

*Full Length Research Paper*

## Eye drops prescription pattern in patients with glaucoma

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Glaucoma is a major public health problem, being the leading cause of irreversible visual impairment worldwide. In most cases, glaucoma is associated with intraocular pressure (IOP) levels that are above those considered normal (IOP  $\geq$  21 mmHg). The aim of the present work is to describe the pattern of eye drops prescription in patients with glaucoma in the state of Sergipe, Brazil. A descriptive cross-sectional study with retrospective documentary analysis, developed at the Eye Institute of Sergipe was performed. Of all glaucoma patients, 41.5% had a family history of the disease. Among the popular drugs, Latanoprost 0.005% is the most requested totaling 34% of prescriptions. In the Region 2, a significant association ( $\chi^2= 48, 45; p<0.05$ ) was observed between monotherapy and high IOP. The present study showed that the pattern of eye drops prescription was as recommended by the Brazilian Society of Glaucoma. Although, these medications were distributed freely, most patients with glaucoma have high IOP. Therefore, considering the importance of glaucoma as the second cause of blindness worldwide it is essential to carry out studies that evaluate the factors that influenced the effectiveness of eye drops use for treatment of glaucoma.

**Key words:** Glaucoma, ophthalmic solutions, prescription drugs.

### INTRODUCTION

Glaucoma is a silent chronic disease that is characterized by progressive alterations of the optic disc, retinal nerve fiber layer, irreversible loss of vision and damage to the optic nerve. In most cases, glaucoma is associated with intraocular pressure (IOP) levels that are above those that are considered normal (IOP  $\geq$  21 mmHg). The total number of patients (aged 40 - 80 years) with glaucoma worldwide was estimated to be 64.3 million in 2013 increasing to 111.8 million in 2040, especially in Asia, Africa and America (Tham et al., 2014). According to the

World Health Organization (WHO), glaucoma accounts for 13% of global blindness, and 2.4 million new cases occur every year (WHO, 2004; WHO, 2013).

Although, glaucomatous damage is deemed irreversible, approximately 90% of the blindness caused by glaucoma could be avoided with early diagnosis and treatment (Susanna, 2015, UN, 2009). Thus, glaucoma is a serious public health problem (William et al., 2014). Depending on the condition, medical, laser, surgical treatments, and antiglaucoma therapy can be used.

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A great number of topical medications are available for use in glaucoma treatment. These eye drops cause IOP reduction by either decreasing production of aqueous humor from the ciliary body, or increasing outflow of the aqueous humor through the trabecular meshwork or uveoscleral pathway, the natural drain of the eye (Sun et al., 2015).

In developing countries, including Asia, Africa and South America, most glaucoma patients are unconscious that they have the disease and visual injury that is also prevalent and severe (Thomas et al., 2012; Leite et al., 2011). Moreover, two reviews highlight that lack of adherence to the antiglaucoma therapy may culminate in the patient's vision loss (Castro, 2009; Leite et al., 2011). The low adherence can be explained because the glaucoma medications do not improve vision, may have important side effects and are relatively expensive (Leite et al., 2011).

Data on the prevalence of the disease in Brazil are scarce (Leite et al., 2011; Castagno et al., 2009; Tham et al., 2014). Sakata et al. (2007) reported that the prevalence of glaucoma in South Brazilian population among people over 40 years old was 3.4%. According to Stillitano et al. (2005), the antiglaucoma therapy in Brazil is expensive, and only a fraction of the economically active population is treated. As reported by Brazilian Ministry of Health and Brazilian Council of Ophthalmology, about 2% of Brazilian population has glaucoma. Although since recently the Brazilian population has received free eye drops, more than one fifth of the glaucoma patients do not follow the drug treatment in an adequate technique (Castro, 2008, 2009). Then, this study aimed to characterize the use of eye drops in patients with glaucoma in part of Brazilian Northeast.

## MATERIALS AND METHODS

### Study design

The present study is a descriptive research that was based on secondary data extracted from medical records that were used by an ophthalmic reference center for glaucoma patients from the Brazilian Public Health Care System (SUS) in the State of Sergipe. The center attends to about 10,000 elderly patients, and its health care team consists of four physicians, one nurse, one nursing technician, and one pharmacist. Sergipe is the smallest state in Brazil, located in the Northeast Region, this is the second most populous and poorer region of the country.

