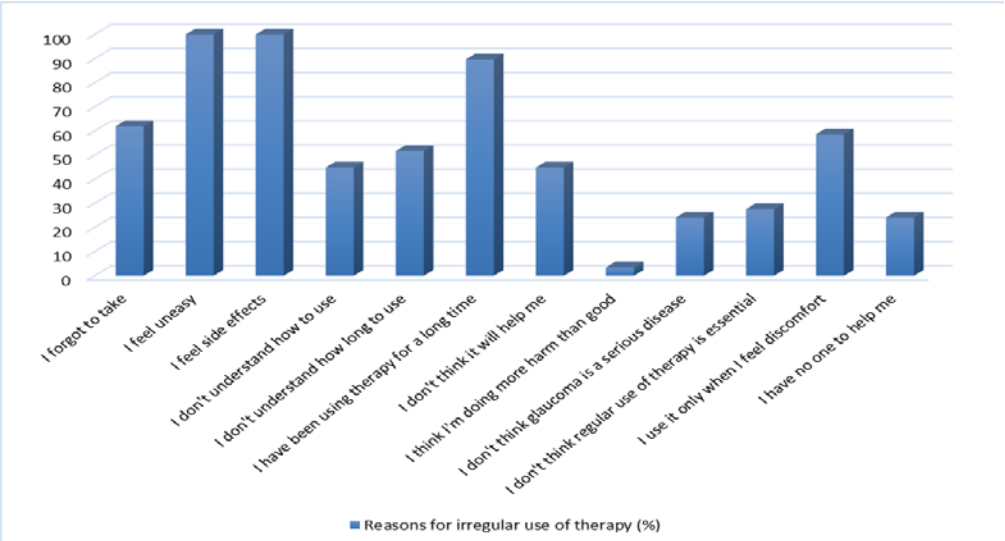

Figure 2. Reasons for irregular use of therapy (%)

Table 2. Correlation between the duration of the disease and the degree of adherence

	Average duration of disease in years
Regular use of therapy	6.71 ± 3.63
Irregular use of therapy	10.97 ± 4.54
p = 0.000014; p < 0.05	

Table 3. Correlation between comorbidities and degree of adherence

	With associated diseases N (%)	**Without associated diseases N (%)**
Regular use of therapy	13 (35.14)	35 (87.5)
Irregular use of therapy	24 (64.86)	5 (12.5)
p = 0.000002; p < 0.005		

Table 4. Correlation between the number of drugs used in therapy and the degree of adherence

	1 drug N (%)	**2 drugs N (%)**	**3 drugs N (%)**	**4 drugs N (%)**
Regular use of therapy	9 (81.81)	22 (88)	12 (42.86)	4 (30.77)
Irregular use of therapy	2 (18.19)	3 (12)	16 (57.14)	9 (69.23)
p = 0.00034; p < 0.05				

Discussion

Patient non-adherence continues to be a significant problem in the treatment of open-angle glaucoma, despite advancements in finding medications and therapeutic regimens that are easier to follow with fewer side effects. The percentage of non-adherent patients in our study was 37.66%. Various studies have shown different rates of non-adherence, with most ranging from 23% (5) to 27.3% (6). A study conducted in the United Kingdom revealed that 77% of respondents claimed to regularly and correctly take their medication. Still, only 55% of them could accurately state the names of the drugs they use and the exact regimen, indicating that a certain number of patients overestimate their discipline (5). Glaucoma belongs to a group of diseases that often progress asymptomatically until late stages, significantly influencing patient non-adherence, as confirmed in numerous studies (4). Due to the lack of symptoms, patients often do not grasp the importance of adherence and regular medication intake. From a medical standpoint, treatment effectiveness is evaluated based on the reduction of intraocular pressure, visual acuity, and structural and functional changes. On the other hand, patients must be aware that it is necessary to undergo treatment, even if they do not feel immediate relief. The assessment of treatment effectiveness, from the patient's perspective, is better in symptomatic diseases (7).

Glaucoma is a disease of older age, with prevalence increasing with age. The prevalence of glaucoma in the population over 50 years is 3%, and in those over 70 years, it rises to 5%, with the highest number of cases occurring between 65 and 75 years of age (7). The average age of our participants was 62.7 years. We demonstrated that the average age of patients who irregularly take medication is significantly higher (71.4 years) compared to the average age of patients who consistently use medication (57.4 years). Older individuals face more difficulties in using medication, including challenges in understanding how and for how long they should use the therapy, memory issues, and, particularly, the use of eye drops (6). Good coordination, dexterity, and good vision are necessary for independently applying eye drops, and these factors are often diminished in older individuals, requiring assistance in administering the therapy (8). Studies by Winfield et al. and Schwartz et al. have shown that around half of older patients experience technical difficulties when applying eye drops, such as aiming, squeezing the bottle, or blinking. The support patients receive from their families has a significant impact on consistency and persistence in therapy application (9). It is crucial for doctors to understand the importance of involving the patient's family in the treatment process, especially for asymptomatic diseases like glaucoma.

The challenge of establishing good adherence becomes more complex when considering other medications patients take for

associated systemic diseases. Different medications with varying application methods make it challenging for patients to use therapy correctly and regularly (4).

A significant number of our patients, especially the elderly, take medications for diabetes, arterial hypertension, asthma, and other diseases regularly. We demonstrated in our study that the presence of concomitant diseases, whether ophthalmological or systemic, significantly reduces patient adherence. The adherence of patients without other diseases except glaucoma was 87.5%, while the adherence of patients with associated diseases was only 35.14%. There is a clear statistically significant correlation between the presence of associated diseases and reduced patient adherence.

