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A COMPARISON OF FIBRIN GLUE WITH SUTURES FOR CONJUNCTIVAL AUTOGRAFTS IN PTERYGIUM EXCISION SURGERY

Lara Sandri

A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Ophthalmology

Johannesburg 2015

DECLARATION

I, Lara Sandri, declare that this dissertation is my own work. It is being submitted for the degree of Master of Medicine in Ophthalmology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or at any other university.

_____

____25th___day of __May__2015

The work reported in this dissertation was carried out at the St John Eye Hospital, Soweto, South Africa. This is the Ophthalmology Unit of the Division of Ophthalmology, Department of Neurosciences of the University of Witwatersrand, situated adjacent to Chris Hani Baragwanath Academic Hospital.

The project was approved by the Human Research Ethics Committee (Medical), University of the Witwatersrand.

Clearance Certificate number: M120242

DEDICATION

To my loving husband – for all his support, understanding, encouragement and unconditional love. Thank you for so often sharing me with my second love: Ophthalmology.

PRESENTATIONS ARISING FROM THIS STUDY

Presentation at the Ophthalmological Society of South Africa (OSSA) Congress in Cape Town, South Africa, March 2013.

Title: A comparison of fibrin glue with sutures for conjunctival autografts in pterygium excision surgery.

Presenter: Lara Sandri

ABSTRACT

Objectives: To assess post-operative patient comfort and graft success following conjunctival autografts with sutures compared with Tisseel glue for pterygium surgery, and to identify which procedure was the more cost-effective surgical option.

Design and Methods: A prospective randomized comparison of 60 patients undergoing primary pterygium surgery at St John Eye Hospital between April 2012 and September 2012. A post-operative comfort scale was used to assess foreign body sensation, sensitivity to light, tearing and itchiness. Graft success was defined as a graft that was still adherent at one month following surgery.

Results: Patients in the Tisseel glue group experienced significantly less foreign body sensation (p=0.038) and itchiness (p=0.018) on day-one after surgery, compared to those in the suture group. At one-month follow-up patients had significantly less foreign body sensation (p=0.042), sensitivity to light (p=0.001), and itchiness (p=0.009) in the Tisseel glue group compared to the suture group. Autograft adherence was seen in all 60 patients at the one-month follow-up visit. Both the surgical time and the indirect costs of the procedure were reduced in the Tisseel glue group.

Conclusions: The use of Tisseel glue for attaching autografts in pterygium surgery is an effective method with global autograft success, less post-operative discomfort and shorter operating times.

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CHAPTER 1

This chapter addresses the research question and aims, its importance and the justification for the study. A brief background of the topic is described, as well as a literature review on the important points regarding this condition and existing research in the field.

INTRODUCTION

A pterygium is a triangular-shaped conjunctival growth that extends onto the cornea, and is usually located nasally.[1] Surgery is commonly used to treat this condition. Pterygium surgery involves excision of the pterygium, and the harvesting of a conjunctival graft from the same eye, which is then placed over the defect. The graft, known as an autograft, is either sutured or opposed with fibrin glue. This study has assessed whether one technique is superior to the other when comparing the patient's post-operative comfort and graft adherence.

1.1 Problem Statement

Pterygium surgery utilizes extensive operating theatre and outpatient resources. The use of a corneal adhesive rather than sutures might reduce theatre time and outpatient visits allowing this time to be better allocated to sight-saving surgery.

1.2 Justification for The Study

Patients with pterygia are frequently seen at St John Eye Hospital, in Soweto, South Africa; and they often require surgery. We currently follow a surgical technique that uses sutures to secure the graft. This is believed to cause significant patient discomfort post-

operatively when compared to the alternative of using fibrin glue. This study has explored whether patients undergoing pterygium surgery at this institute experienced any significant differences in their levels of post-operative discomfort when comparing the two surgical techniques.

1.3 Background and Literature Review

1.3.1 Anatomy and Physiology

The eye is composed of several layers – with the outermost layers consisting of the cornea and sclera and a conjunctival layer covering the sclera. The cornea is the most anterior portion of the globe; and it is responsible for refracting incoming light onto the back of the eye. The cornea is composed of five different layers: the outer epithelium; Bowman's membrane; the stroma; Descemet's membrane and the inner endothelium. The cornea is nourished, protected and kept moist by a constant tear film, which is distributed over the smooth regular surface of the cornea every time a person blinks. A pterygium is a conjunctival growth that extends from the nasal conjunctiva over the limbus and onto the cornea.[1,2] As a pterygium grows towards the centre of the cornea (visual axis), it may interfere with the tear-film stability of the eye resulting in a dry eye.[3] Pterygia may compromise a patient's vision by growing into the visual axis of the cornea or by altering the curvature of the cornea (astigmatism), thereby affecting the refraction of light onto the back of the eye.[4]

1.3.2 Pathogenesis and Clinical Features

The aetiology of pterygia has intrigued researchers for centuries. It appears that a "pterygium belt" of 37 degrees latitude either side of the equator highlights areas with

higher prevalence rates of pterygia.[2,5] In these hot climates, patients are exposed to chronic dryness, ultraviolet (UV) radiation, wind and dust, all of which seem to play a role in the development of pytergia.[1-3,6,7] Research shows that chronic (UV) B radiation may induce cellular changes at the nasal limbus, the area of the eye most likely to be a focal point of any incoming light.[2,6,7]

Population-based studies show independent associations of pterygium prevalence, and these include living in rural areas, increasing age, male sex and outdoor work.[2,4,5,6,7] A hereditary influence on pterygium formation has also been recognized; and a possible genetic predisposition has been reported in both white and black Africans.[8,9]

Several classifications for pterygia exist – ranging from how fleshy and injected the lesion is – to how far it extends onto the cornea. For the purpose of this study, pterygia will be classified clinically as grade 1, 2 or 3 based on the size of the pterygium. This system was adapted from an article by Popat *et al.*[10]

Table 1.1 Clinical grading system of pterygia and associated complications[10]

Grade	Extent	Complications
I	<2mm onto the cornea	Usually asymptomatic. Occasionally becomes red, inflamed and uncomfortable.
II	2-4mm onto the cornea	Distorts the corneal topography. Induces with or against the rule of astigmatism.[4,10] Often inflamed.
III	>4mm onto the cornea	Involves the visual axis.[4,10] Can extend into the conjunctival fornices and limit ocular motility.

1.3.3 Management

Although topical anti-inflammatory and lubricant drops may temporarily reduce the redness and patient discomfort, surgical excision appears to be the treatment of choice for pterygia.[11] The indications for surgery include visual impairment and the restriction of ocular movements, chronic inflammation and discomfort, and also for cosmetic reasons.[11] Surgery should also be considered in pterygia with an unusual appearance, as they may represent a masquerading condition, such as malignancy.[11]

Several surgical techniques are recognized in the treatment of pterygia. Techniques, such as the simple excision leaving bare sclera, or excision and primary closure with conjunctival sutures; but these are seldom used because of high recurrence rates.

