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Analysis of the Ocular Protection Index Against the Body Fat Level of Dry Eye Patients

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Abstract
Background: Obesity is a common health problem today. Its prevalence is increasing day by day. Obesity is known to have the potential to cause various health problems. The Meibom gland in the eye is a fat producer that is responsible for protecting tears from evaporating easily. When this gland is dysfunctional, can lead to damage to the ocular surface. To detect damage to the surface of the eyeball, we can use the Ocular Protection Index parameter.
Objective: The purpose of this study is to determine the Ocular Protection Index (OPI) at various levels of body mass index in patients with dry eye disease, by examining the Tear Film Break Up Time (TFBUT) and measuring the Inter Blink Interval (IBI). **Methods:** The research method was observational analysis with a case-control approach in male and female employees, aged 30 years and above, and suffering from dry eyes. All bivariate data will be analyzed using the Chi-square test if it meets the requirements. If not, the Fisher Test will be used. Results will be considered significant at p <0.05 with a 95% confidence interval. **Results:** A total of 129 subjek berpartisipasi dalam penelitian ini, consisting of 41 men (31,78%) and 88 women (69,22%). A total of 80 respondents (62,02%) have an excess body mass index, and the rest are normal. **Conclussion:** There was no significant relationship between body mass index and ocular protection index in dry eye patients. Meanwhile, a meaningful relationship was obtained between the degree of dry eye and the ocular protection index of men with dry eye.

Keywords: Obesitas, Dry eye disease, Ocular Protection Index, Tear Film Break Up Time, Inter Blink Interval.

Introduction
Obesity is a growing health problem worldwide. *The Body Mass Index* (BMI), which is calculated by dividing a person's weight in kilograms by their height in meters squared, is the most commonly used index to assess adiposity, the neutral amount of lipids stored in adipose tissue in total body mass. The average prevalence of obesity increased from 6.4% to 12.0% between 1980 and 2008, and that overweight increased from 24.6% to 34.4%. In the same time period in Australia, the average prevalence of obesity standardised by age increased from 7.2% to 27.1% for women and from 8.9% to 26.4% for men, and overweight increased from 30.0% to 59.2% for women and from 42.8% to 68.1% for men. Obesity is a risk factor for many health diseases, including hypertension, diabetes mellitus (DM), dyslipidemia, cardiovascular disease, liver disease, osteoarthritis and atherosclerosis.[1] Berdasarkan penelitian Herningtyas, prevalensi obesitas di Indonesia adalah 43,21%.[2]
Dry Eye Disease (DED) is a common condition encountered in eye clinics. This disease primarily affects older individuals, although there is a growing number of younger patients, including children, suffering from DED. The prevalence of DED varies across different countries; in developed countries like the United States, the prevalence in 2013 was approximately 6.8%, or about 16.4 million people from the total population. This prevalence increases with age (18–34 years: 2.7%; ≥ 75 years: 18.6%) and is higher in women (8.8%; 11.1 million) compared to men (4.5%; 5.3 million).[3] In Japan, the prevalence of DED is reported to be 21.6% in women and 12.5% in men.[4]
Dry Eye Disease (DED) is characterized by abnormalities in tear production and the ocular

surface, caused by various factors, including instability of the tear film (TF), increased osmolarity of the TF, and inflammation of the ocular surface. This condition leads to discomfort, a dry sensation in the eyes, a gritty feeling, redness, vision disturbances, and has the potential to damage the ocular surface, thereby reducing the quality of life for those affected.[5] The tear film consists of three layers: a lipid (fat) layer on the surface, an aqueous layer in the middle, and a mucin layer at the deepest level. These three layers work together to maintain eye health by keeping the ocular surface moist, protecting the eyes from irritation and environmental factors. The surface of the eyeball must remain moist to preserve eye health, visual clarity, and comfort around the eyes. Thus, tears are continuously produced to ensure the availability of nutrients for the avascular structures of the cornea and to maintain eye health.[5]

The Meibomian glands, which produce lipids that prevent excessive evaporation of the tear film, play a crucial role in cases of DED. Dysfunction of the Meibomian glands (Meibomian Gland Dysfunction, MGD) is a common chronic cause of eye disease, as these glands primarily contribute to the lipid layer of the tear film. Therefore, MGD affects the lipid layer's integrity, which is suspected to influence the onset of DED. What is the relationship between DED and individuals with excess body fat? The Body Mass Index (BMI) calculation, which determines adiposity, and the amount of neutral lipids stored in adipose tissue may be related to DED.

