



Correlation between the Use of Topical Anti Glaucoma Containing Preservative Benzalkonium Chloride with the Degree of Dry Eye Syndrome in Mohammad Hoesin Hospital Palembang

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DOI: 10.24896/jrmds.2017565

ABSTRACT

There are approximately 67 million glaucoma patients worldwide, half of them are Asian. Most glaucoma treatments use topical agents as the first-line therapy. Long-term antiglaucoma therapy (AGT) treatment, had been shown to have side effects that are not only caused by the active substance of the drug, but also by the preservative such as benzalkonium chloride (BAK). Long duration of AGT drugs use and the number of the drugs can cause discomfort in the eyes of the patient due to decrease in tear secretion as well as vaporizing abnormalities, known as dry eye syndrome. To measure the correlation between the duration of topical anti glaucoma use containing preservative BAK with dry eye syndrome degree in Moehammad Hoesin (RSMH) hospital, Palembang. Method: Descriptive research using correlation test design to find out the correlation between the duration of AGT containing BAK use with the degree of dry eyes syndrome was undertaken in June - December 2016. The samples of the study were glaucomic patients who came to Eye Glaucoma Subdivision clinic, the RSMH hospital Palembang. There were 40 patients recruited, 52.5% of them were women. There were 20 (50%) patients who had been using AGT containing BAK ≥ 20 weeks, while other 20 patients < 20 weeks. It was found that there were significant correlations between the duration of AGT use with Schirmer test ($r = -0.50$, $p = 0.002$), TBUT ($r = -0.24$, $p = 0.004$) and Ferning test ($r = 0.15$, $p = 0.035$). There was a significant correlation between topical drug usage in long-term treatments of AGT with the incidence of dry eyes syndromes ($r = -0.40$, $p = 0.015$). there were 8.6% patients with third degree of dry eyes syndrome, 11.4% with second degree and 57.1% were normal. There was a significant relationship between the duration of AGT use containing preservative BAK with the incidence of the vocational degree in the patient ($r = -0.40$, $p = 0.015$).

Keywords: Anti Glaucoma Topical Treatment, Preservative Benzalkonium Chloride, Degree of Dry Eyes Syndromes

HOW TO CITE THIS ARTICLE: Fidalia, Erial Bahar, Syntia Rizki H, Correlation between the Use of Topical Anti Glaucoma Containing Preservative Benzalkonium Chloride with the Degree of Dry Eye Syndrome in Mohammad Hoesin Hospital Palembang, J Res Med Dent Sci, 2017, 5 (6): 25-29, DOI: 10.24896/jrmds.2017565

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Received: 15/06/2017

Accepted: 10/10/2017

INTRODUCTION

Glaucoma is a group of diseases characterized by optic neuropathy consistent with the presence and functional impairment of neural and connective tissue from optical discs that will

develop into typical visual dysfunction [1, 2]. Based on the sensory health survey of 1993-1996, 1.5% the Indonesian population is blinded by the prevalence of blindness due to glaucoma of 0.20% [3].

Management of glaucoma itself aims to reduce IOP as normal as possible so as to reduce damage from the optic nerve. Therapies include medical, laser, and surgical filtration actions. Most glaucoma therapies, whether open or closed corner, use

topical agents as first-line therapy aimed at increasing the outflow of aqueous fluids or reducing the production of aqueous fluids. Long-term control by using topical therapy has been shown to protect the optic nerve from further damage [4].

Long-term treatment of AGT is associated with side effects that are not only caused by the drug's own active substance, but also preservatives of anti glaucoma drops. Most of AGT's topical agents, containing preservatives that act to inhibit bacterial growth in the drug preparation, make it more durable [4].

Dry Eye Syndrome is a condition with various characterizations characterized by the presence of symptoms of eye discomfort associated with decreased tear production and or tear evaporation abnormalities very quickly. There are several factors that predispose that cause stability in the tear layer, one of which is the use of eye drops containing preservatives and / or systemic drugs for long periods of time. Other factors that can cause tear stability include aging, inflammation, and the use of certain drugs such as oral beta-blockers, oral diuretics and oral anti-depressants.

MATERIALS AND METHODS

Descriptive research using correlation test design was undertaken in June - December 2016. The samples of the study were glaucomic patients who came to Eye Glaucoma Subdivision clinic, the RSMH hospital Palembang. The correlation between the duration of topical anti glaucoma use containing preservative BAK with dry eye syndrome degree was analyzed by Spearman Rho's.

RESULTS

In the period June- December 2016 there are 40 glaucomic patients who meet the criteria of inclusion and exclusion.

Table 1 shows that out of 40 glaucomic patient, there are 19 male (47.5%) and 21 female (52.5%) where the majority of patients are ≥ 45 years old. Patients with glaucoma are in this study the majority of higher education as much as 75% (senior high school and bachelor degree) and the majority work in the room as much as 80%.

