



## Relationship between Progressive Cup Disc Ratio and Intraocular Pressure in Primary Open Angle Glaucoma After 2 Antiglaucoma Agents for 3 Months

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### ABSTRACT

**Introduction:** Primary open-angle glaucoma (POAG) is a subset of glaucoma defined by an open, normal-appearing anterior chamber angle and raised intraocular pressure (IOP) with no other underlying disease. Globally 57.5 million people were affected by primary open-angle glaucoma (POAG) in 2015, rising to 65.5 million by 2020. POAG can further lead to optic nerve damage, which can cause total blindness. POAG cannot be cured but can be controlled with medical therapy, laser, and surgical procedures. Antiglaucoma drugs are a method of treatment that can overcome this disease. This study aims to determine the characteristics of patients with POAG and progressivity of cup to disc ratio and intraocular pressure after 3 months of management of 2 antiglaucoma agents in POAG patients in Dr. Mohammad Hoesin General Hospital Palembang. **Methods:** This study retrospectively reviewed the medical records specific to primary open-angle glaucoma. Data was obtained from the patient register book recorded from February 2022 to May 2022 in Dr. Mohammad Hoesin General Hospital Palembang. The parameters analyzed were patients' profiles, namely gender, intraocular pressure, and cup to disc ratio before and after 3 months of combination 2 antiglaucoma agents. Timolol and latanoprost are the 2 antiglaucoma agents given to patients diagnosed of previous POAG (by an ophthalmologist). **Results:** From 30 patients diagnosed with POAG by an ophthalmologist, the number of primary open-angle glaucoma patients was more female, namely 19 patients (63.3%) than 11 male patients (36.7%), with a ratio of 1.28:1 between women and men. The cup to disc ratio between before and after 3 months of therapy using timolol and latanoprost was  $0.628 \pm 0.04$  before therapy to  $0.645 \pm 0.06$  after therapy ( $p < 0.05$ ). Intraocular pressure before and after 3 months of therapy was  $24.76 \pm 2.63$  before therapy to  $17.75 \pm 2.08$  ( $p < 0.05$ ). Both cup to disc ratio and intraocular pressure differs statistically from before and after therapy. **Conclusion:** Fixed combination therapy of timolol and latanoprost is effective in lowering intraocular pressure and reducing cup to disc ratio progressivity in patients with primary open-angle glaucoma.

### 1. Introduction

The term glaucoma refers to a group of progressive optic neuropathies characterized by an excavated appearance of the optic disc, often described as cupped, together with loss of retinal ganglion cells and their axons and corresponding vision loss.<sup>1</sup> The collection of glaucomatous diseases is subdivided into open-angle and closed-angle glaucoma, both of which can have primary or secondary causes.<sup>2</sup> Primary open-

angle glaucoma (POAG) is a subset of glaucoma defined by an open, normal-appearing anterior chamber angle and raised intraocular pressure (IOP) with no other underlying disease. If there is an identifiable underlying cause for raised IOP, this is termed secondary glaucoma.<sup>3</sup> Globally, 57.5 million people were affected by primary open-angle glaucoma (POAG) in 2015, rising to 65.5 million by 2020.<sup>4</sup> People

over 60 years of age, family members of those already diagnosed with glaucoma, steroid users, diabetics, as well as those with high myopia, hypertension, central cornea thickness of <5 mm, and eye injury are at an increased risk of glaucoma. By 2020, it is expected that approximately 76 million people will suffer from glaucoma, with that number estimated to reach 111.8 million by 2040.<sup>5</sup> In Indonesia, the prevalence of glaucoma is 0,46%. That means that 4 to 5 out of 1.000 people suffer from glaucoma.<sup>6</sup> Primary Open Angle Glaucoma (POAG) is the most common form of glaucoma on up-to-date knowledge of epidemiology, in addition to risk factors and pathogenesis, clinical features, and management options available. POAG cannot be cured but can be controlled with medical therapy, laser, and surgical procedures. Antiglaucoma drugs are a method of treatment that can overcome this disease. Treatment generally begins with the use of eye drops, then laser trabeculoplasty and surgical trabeculectomy can be done to slow the progression of the disease. Some studies have shown good results in management using combinations of antiglaucoma agents in POAG.<sup>7</sup> This study aims to determine the characteristics of patients with POAG, and the progressivity of cup to disc ratio and intraocular

pressure after 3 months of management of 2 antiglaucoma agents in POAG patients in Dr. Mohammad Hoesin General Hospital Palembang.

## 2. Methods

This study retrospectively reviewed the medical records specific to primary open-angle glaucoma. Data obtained from the patient register book recorded from February 2022 to May 2022 in Dr. Mohammad Hoesin General Hospital Palembang. The total sampling method was used for data collection. The parameters analyzed were patients' profiles, namely gender, intraocular pressure, and cup to disc ratio before and after 3 months of combination 2 antiglaucoma agents. Timolol and latanoprost are the 2 antiglaucoma agents given to patients diagnosed with previous POAG (by an ophthalmologist). Cup to disc ratio was measured using optical coherence tomography (OCT), and intraocular pressure was measured using non-contact tonometry (NCT). Data processing was performed using SPSS 24. Normality tests were done using Shapiro-Wilk. Then, pre and post-therapy data were analyzed using a comparative analysis Wilcoxon or Paired T-test. Results are described using the table.

## 3. Results

Profile of primary open-angle glaucoma patients at

Dr. Mohammad Hoesin General Hospital Palembang was described below in Table 1.

