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High HbA1c Level as a Risk Factor of Low Tears Secretion after the Phacoemulsification Surgery



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ABSTRACT

Background: Tears secretion disorder may cause significant discomfort that will interfere with daily activities and quality of life. Diabetes mellitus (DM) patients often have tears secretion disorders as a complication of peripheral neuropathy that affects the lacrimation reflex. The HbA1c level is an indicator of glycemic control in DM patients that can illustrate complication that may occur in DM patients. Surgical procedures involving the cornea, such as phacoemulsification, are thought to interfere with the tear secretion. This study aims to prove that high HbA1c level is a risk factor of low tear secretion in DM patients after the phacoemulsification surgery.

Method: This case-control study was conducted at the Eye

Polyclinic of Sanglah General Hospital and Indera Hospital Denpasar Bali, from June 2013 to November 2013. A total of 70 DM patients who had undergone phacoemulsification surgery 12-16 weeks before the data collection was classified into low tear secretion (Schirmer I test <10 mm) group and normal tear secretion (Schirmer I test ≥10mm) group. The HbA1c levels were measured to assess their glycemic control for the last 3 months.

Result: Based on multivariate analysis using logistic regression, the adjusted odds ratio for HbA1c level was 2.44 (95%CI 0.778 – 7.633).

Conclusion: High HbA1C levels (>7%) increase the risk of low tear secretion in DM patients after phacoemulsification surgery.

Keywords: Dry eye, HbA1C level, phacoemulsification, tear secretion

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INTRODUCTION

Eye discomfort is one of the most common eye problems found in patients that interfere with daily activities. Eye discomfort complaints can be in the form of eye pain, burning sensation, and disruption during reading and driving. Those complaints were caused by disruption on tear films that protect the eye. Further, it may disrupt the patient's quality of life.

The tear film is made up of three layers which are lipid, aqueous, and mucous layers. The aqueous layer occupies almost 90% of tear film thickness. The aqueous layer functions as a solvent for nutrient, oxygen, and specific protein that acts as antimicrobial.^{1,2} Tears secretion, especially the aqueous layer, was secreted by the lacrimal gland. Tears secretion is affected by the nervous system which involves a complex functional lacrimal unit. Stimulus from the ocular surface will stimulate the lacrimation reflex. Any surgical procedure that involves the cornea, such as refractive and cataract surgery, will disrupt the lacrimation reflex.^{3,4} Besides, the existence of a systemic disease, such as diabetes mellitus, will also affect tear secretion.^{5,6}

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemic state.⁷ World Health Organization (WHO) predicts an increase in the number of DM cases in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030. Similar with WHO, the International Diabetes Federation (IDF) also predicts an increase in DM patients from 7.0 million in 2009 to 12.0 million in 2030.^{8,9,10} The complications of DM include macroangiopathy, microangiopathy, and peripheral neuropathy. The peripheral neuropathy will cause a decrease in corneal sensitivity and is suspected to be the cause of neural disorders, either in the afferent or efferent pathway of lacrimation reflex.² The study done by Manaviat et al. in 2008 showed that about 54.3% of DM patients had tears film disorder. This was also supported by another study that showed that poor glycemic control in DM patients will increase the incidence of dry eye syndrome (DES) in DM patients.^{11,12}

A study on the tear film in DM patients found that there was a correlation between HbA1C levels and the quantity of tear secretion.¹² Another study on tear films after the cataract surgery found that

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the phacoemulsification surgery can cause DES.^{13,14} However, there are still no published studies about the association between tear secretion and HbA1c in post-phacoemulsification patients. Therefore, this study aims to describe the magnitude of the risk of poor glycemic control, which is characterized by high levels of glycated hemoglobin (HbA1c), on low tear secretion in post-phacoemulsification patients.

METHOD

This study was an observational study with a case-control study design. This study assesses the role of HbA1c level as a factor associated with tear secretion which is measured using the Schirmer I test in patients who underwent cataract surgery (phacoemulsification). method. This study was conducted at the Eye Polyclinic of Sanglah General Hospital and Indera Hospital Denpasar Bali from June 2013 to November 2013. This study used consecutive sampling method, involving all DM patients who had visit the Eye Polyclinic during the study period and met the inclusion criteria. The inclusion criteria were DM patients who had undergone phacoemulsification surgery 12-16 weeks before the data collection and aged 50 years old or more. The exclusion criteria were using eye drops (antibiotics, antiglaucoma, lubricants, and artificial tears) within the last 2 weeks, using contact lenses within the last 3 months, having local pathological disorders (such as entropion, ectropion, post-Steven Johnson Syndrome, and Bell's palsy), taking certain drugs (non-steroid anti-inflammatory drugs, corticosteroids, antihypertensive, antidepressants, and immunosuppressants drugs) in the last 3 months, and having a history of previous intraocular and refractive surgery.

