A COMPARATIVE STUDY BETWEEN PRESERVATIVE ARTIFICIAL TEARS AND PRESERVATIVE-FREE ARTIFICIAL TEARS ON TEAR FILM STABILITY AMONG DRY EYE PATIENTS

BY

Fortune Obuchi BENJAMIN

LSC1605592

DEPARTMENT OF OPTOMETRY

FACULTY OF LIFE SCIENCES

UNIVERSITY OF BENIN

SEPTEMBER, 2023.

A COMPARATIVE STUDY BETWEEN PRESERVATIVE ARTIFICIAL TEARS AND PRESERVATIVE-FREE ARTIFICIAL TEARS ON TEAR FILM STABILITY AMONG DRY EYE PATIENTS

BY

Fortune Obuchi BENJAMIN

LSC1605592

A PROJECT SUBMITTED TO THE DEPARTMENT OF OPTOMETRY, FACULTY OF LIFE SCIENCES, UNIVERSITY OF BENIN, BENIN CITY, IN PARTIAL FUFILMENT OF THE REQUIREMENTS FOR THE AWARD DOCTOR OF OPTOMETRY (O.D) DEGREE IN OPTOMETRY.

SEPTEMBER, 2023.

CERTIFICATION

DEDICATION

This project is dedicated to you, the silent warriors battling the discomfort and daily challenges posed by Dry Eye Syndrome. Your resilience in the face of persistent discomfort that accompanies dry eye is a proof of your strength. May this work contribute to a better understanding of your condition and pave the way for improved treatment and management plans. With heartfelt respect and empathy, it is an honor to dedicate this project to your unwavering spirit.

ACKNOWLEDGEMENTS

To a more than amazing God, thank you for walking me through every second of my university years. I am grateful to my supervisor Professor E. Iyamu for his excellent guidance and support throughout this project work, also to the HOD, Prof (Mrs) F. K. Idu and the entire staff of the Department of Optometry for the impact and knowledge throughout my academic journey.

I am grateful to my priceless parents Mr. Benjamin Onyekachukwu Ebirika and Mrs. Givings Onyinyechi Ebirika, my precious siblings Ugochukwu, Chukwuakadibia and Chukwudum for being my constant reminder of God's unconditional love on earth.

I must say a big thank you to my grandfather HRH Eze Councillor Nwanadi Olokotor (JP) of blessed memory, who was one of my earliest inspirations to go into the eyecare profession.

I am forever indebted to my beautiful Adventist Students' Fellowship (ASF) family, words cannot express how much gratitude I have in my heart. I am grateful to Dr. G. K. Brobbey for his constant help and guidance in optometry and beyond.

To my friends Oghenerukevwe, Tamarakuro , Chinonye, Vovwero, Frederick, Gregory, Clinton, and Presley, I could not have asked for better people to walk this journey with.

Lastly, I would like to acknowledge myself, for putting in the work of completing my undergraduate education, researching, and carrying out this topic, for throughout the heavens and the earth, I alone am the honored one.

ABSTRACT

This comparative study investigated the effects of preservative and preservative-free artificial tears on tear stability among dry eye patients. The participants completed the OSDI questionnaire to determine their subjective observations. A randomized controlled trial was used to group the participants. Tear film stability was assessed using fluorescein invasive tear break-up time (FTBUT), Schirmer's test was carried out to determine the tear flow rate, the results were compared between the two groups. The results showed that the mean values for TBUT for Hypromellose were 6.25 ± 0.33 before and 6.75 ± 0.31seconds after, for Refresh was 6.40 ± 0.40 before and 7.55 ± 0.42 seconds after. Also, the mean values for TFR for Hypromellose were 8.36 ± 0.50 before and 8.61 ± 0.50 seconds after, for refresh was 9.69 ± 0.54 before and 10.05 ± 0.55 after seconds. The results obtained were analyzed using the SSPS 22.0. T-test and one- way ANOVA were used to compare the mean FTBUT and TFR values between both groups, the p values were 0.64 and 0.68 respectively. There was no statistically significant difference in the tear film stability and tear flow rate between both groups after four weeks ($p > 0.05$). In conclusion, the results of this study showed that there was no notable difference between preservative artificial tears and preservative-free artificial tears on tear film stability and tear flow rate. It is recommended that clinicians can confidently recommend both preservative and preservative-free artificial tears as effective management options for dry eye.

KEYWORDS: Dry eye syndrome, Artificial tears, Preservative, TBUT.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND INFORMATION

Dry eye disease is a prevalent ocular disease which affects millions of people worldwide, it is characterized by a disruption in the tear film homeostasis and subsequent discomfort, visual disturbances, and potential damage to the ocular surface, it presents with symptoms such burning, foreign body sensation, blurred vision, and redness, which causes discomfort and reduces working efficiency and quality of life. These symptoms may cause complications, such as corneal damage and visual impairment. Complications including corneal injury and vision loss may result from these symptoms. The instability of tear film may be due to qualitative or quantitative abnormalities of any of these components. Concentrations of stabilizing substances (such as mucins), the health of the surface epithelia and lipid layer, the presence of proteolytic enzymes in tears, and reflex blinking processes are other elements that can affect tear film stability.

Based on weighted estimates, 6.8% of the US adult population was diagnosed with dry eye disease (~16.4 million people). Prevalence increases with age (18 – 34years 2.7%: > 75years: 18.6%) and was higher among women (8.8%; ~11.1 million) than men (4.5%; ~ 5.3 million).

Dry eye is one of the most common ocular diseases, estimated to affect 14% to 33% of adults and increasing with age. Moss *et al.,* (2000). The integrity and stability of the air-tear film interface, which is the primary refractive surface of the eye, are essential for preserving clear vision and ocular comfort. Artificial tears, which are frequently chosen as the main course of treatment, are crucial for stabilizing the tear film and symptom relief in dry eye patients. The use

of gels, topical or oral secretagogues, blood derivatives, anti-inflammatory therapy, and punctal occlusion are a few other techniques.

However, there are worries regarding the potential effects of preservatives on the health of the ocular surface because they are included in some artificial tears. Preservatives, added to artificial tears to extend their shelf lives and avoid bacterial contamination have been demonstrated to have negative effects on the ocular surface. They have been associated with increased ocular toxicity, destruction of corneal epithelial cells and an inflammatory response, which limit the therapeutic potentials of artificial tears. In contrast, to reduce the danger of issues with the ocular surface, preservative-free artificial tears are produced without these ingredients. The most common preservatives in ocular solutions are benzalkonium chloride (BAK), chlorobutanol, sodium perborate, thiomersal, disodium edetate, and oxychloro complex (SOC). Preservatives can cause toxic epithelial effects and hypersensitivity reactions that range from mild irritation to severe corneal and conjunctival scarring (Noecker, 2001). Even at very low dosages, benzalkonium is known to harm the corneal epithelium and produce cell membrane lysis at the ocular surface. If used as a treatment, its frequency of usage should be restricted to no more than four times per day. (Moshirfar, 2014). Preservative-free eye drops are recommended for patients with severe dry eyes, those who are taking numerous preserved medications, and those who need higher dosages of lubricants, but they have a shorter shelf life, which may influence their effectiveness.

Despite the fact that artificial tears play a crucial therapeutic role in the management of dry eye syndrome, little research has been done on the effectiveness and safety of preservative-versus preservative-free artificial tears. Therefore, careful comparison research is required to assess the

variations in these formulations' effects on the stability of the tear film and their possible effects on the management of dry eyes.

The primary objective of this study is to examine and contrast the effects of artificial tears with preservatives (Refresh) and preservative-free artificial tears (Hypromellose) on the stability of the tear film in dry eye patients. Through the evaluation of a number of clinical measures and subjective results, this study aims to offer relevant information on the relative advantages and disadvantages of these two commonly used artificial tear formulations. This study will adopt a prospective, randomized, clinical single-center design to ensure objective and reliable results. A sample of dry eye patients will be selected, and they will be randomly assigned to receive either preservative or preservative-free artificial tears for a period of 4 weeks. Through objective tests such as tear break-up time (TBUT), ocular surface staining and subjective symptom questionnaires, tear film stability will be evaluated.

The results of this comparative study are anticipated to advance our knowledge of the effects of preservatives on tear film stability and ocular surface health. In addition, they have the potential to guide the clinician and patient in choosing the most appropriate artificial tear formulation based on unique needs and sensitivities.

This project seeks to add to the body of knowledge on dry eye management by providing evidence-based insights into the relative efficacy and safety of preservative artificial tears and preservative-free artificial tears. This research can help to optimize treatment plans and improve the overall life of dry eye patients by shedding more light on the differential impacts if these formulations on tear film stability.

1.1.1 THE TEARS

Tears are clear saline fluid that are continually secreted in small quantities by tear glands, which are located on the outer side of each eye, slightly above the eye and underneath the eyelid It helps to lubricate and clean the eyes by spreading evenly over the front of the eye during blinking. Tears are composed of water, salts, antibodies, and lysozymes (antibacterial enzymes), with the lysozymes being the most important component of the tears.

It is good to note that composition of tears varies among different tear types. Three basic types of tears exist (Masoudi, 2022).

They are:

i. the Basal tears,
ii. the Reflex tears
iii. the Emotional tears

1.1.2 LACRIMAL GLAND

The lacrimal gland is situated in the superolateral region of the orbit. Small ducts that open into the upper fornix carry lacrimal fluid to the ocular surface. The release of tear secretion is controlled by the parasympathetic nervous system. Issues with the gland itself, duct obstruction (induced by scarring), and neurological problems can all cause decreased production of aqueous tears.

1.1.3 NASOLACRIMAL SYSTEM

The nasolacrimal system drains the tear film from the surface of the eye. Fluid is gathered through the punctae and carried along the canaliculi into the lacrimal sac. The fluid drains into

the nasal cavity after leaving the sac and passing through the nasolacrimal duct. Any blockage along the system increases the risk of infection and epiphora (watery eyes).

1.1.4 THE TEAR FILM

The tear film is made up of three layers and the combination of these layers of tears are termed tear film.

The tear film is a distinct, thin fluid coating that covers the ocular surface. It is the outermost fluid of the eye that interacts differently with the environment, and it is approximately 3µm thick and 3µl in volume. This film is transparent and has an aqueous/mucin phase, decreasing in mucin concentration towards a distinct superficial lipid layer Willcox *et al.,* (2017).