Bare Scleral Closure: "Bare scleral closure as a technique generally implies the removal of the pterygium with excision of some of the bulbar conjunctiva nasally, leaving the defect to heal from the surrounding conjunctiva. Occasionally, the conjunctiva may be sutured to the sclera; while at other times, the conjunctiva is left free to adhere to the underlying sclera".[11] Although this is one of the older surgical options, bare scleral closure is commonly used in conjunction with adjunctive therapy, including mitomycin, beta-irradiation, and thiotepa.[11]

Bare scleral closure without adjunctive therapy is by far the fastest method of removal; and it requires minimal skill; however, the disadvantage is the unacceptably high recurrence rates of 11% to 80%.[11,12]

Simple Conjunctival Closure: There is a paucity of literature regarding this technique. It involves a conservative pterygium tissue excision, and then apposition of the remaining conjunctiva with sutures to cover the sclera.[11] This technique appears not to be very promising, as recurrence rates range from 45% to 70%.[11]

***Sliding Conjunctival Flaps*:** Many texts describe the use of a sliding conjunctival graft after pterygium excision, using either the inferior or superior conjunctiva. The merits include the flap maintaining its original blood supply with minimal complications.[11]

Conjunctival Autograft: This technique gained popularity in the 1980s; and involves the excision of the pterygium, leaving a small area of bare sclera, which is closed by using a free conjunctival graft from another area of the bulbar conjunctiva.[11,14] Several prospective studies have looked at the rates of recurrence using this technique; and they show results as low as 2%.[11] This method of surgery attempts to reconstruct the normal anatomy of the

limbus, resulting in a better cosmetic outcome, and lower rates of recurrence, compared with other techniques.[11]

Traditionally, the graft would be fixed using sutures, which requires a high degree of surgical expertise and carries the risk of suture-related complications, such as suture granulomas (mass of granulation tissue), abscess formation, tissue necrosis (cell death) and giant papillary conjunctivitis.[13] Other disadvantages include prolonged surgery time and post operative foreign body sensation and discomfort.[13,14]

An upregulation in the inflammatory response around vicryl sutures in the conjunctiva seems to be responsible for these adverse events;[15] therefore, by replacing sutures with fibrin glue it might be expected that the graft would adhere; and the post-operative discomfort and other complications associated with the suture material might be alleviated.

The use of Tisseel fibrin glue in pterygium surgery was first reported in 1993 by Cohen and McDonald.[16] Nieuwendaal *et al.* in 2006 described replacing absorbable sutures with fibrin glue to attach conjunctival autografts during pterygium surgery.[17] Tisseel fibrin glue (Baxter, USA) is a two-component fibrin sealer, which when combined has haemostatic, adhesive, sealant and wound-support properties.[18] It seems reasonable to try to replace the sutures with an adhesive (fibrin glue) that can be applied to the surface of the eye – not only to secure the graft – but to limit the patient's discomfort.

Recently, Srinivasan *et al*. completed a prospective observer-masked clinical trial, showing that conjunctival grafts secured with fibrin glue are as stable as those secured with sutures and they also produced significantly less inflammation.[19] Bahar *et al*. utilized a self-report questionnaire to compare the level of patient discomfort following pterygium surgery when using either fibrin glue or sutures. They found a significantly lower score for patient

discomfort and pain in the fibrin group.[20] The symptoms reported on included: average pain, sensitivity to light, foreign body sensation, irritation, tearing, itching and redness.[20] This study also showed that operating times were reduced, when using the glue; and that patients in the fibrin group reported far better overall satisfaction than those in the suture group.[20] These outcomes had an impact on the success of pterygium surgery; and they were beneficial to both patient and doctor.[20]

Adjunctive Therapy: Mitomycin C, beta irradiation, and thiotepa are considered as principal medical adjunctive therapies in pterygium surgery to prevent recurrence.[11,21] Recently, the use of bevacizumab intra-operatively as an adjunctive has also been described.[22]

Beta-irradiation has been used predominantly for several years after bare sclera removal; but the outcomes of this adjunctive therapy have, unfortunately, been poorly reported in the literature. Complications following beta radiation, although rare, do exist. These include corneal or scleral melting and endophthalmitis, complications, which probably would not warrant its use in a disease, such as pterygium.[23]

Thiotepa is another adjunctive administered – usually after bare sclera closure – in the form of topical drops for approximately six weeks.[11] This therapy has been used for about as long as beta-irradiation; and it is also poorly reported on in the literature.

Mitomycin C is commonly used in pterygium surgery, both intra- and post-operatively.[21] The main objective with pterygium surgery is to prevent recurrence, which autologous free grafts and concurrent mitomycin C seem to promise.[21] A dose of 0.02% is applied for between 2.5 minutes to 3 minutes during surgery, usually when employing the bare sclera closure or conjunctival closure techniques.[11,21,24] The recurrence rates with intra-operative

mitomycin C appear to be low. A study looking at the long-term follow-up of low-dose intra-operative mitomycin C, compared to conjunctival autografts, showed recurrence rates of 14.3% and 5%, respectively.[24]

Other studies report 3% to 39.7% recurrence rates with the use of intra-operative mitomycin C.[21] Complications of the use of both intra-operative and post-operative mitomycin C with bare sclera and conjunctival closure techniques include scleral ulceration and delayed conjunctival epithelialization.[25] Higher rates of complications are seen with longer exposure times and increased concentrations of mitomycin C.[25]

Post-operative dosages of mitomycin C are still under debate; while we await studies, which report on the long-term follow-up of these patients. A dose of 0.02% daily for two weeks appears to have favourable outcomes showing low recurrence rates.[11]

The American Academy of Ophthalmology recently reported on a literature review of 51 studies with at least 6 months follow-up times, describing the options and the adjunctives in pterygium surgery.[25] Bare sclera excision had higher recurrence rates than the same technique with adjunctive therapy.[25] Autografts had lower recurrence rates than amniotic membrane grafts.[25] The addition of mitomycin C, combined with autografts, further reduced the risk of recurrence of pterygia, when compared to the use of mitomycin C alone, or an autograft without mitomycin C.[25]

A novel approach of using the patient's own blood (autologous blood) to fixate the graft has been suggested in the literature. This would mean no glue and no sutures; and this technique carries several cost and comfort advantages. However, randomized control trials have not been performed as yet.[26]

1.3.4 Cost-Effectiveness

The term cost-effectiveness is very often confused with monetary costs; but rather it compares the costs and health effects of an intervention to assess the extent to which it can be regarded as providing value for money.[27] Analysing the cost-effectiveness of a product or procedure allows decision-makers to determine where to allocate limited healthcare resources.[27] Uy *et al*. reported a significantly shorter operating time, a far less surgically challenging procedure, and a less expensive material, when using the glue instead of sutures.[14] The variables above contribute to the cost-effectiveness of this procedure; and they need to be considered when embarking on pterygium surgery.