STATISTIC

The numeric data, including age and the length of time since diagnosed with DM, were presented as mean and standard deviation. The categorical data, such as gender, education level, occupation, and the HbA1c level, were presented as frequency and proportion. The association between the HbA1c levels and Schirmer 1 test result was assessed through bivariate analysis using the Chi-square test. The magnitude of association is shown as crude odds ratio value. Binary logistic regression test was used as the multivariate analysis to assess the true effect of HbA1c levels to the Schirmer 1 test result. The result of the multivariate analysis was shown as the adjusted odds ratio value.

RESULT

This study involved 70 subjects who had met the inclusion and exclusion criteria. All subjects were classified into the case and control groups with 35 subjects in each group. The case group was DM patients who had undergone phacoemulsification surgery 12-16 weeks before the data collection with Schirmer 1 test <10 mm, while the control group was DM patients who had undergone phacoemulsification surgery 12-16 weeks before the data collection with Schirmer I test ≥ 10 mm.

Subjects in the case group had a mean age of 63.06 ± 6.7 years and the subjects in the control group had a mean age of 58.94 ± 4.7 years. Most subjects in the case group were female (60%), while most subjects in the control group were male (60%). The number of low and moderate education levels were similar in both groups. The number of indoor and outdoor occupation was almost equal in both groups. The mean length of time since diagnosed with DM in the case group was 4.69 ± 3.94 years and in the control group was 4.83 ± 4.89 years. Characteristics of the subjects in this study is provided on Table 1.

Table 2 showed the association between the HbA1c level and tear secretion in DM patients after the phacoemulsification surgery. There are 27 subjects (77.1%) in the case group (Schirmer 1 test <10 mm) who had risk with HbA1c $\geq 7\%$. This study found that there was an association between the HbA1c level and tear secretion in DM patients after the phacoemulsification surgery with crude odds ratio value 2.25.

The crude odd ratio value obtained from the bivariate analysis could not illustrate the true effect of HbA1c level as a risk factor, because it was still affected by the confounding factors. Other variables that had a significance p value < 0.025 were included in the multivariate analysis.

Table 3 showed the result of multivariate analysis to estimate the true effect of HbA1c level against the tear secretion by controlling the confounding variables. The confounding variables were age and sex. The multivariate analysis was done using binary logistic regression with Schirmer 1 test result as the dependent variables and the HbA1c level, age, and sex as the covariates. The method of elimination used was entered. The adjusted odds ratio value obtained from this analysis was 2.44 which means that the post-phacoemulsification DM patients with high HbA1c levels had a 2.44 times greater risk of low tear secretion than those with normal HbA1c levels. The confidence interval range was from 0.778 to 7.633 with a probability value of 0.126 was not statistically significant. Thus, this means that high HbA1c level is a risk factor for the low tear secretion

Table 1. Characteristic of Subjects

Characteristic	Tear Secretion		p value
	Schirmer 1 Test <10mm n=35	Schirmer 1 Test ≥10mm n=35	
Age (years) (Mean±SD)	63,06±6,7	58,94±4,7	0,004*
Gender {n (%)}			
Male	14 (40)	21 (60)	0,094**
Female	21 (60)	14 (40)	
Education level {n(%)}			
Low	18 (52)	21 (60)	0,521**
Moderate	17 (48)	14 (40)	
Occupation {n(%)}			
Outdoor	7 (10,0)	6 (8,6)	0,759**
Indoor	28 (40,0)	29 (41,4)	
Length of time since diagnosed with DM (years) (Mean±SD)	4,69±3,94	4,83±4,89	0,893*

* Independent T-test

** Pearson Chi-square Test

Table 2. Association Between HbA1c Levels and Tears Secretion in DM Patients After Phacoemulsification Surgery

Variable	Schirmer 1 Test		Odds Ratio	p value
	< 10mm	≥10 mm		
HbA1c ≥ 7% n (%)	27 (77.1)	21(60.0)	2.25	0.122*
HbA1c < 7% n (%)	8 (22.9)	14(40.0)		

*Pearson Chi Square Test

Table 3. The Result of Multivariate Analysis Using Logistic Regression Test

Variable	Odds Ratio	95% CI	p value
HbA1c	2.44	0.778-7.633	0.126
Age	0.88	0.796-0.973	0.012
Gender	0.42	0.150-1.198	0.105

p value based on the binary logistic regression test

in DM patients after the phacoemulsification surgery. Meanwhile, younger age was a protection factor against the low tear secretion by 1/0.88 or 1.14 times compared to the older age. Male gender was also a protective factor against low tear secretion by 1/0.42 or 2.36 times compared to the female gender.

