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COMPARATIVE OF FIRST LINE MEDICATIONS FOR PRIMARY OPEN ANGLE GLAUCOMA : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Glaucoma is the second leading cause of blindness globally, of which primary open-angle glaucoma (POAG) is the most common type, and its prevalence is estimated at 2% worldwide. The prevalence of glaucoma contributes to significant medical costs, and the majority of costs are medication related. Most medications used in the management of glaucoma are targeted at decreasing intraocular pressure (IOP), with each millimeter of mercury (mm Hg) IOP reduction shown to reduce the risk of glaucoma progression and subsequent vision loss by 10%.*

The aim: *This study aims to show the comparative of first line medications for primary open angle glaucoma.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search on SagePub brought up 124 articles. The results of the search conducted for the last year of 2013 yielded a total 12 articles for PubMed and 34 articles for SagePub. The result from title screening, a total 10 articles for PubMed and 12 articles for SagePub. In the end, we compiled a total of 8 papers. We included five research that met the criteria.*

Conclusion: *All active first-line drugs are among the most efficacious drugs, although the within class differences were small and may not be clinically meaningful. All factors, including adverse effects, patient preferences, and cost should be considered in selecting a drug for a given patient.*

Keyword: *Glaucoma, medications, first line, POAG.*

INTRODUCTION

Glaucoma is a progressive multifactorial disease characterised by damage to the optic nerve. It is the second leading cause of blindness worldwide and it is predicted by 2020, close to 80 million people will have the disease, the majority affected by primary open angle glaucoma (POAG). POAG is strongly associated with elevated intraocular pressure (IOP) but may also occur with IOP in the normal range. Certain individuals can have elevated IOP without detectable glaucomatous damage. These individuals are at an increased risk of developing POAG and are referred to as having ocular hypertension (OHT).[1]

Despite advances into our knowledge of the aetiology and pathophysiology of POAG, the current mainstay of glaucoma treatment remains lowering of IOP to prevent further progression and visual loss. In this review we discuss different factors that may be important to consider when offering a choice of treatment to newly diagnosed POAG and OHT patients and describe new glaucoma treatments in development and future directions for POAG and OHT treatment.[1]

The goal of medical treatment for glaucoma is to lower an individual's eye pressure to a level that preserves visual function to reduce morbidity such as diminished psychosocial functioning3 and falls, while maintaining a good quality of life. Because of the asymptomatic and insidious nature of most forms of glaucoma, particularly early in the disease process, screening eye examinations including IOP checks and examination of the optic nerve are commonly used to first make a diagnosis. Intraocular pressure is a well-established, modifiable risk factor for glaucomatous optic neuropathy, and medical therapy to reduce IOP has been proven to slow disease progression and reduce vision loss.[2,3]

An increasing number of surgical options are now available to treat glaucoma patients. Subconjunctival filtration surgeries such as trabeculectomy and tube shunts remain very effective in reducing IOP, particularly in advanced or secondary forms of glaucoma or in patients who cannot tolerate or are poorly compliant with topical glaucoma treatments. However, these procedures carry serious risks such as bleb-related infections and endophthalmitis, flat anterior chamber, corneal decompensation, suprachoroidal hemorrhage, bleb dysesthesia, hypotony maculopathy, conjunctival scarring, and bleb failure. For these reasons, they are often reserved for refractory and advanced glaucoma cases. Patients who progress despite topical treatment can therefore be therapeutically challenging, as they require an escalation of treatment but may not warrant surgery with the aforementioned risks.[4]

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we compare and contrast of the comparative effectiveness of first line medications for primary open angle glaucoma. It is possible to accomplish this by researching or investigating the comparative effectiveness of first line medications for primary open angle glaucoma. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about the comparative effectiveness of first line medications for primary open angle glaucoma. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "First line medications for primary open angle glaucoma"; "primary open angle glaucoma" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("Glaucoma"[MeSH Subheading] OR "Open angel glaucoma"[All Fields] OR "Primary open angel glaucoma"[All Fields]) AND ("Medications for glaucoma"[All Fields] OR "Medications for primary open angel glaucoma"[All Fields]) AND ("Therapy for Glaucoma"[MeSH Terms] OR ("Therapy for Primary open angel glaucoma"[All Fields]) OR ("First line medications for open angel glaucoma [All Fields]))* used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