The Ocular Protection Index (OPI) is a parameter used to assess the risk of ocular surface damage due to exposure. This parameter is noted for its accuracy in evaluating the effectiveness of DED treatments and can provide a more functional interpretation of the Tear Film Break Up Time (TFBUT) results. The OPI value is calculated by dividing TFBUT by the duration of the inter-blink interval (IBI). A value greater than one indicates a healthy ocular surface, while an OPI value less than one suggests an unhealthy ocular surface.[6] In this study, we will assess the OPI profile at various levels of body fat in patients with DED by conducting TFBUT examinations and measuring IBI.

Methods

Population and Subjects

The method used is an observational analytic study with a cross-sectional approach. The inclusion criteria are male and female employees aged 30 years and above who suffer from dry eye disease. Subjects with TFBUT > 10 mm, wearing contact lenses, having anatomical abnormalities in their eyes, and those experiencing eye infections were excluded from the study, resulting in a total of 129 research subjects. The study was conducted by the same examiner over 2 days at the Faculty of Medicine, campus of Universitas Trisakti. Subjects underwent measurements of body weight, height, and blink rate. Recordings and examinations were performed only on the right eye.

Body Mass Index (BMI)

Body Mass Index (BMI) is a statistical measure used to estimate the total body fat of an individual based on their height and weight. Height is measured using Microtoise on a flat vertical plane by placing it on the floor then pulling the end of the meter up to 2 meters vertically until it shows a zero number. Have the subject stand upright against a barefoot vertical plane just below the Microtoise, looking straight ahead, arms at sides of the body with palms facing the thighs, knees upright, and in a relaxed state. Lower the Microtoise until it touches the hair, fits snugly against the head, not too much pressure. View and record measurement results in centimeters (cm). Weight measurement using digital scales that have been calibrated using standard weights. Place the scale on a flat floor. Have respondents climb onto the scale by removing footwear, accessories, and other items that have significant weight. Make sure the respondent is not moving and in a relaxed state. View and record measurement results in kilograms (kg).[7]

BMI is calculated by dividing a person's weight in kilograms by the square of their height in meters. The resulting value is then used to categorize individuals into different weight categories, such as underweight, normal weight, overweight, and obese. The BMI formula is weight (kg) / height² (m^2). The interpretation of body mass index (BMI) measurement results according to the Indonesian Ministry of Health Regulation No. 41 of 2014 is as follows: Normal (BMI is within the range of 18.5 to 25 kg/m^2), Overweight (BMI is greater than 25.0 to 27.0 kg/m^2) and Obese (BMI is greater than 27.0 kg/m^2).[7]

Tear film break-up time (TBUT)

Tear film break-up time (TBUT) is a diagnostic test used to assess the stability of the tear film on the surface of the eye. It is a crucial indicator of dry eye syndrome and other ocular surface disorders. During the test, the patient is asked to refrain from blinking while a fluorescein dye is instilled into the eye. The tear film is observed under a slit lamp microscope equipped with cobalt blue light. The clinician then measures the time it takes for the first dry spot or disruption in the tear film to appear. A normal TBUT is typically greater than 10 seconds. If the tear film breaks up in less than 10 seconds, it suggests instability of the tear film and may indicate dry eye disease or other ocular surface disorders.[8]

Inter Blink Interval (IBI)

The blinking process typically occurs every 5-6 seconds or 12 times per minute. However, it will lengthen during certain activities that require concentration, such as reading and working in front of a computer. A decrease in the blinking reflex means that the interval between blinks (IBI) becomes longer. This will increase evaporation. Therefore, if the IBI lengthens, it means that eye protection decreases.[9]