DISCUSSION

Most subjects in the case group (post-phacoemulsification DM patients with low tear secretion) in this study were female (60%). This result was similar to the study done in the United States that estimated there were 3.23 million women and 1.68 million men from a total of 4.91

million Americans aged over 50 years old had DES.^{15,16} Another study done by Manaviat *et al.* in 2008 showed that DM patients who had DES in their study were 58% female and 48.8% male.¹¹

Women more often come with complaints of DES. This was associated with decreased androgen levels in women over 50 years old due to menopause which can lead to low tear secretion.^{17,18} A study done by Susiyanti in 2001 found the severity of DES in accordance with the duration of amenorrhoea postmenopausal which showed the role of estrogen in DES. However, the administration of estrogen hormone replacement therapy in menopausal women increases the prevalence of DES compared to those who did not receive the estrogen replacement therapy.¹⁹ Estrogen can induce regression of the lacrimal glands, reduce its metabolic functions, and reduce tear secretion.¹⁷ The androgen hormone had important roles in regulating the function of meibomian glands and lipid secretion in tears. Androgen acts on the epithelial cells of the glandular acini thereby maintaining the tear stability by preventing evaporation. Therefore, reduced androgen function due to aging is the same in both genders due to atrophy of the meibomian glands and lipid dysfunction.²⁰

A study on the incidence of DES after cataract surgery by Robert *et al.* in 2006 showed that a surgical procedure can aggravate the existing DES conditions.²¹ Other studies on tear films after cataract surgery showed that the phacoemulsification surgery could trigger incidence of DES.^{4,13} Liu *et al.* in 2008 also found that the Schirmer test results in DM patients who underwent a phacoemulsification surgery on day

180 were 86% lower compared to Schirmer test preoperatively. Meanwhile, the Schirmer test results in the non-DM group will return to the preoperative values in 90 days after the surgery. However, a study conducted by Ram *et al.* in 2002 on DES patients undergone phacoemulsification surgery concluded that phacoemulsification was safe and did not alter the results of the Schirmer test in patients with DES.²²

The HbA1c level indicates the amount of glycated hemoglobin due to prolonged exposure to serum glucose. The high HbA1c levels indicate uncontrolled hyperglycemia over the past 3 months.²³ This glycemic control was associated with the incidence of DM complications. Good glycemic control with HbA1c level <7% can reduce the progression of DM complications. A study by Nuho *et al.* in 2004 searched for the relationship between neuropathy using cornea sensitivity and lacrimal glands secretion in DM type 2 patients. This study found that the mean of HbA1c levels of DM patients with neuropathy was higher than the DM patients without neuropathy which was 7.4% and 6.5%, respectively.²⁴

The subjects in this study were the DM patients who had undergone phacoemulsification surgery 12-16 weeks before the data collection. The criteria of 12-16 weeks post-phacoemulsification surgery referred to the healing process of the corneal incision wound due to the phacoemulsification surgery. This healing process was influenced by the corneal endothelial cell layer which had limited mitotic capabilities. The loss of endothelial cells will be followed by cell enlargement and filling of the empty space by other endothelial cells. The stabilization process of changes in the endothelial layer of the cornea occurs approximately within three months.²⁵

This study found that high HbA1c levels ($\geq 7\%$) increase the risk of low tear secretion by 2.44 times in DM patients after the phacoemulsification surgery. The reduction in tear secretion was affected by various factors. This study found that older age tends to have lower tear secretion. Nevertheless, this study already attempted to find the true effect of HbA1c as a risk factor of low tear secretion after considering the age and gender factors.

This study was using a case-control study design to measure the magnitude of HbA1c levels as a risk factor for low tear secretion after the phacoemulsification surgery. The limitation in this study was there was no data on tear secretion before the surgery or before the patients were diagnosed with DM.

Tears secretion disorder may cause significant discomfort. This study concluded that DM

patients with high HbA1c levels ($\geq 7\%$) had a 2.44 times greater risk of low tear secretion after the phacoemulsification surgery than those with normal HbA1c levels ($< 7\%$).

CONFLICT OF INTEREST

None declared

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AUTHOR CONTRIBUTION

All authors have equal contribution

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