Pterygia are a common occurrence; and they frequently require surgery. At our institution, sutures are used to secure the autograft. The use of suture material requires a high degree of surgical expertise; and it may lead to suture-related complications and post-operative eye discomfort. Eye discomfort or pain is typically divided into the following parameters: foreign body sensation, sensitivity to light, tearing and itchiness.[14] In an attempt to alleviate this discomfort, and to provide patients with a less painful recovery – without compromising on autograft success – the use of a fibrin glue needed to be explored at our facility.

1.4 Research Aim

The aim of this study was to compare post-operative patient comfort and graft success following conjunctival autografts for pterygium surgery when using vicryl sutures compared to Tisseel fibrin glue.

1.5 Research Objectives

The primary objective of this study was to compare vicryl sutures and Tisseel fibrin glue for autografts in pterygium surgery, and to establish whether there is any significant difference between the vicryl sutures and Tisseel glue, when assessing post-operative patient comfort and graft success.

The secondary objective of this study was to identify whether Tisseel fibrin glue is a more cost-effective surgical option than the use of sutures.

1.6 Hypothesis

Tisseel fibrin glue used in pterygium excision surgery to secure the autograft would leave the patient more comfortable post-operatively, while still allowing for autograft adherence.

CHAPTER 2

This chapter will discuss the methodology of the study, including the study design, the study population, and the method and materials used for data collection. A description of the surgical procedure and post-operative management will be mentioned, followed by how the data analysis was completed. Both ethical considerations and the issue of the sponsorship of Tisseel fibrin glue will be addressed.

METHODOLOGY

2.1 Study Design

This prospective randomized comparative study included 60 patients undergoing primary pterygium excision surgery at St John Eye Hospital, Soweto.

2.2 Study Population

Patients with pterygia were selected on presentation to the hospital and assigned a number. The patients were numbered from 1 to 60, in the order of presentation; odd numbers were assigned to the Tisseel glue group and even numbers to the suture group.

Inclusion criteria:

- Grade I, II and III pterygia;
- Age >18 years of age;
- No previous pterygium surgery.

Exclusion criteria:

- Patients <18 years of age;
- History of eye trauma or pseudo-pterygium;
- Intra-ocular and local disease.

2.3 Pre-operative Assessment

A pre-operative interview was conducted to obtain a detailed history of the complaint. A slit lamp examination was performed to determine the pterygium size in millimetres, by measuring from the limbus to the corneal limit of the growth in the horizontal plane. The pterygium was to be graded as follows: Grade I pterygia extend less than 2mm onto the cornea; grade II pterygia extend 2mm to 4mm onto the cornea; and grade III pterygia extend more than 4mm onto the cornea.

The patient was examined to exclude any ophthalmic infection, local or uncontrolled systemic disease or infection.

2.4 Informed Consent

Informed consent was obtained pre-operatively from all the eligible patients, and from all those who were willing to participate in the study. The standardized information sheet (Appendix A) and consent form (Appendix B) were printed in English. If necessary, a translator from the nursing staff assisted in obtaining this consent in the patient's first language. Once the patient had agreed to be enrolled in the study, he/she was randomized into one of two groups, as mentioned above. The patients were not informed as to which group they belonged.

2.5 Tisseel Glue Preparation

The Tisseel Kit 1.0ml (Baxter) was mixed by the same Ophthalmology registrar (LS) ten minutes prior to starting with the first surgical case. The following steps were carried out routinely:

The Fibrinotherm heating device was turned on at the amber switch and allowed to heat up to a temperature of 37 degrees Celsius.



Figure 2.1: The Fibrinotherm heating and mixing device

Four vials from the box; two blue-topped, one black-topped and one silver-topped vials (select Thrombin 4 not 500 for pterygium surgery), were placed in their wells, and allowed to heat for a few minutes.



Figure 2.2: The different Tisseel Kit vials required for mixing



Figure 2.3: The different vials in their respective heating and mixing wells

Once heated, the blue-scaled syringe was used to withdraw the entire volume of the fibrinolysis inhibitor (blue top) and injected into the sealer protein concentrate vial.

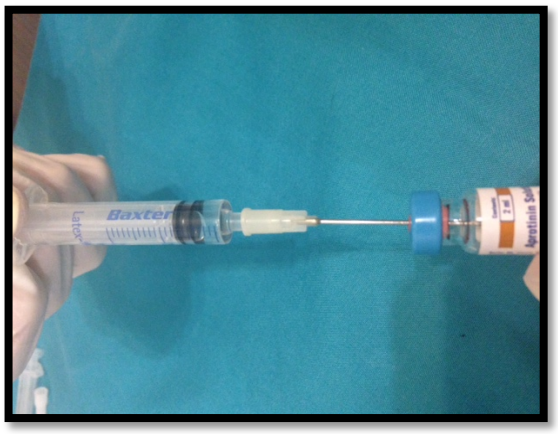


Figure 2.4: Withdrawing the fibrinolysis inhibitor



Figure 2.5: Injecting the fibrinolysis inhibitor into the sealer protein vial

This combination was placed into the stirring well; and the mixer was turned on at the green switch, allowing the solution to mix for 5 minutes to 15 minutes.



Figure 2.6: Turning on the green switch to activate the magnetic stirring well

During this time, the black scaled-syringe was used to withdraw the calcium chloride from the black-topped vial. This was then injected slowly into the thrombin 4 vial and swirled around gently, taking care not to invert the bottles at any time.

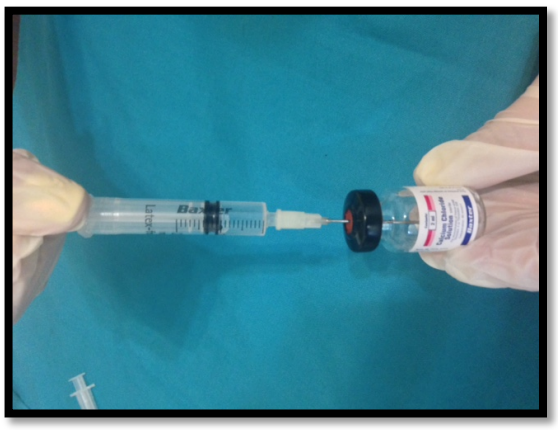


Figure 2.7: Withdrawing the calcium chloride



Figure 2.8: Injecting the calcium chloride into the thrombin vial

At this point, the duploject was opened for the scrub sister onto a sterile field, along with both black and blue-scaled syringes and their needles.

The contents of the blue and black vials were separately aspirated with their respective blue and black syringes and loaded into the duploject.