The tear layer (LAM) is 3 layers of tear components consisting of a lipid layer (fat) on the surface, the aquious layer which is the second layer and the mucin layer which is the deepest layer. These three layers of tears are able to maintain eye health by maintaining ocular surface moisture, protecting the eyes from irritation and the environment. The surface of the eyeball must always be wet, to maintain eye health, clarity of vision and comfort around the eyes. Thus, tears will continue to be produced to ensure the availability of nutrients for the avascular structure of the cornea and ensure eye health.[10]

Before taking the inter blink interval (IBI) measurement, a room setting is carried out, where the measurement room uses an air conditioner but not too cold and the wind from the device does not hit the respondent's eyes directly, to avoid blinking too often. IBI measurements are obtained using a stopwatch and a timer. The researcher conducted a

brief interview with the subjects, while there was an assistant who measured the respondents' blinks from one blink to the next. Measurements were taken several times in a span of 1 minute without being known by the object. Then the result is averaged and recorded in seconds, so if the IBI is 4 seconds, it means that the time between the blinks of the person is 4 seconds. The normal IBI value is 2-10 seconds. An elongated IBI value indicates dryness in the eyes

Ocular Protection Index (OPI)

The Ocular Protection Index (OPI) is defined as the ratio between the time spent keeping the eyes open to the minimum time required to maintain tear stability. Thus, the OPI formula is the TFBUT value divided by the IBI value. Normal OPI values are 1-3, where OPI values above 3 indicate good eye protection and OPI values below 1 indicate poor eye protection. This system has gone through a series of validation and verification so that according to researchers, this system is feasible to use.[11]

Statistical methods

All statistical analyses will be conducted using Microsoft Office Excel 2010 and GraphPad Prism Version 6.00 (GraphPad Software Inc.). The results will be presented as mean ± SEM if the data distribution is normal, and as median if the data distribution is not normal. All bivariate data will be analyzed using the Chi-square test if the conditions are met. If not, the Fisher test will be used. The results will be considered significant at $p < 0.05$ with a 95% confidence interval.

Ethics

This study has passed an ethical review conducted by the Faculty of Medicine, Universitas Trisakti, with the ethical clearance number Each subject signed an informed consent prior to the study.

Results

After complying with the inclusion and exclusion criteria, 129 employees who had dry eye disease participated in this study. Table 1 shows data on subject characteristics, 88 subjects were women (68.22%), 65.12% were aged 30-45 years, generally had an excess body mass index (62.02%). All subjects in this study had dry eye disease after undergoing a Tear Film Break Up Time (TFBUT) examination. If the results of the TFBUT examination were ≤ 10 seconds, it means that he or she have dry eye disease. Generally, humans blink every 5-6 seconds or 12x per minute. If he or she blinks more often, it means the interval between blinks is shorter, and vice versa, if the interval between blinks is longer, it means the person rarely blinks. If the inter-blink interval is prolonged, it will increase the risk of evaporation, thereby disrupting ocular protection. The Ocular Protection Index is a parameter to determine eye protection against exposure, obtained by dividing the TFBUT value by the Inter Blink Interval (IBI) value. If the OPI value is <1, it means that ocular protection is considered poor.[9]

Table 1: Characteristics of research subjects.

Characteristic		n = 129	%
Gender			
	Male	41	31,78
	Female	88	68,22
Age			
	30 - 45 years	84	65,12
	More than 45 years	45	34,88
Body Mass Index (BMI)			
	Normal	49	37,98
	Excess	80	62,02
Degree of Dry Eye			
	Mild	112	86,82
	Severe	17	13,18
Ocular Protection Index (OPI)			
	More than 1	64	49,61
	Less than 1	65	50,39

Body mass index (BMI) indicates an individual's health status. According to the definition of adult overweight and obesity by the Centers for Disease Control and Prevention, a BMI of less than 18.5 implies being underweight, a BMI ranging from 18.5 to < 25 indicates a healthy weight, a BMI ranging from 25.0 to < 30 indicates overweight and a BMI ≥ 30.0 indicates obesity.[12] According to the Indonesian Ministry of Health, a BMI of 18.5 – 25.0 is normal; fat if > 25.0 – 27.0 and obese if > 27.0.[7]

Table 2: Mean ± standard deviation) of age, body mass index (BMI), tear film breaks up time (TFBUT) and inter blink interval (IBI) based on gender.

