Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga

JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
2022 August, XIII (02)

ORIGINAL ARTICLE

Effectiveness of Medication, Surgery, and Combination Therapy to Decrease Intraocular Pressure on Glaucoma Outpatient at Outpatient Ophthalmic Clinic Dr. Soetomo General Hospital Surabaya in January – December 2017

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A B S T R A C T

Introduction: Glaucoma leads to blindness in its end stage. Quality of life drops as visual field loss as progressive optic nerve damage since high intraocular pressure elevation. Glaucoma treatment focused on aqueous humor regulation, thus the intraocular pressure is maintained at normal.

Methods: This was a retrospective analytical study using secondary data gathered from medical records as total sampling data. The sample was determined by the purposive non-probability technique. The mean of intraocular pressure after therapies was defined as the dependent variable while the independent variable was the type of therapy.

Results: Combined therapy (16.00 ± 6.77 mmHg) had the least post-therapy intraocular pressure. The statistical test indicated no significant difference in the effectiveness of medication, surgery, and combination therapy for glaucoma intraocular pressure reduction.

Conclusion: There was no prominent difference in the efficacy of drugs, surgeries, and combined therapies for glaucoma intraocular pressure reduction.

A R T I C L E I N F O

Article history:

Received 1 June 2022

Received in revised form
28 June 2022

Accepted 22 July 2022

Available online 10 August 2022

Keywords:
Glaucoma,
Human & health,
Human & medicine,
Intraocular pressure reduction.

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JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
p-ISSN: 1907-3623; e-ISSN: 2684-9453
DOI: 10.20473/juxta.V13I12022.67-72

Introduction

Glaucoma is one of the most common eye disorders after cataracts which causes blindness. In glaucoma, the intraocular pressure increases to the level that can damage the optic nerve, thus leading to the loss of visual field. Many people with glaucoma do not realize that they have glaucoma in their eyes because glaucoma is not a well-known disease compared to cataracts. Over 45 million people are suffering from open-angle glaucoma and another 16 million people are suffering from angle-closure glaucoma. The prevalence number is estimated to increase every year.[1–4]

The increase of the intraocular pressure is produced by poor drainage of aqueous humor. Aqueous humor drainage is mainly determined by the production rate and the flow of aqueous humor.[5,6] The intraocular pressure can be managed by medication therapy, surgery, or the combination between medical therapy and surgery. This study aimed to compare drugs, surgeries, and combined therapies that provide glaucoma intraocular pressure reduction and represent glaucoma treatments performed at Ophthalmic Clinic Dr. Soetomo General Hospital Surabaya in January – December 2017.

Methods

This was a retrospective analytical study using secondary data gathered from medical records between January – Desember 2017 at the outpatient ophthalmology clinic of Dr. Soetomo General Hospital Surabaya by applying total sampling method. The sample was determined by the purposive non-probability technique. The mean of intraocular pressure after therapies was defined as the dependent variable while the independent variable was the type of therapy. The data were included based on criteria involving: 1) an outpatient with diagnosis of any glaucoma who received any glaucoma therapy from Outpatient Ophthalmology Clinic Dr. Soetomo General Hospital Surabaya between January – December 2017; 2) minimum of follow-up consultations were twice after the first consultation; and 3) post therapy intraocular pressure could be evaluated and recorded in quantitative value (mmHg), while the data were excluded if based on criteria involving: 1) an outpatient without diagnosis of any glaucoma even though they received any glaucoma therapy; 2) an outpatient who did not receive any glaucoma therapy even though the outpatient was diagnosed with any glaucoma; 3) the follow-up consultation was less than twice after the first consultation; and 4) post therapy intraocular pressure could not be evaluated or was not recorded in quantitative value. The data were clustered into descriptive tables and chi-square test was performed to acknowledge the objective of the study.

This study got ethical clearance from the Health Research Ethics Commission (KEPK) of Faculty of Medicine, Universitas Airlangga, Surabaya with number 0283/KEPK/V/2018.

