

Pharmacoepidemiology of the antiglaucoma drugs in Brazil from 2012 to 2018

Farmacoepidemiologia das drogas antiglaucomatosas no Brasil de 2012 a 2018

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ABSTRACT

Purpose: To outline the epidemiological profile of clinical treatments for glaucoma provided by the Brazilian Unified Health System (SUS, acronym in Portuguese) between January 2012 and December 2018. **Methods:** A quantitative and descriptive study was conducted using available data based on the outpatient information system from SUS (SIA/SUS, acronym in Portuguese). The variables were monocular treatment with first, second, and third-line drugs; monocular treatment with combinations of two drugs and three drugs from different lines; binocular treatment with first, second, and third-line drugs; and binocular treatment with combinations of two drugs and three drugs from different lines. **Results:** During the analysis period, the prevalence of clinical therapies for glaucoma increased from 2012 to 2017 and decreased from 2017 to 2018. Of the clinically treated patients, 96% were carriers of binocular glaucoma. Among the regions of Brazil, the Northeast had the highest prevalence of binocular glaucoma (about 60% of the number of cases), and the most common therapy was combinations of two drugs from different lines. The Southeast region had the highest concentration of monocular glaucoma (53% of cases), and the predominant therapy was combinations of three drugs from different lines. The Midwest region had the lowest prevalence of monocular-treatments for glaucoma (less than 6%). **Conclusion:** In Brazil, the highest number of treatments offered by the public health system was in the Northeast and Southeast regions. There is a high national prevalence and potential for the morbidity of this disease. Therefore, it is necessary to strengthen programs aimed at early diagnosis and appropriate treatment to reduce adverse outcomes.

Keywords: Glaucoma/terapia; Intraocular pressure; Eyedrops; Unified Health System; Brazil

RESUMO

Objetivo: Traçar o perfil epidemiológico do tratamento clínico para o glaucoma no Brasil fornecido pelo Sistema Único de Saúde (SUS), no período de janeiro de 2012 a dezembro de 2018. **Métodos:** Estudo quantitativo e descritivo, utilizando a base de dados disponível no Sistema de Informações Ambulatoriais do SUS (SIA/SUS). As variáveis utilizadas foram: tratamento monocular com drogas de primeira, de segunda e de terceira linha; tratamento monocular com combinações de duas drogas e de três drogas de diferentes linhas; tratamento binocular com drogas de primeira, de segunda e de terceira linha; e tratamento binocular com combinações de duas drogas e de três drogas de diferentes linhas. **Resultados:** Durante o período analisado, a prevalência de terapias clínicas para o glaucoma aumentou entre 2012 e 2017 e diminuiu entre 2017 e 2018. Dos pacientes tratados clinicamente, 96% eram portadores de glaucoma binocular. Entre as regiões do Brasil, o Nordeste teve a maior prevalência de glaucoma binocular (cerca de 60% do número de casos), e a terapia mais comum foi a combinação de duas drogas de diferentes linhas. A região Sudeste teve a maior concentração de glaucoma monocular (53% dos casos), e a terapia predominante foi a combinação de três drogas de diferentes linhas. A região Centro-Oeste apresentou a menor prevalência de tratamentos monoculares para o glaucoma (menos de 6%). **Conclusão:** No Brasil, o maior número de tratamentos oferecidos pelo sistema público de saúde foi nas regiões Nordeste e Sudeste. Existe uma alta prevalência nacional e um alto potencial para morbidade desta doença. Portanto, é necessário fortalecer programas voltados para o diagnóstico precoce e para o tratamento adequado a fim de reduzir os resultados adversos.

