



# Macular Alteration of Topical Diclofenac Sodium after Phacoemulsification Surgery in Diabetic Patients

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## Abstract

**Edited by:** Ksenija Bogoeva-Kostovska  
**Citation:** Delfi D, Virgayanti V, Alandy J. Macular Alteration of Topical Diclofenac Sodium after Phacoemulsification Surgery in Diabetic Patients. Open Access Maced J Med Sci. 2021 Jun 04; 9(T3):156-159. https://doi.org/10.3889/oamjms.2021.6287  
**Keyword:** Diclofenac sodium; Phacoemulsification; Macular thickness  
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**Received:** 26-Apr-2021  
**Revised:** 20-May-2021  
**Accepted:** 25-May-2021  
**Copyright:** © 2021 Delfi Delfi, Vanda Virgayanti, Julham Alandy  
**Funding:** This research did not receive any financial support  
**Competing Interests:** The authors have declared that no competing interests exist  
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**BACKGROUND:** Cystoid macular edema (CME) is a serious complication of cataract surgery in a diabetic patient. CME was found 1–19% after phacoemulsification surgery. Nonsteroidal anti-inflammatory drugs inhibit cyclooxygenase-1, cyclooxygenase-2, and endoperoxides. Inhibition of these enzymes also reduces macular thickening.

**AIM:** The aim of the study was to assess macular thickness alteration after application of 1.00 mg diclofenac sodium eye drops in diabetic patients who receive phacoemulsification surgery.

**METHODS:** This study was a quasi-experimental study. A total of 40 eyes diabetic retinopathy patients having phacoemulsification surgery were randomized to 100 mg diclofenac sodium (n = 20) or placebo eye drops (n = 20), three drops daily on 1 day before surgery until 30 days post-operative. The main outcome measures macular thickness using Ocular Coherence Tomography before and after (14 and 30 days) phacoemulsification.

**RESULTS:** Utilizing an independent t-test, this study had significantly inner macular (p = 0.0001) and central macular (p = 0.008) thickness differences in the diclofenac sodium group during surgery until 14 days postoperatively. However, significant changes in the outer macular thickness were absent. There were no notable alterations in the center, inner, and outer macular thickness in the diclofenac sodium group until 30 days postoperatively. In the placebo group, no significant changes were found in the macular thickness at every point of time.

**CONCLUSION:** Two statistically significant central and inner macular thicknesses in the diclofenac sodium group until 14 days postoperatively were present. There were no significant changes in the center, inner, and outer macular thickness in the diclofenac sodium group until 30 days postoperatively.

## Introduction

Diabetes mellitus is one of the endocrine diseases characterized by elevation of blood glucose levels due to insulin impairment [1]. According to Riset Kesehatan Dasar, diabetes mellitus prevalence in 2007 was 1.1% and increased to 2.1% in 2013. One of the most common microvascular complications of diabetes mellitus is diabetic retinopathy (DR) [2]. DR is a progressive microangiopathy characterized by damage and occlusion of small vessels. The first pathological changes are basal membrane thickening of retinal capillary endothelium, diminished pericytes, vessel dilatation, hard exudates, soft exudates, angiogenesis, retinal edema, and scarring [3], [4]. Cystoid macular edema (CME) was first reported by Irvine in 1953 and is one of the most serious complications of cataract surgery in a diabetic patient [5]. Diabetic patients having cataract surgery have an increased risk for developing CME postoperatively, especially if they are also diagnosed with DR [6].

Angiography CME was found 1–19% after extracapsular cataract extraction of phacoemulsification.

Almeida's study in 2011 stated that CME was significantly lower with the use of nonsteroidal anti-inflammatory drugs (NSAID) prophylaxis continued with a combination of NSAID and corticosteroid for 4 weeks after phacoemulsification compared with the corticosteroid-only treatment [7]. NSAID's mechanism of action is inhibition of cyclooxygenase-1, cyclooxygenase-2, and endoperoxides. Inhibition of these enzymes also reduces macular thickening [8]. One of the most popular NSAID is diclofenac sodium eye drop. The objective of this study is to assess macular thickness alteration after the application of 1.00 mg topical diclofenac sodium in diabetic patients who receive phacoemulsification surgery.

## Methods

This was a quasi-experimental study that was conducted from June to November 2019 at Sumatera Utara University Hospital and Medan Baru Medical Centre Medan, Indonesia. DR patients who receive

phacoemulsification surgery and intraocular lens (IOL) implantation were enrolled in this study. HbA1C test performed before surgery and HbA1C higher than 6.4% were included in this study. Exclusion criteria were glaucoma, intraocular inflammation, posterior segment disorder, laser photocoagulation history, and patients having intraoperative and post-operative complications of the surgery. The patients divided into two groups, the first group was treated with 1.00 mg topical diclofenac sodium eye drop 3 times a day, starting 1 day before surgery for a month, and the second group was treated only with artificial tears eye drop after surgery. Ocular tomography coherence was performed at 1-day pre-phacoemulsification, 14 and 30 days post-phacoemulsification. Macular thickness was analyzed using a paired t-test.