Characteristic		Male (n = 41)		Female (n = 88)	
		n(mean ± SD)	%	n(mean ± SD)	%
Age					
	30 - 45 years	18 (40,83 ± 4,66)	43,9	66 (42,12 ± 4,29)	75
	More than 45 years	23 (54,57 ± 4,57)	56,1	22 (47,09 ± 1,31)	25
Body Mass Index					

	Normal	22 (23,86 ± 2,55)	53,7	27 (20,52 ± 3,77)	30,7
	Excess	19 (27,37 ± 4,69)	46,3	61 (28,71 ± 3,08)	69,3
Tear Film Break Up Time (TFBUT)					
	Less than or equal to 5 seconds	34 (7,35 ± 1,29)	82,9	78 (7,81 ± 0,95)	88,6
	More than 5 to 10 seconds	7 (4,14 ± 0,94)	17,1	10 (5,8 ± 1,83)	11,4
Inter Blink Interval (IBI)					
	Less than or equal to 10	32 (5,31 ± 1,83)	78	54 (6,54 ± 1,71)	61,4
	More than 10	9 (10,67 ± 1,25)	21	34 (10,82 ± 1,72)	38,6

Table 3: Distribution of risk factors for OPI in male and female.

		Male (n = 41)			Female (n = 88)			
		OPI ≥ 1	OPI < 1	p	OPI ≥ 1	OPI < 1	p	
Age								
	30 - 45 years	14	10	0,062	28	38	0,407	
	More than 45 years	5	12		11	11		
Body Mass Index								
	Normal	12	10	0,94	13	14	0,754	
	Excess	12	7		27	34		
Degree of Dry Eye								
	Mild	24	8	0,001	39	41	0,086	
	Severe	1	8		2	8		

There is no significant correlation between each factor and the ocular protection index for both men and women, except that the degree of dry eye has $p<0.05$.

Discussion

The tear layer is a dynamic structure because it can react quickly to protect the ocular structure. Tears are liquids that contain water, enzymes, proteins, immunoglobulins, fats, metabolites, epithelial debris and polymorphocklear cells. Tear production will decrease significantly in the 6th decade (50-59 years). The tear layer consists of 3 layers (trilaminar). The innermost layer is the mucin layer produced by goblet cells and conjunctival epithelium. This layer functions in spreading and attaching tears on the ocular surface and preventing foreign objects and pathogenic cells from attaching to the ocular surface.[13]

The second layer is the aqueous layer produced by the tear glands which functions to carry oxygen and essential nutrients, aid the movement of cells on the ocular surface and remove debris, toxins and foreign objects from the ocular surface. This layer contains many growth factors such as EGF (Epidermal Growth Factor), TGF (Transforming Growth Factor), HGF (Human Growth Factor). The outermost layer is the lipid layer produced by the meibomian glands, serving to prevent evaporation and improve the stability of the LAM. The stability of the tears depends largely on the correctness of the composition between the three. The advantages or disadvantages of these three components will cause instability in the LAM. The mucin layer will bind directly to the conjunctival glycocalyx which will produce a hydrophilic layer under the aquifer layer.[13,14]

Dry eye syndrome (DES) is a prevalent ocular condition characterized by a decrease in tear production or an increase in tear evaporation, leading to inflammation and damage to the ocular surface. The most recent definition according to the International *Dry Eye WorkShop* (DEWS) Definition and Classification Sub-committee in 2007 is tear and ocular surface abnormalities, which are multifactorial and cause discomfort, visual impairment and instability of the tear layer (LAM) so that it has the potential to damage the ocular surface.[15] It is associated with symptoms such as dryness, burning, and discomfort, significantly impacting quality of life. Recent studies have begun to explore various systemic factors that may contribute to t he development of DES, including Body Mass Index (BMI).