Figure 2.9: Assembly of the duploject

2.6 Surgical Procedure

The operations were carried out by a senior ophthalmic surgeon (KA) and an ophthalmology registrar (LS) in the ophthalmology theatres at St John Eye Hospital,

Soweto. Peribulbar anaesthesia with bupivicaine 0.5% and a solution of lignocaine 2%, mixed with hyalase on the day of the surgery, was performed by the ophthalmology registrar. A drop of 5% povidone was instilled in the eye after the local anaesthesia had taken effect; and this was done to prevent any post-operative infections. The involved eye underwent standardized ophthalmologic sterile preparation and draping.

All pterygia excisions were performed under an operating microscope, with a lid speculum to expose the surgical site. The surgical time was recorded from placement of the lid speculum to its removal at the end of the procedure. The apex of the pterygium, which is the part that inserts onto the cornea, was dissected off the cornea up to the limbus – using a crescent blade, and taking care to maintain the surgical plane of the pterygium. Blunt dissection was performed to separate the remaining portion of the pterygium from the underlying sclera.

The next step involved harvesting a free conjunctival autograft from the superior conjunctiva. The technique, as described by Starck *et al,* was used in this study.[28] After measuring the defect with callipers, following the resection of the pterygium, an oversized graft, measuring at least 1mm (millimetre) greater than the measured area in both width and length, was marked out on the donor site with a sterile gentian violet marker pen. A balanced salt solution was injected, with a 2ml (millilitre) syringe and a 27 gauge needle, very superficially underneath the conjunctiva of the donor site. This was performed to separate this delicate structure from the underlying connective tissue, referred to as Tenon's capsule.

The marked out area was excised to create a free graft, which was then placed on the cornea, taking care not to flip it over; and it was kept moist by irrigating it with a balanced salt solution.

The free graft was placed over the bare sclera, keeping the orientation of the donor site, so that the graft's limbal side would oppose the limbus, once it was secured. Depending on which group the patient had been allocated to, the conjunctival edges of the graft would be sutured to the surrounding conjunctiva, or opposed with glue. The suturing involved four interrupted vicryl 8/0 sutures and only two single knots were tied on each suture, which were not buried. If glue was to be used, the preparation took place before the surgery; and the duploject device was used to apply the glue to the surgical site.

The cannula on the duploject device allowed for placement of the solution on the bare sclera, and thereafter, the graft was positioned over the defect. The glue set in 60 seconds; and the graft's adherence was ensured before removing the lid speculum.

At the end of the procedure, a combination of a steroid /antibiotic ointment, dexamethasone and neomycin (Maxitrol), was applied to the surgical site, and an eye pad with tape (micropore) was used to cover the eye. This pad remained on the eye until the patient was assessed the following day.

All excised pterygium specimens were placed in formalin, and sent to the laboratory for histological evaluation.

2.7 Data Collection

A data-capture sheet (Appendix C), which included an administrative section, demographics, clinical findings, surgery data and a questionnaire, was filed and kept confidential, using the patient's unique study ID number.

Intra-operative entries documented the name of the surgeon, the surgical time, the technique, the reference numbers for the sample sent to the lab, the post-operative

prescription and the follow-up dates. Following surgery, reviews took take place at day-one, and months-one and three post-surgery. During the follow-up visits, several parameters, including patient comfort and graft integrity were assessed. Patients graded their discomfort, based on the following four categories: foreign body sensation, sensitivity to light, tearing and itchiness on an ordinal 4-point scale ranging from 1 to 4.

Autograft success was defined as a graft that was still adherent by the first month follow-up visit. It follows then that any autograft failure would refer to the dehiscence of the graft within the first month.

2.8 Data Analysis

The data was captured in Microsoft Excel 2011 and imported into IBM SPSS Version 20 for further analysis. The first step in the analysis involved the construction of basic frequency and descriptive tables to examine any variations in the data. This predominantly involved inspection of proportions, means, medians, and standard deviations. A p-value of less than 0.05 was indicative of statistical significance during hypothesis testing. Patient comfort was analysed using the Mann-Whitney U test to assess any significant differences in the four dimensions of discomfort across the two surgical methods on day-one, one-month, and three-months post-surgery.

The Mann-Whitney U test is a suitable test when comparing ordinal data, of two non-parametric variables; and it compares the mean ranking of groups. In essence, the scores of the level of discomfort for each group was converted to ranks and the mean rank for each group was then compared. The Kruskal-Wallis test was also utilized for comparing the ordinal data of three or more non-parametric variables. The Chi-Square test of independence was used to assess if proportional distributions were independent across the

categorical variables, such as recurrence rates in the two different surgical groups, recurrence and age, and recurrence and grade of the pterygium.

In the event of few, sparse or unbalanced data, the Fischers Exact test, Monte Carlo Method tests and odd ratios were included.

2.9 Ethical Considerations

Ethical approval was attained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (Appendix D); and permission was obtained from the Medical Advisory Committee Chris Hani Baragwanath Academic Hospital (Appendix E) before starting this project. Tisseel fibrin glue is registered with the Medical Control Council (Appendix F) as a blood fraction, which is used to achieve haemostasis, to seal or glue tissues, and to support wound healing.

2.10 Sponsorship

Adcock Ingram Pharmaceuticals provided the sponsorship of Tisseel fibrin glue and the fibrinotherm mixing device for the duration of this study (Appendix G).

CHAPTER 3

RESULTS

During the period from April 2012 to September 2012, 60 patients were recruited for the study and underwent pterygium surgery at St John Eye Hospital, Chris Hani Baragwanath Academic Hospital, Soweto.

