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Research Article

The success of glaucoma therapy in diabetes mellitus and non-diabetes mellitus

Nur Shani Meida^{1*}, Ahmad Ikliluddin², Yunani Setyandriana³, Ilma Naafisa Anthrasita⁴

1,2,3) Department of Ophthalmology Faculty of Medicine and Health Sciences Universitas Muhammadiyah Yogyakarta

4) Students of Medical Study Program, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta,

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***Correspondence:**

nurshani_meida@yahoo.com

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ABSTRACT

Glaucoma is a disease marked with damage to the optic nerve, chronic and can cause blindness. Glaucoma needs regular therapy to prevent blindness. This study was an observational study using a case-control approach. Data were analyzed using the Mann-Whitney test to determine the differences in blood sugar levels in the DM and non-DM groups and the Chi-Square test to determine differences in the success of glaucoma therapy in DM and non-DM patients. There were 66 samples of glaucoma patients in this study, consisting of 14 men (21.2%) and 52 women (78.8%). The mean age of the patients was 61.12 ± 9.17 years. The sample was divided into 2 groups, namely 34 DM patients (51.5%) and 32 non DM patients (48.5%). The Mann-Whitney test showed significant differences in blood sugar levels between the DM and non-DM groups ($p < 0.05$). Blood sugar levels in the DM group were 202.59 ± 73.5 mg / dL and in the non-DM group was 106.19 ± 16.3 mg / dL. In conclusion, there is no difference in the success of glaucoma therapy in DM and non-DM patients.



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INTRODUCTION

Glaucoma is an eye condition that causes global blindness. It is the third blindness after uncorrected refractive error and cataract. Glaucoma contributed 8,49% to the world blindness among adults aged 50 years and older (Cvenkel & Kolko, 2020). Glaucoma is characterized by progressive optic nerve damage, retinal ganglion cells death, and corresponding visual field defect with a relative increase in intraocular pressure as one of the risk factors (Gauthier & Liu, 2017); (Tripathi Shweta, 2020); (Cvenkel & Kolko, 2020).

Glaucoma is an incurable disease that can be controlled with therapy. Glaucoma therapy aims to prevent vision loss, disability, and blindness by controlling intraocular pressure (IOP). IOP is the principal known and a modifiable risk factor for the development and progression of glaucoma. The success of therapy in glaucoma can be seen from the intraocular pressure that matches suitable with the therapeutic target (≤ 20 mmHg) or lowering by 20-40% of IOP (Rizka et al. 2020); (Cvenkel & Kolko, 2020). Generally, glaucoma treatment can use drugs with eye drops or oral medications. Five groups of IOP-lowering eye drops have varying mechanisms of action. Some drops, such as β -blocker and α -2 agonist, have potentially serious systemic side effects. Acetazolamide is the only available oral agent, it is effective at lowering IOP, but significant side effects relegate its use, usually to refractory glaucoma. Selective laser trabeculoplasty is a gentle treatment that enhances conventional aqueous outflow. Trabeculectomy is the gold standard surgery to lowering IOP (Paul Riordan-Eva, 2018); (Rizka et al., 2020); (Lusthaus & Goldberg, 2019). Glaucoma patients with Diabetes Mellitus (DM) have additional damage mechanisms to the lamina cribrosa and

trabecular meshwork, and they have relatively higher intraocular pressure (Costa et al., 2015).

Hyperglycemia in DM can increase Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase. It is the major source of Reactive Oxygen Species (ROS) production (Dos Santos et al., 2019). ROS will increase oxidative stress, which can contribute to the pathogenesis of glaucoma, increase IOP and disturb the endothelial function and make a loss of pericytes (Volpe et al., 2018); (Benoist d'Azy et al., 2016); (Tang et al., 2019); (Kida et al., 2015); (J. Zhao et al., 2016). DM can cause microvascular damage and several disorders of the body's regulation of the retina, optic nerve and increase the susceptibility of ganglion cells to oxidative stress damage in glaucoma such as increased intraocular pressure (Torres-Martínez et al., 2016). Therefore, this study aimed to determine the differences in the success of glaucoma therapy in DM and non-DM patients.

METHODS

This study was an observational study using a case-control approach with the ethical clearance number 038/EC-EXEM-KEPK FKIK UMY/IV/2020. The study sample was glaucoma patients with a history of DM, and as control was glaucoma patients non-DM. The data was taken from patients' medical records at Purbowangi Gombong Hospital, Kebumen Eye Center Clinic, and PKU Muhammadiyah Gamping Yogyakarta Hospital from November 2019 to August 2020.

Sampling from this study using a simple random sampling technique. The inclusion criteria in this study were glaucoma patients who were routine visited hospital to take medicine, male or female aged more than 40 years, with routine treatment for at least one year, with a history of Diabetes Mellitus at least 5 years.