Descritores: Glaucoma/terapia; Pressão intraocular; Colírios; Sistema Único de Saúde; Brasil

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INTRODUCTION

Glaucoma is considered a public health problem and is the leading cause of irreversible blindness worldwide. The number of people with glaucoma in the world was estimated to be 64.3 million in 2013 and is expected to rise to 76 million by 2020 and to 1.1 billion by 2040.⁽¹⁻³⁾

Glaucoma is a neurodegenerative disorder in which retinal ganglion cells (RGC) undergo apoptosis, thus producing significant visual impairment.⁽⁴⁾ The most important known risk factors for its development and progression are intraocular pressure (IOP). Only the IOP is currently a modifiable factor and is used to prevent or delay the loss of RGC due to mechanical stress, vascular abnormalities, and other mechanisms.^(5,6)

A variety of clinical, laser, and surgical options are used to achieve the target IOP. In many patients, it is necessary to combine two or more hypotensive drugs for the control to be effective.⁵ The American Academy of Ophthalmology recommends that initial treatments aim at reducing IOP in Primary Open-Angle Glaucoma (POAG) by 25% from baseline. Thus, pharmacotherapy is typically the first approach to IOP reduction. This treatment is commonly initiated with a single topical ocular hypotensive agent, such as prostaglandin analogs or beta-blockers. These agents decrease IOP by decreasing aqueous humor production or by increasing its flow through the conventional (trabecular) or uveoscleral pathways.^(7,8)

In the Brazilian Unified Health System (SUS), antiglaucoma drugs are provided through a high-cost program.^(9,10) The goal of glaucoma treatment is to improve the patient's quality of life by maintaining a vision with minimal adverse effects.⁽⁶⁾ Knowledge of the resource costs and treatment standards for glaucoma patients is essential for assessing the impact of the increased prevalence of health resources.⁽¹¹⁾ Thus, the aim of this study was to discuss the main clinical therapies used for the treatment of glaucoma in Brazil that are made available by SUS, as well as the relationship between regions and the treatments used.

METHODS

This epidemiological, quantitative, and descriptive study was based on records obtained from population data and spatial analysis. Epidemiological information regarding clinical therapy for glaucoma was obtained from the Unified Health System Database (DATASUS, acronym in Portuguese – <http://datasus.saude.gov.br/>).⁽¹²⁾ These data refer to reports from the outpatient information system called Sistema de Informações Ambulatoriais (SIA/SUS, acronym in Portuguese). The data obtained were then organized by region.

The analysis period was selected from 2012 to 2018 for the following reasons. First, it was considered that more recent analyses would provide greater reliability in the data collection due to progressive improvements in the computerization process. Secondly, this period could potentially portray the transition scenario resulting from the introduction of the Glaucoma Program. The clinical protocol and the therapeutic guidelines for the Glaucoma Program in Brazil were approved under Ordinance number 1279/SAS of November 19, 2013.

It should be noted that the effects of the program might occur unevenly between regions, which could potentially influence the analysis. In the Glaucoma Program in Brazil, topical medica-

tions are divided into the following treatment lines: first-line, pilocarpine and timolol; second-line, brimonidine, brinzolamide, and dorzolamide; third-line, bimatoprost, travoprost, and latanoprost.

The research was carried out using the names of the procedures offered by the health system: "Ophthalmic treatment of binocular glaucoma patient (1st line)", "Ophthalmic treatment of binocular glaucoma patient (2nd line)", "Ophthalmic treatment of patient with binocular glaucoma (3rd line)", "Ophthalmic treatment of patient with monocular glaucoma (1st line)", "Ophthalmic treatment of patient with monocular glaucoma (2nd line)", "Ophthalmic treatment of patient with monocular glaucoma (3rd line)", "Ophthalmologic treatment of a patient with 2nd line monocular glaucoma", "Ophthalmic treatment of a second line binocular patient - 1st line associated with glaucoma" - monocular", "Ophthalmic treatment of a glaucoma patient - 1st line associated with 3rd line - binocular", "Ophthalmic treatment of a glaucoma patient - 2nd line a associated with 3rd line - monocular", "Ophthalmic treatment of patient with glaucoma - 2nd line associated with 3rd line - binocular", "Ophthalmic treatment of patient with monocular glaucoma - 1st, 2nd and 3rd line association", and "Ophthalmic treatment of patient with binocular glaucoma - 1st, 2nd and 3rd line combination".