Body Mass Index (BMI) is a widely used measure to classify individuals based on their body weight relative to their height. Obesity has become a growing global health problem, with serious impacts on quality of life and health costs. Obesity, in particular, is associated with various systemic health issues, including metabolic syndrome, diabetes, and cardiovascular diseases. The increasing prevalence of obesity worldwide has prompted researchers to investigate its potential effects on ocular health, specifically dry eye syndrome. Obesity should be considered a significant risk factor for eye disease. Therefore, a multidisciplinary approach in the treatment of obesity, which also considers eye health, such as cataracts, glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy.[16] And in line with our study, there are other studies that have stated that no significant association was found between obesity and DES risk, suggesting that obesity does not increase the risk of dry eye syndrome.[17]

In our study, there was no significant relationship between body mass index and ocular protection index of male and female dry eye sufferers. Only dry eye degrees had a meaningful relationship with the ocular protection index, but even that was only in men. Our study also did not measure meibomian gland dysfunction so it was not possible to know how it relates to the ocular protection index. But almost the same results were obtained from the Mussi study[18] where there was no specific meaningful relationship between body mass index and Meibom's gland dysfunction.

In a study in Japan, the results showed that the prevalence of DED was 23.4%, and there was an inverse relationship between BMI and the prevalence of DED, where an increase in BMI correlated with a gradual decrease in the prevalence of DED, the higher the BMI, the lower the likelihood of developing DED.[19]

Bosello's research on obesity, body fat distribution and eye

diseases, stated that there is strong evidence of a link between obesity and several eye diseases including dry eyes. It is said that the examination of waist circumference (abdomen) and waist/hip ratio has a stronger positive relationship than the examination of body mass index[16]

Several epidemiological studies have reported a correlation between higher BMI and the incidence of dry eye syndrome. For instance, a cross-sectional study found that individuals with obesity were more likely to report symptoms of dry eye compared to those with normal weight. The underlying reasons for this association may be multifactorial, involving both biological and lifestyle factors. In a study by Saud et al, it was stated that the quality of tears is also determined by high BMI levels, where the quality of tears in people with a high BMI is proven to be lower compared to people with normal BMI. But the number of tears was the same between people with a high BMI and people with a normal BMI.[20]

The research of Yingsi Li et al, which intends to evaluate whether there is an association between dyslipidemia and the incidence of dry eye, turns out that there is a meaningful relationship between total cholesterol levels and dry eye disease, especially in women. The same is the case with triglyceride, LDL and HDL cholesterol levels.[21,22]

The Ocular Protection Index is derived from the ratio of tear film break-up time (TBUT) to the frequency of blink rate. It offers an integrated measure of the stability and protective capacity of the tear film. A lower OPI value indicates a reduced protective function of the tear film, which correlates with the severity of dry eye symptoms and ocular surface damage. A low OPI is often observed in patients with severe dry eye, where the tear film is less stable and rapidly breaks down between blinks. This instability can lead to increased ocular surface exposure and exacerbate symptoms of dryness, irritation, and redness. Conversely, a higher OPI suggests a more stable tear film that provides better protection to the ocular surface.[23]

In our study, there was a meaningful relationship between the degree of dry eye in men and the ocular protection index. This is not in accordance with the research conducted by Peck T[24] which stated that post-menopausal women have a much lower OPI value than pre-menopausal or perimenopausal women. This will lead to an increased likelihood of eye exposure and will worsen the condition of dry eyes.

Conclussion

There was no significant relationship between body mass index and ocular protection index in dry eye patients. Meanwhile, a meaningful relationship was obtained between the degree of dry eye and the ocular protection index of men with dry eye.

Conflict of Interest

The authors declare no competing interests

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Author Contribution

The research idea was from Noviani Prasetyaningsih, but Dian Mediana, Noviani Prasetyaningsih, Anggraeni Adiwardhani, Riani Witjaksana also wrote the manuscript. Meanwhile, Monica Dwi Hartanti, Jihan Samira Thabit, Raden Mohammad Ilham Effendi also assisted in data collection

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