Table 1. Epidemiological profile of the patients

| Parameters | Numbers and Percentages |
|------------|-------------------------|
| Gender     |                         |
| Male       | 11 (36.7)               |
| Female     | 19 (63.3)               |

In this study, the number of primary open-angle glaucoma patients was more female, namely 19

patients (63.3%) than 11 male patients (36.7%), with a ratio of 1.28:1 between women and men.

Table 2. Cup to disc ratio before and after 3 months of 2 antiglaucoma agents, timolol and latanoprost.

| Cup to disc ratio                         | Mean ± SD    | P-value |
|---|--------------|---------|
| Before therapy                            | 0.628 ± 0.04 | 0.001   |
| After 3 months of timolol and latanoprost | 0.645 ± 0.06 |         |

Table 3. Intraocular pressure before and after 3 months of 2 antiglaucoma agents, timolol and latanoprost.

| Intraocular pressure                      | Mean ± SD    | P-value |
|---|--------------|---------|
| Before therapy                            | 24.76 ± 2.63 | 0.001   |
| After 3 months of timolol and latanoprost | 17.75 ± 2.08 |         |

The cup to disc ratio between before and after 3 months of therapy using timolol and latanoprost was  $0.628 \pm 0.04$  before therapy to  $0.645 \pm 0.06$  after therapy ( $p < 0.05$ ). Intraocular pressure before and after 3 months of therapy was  $24.76 \pm 2.63$  before therapy to  $17.75 \pm 2.08$  ( $p < 0.05$ ). Both cup to disc ratio and intraocular pressure differs statistically from before and after therapy.

#### 4. Discussion

POAG is the primary cause of irreversible blindness in adults around the world, posing real public health and quality of life problem as well as an economic problem. The progressive and irreversible loss of vision makes POAG a disease that can lead to blindness.<sup>8</sup> Complications of POAG can lead to painless blindness.<sup>2</sup> The pathogenesis of glaucoma is not fully understood, but high intraocular pressure is associated with retinal ganglion cell death. The balance between the secretion of aqueous humor by the ciliary body and its flow through the trabecular and uveoscleral pathways determines the magnitude of intraocular pressure. In POAG patients, there is increased resistance to aqueous outflow through the trabecular meshwork, resulting in a decreased outflow of aqueous humor.<sup>9,10</sup> The mechanism of optic nerve damage caused by increased intraocular pressure is unclear, but ischemia of the optic disc or nerve fiber layer, direct mechanical compression of the axons, local toxicity, or a combination of these are said to cause optic nerve damage in POAG.<sup>11</sup> To this further effects on the eye, The goal of glaucoma therapy is to maintain visual function by lowering intraocular pressure to a pressure that can prevent further optic nerve damage. The treatment regimen chosen should achieve this goal with the lowest risk, the fewest side effects, and the least cost to the patient. The target

pressure is the range of intraocular pressure in which the risk for disease progression is minimal, thereby reducing the patient's risk of blindness. Latanoprost is a prostaglandin analogues that are an ocular hypotensive agent with the ability to penetrate the cornea and is active after hydrolysis by corneal esterase. These drugs decrease intraocular pressure by increasing aqueous outflow through the uveascleral pathway and decreasing resistance to this flow.<sup>12-14</sup> Prostaglandins (PGs) are potent biologically active metabolites of the arachidonic acid that modulate many biological responses in various tissues, including the eye.<sup>15</sup> Timolol is a  $\beta$ -adrenergic antagonist which works by reducing intraocular pressure by inhibiting the production of cyclic adenosine monophosphate in the ciliary body epithelium, thereby reducing aqueous humor secretion by 20%-50%, thereby reducing intraocular pressure by 20%-30%.<sup>16</sup> This study conducted found that intraocular pressure in POAG patients in Dr. Mohammad Hoesin Palembang was reduced by up to  $7.01 \pm 0.55$  using a combination therapy of timolol and latanoprost. Progressivity of cup to disc ratio was also reduced by about 0.017 from  $0.628 \pm 0.04$  to  $0.645 \pm 0.06$ . This result is supported by some others studies that have been done before. A systematic review and meta-analysis studies including 16 trials by Xing Y et al., shows Fixed combination latanoprost timolol (FCLT) is as effective as travoprost and timolol (TTFC) and dorzolamide and timolol (DTFC), but worse than bimatoprost and timolol (BiTFC) in controlling mean IOP and IOP fluctuation for POAG or ocular hypertension patient.<sup>17</sup> Wang T et al. also state that fixed-combination therapeutics offer greater efficacy, reliable security, clinical compliance, and tolerance than non-fixed combination agents and monotherapy agents, which will become a preferred option for the

treatment of glaucoma.<sup>18</sup> Thelen U studies to evaluate the effect of an "escalation" of topical glaucoma therapy by switching from prostaglandin monotherapy to two different prostaglandin-timolol fixed combinations show six months after switching from latanoprost monotherapy to preservative-free prostaglandintimolol combinations, patients being treated with the latanoprost-timolol fixed combination had a mean IOP reduction by 4.16 mm Hg and Tolerability of, and satisfaction with, the fixed combination therapies was high. Side effects were few, such as a burning sensation in only 2 out of 30 patients involved in the study.<sup>19</sup>

## 5. Conclusion

Fixed combination therapy of timolol and latanoprost is effective in lowering intraocular pressure and reducing cup to disc ratio progressivity in patients with primary open-angle glaucoma. In addition, further studies about the side effects of therapy should be done to help clinician considerations of using the fixed combination therapy of antiglaucoma agents timolol and latanoprost in primary open-angle glaucoma.

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