Results

A total of 71 (142 eyes) subject with glaucoma were included in this study. Most of the subjects were between the age of 41-64 years old (43.66%) while fewer subjects were under 40 years old (18.31%) with a mean age of 55.03 ± 17.06 years old. There were more female (56.34%) than male (43.66%) patients in this study. The sample distribution based on age and gender was presented in Table 1. Only 124 of 142 eyes were diagnosed with glaucoma because some subjects did not have glaucoma in both eyes. The most type of glaucoma diagnosed was open-angle glaucoma (29.03%), followed by angle-closure glaucoma (21.77%), absolute glaucoma (16.94%), and normal tension glaucoma (14.52%). The sample distribution based on the type of glaucoma was presented in Table 2.

The medication therapy was the most frequently administered compared to other therapy, as shown in Table 3. According to Table 4, the most frequently administered drug in mono-drug therapy medication was Timolol (65.91%) and Xalatan (20.45%), while Table 5 shows that the most frequently administered drug in multi-drug therapy was the combination of Timolol with Acetazolamide (30.61%), followed by Xalatan with Timolol and Acetazolamide (24.49%), and Xalatan with Timolol (18.37%). Trabeculectomy (60%) was the most frequent surgery in this study as shown in Table 6. Laser Peripheral Iridotomy (41.67%) was the most frequent combination therapy as shown in Table 7. The least post-therapy intraocular pressure was found in the combined therapy (16.00 ± 6.77 mmHg), however the chi-square test (p-value < 0.05) specified that there was no significant difference in drugs, surgeries, and combined therapies efficacy to glaucoma intraocular pressure reduction. Table 8 presents the data on post-therapy intraocular pressure.

Table 1. Sample distribution based on age and gender

Variable	Frequency (f = 71)	Percentage (%)
Age (years old)		
≤40	13	18.31
41-64	31	43.66
≥65	27	38.03
Gender		
Female	40	56.34
Male	71	43.66

Table 2. Eye distribution based on the type of glaucoma

Type of Glaucoma	Frequency (f=124)	Percentage (%)
Normal Tension Glaucoma	18	14.52
Angle-closure Glaucoma	27	21.77

Open-Angle Glaucoma	36	29.03
Aphakic Glaucoma	1	0.81
Exfoliative Glaucoma	1	0.81
Pseudoexfoliative Glaucoma	1	0.81
Phacomorphic Glaucoma	2	1.61
Absolute Glaucoma	21	16.94
Juvenile Glaucoma	4	3.23
Neovascular Glaucoma	1	0.81
Secondary Glaucoma	10	8.06
Suspect Glaucoma	1	0.81
Uveitic Glaucoma	1	0.81

Table 3. Eye distribution based on glaucoma therapy

Type of Glaucoma	Frequency (f=110)	Percentage (%)
Medication	93	84.55
Surgery	5	4.54
Combination	12	10.91

Table 4. Eye distribution based on mono-drug therapy medication

Medication	Frequency (f=44)	Percentage (%)
Betaxolol	3	6.82
Timolol	29	65.91
Xalatan	9	20.45
Acetazolamide	3	6.82

Table 5. Eye distribution based on multi-drug therapy medication

Medication	Frequency (f = 49)	Percentage (%)
Azopt + Betoptima	1	2.04
Timolol + Acetazolamide	15	30.61
Timolol + Azopt	2	4.08
Xalatan + Azopt	1	2.04
Xalatan + Betoxolol	2	4.08
Xalatan + Timolol	9	18.37
Timolol + Atropine + Acetazolamide	1	2.04
Timolol + Atropine + Azopt	1	2.04
Timolol + Latanoprost + Azopt	1	2.04
Xalatan + Timolol + Acetazolamide	12	24.49
Xalatan + Timolol + Azopt	3	6.12
Xalatan + Timolol + Azopt + Acetazolamide	1	2.04

Table 6. Eye distribution based on surgery therapy

Surgery	Frequency (f = 5)	Percentage (%)
Phacoemulsification with Intraocular Lens Implantation	2	40.00%
Trabeculectomy	3	60.00%

Table 7. Eye distribution based on combination therapy

Combination	Frequency (f = 12)	Percentage (%)
LPI + Timolol	5	41.67
Trabeculectomy + Timolol	1	8.33
PE *with* IOL+ Acetazolamide	1	8.33
PE *with* IOL+ Xalatan	1	8.33
PE *with* IOL+ Timolol + Atropine + Azopt	1	8.33
Transscleral Cyclophotocoagulation + Timolol + Azopt + Acetazolamide	2	16.67
LPI + Latanoprost + Timolol + Azopt	1	8.33