Non-DM glaucoma patients were taken as controls. The exclusion criteria were glaucoma



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patients with normotension type glaucoma and secondary glaucoma (including neovascular glaucoma), glaucoma patients who were pregnant, glaucoma patients with a history of glaucoma surgery and other eye surgeries and Diabetes Mellitus patients with severe complications such as heart disease and kidney failure. The success of glaucoma therapy was seen from the level of Intra Ocular Pressure (IOP). It was said to be a success if it meets the IOP therapy target ≤ 20 mmHg and was said unsuccessful if $IOP > 20$ mmHg. The Data

were analyzed using Chi-Square by SPSS to determine differences in the success of glaucoma therapy in DM and non-DM patients.

RESULTS

In this study, 66 samples of glaucoma patients were collected, consisting of 14 men (21.2%) and 52 women (78.8%). The mean age of the patients was 61.12 ± 9.17 years. The sample was divided into 2 groups, namely 34 DM patients (51.5%) and 32 non DM patients (48.5%).

Table 1. Characteristics of subjects based on gender

	Variable	Frequency	Presentage(%)
Sex	Male	14	21.2
	Female	52	78.8
	Total	66	100

Table 2. Characteristics of subjects based on DM status

	Variable	Frequency	Percentage(%)
	DM	34	51,2
	Non DM	32	48,5
	Total	66	100

Table 3. Average blood sugar levels and Intra Ocular Pressure (IOP) of the DM and non-DM groups

Parameter	DM (n=34)	Non DM (n=32)	p
Fasting blood sugar levels (mg/dL)	202,59 \pm 73,5	106,19 \pm 16,3	p < 0,05
IOP (mmHg)	17,94 \pm 7,1	17,41 \pm 7,74	p > 0.05



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Table 4. The success rate of glaucoma therapy on DM status in the right and the left eyes

	Glaucoma therapy		Total	p
	succeed (IOP<20)	Not successful (IOP>20)		
DM	51	17	68	>0,05
Non DM	46	18	64	
Total	97	35	132	

Table 3 shows the mean blood sugar levels and Intra Ocular Pressure (IOP) of the right and left eyes of the DM and non-DM groups. The Mann-Whitney test showed significant differences in blood sugar levels in the DM and non-DM groups ($p < 0.05$). Blood sugar levels in the DM group 202.59 ± 73.5 mg / dL and in the non-DM group and 106.19 ± 16.3 mg / dL. Although the two groups showed significantly different blood sugar levels, blood sugar levels in the DM group showed a not too high increase in blood sugar levels. The patient can control routine blood sugar levels either by diet, exercise, or taking DM drugs.

The mean Intra Ocular Pressure (IOP) of the right and left eyes of glaucoma patients did not show a significant difference ($p > 0.05$) between the DM and non-DM groups. The intraocular pressure in both groups showed a pressure of ≤ 20 mmHg, meaning glaucoma therapy was successful. Even so, the DM group showed a higher Intra Ocular Pressure than the non-DM group, but both of them were still on target therapy ($IOP \leq 20$ mmHg).

The success of glaucoma therapy (right and left eyes) in the DM and non-DM groups, as shown in tables 4 and 5 above, with the Chi-Square test, did not show a significant difference ($p > 0.05$), meaning that they were equally successful.

DISCUSSION

Glaucoma is an eye disease that causes blindness. Glaucoma requires regular therapy to prevent blindness. The success of glaucoma therapy is indicated by the decrease in IOP reaching ≤ 20 mmHg. Several factors influence and obstruct the success of glaucoma therapy.

Diabetes Mellitus is the risk factor of glaucoma (Y. X. Zhao & Chen, 2017). Meta-analysis study reported Relative Risk (RR) effect DM to glaucoma 0,65 – 4,2 (Y. X. Zhao & Chen, 2017); (D. Zhao et al., 2015); (Y. X. Zhao & Chen, 2017). The prevalences glaucoma in DM are 6,8 – 15,6% (Beena et al., 2020); (M et al., 2017); (Dharmadhikari et al., 2015) and in Primay Open Angle Glaucoma (POAG) is 20% (Jayanta et al., 2017).

Andrey G et al., (2020) said that DM is associated with elevated IOP but has no clear association with POAG.

Many hypotheses have been offered it. The first theory suggests that long-standing hyperglycemia might increase the risk of neural stress damage. A second theory is that diabetic eyes have a dysregulation in blood flow due to retinal vascular endothelial cell dysfunction. Another explanation might be a remodeling of the connective tissue of the optic nerve head and dysregulation at the trabecular meshwork and the lamina cribosa. In accordance increased IOP and more significant mechanical stress on the optic nerve head.