The 3 layers of tears include:

i. the outermost lipid layer.
ii. the middle aqueous layer.
iii. the innermost mucin layer

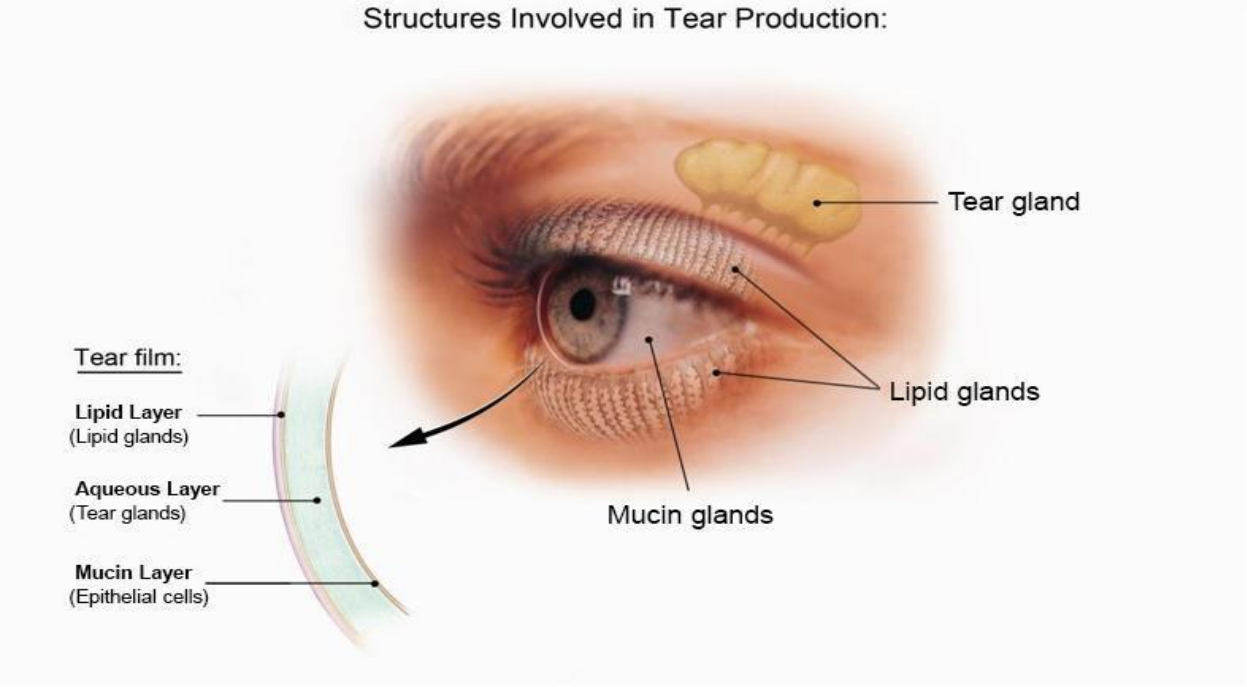

Fig 1: Diagram showing structures involved in tear production.

The Lipid Layer

The lipid layer is the outermost layer of the tear film and being secreted by Meibomian glands, located within tarsal plates of upper and lower eyelids with some small contribution by Moll (modified apocrinic, sudoriferous) and Zeiss (modified subeceous) glands, located within superior and lower eyelids (connected with hair follicles) and possibly epithelial cells (Rolando *et al.,* 2001, Stahl *et al.,* 2012, Holland *et al.,* 2013 and Kopacz *et al.,* 2020).

The most significant role of the lipid layer is in retarding evaporation of tears from the ocular surface thereby enhancing the stability of the tears. Moreover, the lipid layer provides smooth refracting surface, limits contamination of ocular surface from particles (dust) and microorganisms, prevents tear contamination by skin lipids, limits aqueous layer surface tension and counteracts tears overflowing onto the skin (Rolando *et al.,* 2001, Stahl *et al.,* 2012, Dartt *et al.,* 2013, Holland *et al.,* 2013 and Kopacz *et al.,* 2020).

The Aqueous layer

The lacrimal gland and accessory glands (Krause and Wolfring glands, located in the conjunctiva of the superior eyelid and superior conjunctival fornix) supply the tear film with a number of components, most notably the aqueous, which is produced by the accessory gland in a non-reflex manner along with the mucin/aqueous gel. While the main lacrimal gland is responsible for aqueous tears production secondary to deleterious stimulation and plays important, though not entirely clear role in non-reflecting tearing (dry eye syndrome is noted in patients with damaged main lacrimal gland) (Conrady *et al.,* 2016 and Kopacz *et al.,* 2020).

The major functions of aqueous portion of the tear film include the ocular surface lubrication, washing away foreign bodies or contaminations and nourishing avascular cornea (oxygen, inorganic salts, proteins, glucose) Kopacz *et al.,* (2020).

Therefore, dysfunction of these glands results in the loss of aqueous and other products required in ocular surface maintenance and health resulting in dry eye and the potential for significant surface pathology Conrady *et al.,* (2016).

The Mucous layer

The cornea, which is translucent, the conjunctiva, and the inner surfaces of the eyelids are all covered by a wet-surfaced epithelium that is on the eye. Large, highly glycosylated, and hydrophilic glycoproteins known as mucins make it easier for tear film to stick to the ocular surface, lubricate it, and provide a pathogen barrier on this wet surface. This mucous layer of the tear film is produced by both corneal and conjunctival epithelium and the lacrimal gland and conjunctival goblet cells Kopacz *et al.,* (2020)

1.1.5 TEAR FILM STABILITY

Sweeney *et al.,* (2013) reviewed the current knowledge on tear film stability. Their review highlighted a range of both clinical and laboratory techniques that have been used to examine the stability of the tear film.

Tear film stability is probably crucial in a variety of circumstances, such as dry eyes and while wearing contacts. Slit lamp biomicroscopy can be used to measure the time it takes for a tear film to break up after fluorescein injection, although the repeatability of this measurement is low. Non-invasive procedures that frequently entail the observation of a lighted anterior tear surface using a Keratometer, the observation of a grid pattern reflected from the anterior tear surface, or corneal topography systems have all been used in an effort to increase repeatability. Dartt and Willcox (2013), in their work noted that the evaporation rate of the tear film has often been a central point of many studies into tear film stability. Evaporation rate is controlled by the tear film lipid layer. The formation of liquid crystals of tear film lipids oriented at right angles to the surface may brace each other and resist collapse of the lipid layer and hence prevent evaporation.

While TBUT is determined by timing the appearance of dry spots on fluorescein-treated eyes, NIBUT is calculated by timing the distortion or diffusion of keratometric marks on the corneal surface.

In this study, an invasive tear break-up time (i-TBUT) technique was used.

1.1.6 TEAR FLOW RATE

The tear flow rate is said to be the rate at which tear film is being replenished on the ocular surface.

Irritation to the eye and psychologic stimuli can cause rapid fluctuations in the normal tear flow Mishima *et al.,* (1966).

This tear flow rate could clinically be assessed using Schirmer's test or even with a more extensive equipment called fluorophotometer. The use of Schirmer's strip test is done by inserting the strip in the cul-de-sac of the lower conjunctiva fornix. It does not provide an estimation of normal tear flow, since the insertion of filter paper into the cul-de-sac stimulates reflex lacrimation Mishima *et al.,* (1966).

Mishima *et al.,* (1966) noted that another method at which the flow rate could be estimated is by observing the disappearance of dyes instilled in the cul-de-sac. They however pointed out that this method was not capable of showing dynamic changes in the rate of tear flow since the fluorescein concentration was not determined in situ. Also, the quantity of fluorescein solution used was so large that the method may have produced irritation. By following the concentration decay of fluorescein in the tears, the turnover rate of the indicator could be evaluated.

Fluorophotometry is a modern and more accurate method of assessing the tear flow rate. Here, a known quantity of dye is applied to the cul-de-sac of the ocular system, then the rate at which the dye is washed off from the tear film will be assessed using the fluorophotometer.

During this project, Schirmer's strip method of assessing the tear flow rate was used because of non-availability of the fluorophotometer.

1.1.7 DRY EYE DISEASE

The international dry eye workshop (2007) defined dry eye as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film

instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

Instability of the tear film, which can be brought on by either insufficient tear production or poor tear film quality and leads to increased tear evaporation, is one of the hallmarks of dry eye illness. Normal vision depends on the tear film, which works in tandem with the cornea to concentrate light onto the retina. As such, it must be kept in a biologically full state.

Dry eye therefore can be mainly divided into two groups namely:

1. aqueous production deficient dry eye diseases
2. evaporative dry eye disease

Causes of dry eye syndrome

1. Insufficient tears Older individuals, postmenopausal women, and people with autoimmune illnesses including Sjogren's syndrome and rheumatoid arthritis are more likely to experience dry eye due to inadequate tear production by the tear glands. Changes in the tear fluid's composition and unstable tear films brought on by lacrimal functional unit dysfunction result in ocular surface irritation. Because the anti-inflammatory component of the eye is deficient and irritation of the eye is not under control, the eye does not produce enough tears.
2. In cases of evaporative dry eyes, decreased blinking, abnormalities on the lid surface, and increased tear evaporation cause the eyes to become dry. The tear film can be impacted

by environmental variables such central heating, arid weather, air pollution, wind, chemical burns, contact lens wear, or decreased blinking from driving, watching TV, and computer use, which can lead to corneal ulcers, infections, and blindness.

3. Evaporative loss of tear fluid and dry eye is usually associated with inadequate lipid layer. The lipid layer stabilizes and retards evaporation of the underlying aqueous layer. Evaporative dry eyes are primarily caused by rosacea, blepharitis, and meibomian gland dysfunction (MGD)..

Prevalence of Dry Eye

The prevalence of dry eye syndrome increases with age. DES is a common eye disorder that affects a sizable percentage of the population, especially those over 50 years of age, middle aged and older adults are the mostly commonly affected group because of high prevalence of contact lens usage, systemic drug effects, autoimmune diseases, and refractive surgeries in this group. Research shows that DES can affect any race and is more common in women than men, Phadatare *et al.,* (2015).