3.1 Patient Demographics

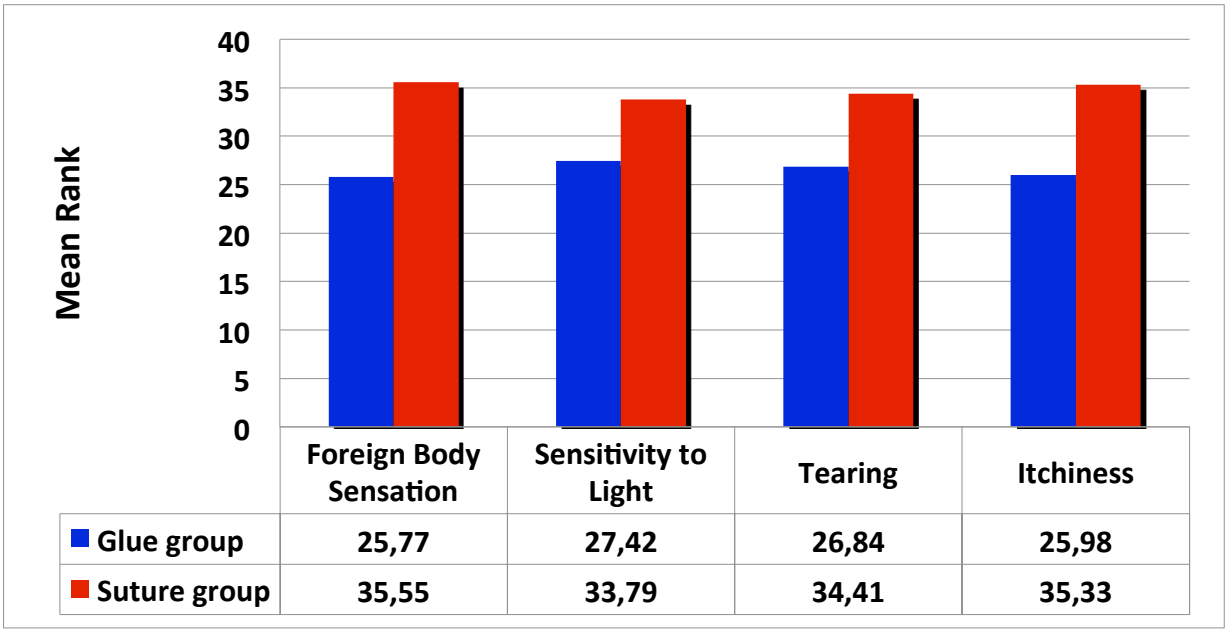
Sixty patients, with a median age of 50 years, were enrolled in the study. Forty-two (70%) were female, 18 (30%) were male and 56 (93.3%) were black African patients.

3.2 Patient Comfort

3.2.1 Tisseel glue compared to sutures

Patients rated their level of discomfort following surgery on a scale of 1 to 4 for foreign body sensation, sensitivity to light, tearing and itchiness, with 1 being indicative of no discomfort, 2 reflecting mild discomfort, 3 for moderate discomfort, and 4 for severe discomfort. The Mann-Whitney U test was used to assess these parameters; the lower the mean rank, the less discomfort the patient had experienced.

Patients in the Tisseel glue group experienced significantly less foreign body sensation and itchiness on the day after surgery, compared to the suture group, with a mean rank of 25.77 versus 35.55 (p=0.038) for foreign body sensation and 25.98 versus 35.33 (p=0.018) for itchiness. Sensitivity to light and tearing showed no statistical difference between the two groups, with mean ranks of 27.42 versus 33.79 (p=0.620) and 26.84 versus 34.41 (p=0.650), respectively.



	Foreign Body Sensation	Sensitivity to Light	Tearing	Itchiness
Glue group	25,77	27,42	26,84	25,98
Suture group	35,55	33,79	34,41	35,33

Figure 3.1: Level of comfort day 1 post-operatively

Similar results were seen at one-month follow-up, with patients in the Tisseel glue group experiencing less discomfort compared to the suture group. Foreign body sensation was statistically lower in the Tisseel glue group compared to the suture group, with a mean rank of 26.40 versus 34.60 (p=0.042), as also were sensitivity to light and itchiness with mean ranks of 24.12 versus 36.88 (p=0.001) and 26.43 versus 34.57 (p=0.009), respectively. The amount of tearing showed no statistical difference between the two groups, showing a mean rank of 29.00 versus 32.00 (p=0.232).

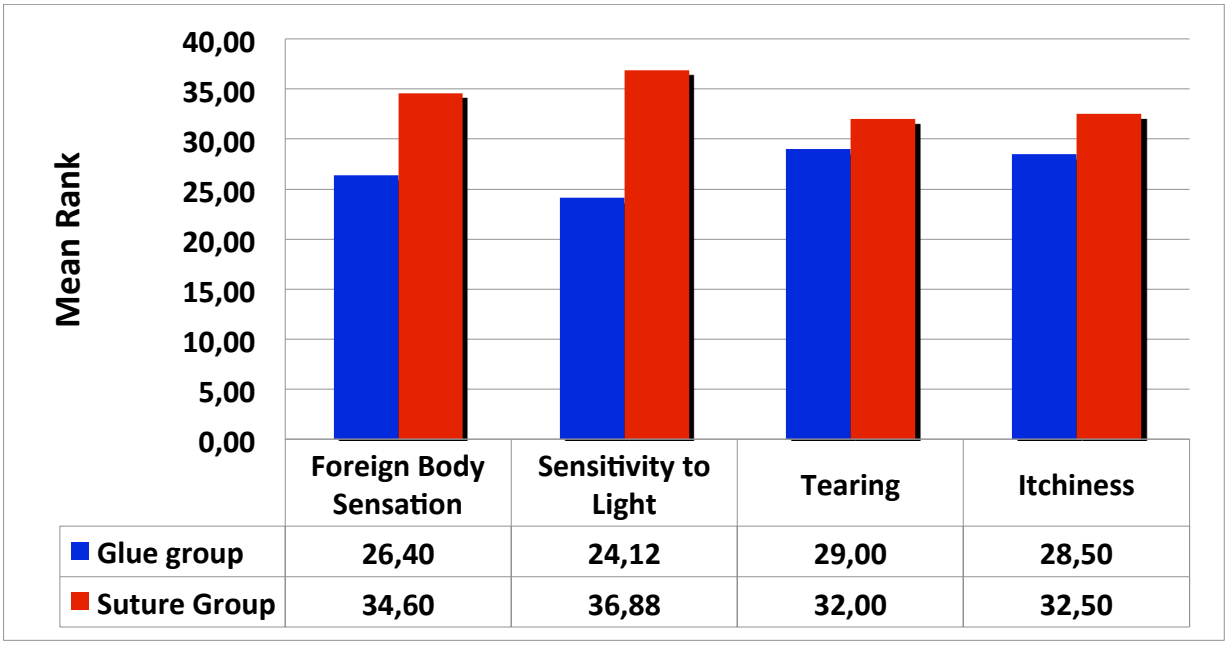
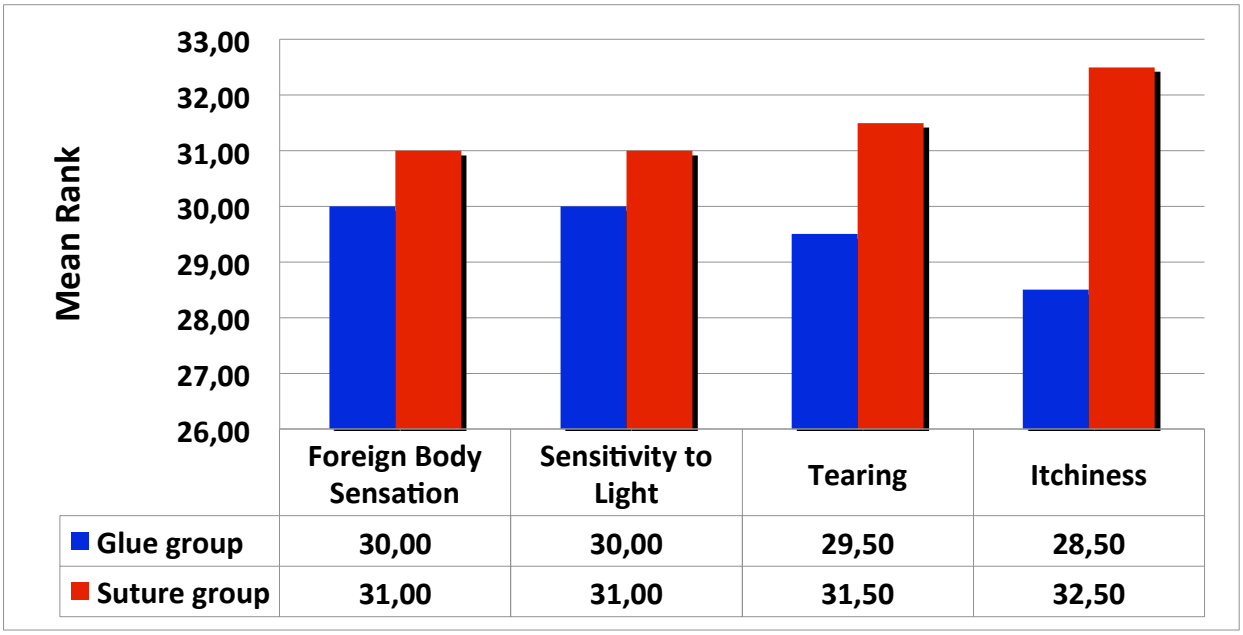