LPI = Laser Peripheral Iridotomy
PE with IOL = Phacoemulsification with Intraocular Lens Transplantation

Table 8. Post therapy intraocular pressure

Therapy	N	Min. Value (mmHg)	Max. Value (mmHg)	Mean (mmHg)	p value
Medication	92	4.90	64.20	22.20 ± 12.61	0.448
Surgery	5	8.50	41.50	16.15 ± 14.21	
Combination	12	8.05	31.80	16.00 ± 6.77	

Min = Minimum
Max = Maximum

Discussion

Combined therapy of drug and surgery had the least intraocular pressure after treatment (16.00 ± 6.77 mmHg). Based on the chi-square test, there was no significant difference in drugs, surgeries, and combined therapy to glaucoma intraocular pressure reduction.

Age-related stress such as oxidative damage or imbalance response to crosslink protein can stimulate the body to produce excessive body factors that cause the accumulation of extracellular matrix in the trabecular meshwork and ciliary muscle. The accumulation of the extracellular matrix and loss of trabecular meshwork cells can lead to the decreased outflow of aqueous humor and finally increase the intraocular pressure.[7] The risk of glaucoma is increased by 1% on people aged 41-65 years old and 5% on people aged above 65 years old, while the risk of glaucoma is relatively small in people aged under 40 years old.[1,8] This study showed that the age of 41-64 years old (43.66%) was the most common age recorded with glaucoma. In a study conducted by Ariesta and Herriadi, most subjects were aged above 40 years old, and in the study conducted by Pusvitasari and Triningrat,[1] age 40-64 years old dominated the subjects. From another study, the mean age of people with glaucoma was 56.23 ± 18.07 years old. The results from the previously mentioned studies are in line with the results of this study and support the theory that the risk of glaucoma is increased with the increase of age.

Most of the subjects were females (56.34%). It is in line with a study conducted by Martinez and Hosaka[9] and Al Obeidan, *et al*.,[10] which stated that females were more dominant compared to males. However, in the study conducted by Ariesti and Herriadi[11] and Pusvitasari and Triningrat,[1] males were more dominant than females. There is still no further explanation about predilection glaucoma related to gender, but females usually have a longer life span, thus they are riskier to be affected with glaucoma.[12] The difference in prevalence by gender from the previously mentioned studies is affected by environment physical activity or other causes, thus gender is not included as the risk factor of glaucoma.[11]

Open-angle glaucoma (29.03%), angle-closure glaucoma (21.77%), absolute glaucoma (16.94%), and normal tension glaucoma (14.52%) were the most common type of glaucoma found among the subjects. According to an article by Jonas, *et al*.[13] open-angle glaucoma was the most common type of glaucoma. In a study conducted by Ariesti and Herriadi,[11] primary open-angle glaucoma (50.25%) was the most common type of glaucoma found followed by secondary glaucoma (19.70%) and primary angle-closure glaucoma (11.82%). In the study conducted by Pusvitasari and Triningrat,[1] primary open-angle glaucoma (33%) is the second most common type of glaucoma found after secondary glaucoma (37%). However, in the study conducted by Al Obeidan, *et al*.,[10] the most common type of glaucoma was primary angle-closure glaucoma (46.6%) followed by primary angle-closure (17.2%) and primary open-angle glaucoma (12.8%). In the study conducted by Alzhuhairy, *et al*.,[14] the most common type of glaucoma found was primary chronic angle-closure glaucoma (46.6%) followed by open-angle glaucoma (25.6%). Based on the results from the previously mentioned studies, the most common type of glaucoma was open-angle glaucoma and angle-closure glaucoma.

Medication therapy (84.55%) was the most frequent therapy administered compared to surgery and combination therapy. Timolol (65.91%) was the most frequent drug administered in medication using mono-drug therapy, while the combination of Timolol with Acetazolamide (30.61%) was the most frequent drug administered in medication using multi-drug therapy. Trabeculectomy (60.00%) was the most frequent surgery therapy performed while the combination of Laser Peripheral Iridotomy with Timolol (41.67%) was the most frequent combination therapy used. In a study conducted by Martinez and Hosoka,[9] the most frequent therapy administered was medication therapy (39.80%) followed by laser therapy (23.14%) and trabeculectomy (17.65%). Primary open-angle glaucoma was mostly treated by medication therapy (63.72%), while angle-closure glaucoma was mostly treated by Trabeculectomy (54.16%) in the study conducted by Ariesti and Herriadi (2018). Trabeculectomy (33.80%) is also often performed in primary open-angle glaucoma.[15]