### Characterization of Brazilian health care

Since 1989, all 200,000 Brazilian have been entitled to free health care at primary, secondary, and tertiary level through a national health system that is unique in Latin America, being funded by taxes and social contributions, such as social security payments. The Brazilian Public Health Care System (SUS) has decentralized care coverage based on Family Health Strategy that proved to reduce common diseases, mortality, and reductions in unnecessary admissions (Victoria et al., 2011). This Health Care System is

divided in territories called Health Regions.

The Health Regions represent the integration of actions and health services of the federative institutions in a territory to qualify the SUS management, and also to ensure integrity. It must be able to cover and solve almost all health needs shown by the population of the region. In this study, the Health Regions were divided into three regions. Each region has a specific number of municipalities: Region 1 (15), Region 2 (11) and Region 3 (10). The division of regions considers geographical proximity defined by cultural, economic and social aspects, provision of health services, communication networks and infrastructure (Duarte et al., 2015; Santos, 2015). In this context, the Brazilian Public Health Care System (SUS) has a Glaucoma Patient support program present in all States and municipalities in Brazil. This program aims to manage patient support, increase public access, and generate mechanisms that can expand the diagnosis, monitoring, and treatment of these patients (Brazil, 2002a,b).

### Databases and analysis instrument

For monitoring glaucoma patients, databases including information on diagnosis and treatment were created. The databases included users who were diagnosed with primary open-angle glaucoma and who were treated between June 2011 and March 2012 in 36 municipalities. These municipalities covered 48%, nearly 1,000,000 inhabitants of the State of Sergipe. The analysis instrument was structured by researchers to evaluate the study population's profile. The database analysis was performed by a team consisting of a pharmacist (C.A.S.S.) and a Pharmacy undergraduate student (C.B.R.) of the Federal University of Sergipe. Both researchers were trained for six hours in order to be able to evaluate the databases. The data collected included a sociodemographic profile for each patient (name, age, gender, and length of stay in the program), the drugs prescribed for ophthalmic use, comorbidity, prescription patterns and outcomes of the users that were monitored for ten months in an ophthalmic reference center. At the end of the study, all of the instruments used were reviewed by the two researchers (F.A.S. and D.P.L.J), the results were further analyzed.

### Population of study

Data collection was obtained from medical records of 9,308 patients who were diagnosed with glaucoma. In order to characterize the prescription patterns of eye drops, the prescribed drugs and types of therapy were analyzed. In Brazil, the respondents reported their ethnicity for classification according to the Brazilian Institute of Geography (IBGE).

### Statistics analysis

The data was analyzed with BioEstat 5.0 and Epi info for Windows, IOP (CDC, 2012) prevalence estimates were examined according to age and monotherapy (the use of a single drug to treat a particular disorder or disease). In order to evaluate the statistical significance of the association between these variables and IOP, Mantel-Haenszel chi-square test was employed. A confidence interval of 95% was set for all of the statistical tests performed, and the differences were considered statistically significant if the p value was equal to or lower than 0.05.

### Ethical aspects

The study was approved by the research ethics commission of the

**Table 1.** Frequency distribution of the variables gender, ethnic group, number of medicines used, existence of comorbidities, familiar glaucoma in the studied population. Sergipe June 2011 to March 2012.

Variable	Frequency	%
<b>Gender</b>		
Male	3222	35
Female	6062	65
<b>Ethnic group</b>		
Brown	4607	49.5
Black	2860	30.7
White	1831	19.6
Indian	5	0.05
Yellow	3	0.03
<b>Number of medicines</b>		
1	8536	92
2	686	7
3	87	1
<b>Co-morbidades</b>		
Hypertension	2454	49
Migraine	1450	29
Diabetes	932	18
Asthma	184	4
<b>Familiar Glaucoma</b>		
No	5442	58.3
Yes	3867	41.5

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## RESULTS

In this study, 65% of the patients were female. Most of the population reported themselves as brown-skinned (49%), 31% as black, and 20% were self-declared white as shown in Table 1. The average age of the population from the three regions was 58 years old (standard deviation: 15.81). Among the comorbidity more commonly reported by patients from the three regions, arterial hypertension, migraine, and diabetes had higher percentages of occurrence (49, 29, and 4%, respectively). In addition, 41.5% of the patients reported a family history of glaucoma as shown in Table 1.