Figure 3.2: Level of comfort 1 month post-operatively

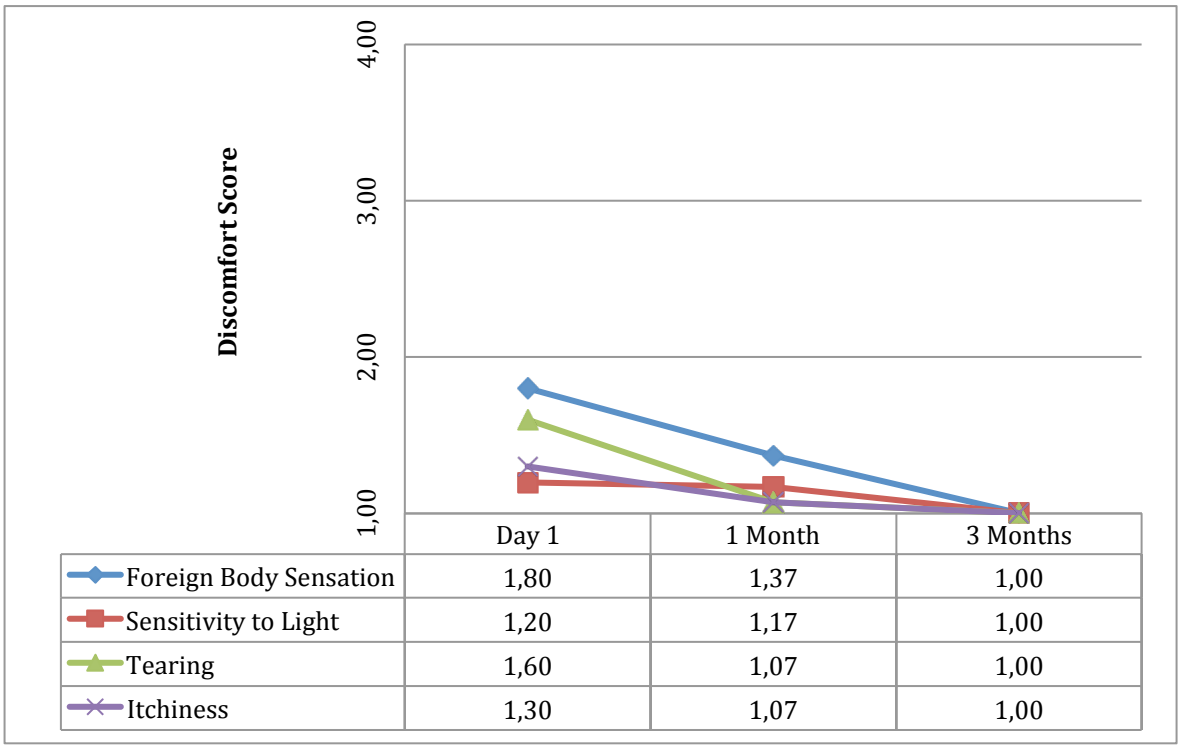
At the three-month follow-up visit, there were no statistical differences between the two groups, when comparing foreign body sensation (mean rank 30.00 vs 31.00, p=0.317), sensitivity to light (mean rank 30.00 vs 31.00, p=0.317) and tearing (mean rank 29.50 vs 31.50, p=0.154). However, the difference in discomfort attributed to itchiness between the two groups proved to be statistically significant, with mean ranks of 28.50 for Tisseel glue group and 32.50 for suture group (p=0.040).



	Foreign Body Sensation	Sensitivity to Light	Tearing	Itchiness
Glue group	30,00	30,00	29,50	28,50
Suture group	31,00	31,00	31,50	32,50