To achieve better adherence, the doctor needs to consider the patient's daily habits and obligations when creating a daily medication schedule. It is also desirable to associate the medication intake time with some daily activity to avoid forgetfulness as a significant reason for non-adherence (10). Studies have shown that monotherapy and once-daily dosing are associated with greater consistency and persistence in medication intake. If combined therapy is necessary, it is better to choose a fixed combination, as it simplifies the dosing regimen, leading to better adherence and satisfactory treatment effectiveness (11). Adding another medication to the treatment regimen significantly decreases patient adherence, as shown in the study by Robin et al. (12). Similar results were obtained in our study, where we demonstrated that the use of a higher number of medications leads to reduced patient adherence. The percentage of non-adherent patients among those using three drugs was 57.14%, and among those using four drugs, it was as high as 69.23%, significantly higher compared to the percentage of non-adherent patients among those using only one drug, which was 18.19%.

We demonstrated in our study that the level of education also influences the degree of adherence. Individuals with lower educational levels are often of lower socioeconomic status, limiting them to using medications covered by the National Health Insurance Fund. These patients frequently cannot afford medications without preservatives (e.g., Benzalkonium Chloride—BAK) due to financial constraints, and they have a significantly lower incidence of side effects. The most common side effects occur as a result of anterior surface eye diseases (chronic inflammation of the eyelid margins, dry eyes, chronic hyperemia, allergic reactions to preservatives in the medication) (13). These side effects were the main reason for patient non-adherence in our study, where all patients (100%) listed discomfort, itching, stinging, and redness as reasons for non-adherence. Many studies conducted worldwide have not found a connection between patient adherence and medication side effects (14, 15). The disparity between our results and theirs likely lies in the different socioeconomic profiles of patients. It is necessary in clinical practice to distinguish between side effects that genuinely require discontinuation of therapy and symptoms of a highly subjective nature not accompanied by objective symptomatology. In any case, patients must be fully informed about the nature of their disease and potential outcomes if they discontinue treatment spontaneously.

Konstans et al. showed in their study that one of the key factors in achieving good adherence is the patient's good understanding of the nature of the disease. Consequently, establishing a good relationship and trust between the doctor and patient, as well as regular check-ups, are essential factors in glaucoma treatment and preventing disease progression (10). In the GAPS study, Friedman et al. demonstrated that regular check-ups are significantly associated with better patient adherence (16). Similar results were obtained in our study, where we showed a statistically significant correlation between regular attendance of follow-up examinations and regular medication intake.

Conclusion

There is a relatively high, but not entirely satisfactory, level of adherence among outpatients with open-angle glaucoma. Optimal therapeutic regimens and medications with fewer side effects, patient education about the nature of the disease and its potential consequences, such as possible blindness, as well as emphasizing the importance of regular medication intake, could lead to an improvement in adherence levels.

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PROCENA ADHERENCIJE BOLESNIKA SA GLAUKOMOM OTVORENOG UGLA LEČENIH U AMBULANTI

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Glaukom je hronična, progresivna neuropatija optičkog živca, koja dovodi do trajnog oštećenja u vidnom polju. Iako jednom dijagnostikovan glaukom nije moguće izlečiti, pravilnim korišćenjem terapije mogu se sprečiti dalja progresija bolesti i gubitak vida. Uspostavljanje dobre adherencije prema farmakoterapijskim preporukama predstavlja jednu od ključnih komponenata u lečenju glaukoma.

Cilj ovog rada bio je da ispita stepen adherencije kod vanbolničkih pacijenata sa glaukomom otvorenog ugla.

Istraživanje je sprovedeno na Odeljenju za glaukom Klinike za očne bolesti Kliničkog centra u Nišu februara 2019. godine uz pomoć anonimne ankete na dobrovoljnoj bazi. Upitnik je popunilo 77 ljudi. Upitnik se sastojao od 11 pitanja u vezi sa demografskim i socio-ekonomskim podacima o ispitanicima, dužinom trajanja bolesti, adherencijom prema preporučenoj terapiji, te razlozima moguće neadherencije.

Od ukupnog broja ispitanika, njih 62,34% navelo je da redovno uzima terapiju; 37,66% bolesnika nije redovno uzimalo propisane lekove. Među onima koji nisu redovno uzimali terapiju više je bilo starijih osoba ($p = 0,00001$; $p < 0,05$). Nije uočena statistički značajna razlika kada je reč o polu. Pacijenti koji su u terapiji koristili više lekova imali su manju adherenciju od onih koji su koristili samo jedan lek ($p = 0,00034$; $p < 0,05$). Bolja adherencija zapažena je kod pacijenata koji nisu imali pridružene bolesti (87,5%) nego kod onih koji su imali neku pridruženu bolest (35,14%); između ovih parametara postojala je statistički značajna korelacija ($p = 0,000002$; $p < 0,005$). Kao razloge neadherencije bolesnici su najčešće navodili neželjene efekte i nelagodnost (100%), dugo korišćenje terapije (89,66%) i zaboravnost (62,01%).

Postoji relativno visok, ali ne i potpuno zadovoljavajući stepen adherencije među vanbolničkim pacijentima sa glaukomom otvorenog ugla. Izbor optimalnog terapijskog režima i lekova sa manje neželjenih efekata, edukacija bolesnika o prirodi same bolesti i njenim posledicama, tj. o mogućem slepilu, kao i naglašavanje značaja redovnog korišćenja terapije mogli bi dovesti do poboljšanja stepena adherencije.

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***Ključne reči**: adherencija, glaukom otvorenog ugla, vanbolnički pacijenti*