## Results

The research subjects were cataract patients with type 2 diabetes mellitus who met the requirements to undergo phacoemulsification at the Medan Baru Eye Hospital (40 subjects). The research subjects were divided into two groups. One group was given artificial tears eye drops and the other group was given 1.00 mg of diclofenac sodium eye drops postoperatively. Data were obtained from June to August 2019 by recording patient demographic data, HbA1C, visual examination, and macular thickness D-1 pre-cataract surgery, D+14, and D+30 after cataract surgery.

## Discussion

Table 1 showed the characteristics of research subjects based on age. It is stated that most subjects aged more than 60 years old. This fact is not in line with the research of Kiziltoprak *et al.* and Becker *et al.* which stated that people with diabetes mellitus have a 5 times more risk of developing cataracts with the age range of 45–54 years [9], [10].

**Table 1: Characteristics of research subjects by age**

Age characteristics (years)	Frequency	n (%)
41–<46	1	2.5
46–<51	1	2.5
51–<55	10	25
56–<60	6	15
>60	22	55
Total	40	100

In Table 3, it is revealed that the research subjects had HbA1C levels with the highest frequency at >10% levels. This level of HbA1C can lead to the formation of mild-to-severe senile cataracts and NPDR with a predominance of mild types.

**Table 2: Characteristics of research subjects based on gender**

Gender	Frequency	(%)
Male	20	50
Women	20	50
Total	40	100

In Table 4, the characteristics of research subjects based on the results of visual acuity showed that there are no statistically significant differences between pre-operative and post-operative visual acuity in the control group and the treatment group with a value of  $p > 0.005$  ( $p = 0.0374$ ).

**Table 3: Characteristics of Research Subjects based on HbA1C**

Levels	Frequency	n (%)
7.0–8.0	1	2.5
8.1–9.0	1	2.5
9.1–10	10	25
10+	28	70
Total	40	100

In this study, the macular evaluation was performed using optical coherence tomography (OCT). Walkden's research in 2017 stated SD-OCT to detect subclinical CME in patients having routine phacoemulsification and IOL insertion [11]. Bellocq's research in 2019 stated SD-OCT appears to be the procedure of choice for confirming the diagnosis CME [12].

**Table 4: Overview of pre-operative visus at D-1 in the control and treatment groups**

Pre operation vision	Eye drop		Diclofenac sodium		Amount		p
	n	%	n	%	n	%%	
Poor	7	43.8	9	56.3	16	100.0	0.519
Worse	13	54.2	11	45.8	24	100.0	

In Table 5, a comparison of macular thickness a day before the surgery between control and treatment groups showed no significant difference. This is known with  $p > 0.05$ , namely, at central 0.721, inner 0.386, and outer 0.688. This indicates that there is no statistically significant difference in macular thickness. In Table 6, the comparison of macular thickness at 1 day before surgery, 14 and 30 days after surgery in the control group shows no significant difference because the p-value appears to exceed  $p > 0.05$ . In Table 7, the comparison of the macular thickness at 1 day before surgery, 14 and 30 days after surgery in the treatment group shows a  $p < 0.05$ , that is, with a value of  $p = 0.008$  and  $p = 0.0001$ . This study is in line with Yang in 2016 and Katsimpris in 2011 which stated that topical administration of diclofenac sodium can prevent thickening of the macula after phacoemulsification surgery in senile cataract patients with diabetes mellitus.

**Table 5: Comparison of macular thickness in D-1 control and treatment groups**

Macular thickness	n	$x \pm \Sigma\Delta$	p
Central on D-1			
Artificial tears	20	245.75 ± 34.469	0.721
Diclofenac sodium	20	248.85 ± 17.101	
Inner on D-1			
Artificial tears	20	302.95 ± 46.440	0.386
Diclofenac sodium	20	312.70 ± 16.874	
Outer on D-1			
Artificial tears	20	273.85 ± 31.925	0.688
Diclofenac sodium	20	277.00 ± 13.765	

Patients treated with diclofenac sodium before and after cataract surgery had lower levels of intraocular interleukin-12 and may reduce the incidence of postoperative macular edema in patients with DR [13].

**Table 6: Changes in macular thickness in D - 1, D + 14, and D + 30 control group**

Thickness macula	n	x ± ΣΔ	p
<b>Central</b>			
On D - 1	20	245.75 ± 34.469	0.937
On D + 14	20	245.40 ± 22.883	
<b>Inner</b>			
On D - 1	20	302.95 ± 46.440	0.946
On D + 14	20	302.60 ± 31.426	
<b>Outer</b>			
On D - 1	20	273.85 ± 31.925	0.571
On D + 14	20	276.65 ± 21.902	
<b>Central</b>			
On D + 14	20	245.40 ± 22.883	0.247
On D + 30	20	241.30 ± 19.027	
<b>Inner</b>			
On D + 14	20	302.60 ± 31.426	0.895
On D + 30	20	301.80 ± 14.609	
<b>Outer</b>			
On D + 14	20	276.65 ± 21.902	0.711
On D + 30	20	278.55 ± 14.497	

Meanwhile, the outer macular thickness before surgery and 14 days after surgery show a  $p > 0.05$ , which means that there is no statistically significant difference. The same result can also be found in central, inner, outer macular thickness in 14 days and 30 days after the surgery.

