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Aqueous Humour Malondialdehyde Level as Oxidative Stress Marker In Types Of Glaucoma



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ABSTRACT

Background: Angle-closure glaucoma is Asia's most common type of glaucoma, leading to worse damage due to its oxidative stress. Another type is open-angle glaucoma in the second line. The oxidative stress level can be known by malondialdehyde level examination. The study about MDA levels in aqueous humour in primary angle-closure and open angle glaucoma has not been done before. Therefore, the objective of this study was to determine the difference of malondialdehyde levels in aqueous humour between primary open-angle glaucoma and primary angle-closure glaucoma.

Methods: This study was an analytical observational study. Nine subjects were primary open-angle glaucoma patients, and ten subjects were primary angle-closure glaucoma patients. The aqueous humour was aspirated from the anterior chamber during trabeculectomy and measured the MDA levels using a spectrophotometer. Data were analyzed by the Mann-Whitney test.

Results: There was no significant difference ($p=0.095$) of MDA levels in aqueous humour between primary open-angle glaucoma ($62.913 \pm 17.259 \mu\text{mol/L}$) and primary angle-closure glaucoma ($53.485 \pm 9.670 \mu\text{mol/L}$).

Conclusion: The oxidative stress level in primary open-angle glaucoma and primary angle-closure glaucoma is the same, indicating that the inflammation status in both conditions could be similar.

Keywords: Malondialdehyde (MDA), primary open-angle glaucoma, primary angle-closure glaucoma

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INTRODUCTION

Glaucoma is the second largest cause of blindness after Cataracts.¹ The blindness due to glaucoma in Indonesia reached 0.16% of the total population.² The glaucoma prevalence in Indonesia, according to the Basic Health Research (Riset Kesehatan Dasar or Riskesdas) in 2007, was around 4.6%. In Central Java, the glaucoma prevalence in 2007 was 2,3%.³

Definition of glaucoma is a group of progressive optic neuropathies characterized by degeneration of retinal ganglion cells and resulting optic nerve head.⁴ Degeneration of these nerves results in cupping, a characteristic appearance of the optic disc and visual loss.⁵ Glaucomas can be classified into open-angle glaucoma (POAG) and angle-closure glaucoma (PACG).⁴ Primary open-angle glaucoma (POAG) is a chronic,

progressive optic neuropathy in adults characterized by acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons.⁶ Primary Angle Closure Glaucoma (PACG) is responsible for half of glaucoma-related blindness. PACG is characterized by appositional approximation or contact between the iris and trabecular meshwork.⁷ Pathogenesis of glaucoma is not fully understood, but some factors are associated with this condition, such as high intraocular pressure (IOP), increased oxidative stress, aging, glutamate neurotoxicity, and susceptibility genes such as optineurin and myocilin.⁸⁻¹⁰

Oxidative stress is an important risk factor in the pathogenesis of glaucoma. Increasing ROS (Reactive Oxygen Species) production and imbalance between oxidative and antioxidant capacity have been postulated as the crucial factors in early retinal injury, together with the

reduced ocular perfusion pressure in the blood vessels (the vascular theory of glaucoma).¹¹ Studies conducted on aqueous humour and the blood of glaucoma patients reported an increase in the level of oxidative stress of malondialdehyde (MDA) and decreased total capacity of antioxidants.¹² Analysis of some studies showed an increase in oxidative damage to the nucleus and mitochondria of DNA in patients with glaucoma compared to normal people.¹³⁻¹⁴ The increase of oxidative stress in patients with glaucoma is the cause of apoptosis reaction in TM.¹⁵⁻¹⁶ The study by Ghanem *et al.* (2010), which assessed the correlation between oxidative stress and glaucoma severity, found higher MDA levels in glaucoma patients compared to the control group and a positive correlation between high MDA levels and the damage to the visual field.¹⁷ Based on the study of Faschinger *et*

al. (2006), there was a positive correlation between the MDA serum levels and MDA levels in aqueous humour of patients with angle-closure glaucoma. The study also found no significant difference between MDA levels in aqueous humour compared with levels in serum and plasma.¹⁸

Both Primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG) are glaucoma types that need to be studied about oxidative stress, such as MDA. The fact is that MDA has been increasing in glaucoma condition, but the level in POAG and PACG has not been understood. Therefore, this study tried to explain the MDA level in POAG and PACG for early study in Indonesia.

METHODS

This was an analytical observational study with a cross-sectional design. We conducted the study in the Ophthalmology Department of Dr. Kariadi Hospital and the GAKI laboratory of the Faculty of Medicine of Diponegoro University from November 2016 to July 2017.