When comparing the average number of prescribed eye drops used by patients in the three regions, the majority (93% of the prescriptions) were for only one drug as shown in Figure 1. Thirteen drugs were used for the treatment of glaucoma as shown in Table 2, and prostaglandin analogs (Xalatan®) accounted 34% of the

total as shown in Figure 2. In Region 2, a statistically significant association ( $\chi^2 = 48.45$ ;  $p < 0.05$ ) was observed between monotherapy and abnormal IOP as shown in Table 3. Therefore, individuals with glaucoma who were treated with monotherapy were 1.76 times more likely to present an IOP  $\geq 21$  mmHg compared to individuals who were treated with more than one drug as shown in Table 3.

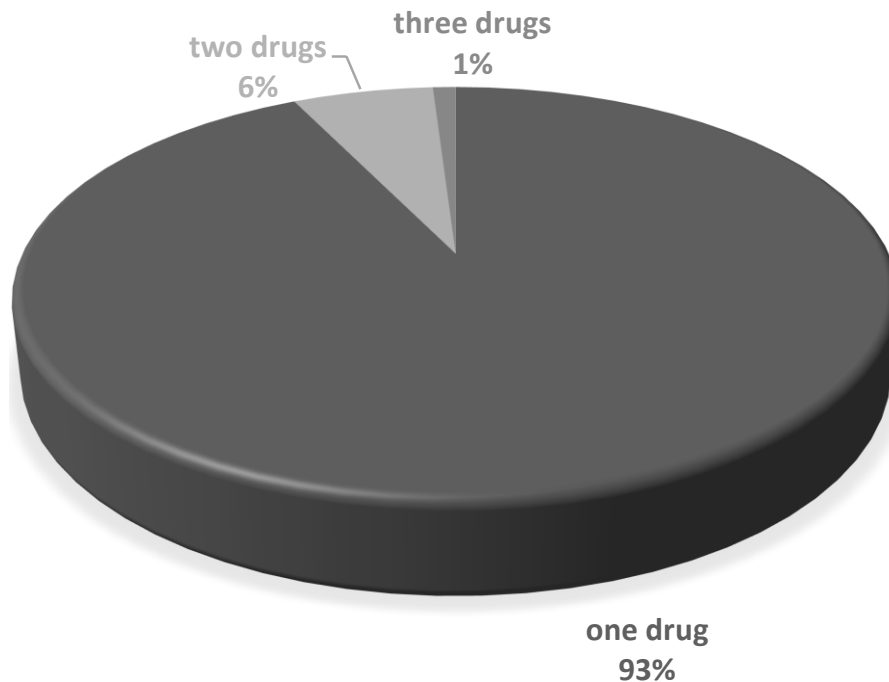
## DISCUSSION

In this study, majority of the population was composed of female patients. Though, no associations between gender and the percentage of individuals affected by glaucoma have been reported, and the prevalence of the disease is similar in both genders (Lima et al., 2010). This phenomenon may be related to observations that women use healthcare services more often, especially for social and reproductive issues, which results in a greater demand of drugs by this gender (Quigley, 2006; Le A et al., 2003; Travassos et al., 2002; Fleith et al., 2008).

Regarding ethnicity, the majority of patients with glaucoma who were included in this study reported themselves as black or brown-skinned. According to the Brazilian glaucoma society (Brazil, 2009; Brazil, 2011; BCO, 2015), morbidity develops earlier in black-skinned individuals compared to whites. In this study, the majority of the patients were brown-skinned, and this could be related to the racial miscegenation in the state of Sergipe.