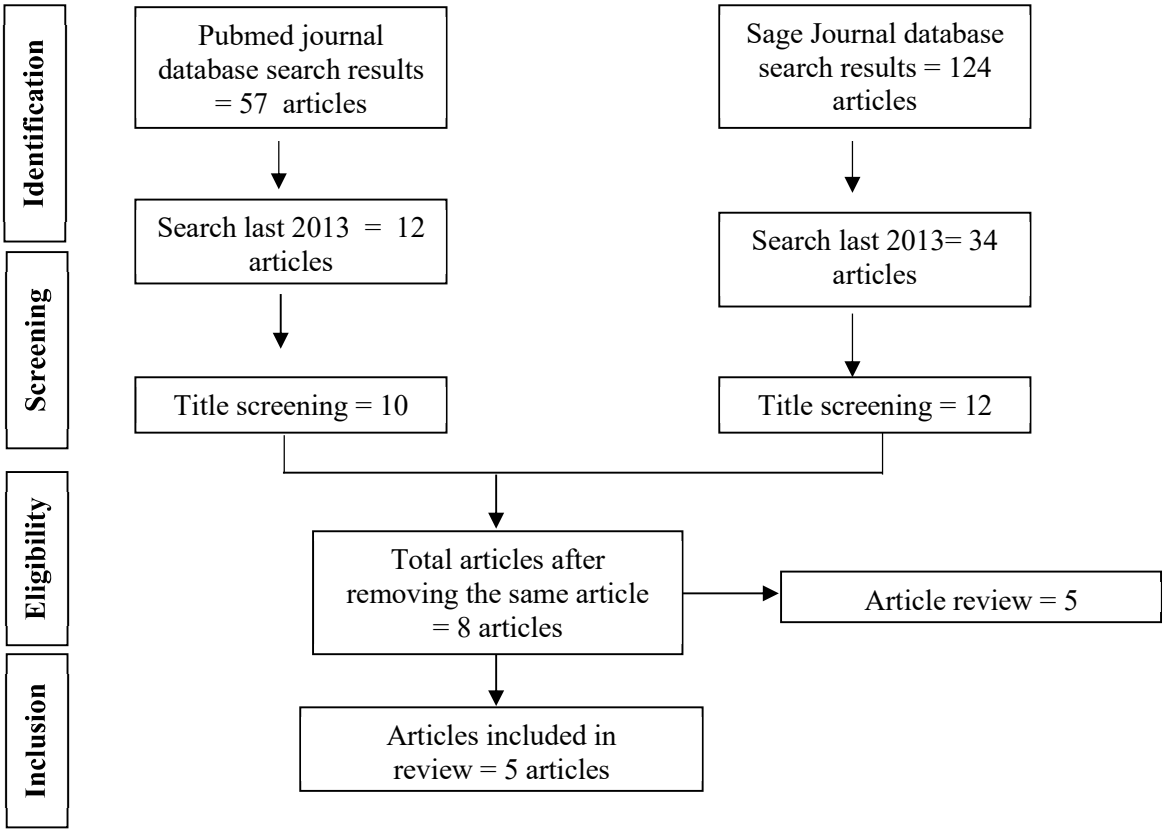

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 57 articles, whereas the results of our search on SagePub brought up 124 articles. The results of the search conducted for the last year of 2013 yielded a total 12 articles for PubMed and 34 articles for SagePub. The result from title screening, a total 10 articles for PubMed and 12 articles for SagePub. In the end, we compiled a total of 8 papers. We included five research that met the criteria.

Paul, C (2023) showed significant IOP reduction with preserved tafluprost 0.0015% in a real-world setting. As first-line monotherapy in patients with OHT and in POAG–naïve patients, preserved tafluprost 0.0015% significantly reduced IOP at 3 months. Even as second-line therapy in nonresponders (POAG-Switched) to various drugs (same class [PGAs] versus different class), treatment with preserved tafluprost 0.0015% resulted in significant IOP reduction at 3 months.