1.1.8 ARTIFICIAL TEARS

Artificial tears are a mainstay in the treatment of dry eye illness, but they also help with corneal abrasion and wound healing, controlling pain and inflammation, treating conjunctivitis and keratitis, removing foreign bodies from the eyes, and rewetting contact lenses.

Formulation

Most artificial tears are aqueous-based and contain viscosity-enhancing agents such as carbomer 940, carboxymethyll cellulose (CMC), dextran, hyaluronic acid, sodium hyaluronate (which has a smaller molecular size), hydroxypropyl guar (HP-guar), hydoxypropyl methycellulose (HPMC

hypromellose), polyvinyl alcohol, polyvinylpyrrolidone and polyethylene glycol, which aid lubrication and increase on-eye retention time. Other ingredients may include osmotic agents, Osmo-protectants, antioxidants, preservatives and inactives such as Ph buffers, excipients, and electrolytes.

Aqueous-based artificial tears have been found to ameliorate dry eye syndrome associated with all subtypes of DED. They primarily target the muco-aqueous phase of the tear film.

Preservatives

Preservatives are frequently used in multi-dose eye drops, both synthetic and medicated topical ocular drops, to maintain sterility and extend shelf life, however they are known to produce toxicity.

DED may be caused by or made worse by the toxic post-inflammatory and detergent effects of benzalkonium chloride, which is frequently found in multi-dose drops. Preservative-free and unit dose formulations have become more popular as a result.

In more recent preparations, less harmful preservatives such polyquaterium, "vanishing" preservatives like sodium perborate and purite, or bottles with specific designs that prevent the entry of germs may be present.

For all forms of dry eye, preservative-free formulations are advised; however, for severe dry eye or sensitive people, this is even more crucial; more information may be found in the TFOS DEWS II iatrogenic study.

1.2 STATEMENT OF PROBLEM

This study aims to compare the effects of preservative and non-preservative artificial tears on tear stability among adults with dry eye syndrome. The use of preservatives in artificial tears can cause ocular surface toxicity and exacerbate dry eye symptoms, while non-preservative artificial tears may be less effective because they have a shorter shelf life. This study aims to provide evidence-based recommendations, potential benefits, and drawbacks of each treatment option for dry eye syndrome.

1.3 AIM AND OBJECTIVES

Aim of study

The aim of this study is to compare the effect of preservative artificial tears and non-preservative artificial tears on tear stability among adults with dry eye syndrome.

Objectives of study

1. To identify any adverse effects associated with the use of preservative artificial tears and non-preservative artificial tears among adults with dry eye disease in the study area.
2. To compare the tear stability (measured by non-invasive tear break-up time) between preservative artificial tears and non-preservative artificial tears among adults in the study area with dry eye syndrome, before and after 4 weeks of treatment.
3. To compare the tear secretion (measured by Schirmer's test) between preservative artificial tears and non-preservative artificial tears among adults with dry eye syndrome in the study area, before and after 4 weeks of treatment.

1.4 HYPOTHESIS

- Null hypothesis (H0): there is no significant difference between preservative artificial tears and non-preservatives artificial tears on tear stability of adults.

- Alternate hypothesis (Ha): there is significant difference between preservative artificial tears and non-preservative artificial tears on tear stability of adults.

1.5 SIGNIFICANCE OF STUDY

1. Clinical significance: This study has the potential to provide valuable information on the efficacy and safety of different types of artificial tears in improving tear stability and reducing subjective dry eye symptoms among adults with dry eye syndrome, thus guiding clinical decision-making and improving patient outcomes.

2. Economic significance: The results of this study could help healthcare providers and policymakers to make more informed decisions regarding the optimal use of artificial tears in the treatment of dry eye syndrome, potentially reducing healthcare costs and improving the quality of life of patients.

3. Scientific significance: This study will add to the growing body of literature on the use of artificial tears in the treatment of dry eye syndrome, particularly with regard to tear stability as a key outcome measure. The findings of this study could help to fill gaps in knowledge and inform future research in this area, thus contributing to the advancement of the field.

1.6 DEFINITION OF TERMS

Dry eye syndrome: Dry eye is a condition that occurs when tears are unable to adequately lubricate the eyes. This is caused by either a decrease in tear secretion or an increase in tear evaporation.

Artificial tears: are lubricating eye drops that are used to treat dry eyes and ocular surface irritation.

Tears: Lacrimal glands (tear glands), which are present in the eyes of all land mammals, produce tears, a clear liquid. Water, electrolytes, proteins, lipids, and mucins make up the layers of tears that cover the surface of the eyes.

Tear film: Tear film is a thin layer of fluid that covers the eye and is made up of three layers: lipid, aqueous, and mucin. It is critical for eye health, protection, comfort, and vision.

Preservatives: Preservatives are substances or chemicals that are added to a variety of products, including food, drinks, pharmaceutical medications, paints, biological samples, cosmetics, wood, and many others, to stop microbial development or unfavourable chemical changes from causing the objects or substances to decompose.

Schirmer's test: Schirmer test is a test that measures tear production.

TBUT: Tear Breakup Time (TBUT) is a clinical test used to assess for evaporative dry eye disease.

Slit lamp bio-microscopy: Slit lamp bio-microscopy is a procedure that uses a slit lamp, which is a device that combines a microscope and a bright light, to examine the eye.

Fluorescein dye: a yellow dye that is visible even when highly diluted; used as an absorption indicator when silver nitrate solution is added to sodium chloride in order to precipitate silver

chloride (turns pink when no chloride ions are left in solution and negative fluorescein ions are then absorbed).

Tear film stability: Tear film stability refers to the ability of the tear film to maintain its integrity and resist breakup.

Tear flow rate: The rate at which tears are produced by the lacrimal gland and drained through the nasolacrimal duct is known as the tear flow rate. It can be used to diagnose dry eye syndrome and is measured in microliters per minute (µl/min).

Lacrimal gland: The lacrimal gland is a paired almond-shaped gland that secretes the aqueous layer of the tear film. It is in the upper, outer portion of each orbit, in the lacrimal fossa of the orbit formed by the frontal bone.

Nasolacrimal system: The nasolacrimal system is a conduit for tear flow from the external eye to the nasal cavity. It consists of the puncta, canaliculi, lacrimal sac, and nasolacrimal duct. The nasolacrimal duct is located beside the nose and is the final step of the eye's drainage system.

CHAPTER TWO

2.0 LITERATURE REVIEW

In quest for more knowledge on how preservatives artificial tears and preservative-free artifice/al tears interact with the ocular surface, so much research and studies has been carried out. Some of those research works were reviewed in this chapter to further support this project.

2.1 PREVALENCE OF DRY EYE

Lin *et al.,* (2003) did a study to describe the epidemiology of dry eye in an elderly Chinese population in Taipei, Taiwan. It was noted the prevalence of dry eye disease was high among the elderly patients with the aid Schirmer's test.

Moss *et al.,* (2000) carried out research on the prevalence of and Risk Factors for Dry Eye Syndrome, He concluded that Dry eye is one of the most common ocular diseases, estimated to affect 14% to 33% of adults and increasing with age. Furthermore, dry eye syndrome was found to be more common in females than in males in normal population.

Dogru *et al.,* (2018) demonstrated that oxidative stress damages the ocular surface and plays an important role in the mechanism of dry eye disease. They investigated the therapeutic modalities employing topical/systemic use of antioxidants in dry eye disease.

2.2 TEAR FILM STABILITY

Tear stability in young adults was measured by Amaechi *et al.,* (2004) using an invasive and non-invasive tear break-up time (TBUT and NIBUT). In their study, forty –five subjects aged 20 to 30 years were selected from among the students of University of Benin, Edo State. NIBUT was measured by noting the time taken for distortion or diffusion or diffusion of the Keratometric mires on the corneal surface while TBUT was assessed by noting the time taken for dry spots to appear on fluorescein treated eye. The mean NIBUT of the sample was 15.3±3.0 seconds and 15.2±3.1 seconds for TBUT. The relation between TBUT and NIBUT was not

statistically significant (P>0.05). The difference in mean TBUT and NITBUT was also not significant (P>0.05). There was no significant difference in mean TBUT and NIBUT between males and females (P>0.05). TBUT and NIBUT values were independent of subject's age. The TBUT values were comparable to NIBUT values and as such either of the two techniques can assuredly be used to assess the tear film stability. The status of tear stability would help in selecting suitable candidates for contact lens wear.

Mishima *et al.,* (1966) studied dynamics of tear flow in human subjects using fluorescein as an indicator. A new fluorophotometer attachable to a slit lamp was designed to determine fluorescein concentration of tears in situ. After the instillation of about 1 µl of fluorescein solution (1.0 Gm. L.-1) into the cul-de-sac, its concentration in the tears was found to decay in a single exponential pattern. In most cases, the turnover rate was initially fast and became slower after about five minutes. The initial faster turnover rate was interpreted as the result of stimulation of lacrimation due to the application of solution, and the subsequent slower decay interpreted as the physiologic turnover. The initial turnover showed individual variation and was lower in older than in younger people. The physiologic turnover rate was fairly constant among normal subjects, the average being about 16 per cent min-1. The tear volume in the cul-de-sac was measured with two methods. The dilution method consisted of instilling 16.2 µl of fluorescein solution (0.10 Gm. L.-1) sampling after blinking and determining the dilution ratio. This method was found to be subject to large errors due to lacrimation. The second method involved the construction of a semilog plot of concentration decay after the application of a known amount (about 1 µ; l) of fluorescein solution 30(1.0 Gm. L.-1), the extrapolation of the decay curve to zero time, and the computation of the tear volume from the zero-time concentration. The latter method gave very consistent results. The average tear volume obtained

was 7.0 ± 2.0 µl, with no significant difference between age groups, sexes, and fellow eyes. This value agreed well with the probable tear volume calculated from anatomical considerations. The combination of the tear volume and turnover rate determinations gave an average tear flow of 1.2 µl min-1 with a range of 0.5 to 2.2 µl min-1. The tear volume was found to increase with increasing tear flow. Since the tear volume obtained with the zero-time method corresponds to an initial faster tear flow, the normal tear volume with a normal tear flow was estimated from the volume-flow relationship; the average normal tear volume was 6.2 ± 2.0 µl.