**Table 7: Changes in Macular Thickness in D-1, D + 14, and D + 30 treatment group**

Macular thickness	n	x ± ΣΔ	p
<b>Central</b>			
On D - 1	20	248.85 ± 17.101	0.008 *
On D + 14	20	241.80 ± 19.632	
<b>Inner</b>			
On D - 1	20	312705 ± 16.874	0.0001*
On D + 14	20	300.35 ± 15.786	
<b>Outer</b>			
On D - 1	20	277.00 ± 13.765	0.490
On D + 14	20	279.55 ± 16.669	
<b>Central</b>			
On D + 14	20	241.80 ± 19.632	0.133
On D + 30	20	236.55 ± 14.713	
<b>Inner</b>			
On D + 14	20	300.35 ± 15.786	0.172
On D + 30	20	295.60 ± 18.112	
<b>Outer</b>			
On D + 14	20	279.55 ± 16.669	0.074
On D + 30	20	271.50 ± 13.271	

It is known that the energy generated by phacoemulsification does not affect changes in the thickness of the retina as well as the macula (Figures 1 and 2). This is also in accordance with Liu's research in 2015 which stated that inappropriate selection of phacoemulsification type will affect the thickening of the macula, especially in mild-to-moderate NPDR patients [14], [15].

Mentes' study in 2003 stated the incidence of CME after phacoemulsification surgery, it was reported that 23 out of 252 eyes experienced CME angiography and disappeared after being evaluated for 45 days [16].

The use of topical NSAIDs may reduce the risk of developing macular edema after cataract surgery, although there is still much debate about clinical

uncertainty regarding the benefits of administering topical NSAIDs as prophylaxis. In addition, research done by Kessel in 2014 stated that topical NSAIDs are more effective in controlling postoperative inflammation after cataract surgery, especially regarding macular edema compared to the use of topical steroids, so there is no harm in continuing to provide regular topical NSAIDs such as diclofenac sodium to prevent inflammation and macular edema in post-cataract surgery [17].

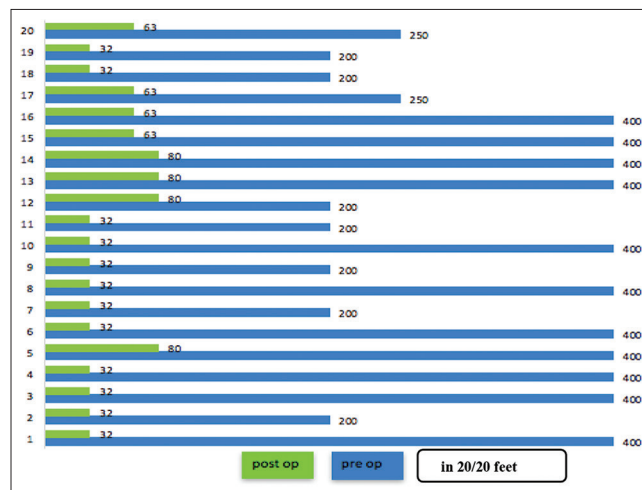


Figure 1: Results of pre- and post-cataract surgery virus research subjects control group

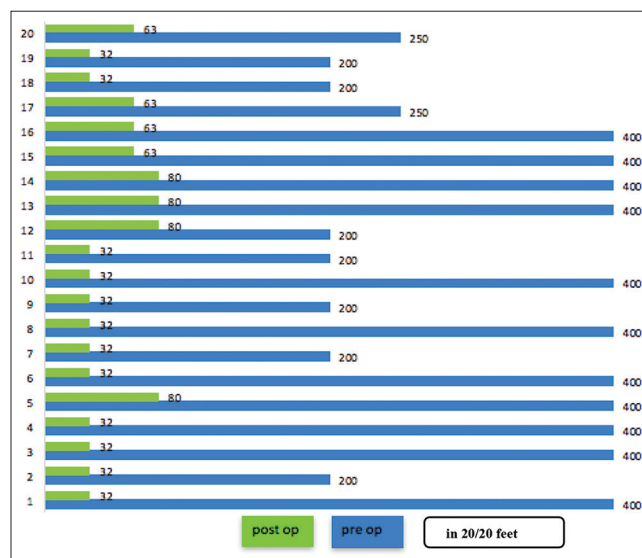


Figure 2: Results of pre- and post-cataract surgery virus research subjects treatment group

## Conclusion

There were significant changes in central and inner macular thickness during observation 1 day before surgery until 14 days in the diclofenac sodium group. Moreover, there were no significant changes in central, inner, and outer macular thickness during observation

14–30 days postoperatively in the diclofenac sodium group.

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