Table 1: Characteristics demographics of research subject

Characteristics	Total	Percentage (%)
Age (n,%)		
• < 45 years old	15	37.5
• ≥ 45 years old	25	62.5
Sex (n,%)		
• Male	19	47.5
• Female	21	52.5
Education, (n,%)		
• Elementary School	2	5.0
• Junior High School	8	20.0
• Senior High School	15	37.5
• Bachelor Degree	15	37.5
Occupation, (n,%)		
• Indoor	32	80.0
• Outdoor	8	20.0

Table 2 shows data on the degree of dry eye syndrome in right eye divided into 5 groups, 1 to 4 degrees and normal. There were no subjects with dry eye syndrome 4 degree; 3 degrees obtained 3 subjects (7.5%), 4 subjects who had 2 degrees and 9 subjects (22.5%) who had degree 1. The highest number of frequencies was 24 subjects or 60% of subjects with normal group. On the left eye, the result showed no subjects who had dry eye syndrome of degree 4, degree 3 got 4 subjects (10%), 3 (7.5%) subjects with degree 2 and 12 subjects (30%) who had degree 1. Total the most frequencies are 21 subjects or 52.5% of subjects with normal groups.

Table 2: Degree of Dry Eye Syndrome

Degree of Dry Eye	Right Eye n (%)	Left Eye n (%)
Normal	24 (60.0)	21 (52.5)
Degree 1	9 (22.5)	12 (30.0)
Degree 2	4 (10.0)	3 (7.5)
Degree 3	3 (7.5)	4 (10.0)
Degree 4	0 (0)	0 (0)
Total	40 (100)	40 (100)

The table below shows there was a significant relationship (P = 0.002) between the duration of AGT use containing preservative BAK with Schirmer test. There was a correlation relationship between the duration of AGT use containing preservative BAK with TBUT and there was a no significant correlation relationship between the duration of AGT use containing preservative BAK with the Ferning test.

In this study with statistical analysis using Spearman analysis obtained a meaningful relationship between the duration of use of AGT with the degree of SMK as listed in table 4.26. We

found moderate negative correlation significant ($r = -0.40, p = 0.015$).

Table 3: Correlation between long use of AGT with Schirmer, TBUT and Ferning Test

Correlation	r	p
Long Use of AGT		
<i>Tes Schirmer</i>	-0.50	0.002
<i>TBUT</i>	-0.24	0.005
<i>Tes Ferning</i>	0.15	0.357

Table 4: Correlation between long use of AGT with Degree of Dry Eye

Correlation	r	p
Long Use of AGT		
Degree of Dry Eye	- 0.40	0.015*

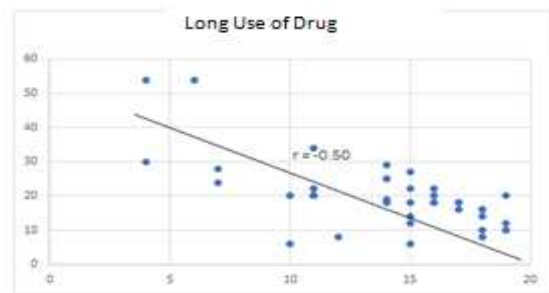
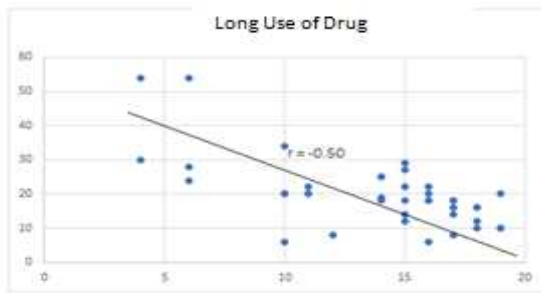


Figure 1: Graph of correlation Schirmer test with old drug usage

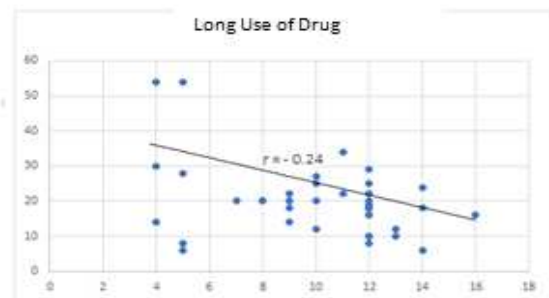
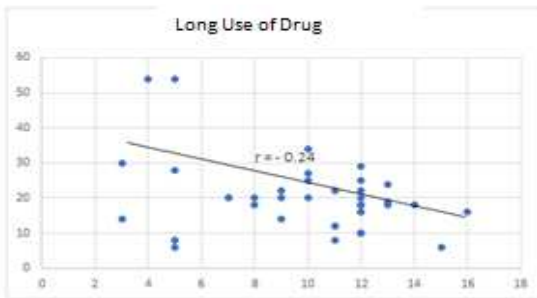