The tear clearance rate is proposed as a simple and useful way to estimate basal tear turnover and tear flow, and measure tear drainage indirectly. This conclusion was made by Xu and Tsubota (1995) in their study to determine the dynamic changes and theoretical bases of a clinical diagnostic test, the tear clearance rate.

In this study, thirty-four healthy subjects ranging in age from 22 to 84 years underwent examination of tear clearance rate, the Schirmer test with anesthesia, as well as fluorophotometric measurement of tear turnover, tear volume, and tear flow. By applying 0.5% fluorescein into the conjunctival sac and subsequently measuring color fades on a Schirmer strip, the tear clearance rate for assessing tear drainage was divided into nine grades. The results of the tear clearance rate were compared with those of the basal tear turnover and tear flow obtained from fluorophotometry.

The result shows that significant relations were found between the tear clearance rate and the basal tear turnover or tear flow ($r = 0.91$ and 0.79, respectively, $p = 0.0001$). Considering the grades of progression from low to high, each grade of tear clearance rate showed a 12.5% increase in basal 31tear turnover (3.59%/min) and tear flow (0.38 microliter/min). It also showed

that there was no significant correlation between age and the basal tear turnover, tear volume, tear flow, or the tear clearance rate.

Iyamu and Ajayi (2005) studied the effect of age and topical antibiotics on the non-invasive tear break-up time (NIBUT) in young adults, in a defined population was investigated. Forty healthy young adults with age range of fifteen to 30 years and mean age 23.9 + 2.9 years, from among the students at University of Benin, were recruited for this study. Noting the time taken for the images of the Keratometer mires on the corneal surface to show distortion or diffusion assessed the NIBUT. The NIBUT was measured before and 10 minutes after instilling either chloramphenicol 0.5% or gentamicin 0.3% guttae. The results showed that the mean NIBUT for the sample population was 14.1+ 3.0 seconds. The majority (60%) of the eyes had NIBUT values within eleven to 15 seconds. The difference in mean NIBUT between males and females was not statistically significant by Mann-Whitney U test ($Z=0.16$, $p=0.56$). The NIBUT was not affected by age ($r=+0.16$, $p>0.05$). The difference in mean NIBUT before and after instilling 0.5% chloramphenicol guttae was statistically significant for both males and females. Also, the difference in mean NIBUT before and after instilling 0.3% gentamicin was statically significant for females. Eye care practitioners should discourage the indiscriminate use of topical antibiotics. The tear film stability of candidates desiring to wear contact lenses should be assessed by either NIBUT or invasive tear break-up time (TBUT) and used as the determinant for suitability for successful contact lens wear.

2.3 TREATMENT OF DED WITH PRESERVATIVE-FREE ARTIFICIAL TEARS

Hynnekleiv *et al.,* (2022) carried out a prospective longitudinal, single-arm interventional cohort study which involved 20 patients with dry eye (40 eyes). Preservative-free artificial tears were administered every 3h. The participants underwent clinical and instrumental evaluations at

baseline, 15, 30, 60, 90 and 120 min after instillation and 1 week and 1 month after treatment. Baseline values were considered as controls. He concluded that a combination of 0.4% hyaluronic acid and 0.2% galactoxyloglucan artificial tears seems effective for treating dry eye. Keratograph 5M can objectively detect these changes during the follow-up period**.**

Mateo-otobia *et al.,* (2022) studied the Evaluation of ocular surface disease symptoms and patient satisfaction in dry eye disease after 84 days of treatment with preservative-free eye drops containing sodium hyaluronate and trehalose. Conclusions results confirm that continued use of eye drops containing sodium hyaluronate and trehalose SH-THL reduced DED signs and symptoms, OSDI scores, and result in a very high patient satisfaction.

2.4 EFFECTS OF OPHTHALMIC PRESERVATIVES

Noecker, R. (2001) compared the effects of common ophthalmic preservatives on ocular health The most common preservatives in ophthalmic preparations for glaucoma and surface eye disease-benzalkonium chloride (BAK), chlorobutanol, sodium perborate, and stabilized oxychloro complex (SOC)-were reviewed. Compared with other preservatives, they concluded that SOC caused the least amount of damage to rabbit corneal epithelial cells. BAK has demonstrated cytotoxic effects in cell culture, as well as in animal and human studies. Physicians should consider treatment with new-generation preparations containing low-risk preservatives such as SOC, especially in patients receiving multiple ophthalmic medications.

Fineide *et al.,* (2022) carried out a study on Preservatives, generics and ocular surface and deduce that in general, preservatives have a negative effect on the surface of the eye due to their toxic effect on, among other things, the ocular surface cells and on the tear film.

Benzalkonium is known to cause corneal epithelium damage and induce cell membrane lysis at the ocular surface even at very low doses, and, if chosen for treatment, its frequency of use has to be limited to no more than four times a day Moshirfar *et al.,* (2014).

Maiti *et al.,* (2016) Clinical studies suggest that the long-term use of ophthalmic preparations for effective therapy may induce major and frequent ocular surface changes causing allergic or inflammatory reactions such as redness, stinging, burning, irritation, eye dryness, or less frequently conjunctivitis or corneal damage.

2.5 COMPARISON BETWEEN PRESERVATIVE ARTIFICIAL TEARS AND PRESERVATIVE-FREE ARTIFICIAL TEARS

Nasser *et al.,* (2018) assessed the clinical benefit of using a switch from preservatives artificial tears drops to preservative-free artificial tears containing hyaluronate in patients with Dry Eye Disease. 1249 people participated in the study, OSDI questionnaire and cornea staining was used to detect patients suffering from DED and they were treated with a preserved artificial tear for some weeks and later switched to a preservative-free artificial tears, this provided clinical benefit by decreasing the severity of DED and reducing the prevalence of SPK, even after only 3 weeks of daily use of the preservative-free artificial tears.

Jee *et al.,* (2014) performed a comparative study on the levels of inflammatory and antioxidant cytokines in patients with dry eye condition who received preserved versus preservative-free eye drops. They concluded Patients with dry eye syndrome who received treatment with preservative-free artificial drops saw substantial improvements in their symptoms, tear film breakup time, Schirmer's I score, and impression cytologic abnormalities compared to those who received treatment with preservative artificial eye drops.

Nasser *et al.,* (2018) carried out a study on Real-life results of switching from preserved to preservative-free artificial tears containing hyaluronate in patients with dry eye disease. The mean age was 51.0±15.4 years, ranging from 6 to 96 years. The majority (61.4%) was female. The patients using ATs containing "soft" or "vanishing" preservatives presented the same clinical pattern (level of OSDI and frequency of SPK) as those using ATs containing classical preservatives such as benzalkonium chloride (BAK). After switching to preservative-free AT containing hyaluronate (Hyabak®), the OSDI of 97.0% of the patients improved, decreasing from an average of 56.0 to an average of 28.2, with 23% of patients reporting a normal value of OSDI. The SPK frequency as well improved dramatically, with a frequency of positive fluorescein staining dropping from 73% to 46.1% of patients. A total of 94.0% of the patients considered that they preferred being treated with the preservative-free AT. He concluded that in patients suffering from DED and treated with a preserved AT, switching to a preservative-free AT provides clinical benefit by decreasing the severity of DED and reducing the prevalence of SPK, even after only 3 weeks of daily use of the preservative-free AT.

Safarzadeh *et al.,* (2017) compared the efficacy of preservatives artificial tears is and non-preservatives artificial tears on two groups. Group A with single dose of artificial tear, containing dextran 70, 1mg/ml and Hypromellose, 3mg/ml hydroxypropyl methylcellulose (HPMC) and group B with multidose of artificial tear, containing 0.3g HPMC and 0.1g of dextran 70, with 0.01% benzalkonium chloride (BAK) as preservatives. At the end of the study there was improvement with the use both products and there was no statistical difference between both.

Maharana *et al.,* (2017) compared the efficacy of carboxymethylcellulose 0.5% (CMC with dry eye. A retrospective evaluation of cases presenting with symptoms of dry eye from July 2014 to June 2015 was done in conclusion Hydroxypropyl-guar containing PEG/PG and),

hydroxypropyl-guar containing polyethylene glycol 400/propylene glycol (PEG/PG), and hydroxypropyl methylcellulose 0.3% (HPMC) as tear substitutes in patients HPMC as tear substitutes are better than CMC. While HPMC was comparable to PEG/PG in subjective improvement, the objective improvement was not consistent.

CHAPTER THREE

3.0 METHODOLOGY

3.1 RESEARCH DESIGN

This is a randomized controlled trial research study.

3.2 SAMPLING TECNHIQUE

Convenience sampling technique was used for this study.

3.3 STUDY LOCATION

This study was conducted at Smart View Eye Clinic Nigeria Limited, Mile 4 Port Harcourt, Rivers State.

3.4 STUDY POPULATION

Participants who scored greater than 13 using the OSDI questionnaire were randomly selected in Port Harcourt with their age ranged between 18 – 69 years. The population consists of participants who were dry eye patients and had not previously been on any dry eye medication.

3.5 SAMPLE SIZE

After much screening, a total of 80 subjects were marked fit to participate in the study. The selected participants were divided into two groups, 40 participants in each group. Each group of the 40 participants were given a bottle of preservative artificial tears (Hypromellose**)** while the other group of 40 participants were given a bottle of preservative-free artificial tears (Refresh**)** each.

3.6 STUDY DURATION

This study was carried out within a period of 4 weeks.

3.7 STUDY MATERIALS

- Fluorescein strip
- Snellen Visual Acuity Chart
- Near card
- Penlight
- Disposable gloves
- Recording book and pen
- Schirmer's strip
- Preservative artificial tears (Hypromellose**)**
- Preservative-free artificial tears **(**Refresh**)**
- Stopwatch
- Slit Lamp (SL-110 Digital LED Slit lamp)
- OSDI questionnaire

3.8 INCLUSION CRITERIA

Subjects aged 18 years above and have been diagnosed with dry eye syndrome based on clinical criteria. Participants who were able to provide informed consent and follow the study protocol.