The most frequent comorbidity was arterial hypertension, but no correlation was found between glaucoma and systemic arterial hypertension. Although this study did not find any associations between these variables, several studies have reported a correlation of increased blood pressure and glaucoma susceptibility (Bonomi et al., 2000; Dielemans et al., 1995; Goldberg et al., 1981; Sun et al., 2012). The blue mountains eye study and rotterdam eye study reported an association between systemic arterial hypertension and glaucoma susceptibility (Mitchell et al., 2004; Hulsman et al., 2007). Although the percentage of patients with diabetes and glaucoma was small, the role of diabetes is important in glaucoma. Previous studies (Kanamori, 2004; Pasquale, 2006; Minwen, 2014) have suggested that people with diabetes are more likely to have high IOP and glaucoma. In a cross-sectional study, Bonovas et al. (2004) suggested that increased IOP is linearly correlated with the severity of diabetes.

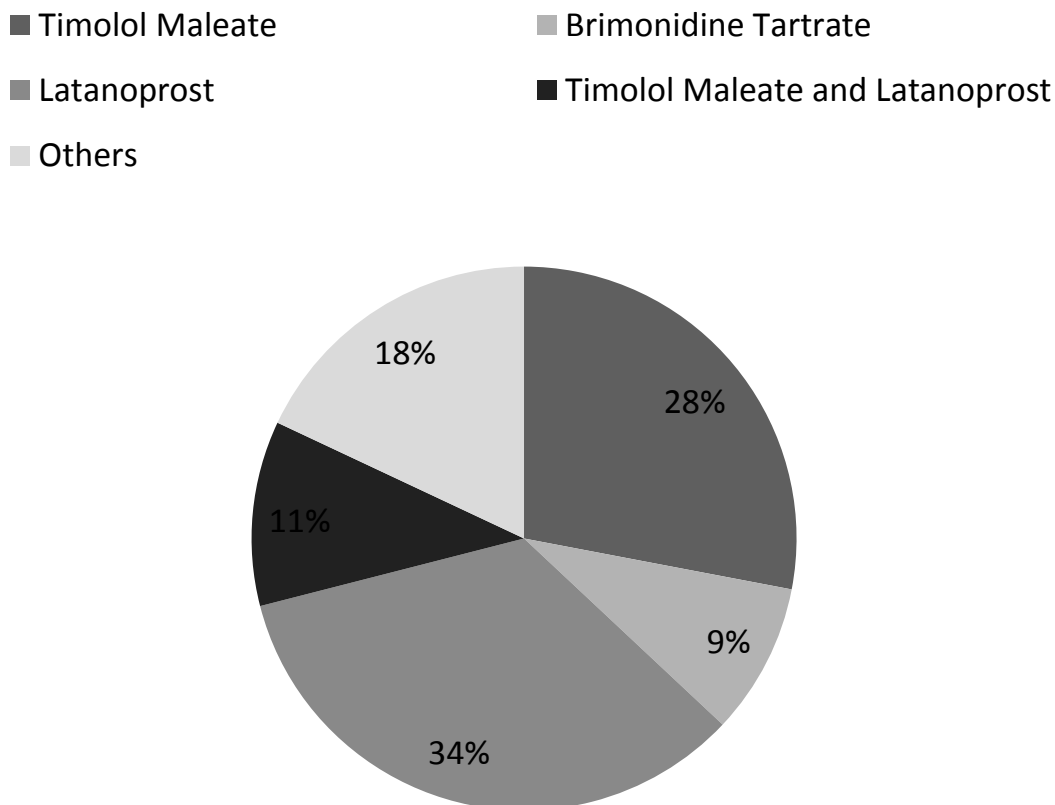
This study showed that physicians initially prioritized treatment with only one drug, typically prostaglandin analogs, because prostaglandins and beta-blockers are recommended in the initial treatment of glaucoma (Heijl, 2002; Van der Valk et al., 2005; Li et al. 2006 Brazil, 2009; Burr et al., 2012; Estacia and Tognon, 2008). However, the analysis of the three regions showed that most of the patients in region 2 who were treated with only one drug had higher IOP values than the