Figure 3.3: Level of comfort 3 months post-operatively

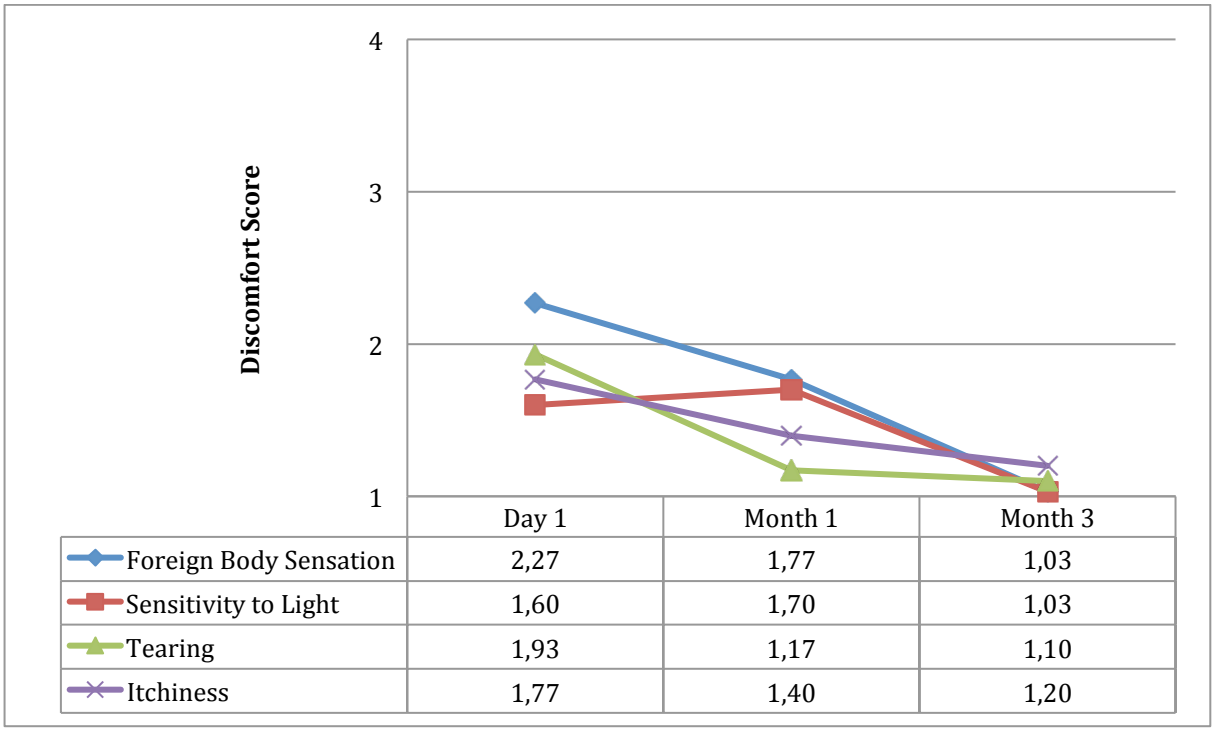
Figure 3.4 demonstrates mean comfort scores over the three-month follow-up period in the Tisseel glue group. The lower the mean value, the less discomfort the patient experienced. When analysing, which dimension of discomfort was the most noticeable, Figure 3.4 shows that foreign body sensation caused the most discomfort day-one, and one-month following surgery, when compared to sensitivity to light, tearing and itchiness.



	Day 1	1 Month	3 Months
Foreign Body Sensation	1,80	1,37	1,00
Sensitivity to Light	1,20	1,17	1,00
Tearing	1,60	1,07	1,00
Itchiness	1,30	1,07	1,00

Figure 3.4: Tisseel glue group - changes in level of comfort on follow-up visits

The Figure 3.5 demonstrates mean comfort scores over the three-month follow-up period in the suture group. Foreign body sensation caused the most discomfort on day-one and one month following surgery.



	Day 1	Month 1	Month 3
Foreign Body Sensation	2,27	1,77	1,03
Sensitivity to Light	1,60	1,70	1,03
Tearing	1,93	1,17	1,10
Itchiness	1,77	1,40	1,20

Figure 3.5: Suture group - changes in level of comfort on follow-up visits

3.2.2 Discomfort and pterygium size

Pterygia were graded clinically (Table 1.1 Clinical grading system of pterygia and associated complications), according to how far they extend onto the cornea. The Kruskal Wallis test was used to ascertain whether the grade of the pterygium would impact on patient comfort following surgical excision; the lower the mean rank, the less the discomfort. However, the numbers of grades I, II and III pterygia were unbalanced and few (grade I= 9 patients, grade II= 34 patients, grade III= 17 patients); and therefore, the Monte

Carlo Test was utilized to show any significant differences in comfort between the different grades of pterygia at all follow-up appointments.

Day one following surgery, the mean ranks for foreign body sensation for grades I, II and III pterygia were: 26.72, 30.37 and 34.56 respectively (p=0.491); sensitivity to light: 27.22, 32.39 and 30.15 respectively (p=0.560); tearing: 23.33, 31.33 and 34.38 respectively (p=0.249); and itchiness: 29.11, 32.02 and 29.88 respectively (p=0.828) [Figure3.6]. Therefore, on day-one following surgery, no significant differences between the level of comfort and pterygium size were noted.

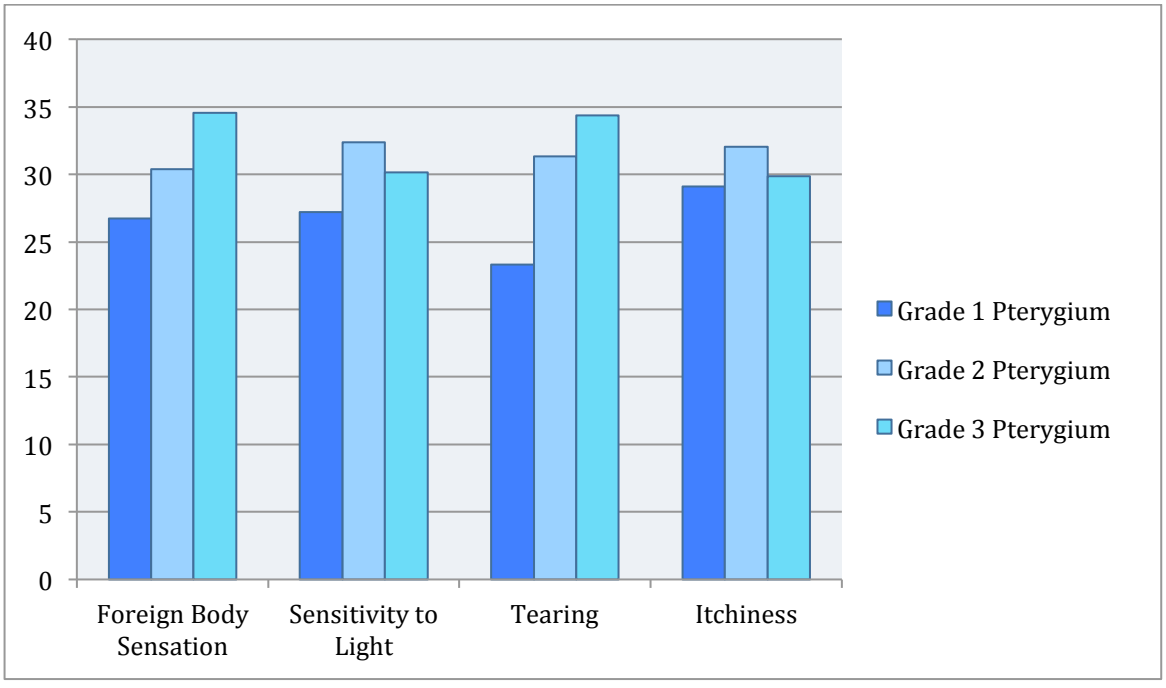


Figure 3.6: Grade of pterygium and level of comfort day 1 post-operatively

One month following surgery, the mean ranks for foreign body sensation for grades I, II and III pterygia were: 34.61, 30.85 and 27.62 respectively (p=0.570); sensitivity to light: 32.33, 31.28 and 27.97 respectively (p=0.676); tearing: 27.00, 32.29 and 28.76 respectively (p=0.285); and itchiness: 27.72, 29,79 and 33.38 respectively (p=0.469) [Figure 3.7]. This shows that one month following surgery, no significant difference between the level of comfort and pterygium size was shown.