A descriptive analysis was carried out on the relationships between treatments according to the regions of Brazil from 2012 to 2018 using data from SIA/SUS. The data were organized into frequency tables. The data used are public, and there were no identifying elements about the individuals studied, so there was no need to obtain informed consent. Also, consideration by an ethics committee was not required because the data is in the public domain with unrestricted access.

RESULTS

During the period analyzed, more than 200,000 treatments were offered for monocular glaucoma and approximately 6,500,000 for binocular glaucoma. The most populous regions in Brazil (the Northeast and Southeast) presented the highest number of clinical treatments for glaucoma. The clinical treatment rate for glaucoma in Brazil increased from 2012 to 2017 and decreased from 2017 to 2018 (Figure 1).

Furthermore, 96% of clinical treatments performed in 2018 corresponded to binocular-treatment (Figure 2). The region of Northeast Brazil had a higher prevalence of binocular-treatment (about 60% of the number of cases), and the most common therapeutic alternative

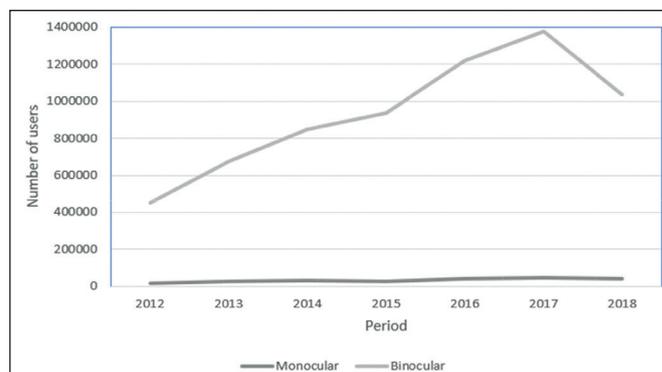


Figure 1: Clinical treatment for glaucoma provided by the Brazilian Unified Health System from 2012 to 2018, monocular-treatment vs. binocular-treatment.

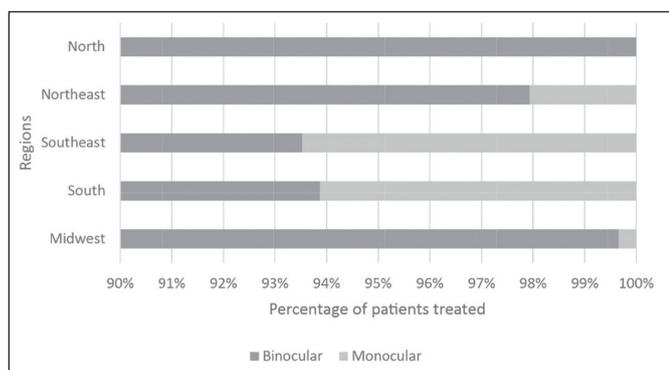


Figure 2: Clinical treatment for glaucoma provided by the Brazilian Unified Health System in 2018 by region: monocular-treatment vs. binocular-treatment.

was combinations of two drugs, considering all combinations of drug lines. The main combination was a first-line drug combined with a third-line drug.

None of the three other combinations exceeded the combination of three drugs in terms of the number of users until December 2018, when segmenting therapies combining two eye drops (1st line + 2nd line, 2nd line + 3rd line or 1st line + 3rd line), as shown in table 1.

The Southeast region showed the highest concentration of monocular treatment registered in DATASUS (53% of cases), and the predominant therapy was a combination of three different drugs (Figure 2). The Midwest region had the lowest prevalence of monocular-treatments for glaucoma at less than 6% of the cases (Figure 2).

DISCUSSION

This epidemiological study was carried out with data obtained from population strata, which means that the applicability of the results cannot be extended to the individual level (but only to the regional and national levels). Also, the possibility of underreporting, overdiagnosis, and misfiling of guides (monocular treatment when using binoculars) should be noted. Some regions might have more of these errors than others.

The number of glaucoma cases in the world is increasing as a result of demographic expansion and aging populations.⁽²⁾ Consequently, the number of treatments for this condition is expected to increase.