**Figure 1.** Percentage of drugs used in the treatment of glaucoma. Aracaju, June 2011 to March 2012.

**Table 2.** Prescribed drugs for glaucoma's treatment.

Marketed drug	Active substance	Drug group	Frequency	Percentage
Azopt®	Brinzolamide 1%	Carbonic anhydrase inhibitor	62	1
Combigan®	Brimonidine tartrate 0.2% + Timolol maleate 0.5%	$\alpha_2$ -Adrenergic agonist and $\beta$ -Adrenergic blocker	235	3
Drusolol®	Dorzolamide hydrochloride 2% + Timolol maleate 0.5%	Carbonic anhydrase inhibitor and $\beta$ -Adrenergic blocker	46	1
Ganfort®	Bimatoprost 0.03% + Timolol maleate 0.5%	$\beta$ -Adrenergic blocker and Prostaglandin analogue	67	1
Timolol maleate	Timolol maleate 0.25%/0.5%	$\beta$ -Adrenergic blocker	2417	28
Brimonidine tartrate	Brimonidine tartrate 0.2%	$\alpha_2$ - Adrenergic agonist	744	9
Xalacom®	Latanoprost 0.005% + Timolol maleate 0.5%	Prostaglandin analogue and $\beta$ -Adrenergic blocker	927	11
Xalatan®	Latanoprost 0.005%	Prostaglandin analogue	2944	34
Cosopt®	Dorzolamide hydrochloride 2% + Timolol maleate 0.5%	Carbonic anhydrase inhibitor and $\beta$ -Adrenergic blocker	15	1
Duo-travatan®	Travoprost 0.004%+ Timolol maleate 0.5%	Prostaglandin analogue and $\beta$ -Adrenergic blocker	362	4
Lumigan®	Bimatoprost 0.03%	Prostaglandin analogue	186	2
Ocupress®	Dorzolamide hydrochloride 2%	Carbonic anhydrase inhibitor	65	1
Travatan®	Travoprost 0.004%	Prostaglandin analogue	470	4



**Figure 2.** Percentage of most prescribed drugs. Aracaju, June 2011 to March 2012.

**Table 3.** Distribution of final IOP, according to the variable monotherapy. Estância, June to March 2012.

Monotherapy	IOP (mmHg)		Prevalence (%)	RP <sup>a</sup>	$\chi^{2b}$	p-value
	≥21	< 21				
Yes	483	988	32.8	1.76	48.45	0.0000001
No	116	84	58	1.00		

recommended standards. A reason for the lack of IOP control in this study may be a lack of adherence to the pharmacotherapy, as most of the patients reported eye irritation from the eye drops during the beginning of treatment in the medical records. In addition, several studies have reported that some patients who are diagnosed with glaucoma do not respond to first-line treatment drugs, and two or more antihypertensive drugs are required to achieve the target IOP (Cheng et al., 2012; Broadway and Cate, 2015; Kass, et al., 2002).

When analyzing the final IOP of the patients from Region 3, age was observed to be a risk factor for increased IOP. This conclusion was found to be in agreement with other studies that reported a positive association between high IOP and age (Kawai, 2001; Quigley, 2006; Schneck et al., 2004). Studies that were performed in Australia and the US have shown that the

prevalence of the disease steadily increases with each decade of life, starting at 55 years old (Mitchell et al., 1996; Wensor, 1998; Quigley et al., 2001). Owsley (2011), in his research, describes the problems caused in vision due to aging and its impact on economic and personal life of the population.

The present study showed that, even though eye drops are prescribed for the treatment of glaucoma as recommended in the literature, patients have high IOP in the analyzed cities. These results could be associated to low adherence to glaucoma pharmacotherapy. Several studies have demonstrated that roughly 50% of patients were not adherent to their medication over 75% of the time (WHO, 2000; Okeke et al., 2009; Robin and Grover, 2011; Costa et al., 2011). Cohen et al. (2014) related that low adherence to glaucoma pharmacotherapy is related to patients, medication, physician and environmental

factors. According to Robin and Grover (2011), some barriers influenced to adherence, such as forgetfulness, other priorities, lack of information and emotional factors. Another study carried out by Newman-Casey and colleagues (2015) also pointed to the difficulty with drop administration and the medication schedule as barriers associated with poor adherence, even in developing countries.

This study showed the prevalence among brown-skinned and elderly patients that use monotherapy of eye drop glaucoma. Although, these medications were distributed freely, most patients have high IOP. Because of the prevalence of glaucoma and the high costs of this disease, it is essential to perform further studies that adequately evaluate the factors that influenced the effectiveness of the use of eye drops, especially to patients' knowledge and attitudes, in the treatment of glaucoma.

### Conflict of Interests

The authors have not declared any conflict of interests.

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