Philippin, H *et al* (2021) showed elective laser trabeculoplasty (SLT) is a rapid outpatient procedure used to reduce IOP. SLT increases aqueous fluid outflow from the eye, which drains through the trabecular meshwork. There is increasing evidence supporting its use as a primary intervention.13, 14 Lasers, especially SLT, could be part of future treatment for glaucoma.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Paul, C., 2023[5]	India	Retrospective study	88 patients	The mean IOP of the study population reduced significantly from baseline level by 20.6% and 25.5% at 1 month and 3 months after preserved tafluprost 0.0015% treatment ($P < 0.001$ for both). The mean IOP in patients with only OHT reduced significantly from baseline level by 21% and 26% at 1 month and 3 months after preserved tafluprost 0.0015% treatment ($P < 0.001$ for both). The mean IOP in patients with POAG reduced significantly from baseline level by 19% and 24% at 1 month and 3 months after preserved tafluprost 0.0015% treatment ($P < 0.001$ for both). The baseline IOP ± SD in POAG treatment naïve patients was 25.3 ± 0.3 mmHg, which reduced significantly by 24% and 28% at 1 month and 3 months after preserved tafluprost 0.0015% treatment ($P < 0.001$ for both). The baseline IOP ± SD in POAG switched patients was 24.3 ± 0.1 mmHg, which reduced significantly by 18% and 22% at 1 month and 3 months after preserved tafluprost 0.0015% treatment ($P < 0.001$ for both). In the POAG switch group, the percent reduction in IOP at 3 months after preserved tafluprost 0.0015% treatment was 23% with timolol as first line, 22% with bimatoprost as first line, 20% with latanoprost as first line, and 19% with travoprost as first line ($P < 0.001$ for all).
Philippin, H *et al*., 2021[6]	East Africa	Single-masked randomised controlled trial	840 patients	840 patients were screened for eligibility, of whom 201 (24%) participants (382 eligible eyes) were enrolled between Aug 31, 2015, and May 12, 2017. 100 (50%) participants (191 eyes) were randomly assigned to the timolol group and 101 (50%; 191 eyes) to the SLT group. After 1 year, 339 (89%) of 382 eyes were analysed. Treatment was successful in 55 (31%) of 176 eyes in the timolol group (16 [29%] of 55 eyes required repeat administration counselling) and in 99 (61%) of 163 eyes in the SLT group

				(33 [33%] of 99 eyes required repeat SLT; odds ratio 3·37 [95% CI 1·96–5·80]; p<0·0001). Adverse events (mostly unrelated to ocular events) occurred in ten (10%) participants in the timolol group and in eight (8%) participants in the SLT group (p=0·61).
Shi, Y *et al* ., 2023[7]	China	Prospective, randomized clinical trial	45 patients	A total of 45 glaucoma patients from Beijing, China, were enrolled in this clinical trial to compare the short-term efficacy of primary single-selective laser trabeculoplasty (SLT) to 0.005% latanoprost eye drops for the treatment of 24-h intraocular pressure (IOP) in patients with newly diagnosed primary open angle glaucoma (POAG) and ocular hypertension (OHT). Both SLT and latanoprost significantly decreased mean 24-h IOP and peak IOP, although the latanoprost group effect was more potent when compared to the SLT group (both Ps < 0.05). Compared with the SLT group, the latanoprost group had a significant and stable decrease in IOP after treatment. The latanoprost group had a more pronounced reduction in IOP at weeks 4 and 12 (P < 0.05) but had no difference at week 1 (P = 0.097). As a first-line treatment, both SLT and latanoprost eye drops are effective in newly diagnosed POAG and OHT patients. However, the latanoprost eye drops may be better in decreasing mean and peak 24-h IOP and thus controlling 24-h IOP fluctuation compared to SLT.
Dixit, A *et al*., 2020[8]	India	Prospective, randomised, single-blind study	104 patients	Significant reduction (p < 0.001) in intraocular pressure by 27.99% and 30.49% at 12th-week visit as compared with baseline was observed in monotherapy and fixed-dose combination group, respectively. Significant changes in pulse rate (9 beats/min) and systolic blood pressure (2.35 mmHg) was observed in fixed-dose combination group. No cup disc ratio reversibility was observed at the end of study.