3.9 EXCLUSION CRITERIA

- Participants with a history of ocular surgery in the previous 6 months.
- Participants with a history of ocular trauma or infection in the previous 3 months.
- Participants with a history of systemic diseases or conditions that may affect ocular surface health (e.g., Sjögren's syndrome, rheumatoid arthritis, or diabetes).
- Participants who are pregnant or breastfeeding.
- Participants with a known allergy or sensitivity to any of the ingredients in the study medication (either preservative artificial tears or non-preservative artificial tears).
- Participants who are currently using any other ocular medications or therapies for dry eye syndrome, such as cyclosporine or punctal plugs.

3.10 ETHICAL CONSIDERATIONS

- Ethical approval was obtained from the departmental Research and Ethics committee of the department of Optometry, University of Benin in accordance with the tenet of the declaration of Helsinki. This was to ensure that all procedures that were performed on each subject were not against public interest or inflict unnecessary harm to them.
- Informed consent was sought from each of the participants and only consenting participants were recruited for the study.

3.11 DESCRIPTION OF PROCEDURE

OSDI questionnaires were given to all participants, and they were divided into two (2) groups of 40 each. Artificial tears with and without preservatives; **(**Hypromellose) and **(**Refresh**)** were given to each group. Participants were to instill the eye drops 4 times daily for 4 weeks, tear flow rate and tear film stability was recorded at the end of the fourth week. At the end, five readings were recorded for each participant – Pre-task and after 4 weeks.

The Tear Film Stability was assessed using Fluorescein and slit lamp method - Invasive break-up time (Invasive-BUT).

The Tear flow rate was assessed using Schirmer Strip test techniques.

All the participant's visual acuity, external examination and case history were taken prior to the proper test.

Then their normal tear flow rate and tear film stability reading was taken before they started using the eye drops

The examination was carried out in the following order:

1. Participants filled out the OSDI questionnaire and it was used to screen out and select participants.
2. Case history.
3. Visual acuity
4. External examination with pen light

5. Tear flow rate was assessed using Schirmer's strip.
6. Tear film stability was assessed using fluorescein dye and slit lamp for the invasive tear break-up time.

3.11.1 OCULAR SURFACE DISORDERS INDEX (OSDI) QUESTIONNAIRE

Ocular Surface Disease Index Questionnaire (OSDI): It is a questionnaire which includes 12 questions related to symptoms, environmental conditions which can cause dry eye and functional limitations. Each question has 5 like type response options. 0 (none of the time) to 4 (all the time). Total OSDI score is calculated by the formula given below.

OSDI = Sum of scores x 25/ total no of questions answered. Scores range from 0 to 100.

0–12 representing normal,

13- 32 representing mild to moderate DED

≥33 representing severe DED.

Higher scores represent more disability. Scores are matched with the graph with different color coding. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eyes and is a valid and reliable instrument for measuring the severity of dry eye disease.

3.11.2 CASE HISTORY:

Detailed case history was carried out on each participant to determine their age, gender, oculo-visual history, medical history.

3.11.3 VISUAL ACUITY:

Visual acuity was measured to determine the level of vision available. This was tested using the Snellen's distant acuity chart for distance (6m) and near point card for near (40cm) testing. Illiterate E chart was provided for persons who cannot read.

3.11.4 EXTERNAL EXAMINATION:

This was carried out using penlight with a loupe to view the anterior segment such as adnexa, upper and lower eyelids, cornea, conjunctiva, sclera, to determine the integrity of these structures.

Assessment of Tear Flow Rate Using Schirmer's Strip

- While the participant was still seated, the closed lids were gently dried. The sterile pouch was carefully opened, and the strip removed. Care was taken not to contaminate the wick end of the strip.
- The participant was asked to look up while the lower lid was pulled down and temporally. The bent hooked end of the strip was placed at the junction of the temporal and central third of the lower eyelid margin. The eyelid was released while the patient continued to look up, blinking normally although excessive blinking was discouraged as it may lead to significant reflex tearing. These were done to both eyes at almost the same time.
- The time of insertion was noted. The strip was removed after 5 minutes or when it was completely wet, whichever comes first.
- The wetted portion of the strip was measured from the notch towards the flat end in mm.
- The value was recorded in seconds.
- This test was performed without anesthetic because aqueous tear production decreases after anaesthetizing the ocular surface Mishra *et al.,* (2022).

- Test value less than 10mm of wetting in 5 minutes is highly suggestive of aqueous deficiency (Bartlett & Jaanus 2008).

Assessment of Tear Film Stability using Invasive tear break-up time (i-BUT)

- While the participant was still seated comfortably.
- A fluorescein strip was wetted with 2 to 3 drops of normal saline and applied to the interior temporal bulbar conjunctiva or lower eyelid fornix.
- The participant was asked to blink about three times in order to distribute the fluorescein efficiently and evenly over the cornea.
- The subjects were asked to place their chin on the chin rest and forehead on headrest of the slit lamp.
- The slit lamp with a low magnification and a broad beam covering the cornea was used. The lamp was switched to a cobalt blue filter.
- The subject was asked to blink once and refrain from blinking.
- A stopwatch was clicked to start reading immediately after the last complete blink.
- With the participant's eye wide open, a cobalt blue filter was used to assess the time taken for a random dry spot to appear on the cornea from the last complete blink.
- At the first appearance of a black spot indicating a dry area, the stopwatch was clicked to stop reading and the time was noted.
- In a situation where the subject blinked between the measurements, the test was halted, and then repeated after several blinks.
- The interval between the last blink and the appearance of black spot was recorded in seconds as the i-BUT.

- Five measurements were taken for each subject and the average of three closest i-BUT values were taken as the mean value.

3.12 DATA ANALYSIS

Data obtained was analyzed using statistical package for social sciences (SPSS version 22.0; SPSS Corporation Chicago, IL. USA). Normality of distribution of data was tested using Kolmogorov Smirnov z-test. An Independent-Samples T Test and One-Way ANOVA Statistic was used to compare the data collected. A post hoc test: Bonferroni pairwise and LSD comparison test was also used. And then, statistical significance was declared when $p \leq 0.05$.

3.13 LIMITATION OF STUDY

1. Financial constraints: this is due to the current high cost of the needed materials in the market, especially the eye drops.

2. Lack of total compliance: some participants need to be constantly reminded of the need to comply with the instructions and some at a time pulled out of the research.

CHAPTER FOUR

4.0 RESULTS

A total of eighty (n = 80) participants were selected randomly, after filling the OSDI questionnaire and had the OSDI scores of 13 and above. The selected participants fell within the age range of 19 to 69 years with the mean age of 46 ± 10.46 years made up of males (n = 40) and females (n = 40) were used for this study. The subjects were divided into two groups, 40 participants in each. The first groups of the 40 participants were given a bottle of artificial tears with preservatives (Hypromellose) eye drop while the other second groups of 40 participants were given a bottle of preservative free artificial (Refresh) eye drop each. The monocular distant visual acuity of each participant was also recorded in the study and converted to their logMAR equivalent.

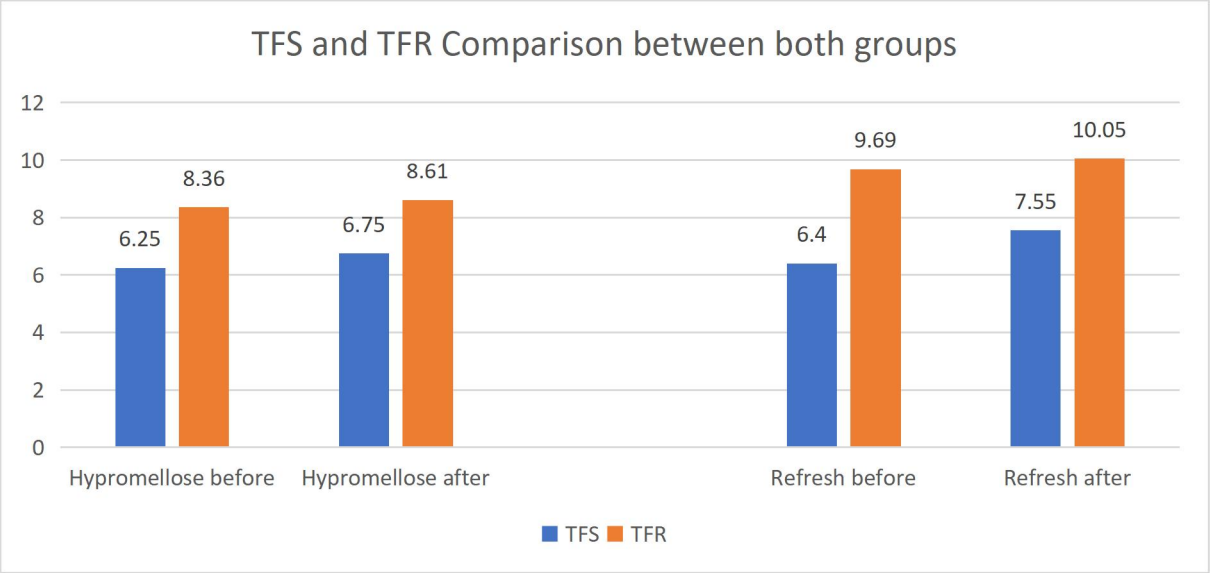

Fig 2: A bar chart showing the comparison of both artificial tear groups on TFS and TFS

The bar chart above, figure 2, shows the mean values for the tear film stability and tear flow rate for both artificial tears groups before and after instillation. The value for TFS before and after instillation of Hypromellose are 6.25 ± 0.33 and 6.75 ± 0.31seconds respectively, and the values for TFS before and after instillation of refresh are 6.40 ± 0.40 and 7.55 ± 0.42 seconds respectively. The mean value for TFR before and after instillation of Hypromellose are 8.36 ± 0.50 and 8.61 ± 0.50 seconds respectively, and the values for TFR before and after instillation of refresh are 9.69 ± 0.54 and 10.05 ± 0.55 seconds respectively.