According to Hazhar, Nurwasis, and Apriliawati,[16] the most therapy administered was multi-drug therapy medication (77.20%) with the most drug combination used was beta blocker with carbonic anhydrase inhibitor (39.50%). In the study conducted by Mustofa, Ulfa, and Suryandari,[17] the most common drug administrated in medication therapy was Timolol (32.67%) followed by Acetazolamide (30.99%) and a combination of Latanoprost with Timolol (20.51%). In the study conducted by Linden, *et al*.,[18] the most frequent drug administered in mono-drug therapy medication was prostaglandin analogue (81.00%) and Timolol (19.00%), while the most frequent drug combination administered in multi-drug therapy medication was Timolol with Bimatoprost or Timolol with Dorzolamide and Latanoprost.

According to Alzhuhairy, *et al*.,[14] primary open-angle glaucoma was primarily treated using medication therapy, but if the intraocular pressure did not reach the target, surgery is recommended. Meanwhile, primary angle-closure glaucoma was treated using combination of laser iridotomy with drugs. Other glaucoma treated using surgery therapy was continued by medication therapy if the post-surgery intraocular pressure was still above 22 mmHg. Based on the results from the previously mentioned studies, medication therapy was the most common therapy used in glaucoma because it is the most appropriate therapy for newly diagnosed patients or patients with their first consultation. It is the safer than surgery therapy. Surgery therapy is administered to patients with uncontrolled intraocular pressure using medication therapy. Trabeculectomy is still the gold standard method in surgery therapy although it has some complications that can damage the eyes.[19] Removal of cataracts is more needed in glaucoma cases with cataracts. Combination therapy is administered to patients who had received surgery but the post-surgery intraocular pressure was still above 22 mmHg.[14]

The mean of post-therapy intraocular pressure of medication, surgery, and combination therapy were 22.20

± 12.61 mmHg, 16.15 ± 14.21 mmHg, and 16.00 ± 6.77 mmHg respectively. Combination therapy resulted in the lowest post-therapy intraocular pressure (16.00 ± 6.77 mmHg), however the chi-square test (p-value < 0.05) specified that there was no significant difference in effectiveness of medication, surgery, and combination therapy. The result is in line with Burr, *et al*.[20] which there was no significant difference visual field score according to initial medication or initial trabeculectomy to primary open angle glaucoma. By the end of their study, they found there were also no difference in visual acuity after five years after initial treatment. In a study performed by Motlagh,[15] there was no significant difference in efficacy between medication and surgery therapy on primary open-angle glaucoma. Trabeculectomy had a success rate of 48.00-98.00% on this type of glaucoma, while the failure rate of medication therapy was 34.00%, which is associated with younger age, higher intraocular pressure at diagnosis, and pharmacology agents needed in initial therapy. Based on the previously mentioned studies, the medication therapy had not been able to decrease the intraocular pressure as far as the other therapies, and there was no significant difference in the effectiveness of medication, surgery, and combination therapy for glaucoma intraocular pressure reduction.

Conclusion

Age 41-64 years old dominated the subjects and there was no big difference between males and females. The most common type of glaucoma was open-angle glaucoma, while the most frequent therapy provided was drug therapy. Timolol was the most frequent drug administered in mono-drug medication therapy, while the combination of Timolol with Acetazolamide was the most frequent drug administered in multi-drug medication therapy. Trabeculectomy was the most frequent surgery performed, while the combination of Laser Peripheral Iridotomy with Timolol was the most frequent combination used. The least therapy intraocular pressure was found in the combination therapy. The statistical test indicated that there was no significant difference in drugs, surgeries, and combined therapies for glaucoma intraocular pressure reduction.

Acknowledgments

The authors would like to thank all participants for sharing their experiences. Deepest gratitude is given to our teachers, Department of Ophthalmology Dr. Soetomo General Hospital Surabaya, and Department of Public Health and Preventive Medicine Universitas Airlangga Surabaya. We also appreciate the support from our fellow colleagues and help from our college friends during the process of this study.

Conflict of Interest

The authors declared there is no conflict of interest.

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