Figure 2: Graph of correlation TBUT test with old drug usage

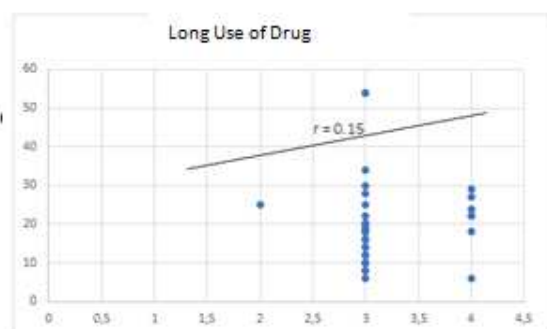
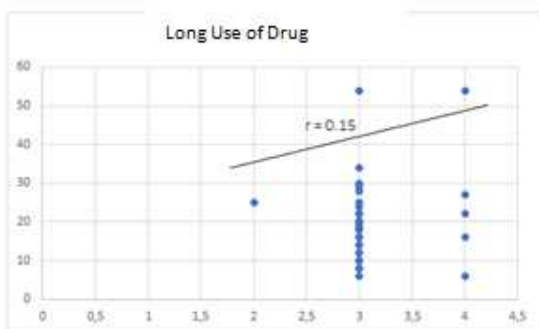


Figure 3: Graph of correlation Ferning test with old drug usage

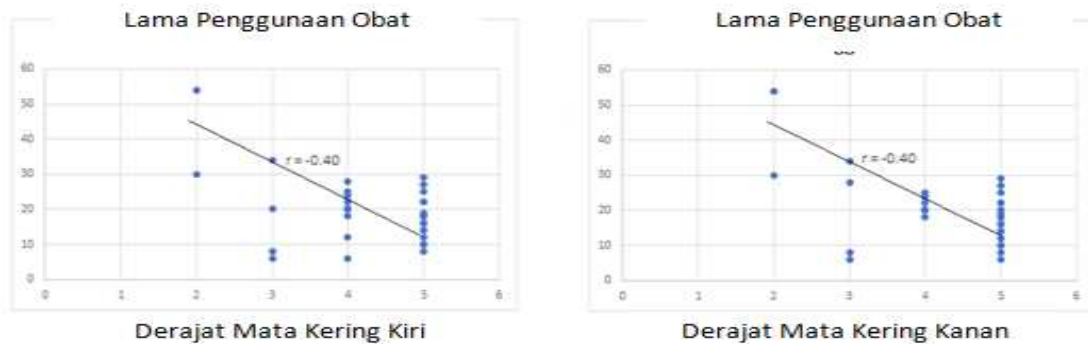


Figure 4: Graph of correlation long use AGT with degree of dry eye

DISCUSSION

In this study, the number of female subjects has a greater percentage of male subjects deripada, which amounted to 52.5%. In accordance with what Sangmon lee et al stated, the risk of dry eye syndrome occurrence in female subjects using AGT with preservatives is greater when compared with subjects not using AGT, and this condition will be exacerbated by the influence of hormonal, age and occupational factors [5].

There are several preservatives that can be used in drip preparations, one of which is benzalkonium chloride. Benzalkonium chloride (BAK), is the most common preservative of eye drops, including anti glaucoma eye drops [6].

Duration of AGT drug use is long, sometimes even until lifetime, causing long duration of exposure between active substance and preservative substances contained in topical antiglaucoma preparations with tissue in the conjunctiva, cornea and sclera causing increased toxicity on the ocular surface [6].

In this research, it is found that the relationship between AGT duration that contains preservative BAK with dry eye syndrome degree has a significant correlation level. This is similar to research from Sangmon Lee *et al* in South Korea in 2013. In addition, there was a change of TBUT value on the subject using AGT with long-term preservative BAK. This change shows the presence of SMK associated with evaporation disorders [7].

The Ferning Test results show that there is a significant correlation relationship between AGT duration that contains preservative BAK and

Ferning Test. This is similar to a study of Norn M, 1944 on dequous-deficient dry eye. In the research, the result of positive Ferning test on AGT patient patients showed that there was a goblet cell disorder in the examined subjects. In a study conducted by Sangmon Lee et al in South Korea in 2013, it was found that a significant outcome of TBUT values on subjects using AGT with BAS [7].

In this study it is explained that the BAK can damage the lipid layer in the tear layer so as to interfere with the evaporation process in the tear layer. This evaporative disturbance led to the emergence of a compensatory mechanism aimed at re-enlarging the tear layer which can ultimately be detected by the presence of a split on the Schirmer test results indicating a disturbance in the aquatic layer of the tear film [7].

CONCLUSION

There was a significant relationship between the duration of AGT use containing preservative BAK with the incidence of the vocational degree in the patient ($r = -0.40$ $p = 0.015$).

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