4.1 Descriptive Statistics of Measured Variables

variable	N	Range	Minimum	Maximum	Mean ±	Std. Deviation	Variance	Skewness	Kurtosis			
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
TOT_AGE	80	50	19	69	46.00 ±	1.199	10.724	115.013	-.559	.269	.782	.532
FTBUT HYP_B	40	7	2	9	6.25±	.333	2.109	4.449	-.485	.374	-.756	.733
FTBUT HYP (A)	40	8	2	10	6.75±	.310	1.958	3.833	-.666	.374	-.301	.733
FTBUT REF_B	40	9	1	10	6.40±	.400	2.530	6.400	-.707	.374	-.364	.733
FTBUT REF_A	40	11	2	13	7.55±	.424	2.679	7.177	-.020	.374	-.344	.733

SCHIRMER'S TEST HYP_B	40	12.0	1.0	13.0	8.363 ±	.5035	3.1845	10.141	-.623	.374	-.302	.733
SCHIRMER'S TEST HYP_A	40	11.5	2.0	13.5	8.610 ±	.5027	3.1796	10.110	-.587	.374	-.607	.733
SCHIRMER'S TEST REF_B	40	13.0	1.0	14.0	9.688 ±	.5417	3.4263	11.740	-.960	.374	.170	.733
SCHIRMER'S TEST REF_A	40	13.5	1.0	14.5	10.050±	.5509	3.4840	12.138	-.989	.374	.320	.733
LogMAR VA (6M)	80	1	0	1	.22±	.033	.293	.086	.368	.269	-1.035	.532
LogMAR VA (40 CM)	80	1	0	1	.59±	.023	.205	.042	-.652	.269	2.081	.532
Valid N (listwise)	40											

Table 4.1 Normality distribution of Age, Tear Flow Rate and Tear Film stability of all the participants

4.2 Data presentation of Comparison effects of Hypromellose on tear film stability and tear flow rate.

Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 FTBUT BEF - FTBUT AFT	-.500	.751	.119	-.740	-.260	-4.210	39	.000
Pair 2 SCHIRMER'S TEST BEF - SCHIRMER'S TEST AFT	-.2475	.5961	.0943	-.4382	-.0568	-2.626	39	.012

Table 4.2 shows the paired T-test result of Tear Film stability with FTBUT and Tear Flow Rate with Schirmer's test before and after instilling Hypromellose.

Table 4.2 shows the presentation of the comparison of participants' Tear Film Stability (TFS) with Fluorescein Invasive break-up time (FTBUT) and Tear Flow Rate (TFR) with Schirmer's Test findings before they were given the artificial tears with preservatives (Hypromellose) and after four weeks of instilling the artificial tears. With (p-value 0.05) the t test result failed to accept the null hypothesis for FBUT. This means there is a significant difference between the initial TFS and the use of artificial tears with preservatives (Hypromellose). While for the TFR the t test result accepts the null hypothesis which means that there is no significant difference between the initial TFR and after the use of artificial tears with preservatives (Hypromellose).

4.3 Data presentation of Comparison effects of Refresh on tear film stability and tear flow rate.

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	FTBUT BEF – FTBUT AFT	-1.150	1.145	.181	-1.516	-.784	-6.354	39	.000
Pair 2	SCHIRMER'S TEST BEF - SCHIRMER'S TEST AFT	-.3625	.5187	.0820	-.5284	-.1966	-4.420	39	.000

Table 4.3 shows the paired T-test result of Tear Film stability with FTBUT and Tear Flow Rate with Schirmer's test before and after instilling Refresh.

Table 4.3 shows the presentation of the comparison of participants' Tear Film Stability (TFS) with Fluorescein Invasive break-up time (FTBUT) and Tear Flow Rate (TFR) with Schirmer's Test findings before they were given the preservative-free artificial tears (Refresh) and after four weeks of instilling the artificial tears. With (p-value 0.05) the t test result failed to accept the null hypothesis for FBUT and Schirmer's Test. This means there is a significant difference between the initial TFS and TFS and the use of preservative-free artificial tears (Refresh).

4.4 Data presentation of Comparison between Initial Tear Film Stability Before and After Instilling Hypromellose and Refresh

ANOVA

FBUT

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	40.475	3	13.492	2.469	.064
Within Groups	852.500	156	5.465		
Total	892.975	159			

Table 4.4 One-way ANOVA result of comparison of Tear Film stability using FTBUT of the participants four weeks after instilling Hypromellose and Refresh

Table 4.2 shows the presentation of the comparison of participants' Tear film stability using FTBUT test after the instillation of artificial tears with preservatives and non-preservative Artificial tears drop, with p-value > 0.05, One-Way ANOVA result showed it accepts the null hypothesis. This means there is no significant difference in tear film stability of the participants in both groups after the instillation of artificial tears with preservatives and non-preservative Artificial tears.

4.5 Data presentation of Comparison between Initial Tear Flow Rate Before and After Instilling Hypromellose and Refresh

ANOVA

SCHIRMER'S TEST

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	80.306	3	26.769	2.426	.068
Within Groups	1721.014	156	11.032		
Total	1801.319	159			

Table 4.5 One-way ANOVA result of comparison of Flow Rate using Schirmer's Test of the participants four weeks after instilling Hypromellose and Refresh

Table 4.3 shows the presentation of the comparison of participants' Tear flow rate with Schirmer's test after the instillation of artificial tears with preservatives and non-preservative Artificial tears drop, with p-value > 0.05, One-Way ANOVA result showed it accepts the null hypothesis. This means there is no significant difference in tear flow rate of the participants in both groups after the instillation of artificial tears with preservatives and non-preservative Artificial tears.

CHAPTER FIVE

5.0 DISCUSSION

This study showed the relationship between the effects of artificial tears with preservatives and non-preservative artificial tears on tear flow rate and tear film stability. The participants in the study were selected randomly from the population of people who had scores of 13 and above in the OSDI questionnaire. 80 persons were selected randomly; the participants comprised 40 males and 40 females with an age range of 19 to 69 years and a mean age of 46 ± 10.46. The figure confirms Lin *et al.,* (2003) and Moss *et al.,* (2000) about the prevalence of dry eye syndrome among the elderly. Selecting the participants in the various groups, the number of male and Females were selected equally to avoid bias in the selection.

The visual acuity of both distance and near was recorded to help give knowledge on the vision of the subjects and ensure no ocular surface pathology, which can affect the findings, was involved in the research.

The assessment of the participants' tear flow rate and tear film stability was done before the instillation of artificial tears. The mean Schirmer's test was 9.025 mm, which is below the

normal value of >10 mm, while the mean value of the fluorescein tear breakup test was 6.32 seconds, which is less than the normal value of >8–10 seconds. Based on both the tear flow rate and tear film stability, this indicated the presence of dry eye syndrome among the participants after the OSDI findings.

The results of a paired-sample t test with a p-value of 0.05 failed to accept the null hypothesis for FTBUT, which means that there is a significant difference between tear film stability before and four weeks after using artificial tears with preservatives, while the results accepted the null hypothesis for the Schirmer's test, which means there is no significant difference between the tear flow rate after using artificial tears with preservatives (Hypromellose) for four weeks.

The results of a paired-sample t test with a p-value of 0.05 failed to accept the null hypothesis for FTBUT and Schirmer's test, which means that there is a significant difference between tear film stability and tear flow rate before and four weeks after using preservative-free artificial tears (Refresh) for four weeks.

The findings of a one-way ANOVA test with a p-value > 0.05 accepts the null hypothesis, indicating that there is no significant difference between the Tear Flow Rate following four weeks of using artificial tears with preservatives (Hypromellose) and artificial tears without preservatives (Refresh). Comparing the tear flow rate of the participants before and after applying Refresh (non-preservative) artificial tears the result from this study supports Safarzadeh *et al.,* (2017) who concluded that was no statistical difference between both groups. Comparing the tear flow rate and tear film stability of the participants before and after applying Refresh (preservative-free) artificial tears supports Hynnekleiv *et al.,* (2022), who stated that applying non-preservative artificial tears influences patients' satisfaction. Although there is no record of allergies or red eye to support Maiti *et al.,* (2016), Comparing the findings on Tear Flow Rate

with the use of both preserved and non-preservative artificial tears shows no significant difference. The outcome is different from the results from Nasser *et al.,* (2018).

The findings of a one-way ANOVA test with a p-value > 0.05 accepts the null hypothesis, indicating that there is no significant difference between the FTBUT following four weeks of using artificial tears with preservatives (Hypromellose) and artificial tears without preservatives (Refresh).

Regarding side effects, the reason for the current selection of preservative-free eye drops, no significant adverse effects were observed in any of the groups in this study. Safarzadeh *et al.,* (2017) did not observe any adverse effects in the group that used preserved eye drops and attributed the results to the short treatment time in this study**.** Perez-Balbuena *et al.,* (2016) reported that side effects were not associated with the intervention in their study. Astakhov *et al.,* (2016) described that both treatments were well tolerated in their results, without significant topical or systemic adverse effects, or discontinuation of treatment for any reason. Only two cases of corneal edema were reported in the group that used preservative-free lubricants, and one case of corneal edema in the preserved artificial tears group, which were attributed to LASIK surgery and not to the lubricants studied. Finally, Nelson *et al.,* (2000) reported that no side effects were observed in any of the groups included in their studies.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 CONCLUSION

This comparative study aimed at evaluating the impact of preservative artificial tears and preservative-free artificial tears on tear film stability among dry eye patients. From the analysis of data and extensive testing, the findings from this study indicates that there is no statistically significant difference between preservative artificial tears and preservative-free artificial tears with regards to tear flow rate and tear film stability. This result will contribute significantly to the management of dry eye in eyecare professionals. The perfect artificial tear should be able to repair the damaged tear film with less frequency of instillation and with minimal side effects. The short time duration in the cornea, in addition to the limited time of symptom improvement, is a common problem of lubricants. Although preservative-free artificial tears are now recommended for dry eyes, single unit-dose tear substitutes are more expensive for the manufacturers and consumers, and less convenient to use than bottled artificial tear drops.

The methodology of this study ensured the inclusion of diverse groups of dry eye patients in order to enhance generalizability of our results.

6.2 RECOMMENDATION

- Clinicians can confidently prescribe both preservative and preservative-free artificial tears as viable treatment options for the management of dry eye, patients should be able to make informed choices about their preferences and tolerances on both types of artificial tears.

- Although this study did not prove a significant difference between tear film stability, further research should be done to investigate the long-term effects using these artificial tears, the variations in outcomes over extended periods.