The results of this study could be used to plan health budgets more effectively for the purchase of drops. They could also be used to avoid medication shortages, which would reduce adherence to treatment and possibly worsen disease progression.⁽¹³⁾ The data could also be used to develop government measures to inform the population about glaucoma and the importance of early diagnosis, which would reduce the number of eye drops used per person in most cases. An early stage of the disease would imply a lower reduction of baseline IOP, thus requiring less medication.⁽¹⁴⁾

We observed an increase in the number of treatments until 2017, with is in line with the findings of a study performed in Scotland⁽¹⁵⁾, with National Health Service (NHS) data, demonstrating the rise in prevalence is far more than that which would have been predicted by growth and aging of the population over the period 2010–2017. These authors⁽¹⁵⁾ proposed that this could repre-

Table 1
Comparing the prevalence of treatments (Northeast region vs. all of Brazil) with more than one drug in December 2018.

December 2018	Northeast	Brazil
Combination of two drugs (first- + third-line)	7672	13164
Combination of two drugs (first- + second-line)	4412	8473
Combination of two drugs (second- + third-line)	2857	5684
Combination of three drugs (first- + second- + third- line)	11921	21506

sent an increasing detection rate for patients receiving intraocular pressure-lowering medications across the whole community.⁽¹⁵⁾

However, in Brazil in 2018, a decrease in the number of treatments was observed. This observation could reflect a failure to identify new cases (not registering), or even the use of definitive techniques for the treatment (such as trabeculoplasty and trabeculectomy) or, on the other hand, an improvement in diagnostic criteria (using standard methods) to accurately detect patients who really need treatment for glaucoma (suspending the prescription of eye drops for those who did not need it).

A study of 420 cases that met the criteria for the diagnosis of severe glaucoma examined the number of hypotensive drugs needed to control IOP. It was concluded that the majority of cases (73.3%) achieved IOP stabilization with the use of only one (38.1%) or at least two (35.2%) topical hypotensive agents in combination, which differs from our findings. Also, the most commonly used drug at the time of treatment initiation was a topical beta-blocker (a first-line drug).⁽¹⁶⁾ In our study, if considering patients treated with only one medication, the most prevalent class was third-line drugs (prostaglandin analogs). A possible reason for this difference is that the previous study was carried out with data collected from the hospital records, in which the medicated patients could choose to buy or receive for free (from SUS) the eye drops. The last option being more complicated and time-consuming for the patient, taking the same to prefer to buy an eye drop and the cheapest (in this case, the beta-blocker).

Another study carried out with patients admitted to a university hospital in São Paulo (in the Southeast region) concluded that 75.3% of glaucoma patients used medication bilaterally, while 24.7% used it in only one eye. Also, 31.5% of the interviewees used only one type of eye drops, 37.7% used two classes, and 21.2% used three types.⁽¹⁷⁾ This data differs from our findings, where we found a higher percentage of monocular treatment in the Southeast region and a higher prevalence of treatment with three different drugs.

The number of patients undergoing treatment for glaucoma in Brazil with combination therapies has been high. In general, the Glaucoma Program makes these medications available separately, which increases the chance of non-adherence to treatment. Studies show that decreasing the number of bottles needed for combinations of drugs increases adherence among users.⁽¹⁸⁾ Thus, the current approach is likely increasing the risk of progression of glaucoma in this population.

However, the results of this study need careful interpreta-

tion. The prevalence derived from this method is not an estimate of the actual prevalence of glaucoma since it did not include patients with glaucoma who did not take medication (because they underwent successful glaucoma surgery) or patients with glaucoma who preferred to buy their own eyedrops.

A possible limitation of this study might derive from the impossibility of separating data by gender or age and to evaluate the patient's clinical history. Also, it is not possible to associate the search terms available on the platform with the International Classification of Diseases (ICD-10).

CONCLUSION

There is a high national prevalence of glaucoma. In Brazil, the most significant numbers of treatments offered by the public health system were in the Northeast and Southeast regions.

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