				Conjunctival hyperaemia (n = 14) and transient blurring of vision (n = 16) were most commonly reported adverse drug reaction in monotherapy and fixed-dose combination, respectively.
Lanza, M *et al*., 2022[9]	Italy	Retrospective study	190 patients	The molecules explored showed some discrepancies in terms of mean duration of efficacy; however, no significant differences were demonstrated ($p > 0.05$). Furthermore, when evaluating the overall cohort, no systemic or ocular features correlated significantly with the effectiveness of the molecules explored. However, the same analysis carried out upon stratifying the different groups according to the IOP-lowering drops they received, demonstrated that the drug efficacy could be influenced by several ocular and systemic features.

Shi, Y *et al* (2023)[7] showed as a first-line treatment, both SLT and latanoprost eye drops are effective in newly diagnosed POAG and OHT patients. The latanoprost eye drops may be better in decreasing mean and peak 24-h IOP and controlling 24-h IOP fluctuation compared to SLT.

Dixit, A *et al* (2020)[8] showed 0.5% timolol/0.2% brinzolamide FDC was superior to 0.004% travoprost monotherapy in reducing IOP among drug-naïve OAG patients. Timolol/brinzolamide FDC diminished pulse rate and systolic BP while travoprost monotherapy had no such effect. No significant variations were recognised in diastolic BP, mean arterial pressure and CDR by both pharmaceutical groups. Both medications were well tolerated, and no new safety findings were established.

Lanza, M *et al* (2022)[9] showed an accurate evaluation of the glaucomatous patient with POAG is crucial to selecting a proper IOP-lowering regime, in agreement with the most relevant international guidelines. A treatment selected with the awareness of the molecule interval of efficacy, indeed, would provide an adequate IOP reduction along with avoiding unexpected VF damage progressions and a concomitant reduction of quality of life.

DISCUSSION

Glaucoma is the second leading cause of blindness worldwide and comprises a group of irreversible, progressive, and chronic optic neuropathies that result in vision loss owing to the death of retinal ganglion cells. Age is considered a major risk factor for glaucoma and the prevalence of this pathology increases with age. Reports indicate a prevalence of 2.93% among patients aged 40–80 years and 10.0% among those over the age of 90. Although the exact mechanism is unknown, several factors seem to contribute. Firstly, increasing age may affect neuronal function, making older patients more susceptible to glaucoma. Additionally, fewer neurons may be detected, allowing for earlier identification of progressive changes in the optic nerve.[10]

Primary open-angle glaucoma (POAG) is associated with high IOP. Elevation of IOP often leads to degeneration of the optic nerve. The main clinical features of glaucomatous damage to the optic nerve include deepening of excavation of the optic disc, bleeding of the optic disc (often seen in normal tension glaucoma) and defects of the retinal nerve fibre layer. Visual field loss may follow optic nerve damage. Previous research has shown that the extent of damage to the optic nerve depends on the extent of IOP elevation. Reduction of IOP both decreases the incidence rate of POAG and delays progression of POAG. In clinical practice, medications and surgeries may help decrease IOP and prevent progression of the disease. Unless contraindicated, drug initial therapy, and potential cost, side-effects, and dosing schedules my influence medication choice.[11]

PGAs (bimatoprost, latanoprost, travoprost, tafuprost and omidenepag isopropyl) are the most efficacious drugs in controlling IOP, followed by β-blockers, α-2 agonists, and carbonic anhydrase inhibitors. Several clinical trials have compared the efficacy and side effects of various PGAs. However, the results of these studies are inconsistent. For example, Florent Aptel demonstrated that 0.03% bimatoprost is more effective in reducing IOP than 0.005% latanoprost and 0.004% travoprost. Conversely, Denis reported that 0.004% travoprost and 03% bimatoprost might have a greater efficacy in reducing IOP than 0.005% latanoprost.[10]