REFRENCES

Amaechi, O. and Osunwoke, C. (2011). The relation between invasive and non-invasive tear break-up time in young adults. *Journal of the Nigerian Optometric Association*, [online] 11(1). doi:https://doi.org/10.4314/jnoa.v11i1.64443.

Astakhov, S.Y. and Tkachenko, N.V., 2016. Trehalose efficacy in dry eye syndrome treatment after phacoemulsification. *Ophthalmology journal*, *9*(4), pp.79-89.

Bartlett, J.D. and Jaanus, S.D., 2008. Clinical ocular pharmacology . St. Louis, Mo.

Conrady, C.D., Joos, Z.P. and Patel, B.C., 2016. The lacrimal gland and its role in dry eye. *Journal of ophthalmology*, *2016*.

Dartt, D.A. and Willcox, M.D.P., 2013. Complexity of the tear film: importance in homeostasis and dysfunction during disease. *Experimental eye research*, *117*, p.1.

Dogru, M., Kojima, T., Simsek, C. and Tsubota, K. (2018). Potential Role of Oxidative Stress in Ocular Surface Inflammation and Dry Eye Disease. *Investigative Opthalmology & Visual Science*, 59(14), p.DES163. doi:https://doi.org/10.1167/iovs.17-23402.

Fineide, F., Lagali, N., Adil, M.Y., Arita, R., Kolko, M., Vehof, J. and Utheim, T.P., 2022. Topical glaucoma medications–Clinical implications for the ocular surface. *The ocular surface*.

Hodges, R.R. and Dartt, D.A., 2013. Tear film mucins: front line defenders of the ocular surface; comparison with airway and gastrointestinal tract mucins. *Experimental eye research*, *117*, pp.62-78.

Holland, E.J., Mannis, M.J. and Lee, W.B., 2013. *Ocular surface disease: cornea, conjunctiva and tear film: expert consult-online and print*. Elsevier Health Sciences.

INTRODUCTION TO THE 2007 REPORT OF THE INTERNATIONAL DRY EYE WORKSHOP DEWS. (n.d.). Available at: https://www.tearfilm.org/dewsreport/pdfs/TOS-0502-DEWS-noAds.pdf.

Iyamu, E. and Ajayi, O.B., 2005. Effect of age and tropical antibiotics on the non-invasive tear break-up time in young Nigerian adults. *Annals of Biomedical Sciences*, *4*(2), pp.10-18.

Jacobi, C., Kruse, F.E. and Cursiefen, C. (2012). Prospective, Randomized, Controlled Comparison of SYSTANE UD Eye Drops Versus VISINE INTENSIV 1% EDO Eye Drops for the Treatment of Moderate Dry Eye. *Journal of Ocular Pharmacology and Therapeutics*, 28(6), pp.598–603. doi:https://doi.org/10.1089/jop.2012.0066.

Jee, D., Park, S.H., Kim, M.S. and Kim, E.C. (2014). Antioxidant and Inflammatory Cytokine in Tears of Patients With Dry Eye Syndrome Treated With Preservative-Free Versus Preserved Eye Drops. *Investigative Opthalmology & Visual Science*, 55(8), p.5081. doi:https://doi.org/10.1167/iovs.14-14483.

Kopacz, D., Niezgoda, Ł., Fudalej, E., Nowak, A. and Maciejewicz, P., 2020. Tear film–physiology and disturbances in various diseases and disorders. *Ocular Surface Diseases—Some Current Date on Tear Film Problem and Keratoconic Diagnosis*, pp.137-44.

Lin, P. Y., Tsai, S. Y., Cheng, C. Y., Liu, J. H., Chou, P., & Hsu, W. M. (2003). Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology, 110(6), 1096–1101. https://doi.org/10.1016/S0161-6420(03)00262-8

Maharana, P. K., Raghuwanshi, S., Chauhan, A. K., Rai, V. G., & Pattebahadur, R. (2017). Comparison of the Efficacy of Carboxymethylcellulose 0.5%, Hydroxypropyl-guar Containing Polyethylene Glycol 400/Propylene Glycol, and Hydroxypropyl Methyl Cellulose 0.3% Tear Substitutes in Improving Ocular Surface Disease Index in Cases of Dry Eye. Middle East African journal of ophthalmology, 24(4), 202–206. https://doi.org/10.4103/meajo.MEAJO_165_15

Maiti, S., Sadhukhan, S. and Bakshi, P., 2016. Ocular Preservatives: Risks and Recent Trends in Its Application in Ocular Drug Delivery (ODD). *Nano-Biomaterials For Ophthalmic Drug Delivery*, pp.253-276.

Masoudi, S., 2022. Biochemistry of human tear film: A review. *Experimental Eye Research*, *220*, p.109101.

Mateo-Otobia, A., Del Prado Sanz, E., Martínez, A.B., Corta, M.I., Sanz, M.R., Pablo Júlvez, L.E. and Farrant, S., 2022. Evaluation of ocular surface disease symptoms and patient satisfaction in dry eye disease after 84 days of treatment with preservative-free eye drops containing sodium hyaluronate and trehalose. *Acta Ophthalmologica*, *100*.

Mishima, S., Gasset, A., Klyce, S.D. and Baum, J.L. (1966). Determination of Tear Volume and Tear Flow. *Investigative Ophthalmology & Visual Science*, [online] 5(3), pp.264–276. Available at: https://iovs.arvojournals.org/article.aspx?articleid=2203634.

Mishra, S., Bista, B., Basnet, P., Chaudhary, P., Chaudhary, S., Gupta, S. and Bista, P.R., 2022. Evaluation of tear secretion and tear film stability in patients with pterygium and normal individuals. *Journal of National Medical College*, *7*(1), pp.14-18.

Moshirfar, M., Pierson, K., Hanamaikai, K., Santiago-Caban, L., Muthappan, V. and Passi, S.F. (2014). Artificial tears potpourri: a literature review. *Clinical Ophthalmology (Auckland, N.Z.)*, [online] 8, pp.1419–1433. doi:https://doi.org/10.2147/OPTH.S65263.

Moss, S. E., Klein, R., and Klein, B. E. (2000).Prevalence of and Risk Factors for Dry Eye Syndrome.Archives of Ophthalmology, 118(9), 1264.https://doi.org/10.1001/archopht.118.9.1264

Nasser, L., Rozycka, M., Gomez Rendon, G. and Navas, A. (2018). Real-life results of switching from preserved to preservative-free artificial tears containing hyaluronate in patients with

dry eye disease. *Clinical Ophthalmology*, Volume 12, pp.1519–1525. doi:https://doi.org/10.2147/opth.s160053.

Nelson, J.D., Helms, H., Fiscella, R., Southwell, Y. and Hirsch, J.D., 2000. A new look at dry eye disease and its treatment. *Advances in therapy*, *17*, pp.84-93.

Noecker, R. (2001). Effects of common ophthalmic preservatives on ocular health. *Advances in Therapy*, [online] 18(5), pp.205–215. doi:https://doi.org/10.1007/BF02853166.

P. Molina-Solana, de, F., A.M. Garrido-Hermosilla, Jesús Montero-Iruzubieta, Fernández-Palacín, A., Rodríguez-de-la-Rúa-Franch, E. and Caro-Magdaleno, M. (2020). Improved Tear Film Stability in Patients with Dry Eye After Hyaluronic Acid and Galactoxyloglucan Use. *Clinical Ophthalmology*, Volume 14, pp.1153–1159. doi:https://doi.org/10.2147/opth.s248949.

Pérez-Balbuena, Ana L., Juan C. Ochoa-Tabares, Sandra Belalcazar-Rey, Cristian Urzúa-Salinas, Laura R. Saucedo-Rodríguez, Regina Velasco-Ramos, Raúl G. Suárez-Sánchez, Adolfo D. Rodríguez-Carrizalez, and Aldo A. Oregón-Miranda. "Efficacy of a fixed combination of 0.09% xanthan gum/0.1% chondroitin sulfate preservative free vs polyethylene glycol/propylene glycol in subjects with dry eye disease: a multicenter randomized controlled trial." *BMC ophthalmology* 16, no. 1 (2016): 1-6.

Phadatare, S.P., Momin, M., Nighojkar, P., Askarkar, S. and Singh, K.K., 2015. A comprehensive review on dry eye disease: diagnosis, medical management, recent developments, and future challenges. *Advances in Pharmaceutics*, *2015*.

Phillips, A.J. and Speedwell, L. (2018). *Contact Lenses*. [online] *Google Books*. Elsevier Health Sciences. Available at: https://books.google.com.ng/books?id=AON8DwAAQBAJ&lpg=PA344&ots=YbnNY-XrNn&dq=bartlett%20%26%20jaanus%202008&lr&pg=PA339#v=onepage&q=bartlett%20&%20jaanus%202008&f=false [Accessed 25 Apr. 2023].

Ribeiro, M.V.M.R., Barbosa, F.T., Ribeiro, L.E.F., Sousa-Rodrigues, C.F. de and Ribeiro, E.A.N. (2019). Effectiveness of using preservative-free artificial tears versus preserved lubricants for the treatment of dry eyes: a systematic review. Arquivos Brasileiros de Oftalmologia, 82(5). doi:https://doi.org/10.5935/0004-2749.20190097.

Rolando, M. and Zierhut, M., 2001. The ocular surface and tear film and their dysfunction in dry eye disease. *Survey of ophthalmology*, *45*, pp.S203-S210.

Safarzadeh, M., Azizzadeh, P., & Akbarshahi, P. (2017). Comparison of the clinical efficacy of preserved and preservative-free hydroxypropyl methylcellulose-dextran-containing eyedrops. Journal of optometry, 10(4), 258–264. https://doi.org/10.1016/j.optom.2016.11.002

Stahl, U., Willcox, M. and Stapleton, F., 2012. Osmolality and tear film dynamics. *Clinical and Experimental Optometry*, *95*(1), pp.3-11.

Sweeney, D.F., Millar, T.J. and Raju, S.R., 2013. Tear film stability: a review. *Experimental eye research*, *117*, pp.28-38.

Willcox, M.D., Argüeso, P., Georgiev, G.A., Holopainen, J.M., Laurie, G.W., Millar, T.J., Papas, E.B., Rolland, J.P., Schmidt, T.A., Stahl, U. and Suarez, T., 2017. TFOS DEWS II tear film report. *The ocular surface*, *15*(3), pp.366-403.

www.nei.nih.gov. (n.d.). *How Tears Work | National Eye Institute*. [online] Available at: https://www.nei.nih.gov/learn-about-eye-health/healthy-vision/how-eyes-work/how-tears-work.