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Glaucoma in DM (with hyperglycemia condition) is suspected of obstructing the success of glaucoma therapy. Hyperglycemia can increase Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase. It is the major source of Reactive Oxygen Species (ROS) production (Dos Santos et al., 2019). ROS will increase oxidative stress, which can contribute to the pathogenesis of glaucoma, increase IOP and disturb the endothelial function and make a loss of pericytes (Volpe et al., 2018); (Benoist d'Azy et al., 2016); (Tang et al., 2019); (Kida et al., 2015).

In this study, the success of glaucoma therapy in the DM and non-DM groups did not show a significant difference. DM patients may have fasting blood glucose levels that are not too high (202.59 ± 73.5 mg / dL). It is possible for the patient to control routine blood sugar levels either by diet, exercise, or taking DM drugs. From the interviews conducted, most DM patients control and routinely seek treatment to treat their disease.

Patients who receive routine diabetes medication do not appear to be detrimental to the success of glaucoma therapy. The relationship of DM and anti-DM drug to glaucoma remain unclear. It might be the neuroprotective effect of anti-DM (particularly metformin), but there are poorly understood and should be studied (Hou et al., 2019).

The mean Intra Ocular Pressure (IOP) of the right and left eyes of glaucoma patients did not show a significant difference ($p > 0.05$) between the DM and non-DM groups. The glaucoma patient group with DM showed a higher IOP than the non-DM group, but both of them were still on target therapy ($IOP \leq 20$ mmHg). Constancy in using drugs and constancy to visits to health services are factors for the success of glaucoma therapy (Rizka et al., 2020).

In glaucoma patients who have good constancy will affect the success of glaucoma therapy.

Patients who routinely seek treatment will increase the success of treatment which is indicated by $IOP \leq 20$. Communication factors, patient knowledge, health facilities, individual factors, family support, social and health workers affect the level of patient compliance (Rizka et al., 2020).

The results of this study are not in line with research conducted by (Baisakhiya et al., 2017); (Pimentel et al., 2015); (Hanyuda et al., 2020) and (Rizka et al., 2020), who stated in their research that there was a significant influence between blood sugar levels with increased IOP. The study noted that blood sugar levels affected IOP in both DM and non-DM patients. Choudhary and Sinha, 2019 reported that the first mean IOP was higher in the DM group than the non-DM group and the second mean IOP was higher in the uncontrolled DM group than the controlled DM group. A study by Pandey and Tiwari, 2020 showed significantly higher IOP in a patient with type 2 DM than non DM.

In the study of (Lavaju et al., 2017), the results are following this study, it showed there is no effect between DM and IOP on glaucoma. In this study, the results of significance ($p = 0.757$) and it was stated that the prevalence of DM in glaucoma patients was 27.4%. In this study, it was noted that patients routinely take anti-glaucoma drugs, so this can cause a decrease in the IOP number in patients. The reduction in IOP in the patient indicates that there is a successful treatment for glaucoma. This study used a cross-sectional method with 113 patients with type 2 diabetes and 76 patients without diabetes.

Desai *et al.*, 2018 research results stated no significant effect between blood sugar levels and TIO. This study says that the impact of DM on glaucoma is still controversial, in several studies showing that the eyes of people with diabetes have decreased ability to regulate blood flow so that it can cause hypoxia and



respond to increased Intra Ocular Pressure (IOP) in the eyes. However, this study states that the decrease in Intra Ocular Pressure (IOP) can be caused by the influence of routine glaucoma therapy performed by patients.

Another study, Hou *et al.*, 2019 with a total of 197 eyes (55 eyes with type 2 Diabetes Mellitus (DM) in POAG and 142 without type 2 DM in POAG) compare the rates of visual field (VF) loss and retinal nerve fiber layer (RNFL) thinning in both groups. It concluded that there was no statistically significant difference between the two groups, although POAG patients with treated type 2 DM had significantly slower rates of RNFL thinning than those without diagnosed DM. Li *et al.*, 2020 studied in Primary Close Angle Glaucoma (PACG), and it concluded that oxidative stress was involved in the onset and development of PACG. It can be shown that increased Malondialdehyde (MDA) levels were associated with VF progression in a patient with PACG. MDA level is the primary indicator of lipid peroxidation. It is used as the predictor of oxidative stress. MDA level in a patient with glaucoma is higher than usual (Javier & Martinez, 2017).

Several factors cause the hypothesis in this study not to be proven. Blood sugar levels in DM patients were well controlled, as seen from the mean blood sugar levels of 202.59 ± 73.5 mg / dL. It is possible for the patient to take regular diabetes medication or maintain blood sugar levels with diet and exercise. DM patients with controlled blood sugar levels have the same glaucoma therapy success as glaucoma patients without DM. There is a limitation of this study. This study was a retrospective study; therefore, we could not control the routine medication of the sample.

CONCLUSION

From this research, it can be concluded that there is no difference in the success of glaucoma therapy in DM and non-DM patients. DM patients with controlled blood sugar levels will not interfere with the success of glaucoma therapy.

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