Medical treatments act to decrease IOP in three main ways: increase outflow of aqueous humour, decrease secretion of aqueous humour and decrease intra-ocular volume. Prostaglandins (PGA), AA, BB, CAI and miotics (MIO) are the drugs most widely used to treat POAG. Previous meta-analysis demonstrated that medical treatment was effective in prevention of visual field loss (Maier et al. 2005). However, different drugs decrease IOP through various mechanisms, thus leading to different efficacies with regard to lowering IOP. Monotherapy, dual therapy and occasionally, triple therapy have all been carried out on patients. The wide variety of drug treatment options makes it difficult for doctors to choose a specific regimen.[11]

CONCLUSION

All active first-line drugs are among the most efficacious drugs, although the within class differences were small and may not be clinically meaningful. All factors, including adverse effects, patient preferences, and cost should be considered in selecting a drug for a given patient.

REFERENCES

[1] Garg A, Gazzard G. Treatment choices for newly diagnosed primary open angle and ocular hypertension patients. Eye. 2020;34(1):60–71.

[2] Cheema A, Chang RT, Shrivastava A, Singh K. Update on the medical treatment of primary open-angle glaucoma. Asia-Pacific J Ophthalmol. 2016;5(1):51–8.

[3] Li T, Lindsley K, Rouse B, Hong H, Shi Q, Friedman DS, et al. Comparative Effectiveness of First-Line Medications for Primary Open-Angle Glaucoma. Ophthalmology. 2016;123(1):129–40.

[4] Shultz M, Chorbajian A, Zohouralen A. Comparative Effectiveness and Safety of Two Different Trabecular MIGS Devices With and Without Ab Interno Canaloplasty in Patients with Primary Open-Angle Glaucoma. Ophthalmol Ther [Internet]. 2023;12(6):3307–22. Available from: https://doi.org/10.1007/s40123-023-00819-5

[5] Balasopoulou A, Kokkinos P, Pagoulatos D, Plotas P, Makri OE, Georgakopoulos CD, et al. Symposium Recent advances and challenges in the management of retinoblastoma Globe - saving Treatments. BMC Ophthalmol [Internet]. 2017;17(1):1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28331284%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5354527%5Cnhttp://bmcpsychiatry.biomedcentral.com/articles/10.1186/1471-244X-11-49%5Cnhttp://bmcophthalmol.biomedcentral.com/articles/10.1186/s12886

[6] Philippin H, Matayan E, Knoll KM, Macha E, Mbishi S, Makupa A, et al. Selective laser trabeculoplasty versus 0·5% timolol eye drops for the treatment of glaucoma in Tanzania: a randomised controlled trial. Lancet Glob Heal. 2021;9(11):e1589–99.

[7] Shi Y, Zhang Y, Sun W, Huang AS, Chen S, Zhang L, et al. 24-Hour efficacy of single primary selective laser trabeculoplasty versus latanoprost eye drops for Naïve primary open-angle glaucoma and ocular hypertension patients. Sci Rep [Internet]. 2023;13(1):1–10. Available from: https://doi.org/10.1038/s41598-023-38550-7

[8] Dixit A, Ashish A, Sharma R. A comparative study on efficacy of fixed combination timolol/brinzolamide versus travoprost monotherapy in drug-naïve open-angle glaucoma patients. Ther Adv Ophthalmol. 2020;12.

[9] Lanza M, Leone A, Scognamiglio G, Serra L, Iodice CM, Melillo P, et al. Evaluation of the Efficacy Duration of Topical Therapies in Eyes with Primary Open-Angle Glaucoma. J Clin Med. 2022;11(20).

[10] Zhou L, Zhan W, Wei X. Clinical pharmacology and pharmacogenetics of prostaglandin analogues in glaucoma. Front Pharmacol. 2022;13(October):1–9.

[11] Li F, Huang W, Zhang X. Efficacy and safety of different regimens for primary open-angle glaucoma or ocular hypertension: a systematic review and network meta-analysis. Acta Ophthalmol. 2018;96(3):e277–84.