Xu, K.P. and Tsubota, K., 1995. Correlation of tear clearance rate and fluorophotometric assessment of tear turnover. *British journal of ophthalmology*, *79*(11), pp.1042-1045.

APPENDICES

Ocular Surface Disease Index

A. Have you experienced any of the following during the last week:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty? (feeling sand is in the eyes)	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision? (Image not clear enough)	4	3	2	1	0
5. Poor vision? (Barely see things)	4	3	2	1	0

Subtotal score for answers 1-5

_____

B. Have your eyes limited you in performing any of the following during the last week:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer /phone or ATM?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 69 _____

C. Have your eyes felt uncomfortable in any of the following situations during the last week:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places with low humidity (very dry)?	4	3	2	1	0	N/A

12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 -12 _____

D. Add subtotals of A, B, and C (Sum of scores from all questions answered)_____

E. Total Number of questions answered (do not include questions answered n/a)_____

OSDI SCORE_____

RAW DATA COLLECTED FROM PARTICIPANTS FOR HYPROMELLOSE GROUP

GENDER	**AGE**	**OD: VA (6M)**	**OS:VA (6M)**	**OD: VA (40 CM)**	**OS: VA (40 CM)**	**OSDI SCORES**	**SCHIRMER'S TEST**
female	60	6/36	6/24	N12	N12	31.81	9.00
male	39	6/5	6/12	N6	N6	14.50	13.00
female	45	6/6	6/9	N12	N12	47.22	5.00
female	42	6/5	6/6	N6	N6	25.00	11.00

male	49	6/9	6/12	N8	N8	20.45	10.00
female	47	6/5	6/6	N10	N10	55.56	7.00
female	65	6/18	6/18	N10	N10	64.58	4.00
male	45	6/5	6/6	N10	N10	36.36	9.00
male	45	6/4	6/7.5	N12	N12	50.00	6.00
female	21	6/9	6/7.5	N5	N5	31.81	10.00
male	55	6/6	6/7.5	N10	N10	20.45	10.00
male	61	6/36	6/36	N12	N12	45.45	5.00
female	60	6/18	6/18	N18	N18	22.22	11.00
male	58	6/12	6/12	N12	N12	38.63	9.00
female	59	6/4	6/9	N12	N12	13.64	12.00
male	39	6/12	6/12	N14	N14	27.27	10.00
female	33	6/6	6/6	N8	N8	58.33	1.50
female	48	6/36	6/24	N12	N12	36.50	10.00
male	48	6/5	6/12	N6	N6	36.77	7.00
male	48	6/6	6/9	N12	N12	36.50	6.50
male	48	6/5	6/6	N6	N6	37.02	10.00
female	48	6/9	6/12	N8	N8	37.15	12.00
male	48	6/5	6/6	N10	N10	37.50	7.00
female	48	6/18	6/18	N10	N10	35.50	7.00
male	48	6/5	6/6	N10	N10	37.50	12.00
male	47	6/4	6/7.5	N12	N12	37.66	6.00
female	47	6/9	6/7.5	N5	N5	37.78	10.00

female	47	6/6	6/7.5	N10	N10	37.92	10.00
male	47	6/36	6/36	N12	N12	38.04	8.00
female	47	6/18	6/18	N18	N18	38.10	13.00
male	47	6/12	6/12	N12	N12	38.29	12.00
male	47	6/4	6/9	N12	N12	38.42	8.00
female	47	6/12	6/12	N14	N14	38.51	8.00
female	47	6/6	6/6	N8	N8	38.65	11.00
male	49	6/18	6/4	N8	N8	41.46	1.00
Female	48	6/5	6/6	N14	N14	62.50	2.00
female	22	6/12	6/18	N6	N6	65.00	5.00
male	49	6/12	6/12	N14	N14	27.00	10.00

FTBUT (OD)	**FTBUT (OS)**	**OSDI SCORES AFTER**	**SCHIRMER'S TEST AFTER**	**FTBUT (OD) AFTER**	**FTBUT (OS) AFTER**
5	6	25.65	9.00	6	6
9	7	11.50	13.50	9	8
3	4	39.52	5.90	4	5
8	8	21.92	11.00	9	7
9	8	13.40	10.50	9	8
5	2	43.50	7.00	6	3
3	3	44.80	4.00	4	5
6	7	31.96	9.50	6	8
5	7	44.40	7.00	5	8

9	8	27.80	9.00	9	8
7	7	15.45	11.00	8	6
2	4	28.45	4.00	3	6
6	5	10.65	11.00	7	6
6	8	31.62	9.00	6	8
9	10	8.54	12.00	10	11
8	8	21.57	11.00	8	9
3	4	38.30	2.00	4	6
8	7	15.50	10.50	8	7
6	6	12.65	8.00	7	6
5	7	25.50	6.00	7	8
7	5	19.02	11.00	8	5
9	8	22.57	12.00	9	8
8	8	21.90	7.50	8	8
8	7	15.50	7.00	9	7
6	7	27.00	12.50	7	7
9	7	22.61	6.00	8	8
8	9	19.80	9.50	8	9
7	6	22.24	10.00	7	7
7	5	24.98	8.50	6	6
6	8	27.71	12.00	8	8
7	9	19.97	12.00	7	9
5	7	23.94	8.00	6	8

8	6	31.61	9.00	8	7
5	8	26.60	11.50	6	8
5	3	39.67	2.50	5	5
3	3	59.50	2.00	3	4
3	2	55.00	4.50	2	4
8	8	21.97	11.00	8	9

RAW DATA COLLECTED FROM PARTICIPANTS FOR REFRESH GROUP

GENDER	**AGE**	**OD: VA (6M)**	**OS:VA (6M)**	**OD: VA (40 CM)**	**OS: VA (40 CM)**	**OSDI SCORES**	**SCHIRMER'S TEST**
male	47	6/5	6/6	N10	N10	29.55	10.00
female	57	6/9	6/12	N12	N12	62.50	6.00
male	48	6/6	6/6	N10	N10	13.64	11.00
male	61	6/12	6/18	N10	N10	25.00	10.00
female	54	6/36	6/36	N10	N10	25.00	9.00
female	40	6/9	6/9	N6	N6	18.45	13.00

female	44	6/24	6/24	N10	N10	25.00	14.00
female	69	6/18	6/12	N14	N14	31.81	9.00
male	46	6/18	6/18	N14	N14	15.00	12.00
male	46	6/5	6/5	N12	N12	16.67	11.00
female	31	6/24	6/15	N6	N6	39.29	10.00
female	48	6/6	6/12	N8	N8	25.45	12.00
female	41	6/36	6/36	N10	N10	25.25	11.00
male	48	6/7.5	6/9	N12	N12	29.55	9.00
female	40	6/5	6/6	N10	N10	22.22	13.00
female	45	6/9	6/12	N12	N12	25.25	10.00
male	39	6/18	6/18	N14	N14	39.58	11.50
male	19	6/5	6/12	N5	N5	30.00	11.00
female	52	6/18	6/18	N12	N12	20.45	14.00
female	49	6/7.5	6/9	N12	N12	49.55	6.50
male	65	6/18	6/18	N10	N10	52.50	4.00
female	20	6/7.5	6/7.5	N5	N5	39.45	12.00
male	40	6/5	6/5	N12	N12	63.89	3.00
female	58	6/18	6/18	N8	N8	50.55	7.00
male	19	6/36	6/36	N6	N6	45.55	6.00
male	39	6/7.5	6/18	N6	N6	25.00	10.00
male	52	6/4	6/9	N10	N10	15.45	13.00
male	50	6/12	6/12	N10	N10	22.22	10.00
male	39	6/6	6/6	N18	N18	15.45	13.00

male	44	6/7.5	6/6	N12	N12	15.45	13.00
female	29	6/18	6/6	N6	N6	25.00	12.50
female	33	6/4	6/4	N6	N6	50.55	2.00
male	46	6/18	6/12	N14	N14	65.63	1.00
female	25	6/18	6/18	N5	N5	20.45	11.00
male	52	6/12	6/12	N10	N10	21.22	14.00
female	43	6/4	6/9	N12	N12	37.05	12.00
Female	48	6/5	6/6	N14	N14	62.50	2.00
female	22	6/12	6/18	N6	N6	65.00	5.00
male	49	6/12	6/12	N14	N14	27.00	10.00

FTBUT (OD)	**FTBUT (OS)**	**OSDI SCORES AFTER**	**SCHIRMER'S TEST ATER**	**FTBUT (OD) AFTER**	**FTBUT (OS) AFTER**
7	5	17.45	10.00	8	6
7	8	46.65	6.50	7	9
8	8	7.43	10.50	11	9
6	5	12.76	11.00	7	5
7	8	17.77	9.00	7	9
9	11	8.95	13.00	12	14
6	8	15.88	14.50	7	6
6	6	21.51	9.00	8	7

10	8	8.99	12.50	12	9
9	7	11.07	12.00	10	8
8	7	20.19	10.00	8	7
7	7	16.38	12.50	9	9
7	5	14.24	11.00	8	8
6	6	18.25	10.00	7	9
10	8	18.00	13.50	13	9
8	9	20.05	10.00	8	10
5	8	22.87	12.00	7	7
8	8	19.39	11.50	6	8
7	8	10.55	13.00	9	9
2	4	31.72	7.50	3	6
2	3	30.91	4.00	4	3
5	1	22.65	12.00	5	2
1	2	45.79	4.00	3	3
2	1	43.61	7.50	5	2
4	5	28.09	6.00	7	6
8	7	10.98	11.00	8	8
8	9	6.89	14.00	7	11
9	7	14.22	11.00	10	8
9	6	5.45	14.50	10	10
10	10	3.93	14.00	12	14
7	7	15.00	13.00	8	7

4	1	42.55	2.00	4	3
1	2	51.60	1.00	2	5
7	5	11.45	11.00	7	6
6	5	12.52	14.00	8	6
3	3	29.05	12.00	4	5
9	9.92	11.50	9	11	
3	3	44.80	4.00	4	5