The subject of this study was patients with POAG and PACG who underwent trabeculectomy. Patients with diseases that cause increased MDA levels such as diabetes mellitus, infection or inflammation and cancer, also patients who consumed antioxidants were excluded in this study.

Nine patients with POAG and 10 patients with PACG met with exclusion criteria. Aqueous humour was taken by aspiration during trabeculectomy surgery. It needed at least 0.025 ml using a 1cc disposable syringe. Samples were stored in tubes at a -20° C temperature for the examination. The samples were examined for MDA level in GAKI laboratory using the Quantikine Immunoassay Kit and read the results with a spectrophotometer at the excitation wavelength of 515 nm and an emission wavelength of 553 nm. Computer programs analyzed data. We performed the normality test and Mann-Whitney test. $P < 0.05$ was significant.

This study obtained ethical approval from the Research Ethics Commission of the Faculty of Medicine of Diponegoro University. All the subjects in this study have declared to join and signed the informed consent form.

RESULTS

Table 1. shows the subject of the characteristics in this study. Subjects with both primary open-angle glaucoma (POAG) types consist of 7 male (77.8%) and 2 (22.2%) females; meanwhile, subjects with primary angle-closure glaucoma (PACG) types consist of 2 male (20%) and 8 (80%) female. The median age subject with POAG is 57.78 ± 9.271 , and PACG is 58.8 ± 9.852 . The next analysis performed the difference test for MDA level in aqueous humour between POAG and PACG. Table 2 showed no significant difference in MDA levels in aqueous humour between POAG and PACG. MDA levels of the subject with POAG are higher than subjects with PACG.

DISCUSSION

Malondialdehyde (MDA) is one of the free radicals used as a marker for glaucoma.¹⁹ Nucci et al., (2013) showed an increase in the level of malondialdehyde and decreased total capacity of antioxidants in the blood and aqueous humor of patients with primary open-angle glaucoma.¹² Yildirim et al. (2005) showed an increase in MDA plasma levels in patients with glaucoma compared to the control group, and there was no significant difference in MDA levels in the blood and aqueous humour.²⁰

The study by Ghanem et al. (2010) assessed the correlation between the oxidative stress marker and the severity

of glaucoma in the primary open-angle glaucoma showed MDA levels in aqueous humor patients with aqueous humor glaucoma were higher compared to the control group. The study also showed a positive correlation between MDA level and the visual field damage.¹⁷

Glaucoma is a multifactorial disease and intraocular pressure is one of the most suspected risk factors causing damage to the retinal ganglion cells. Increased intraocular pressure and the visual field abnormalities occurring in glaucoma are associated with oxidative damage to DNA in the trabecular meshwork.¹⁴ Both POAG and PACG have suffered damage in the retinal ganglion cells, visual field abnormalities, and damage in the trabecular meshwork due to increased intraocular pressure. This almost identical pathophysiology and damage process cause the non-significant difference in MDA levels in the aqueous humour.

Primary angle-closure glaucoma consists of several stages, and most patients who come to the hospital are patients suffering from acute stage episodes and chronic stage patients. In this study, we selected the chronic stage patients who didn't show signs of inflammation to avoid bias from high MDA levels due to the inflammatory process in the acute stage. Therefore, we found clinical features and damages almost the same as those found in the primary open-angle glaucoma.

This study was preliminary that needs to explore more deeply with a larger

Table 1. The characteristics of subjects in the study

Characteristics	POAG	PACG	P
Gender			
Male N (%)	7 (77.8)	2 (20.0)	
Female N (%)	2 (22.2)	8 (80.0)	
Age (Median \pm SE)	57.78 ± 9.271	58.8 ± 9.852	0.455

Table 2. MDA level in POAG and PACG

Variable	Glaucoma groups (Median \pm SE)		P
	POAG	PACG	
MDA level ($\mu\text{mol/L}$)	62.913 ± 17.259	53.485 ± 9.670	0.095*

* = not significant

number of patients, both POAG and PACH. Furthermore, it is difficult to analyze the MDA level at various POAG and PACG. This study also did not determine the correlation between MDA level and variable of clinical visual damage. These limitations need to be evaluated in the next study.

CONCLUSIONS

The oxidative stress level in primary open-angle glaucoma and primary angle-closure glaucoma is the same, indicating that the inflammation status in both status could be similar.

CONFLICT OF INTEREST

No conflict of interest

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CONFLICT OF INTEREST

All authors declared that there is no conflict of interest regarding this article

ETHICS APPROVAL

Research Ethics Commission has ethically approved this study of the Faculty of Medicine of Diponegoro University with ethical clearance number 224/EC/FK/RSDK 2020. All the subjects in this study have declared to join and signed the informed consent form

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AUTHOR CONTRIBUTION

All authors contributed equally in the research and writing process of this article

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