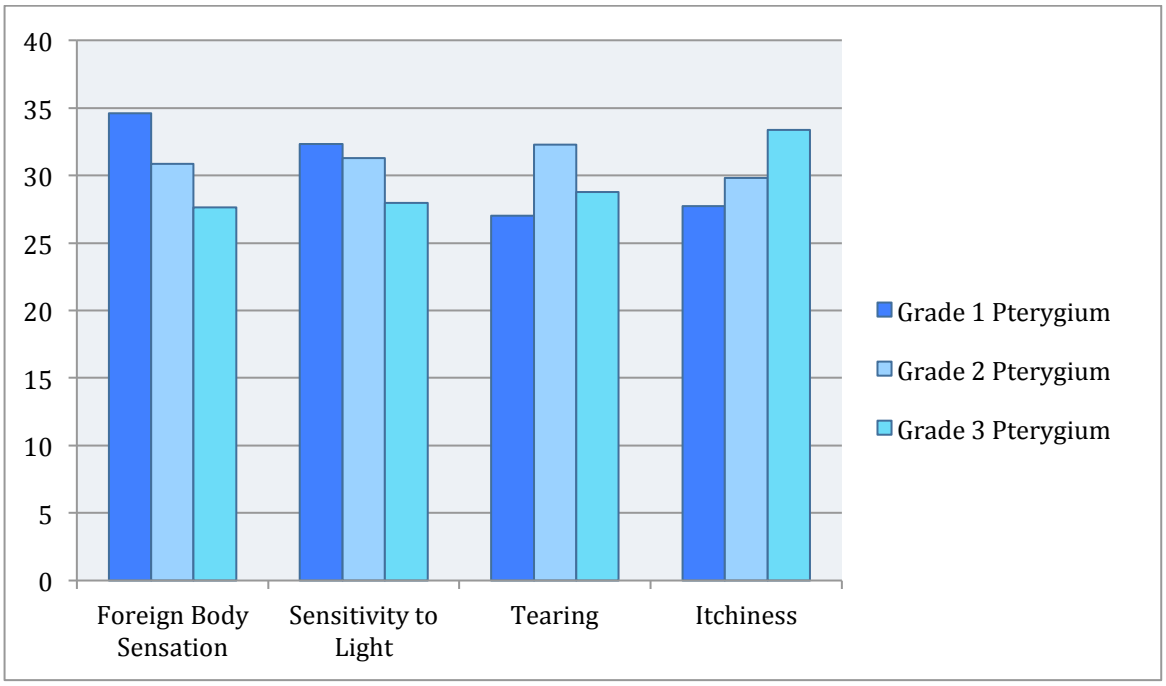


Figure 3.7: Grade of pterygium and level of comfort 1 month post-operatively

It was expected that at three-months follow-up, the grade of the pterygium pre-operatively would still not impact on the patient's level of comfort. At three months, there was no significant difference between the grade of the pterygium and the four dimensions of discomfort: foreign body sensitivity; sensitivity to light; tearing and itchiness, showing p-values of 1.000, 1.000, 1.000 and 0.598, respectively.

3.3 Graft Adherence

Autograft success was defined as a graft that was still adherent and intact at the one-month follow-up visit. This study showed a 100% graft success in both groups of patients on day-one, and at one and three-months follow-up.

3.4 Recurrence

Pterygium recurrences at three months were seen in seven patients (11.7%): four females and three males. Of these recurrences, four (6.7%) patients were from the Tisseel glue group and three (5%) from the suture group of the study. Due to the small study population of 60 patients and the few recurrences seen, Fischer's Exact test was used to demonstrate that there was no statistically significant difference in the rates of pterygium recurrence between the Tisseel glue group and suture group. All the patients with recurrent pterygia were less than 40 years of age.

3.5 Cost-Effectiveness

In this study, the objective costs included Tisseel fibrin glue (Tisseel Kit 1.0H), suture material (vicryl 8-0), and theatre time. The subjective cost would be the patient's level of comfort following the surgical procedure.

3.5.1 Tisseel Glue and Suture Material

Tisseel Kit 1H cost R1850 and was shared among four patients. This equated to a cost of R462.50 per patient if glue was used to secure the autograft.

The alternative material in this study was vicryl 8-0 sutures single arm, at a cost of R204, which could only be used on one patient. Therefore, the cost of the product to secure the

autograft in the suture group was R204 per patient. Other consumables were used during the surgery; but these were consistent with both techniques; and therefore, would equally affect the costs of both procedures.

3.5.2 Surgical Time

The surgical time was recorded from the time the lid speculum was inserted into the eye to the time when the speculum was removed at the end of the surgical procedure. This was recorded on the data-capture sheet. The average surgical time for the Tisseel glue group was 7 minutes and 12 minutes for the suture group. Most institutions bill for every minute that the patient is in the operating room. The average theatre charges approximately R200 per minute that the patient is in theatre.

3.5.2 Surgical Time and Pterygium Size

Pterygia were graded clinically (Table 1.1 Clinical grading system of pterygia and associated complications), according to how far they extend onto the cornea. In both the Tisseel glue group and the suture group, the numbers of grades I, II and III pterygia were unbalanced. Therefore, the Monte Carlo test was used to interpret whether the size of the pterygium impacted on the duration of the surgical procedure. In both the Tisseel glue group and suture groups, the size of the pterygium did not impact on the time of the procedure ($p=0.076$ and $p=0.800$, respectively).

3.5.3 Patient Comfort

Patients in the Tisseel glue group experienced significantly less foreign body sensation and itchiness on the day after surgery compared to the suture group. Similar results were seen at the one-month follow-up, with patients in the Tisseel glue group experiencing less

discomfort compared to the suture group. Foreign body sensation was significantly lower in the Tisseel glue group compared to the suture group, and there was less sensitivity to light and itchiness experienced by patients in the Tisseel glue group at this one-month follow-up visit.

At the three-month follow-up visit, there was no statistical difference between the two groups, when comparing foreign body sensation, sensitivity to light and tearing. However, the difference in discomfort attributed to itchiness between the two groups proved to be statistically significant.

Overall patients in the Tisseel glue group on day-one and one-month following surgery were more comfortable than those in the suture group.

CHAPTER 4

DISCUSSION

This study was conducted at the St John Eye Hospital, Soweto. This is the Ophthalmology Unit of the Division of Ophthalmology, Department of Neurosciences of the University of Witwatersrand situated adjacent to Chris Hani Baragwanath Academic Hospital. This is a referral centre for the greater Johannesburg area.

During the period from April 2012 to September 2012, 60 patients were recruited for the study. The median age was 50 years, 42 (70%) were females, 18 (30%) were male and 56 (93.3%) were black African patients. A female predominance was noted in this study. This finding was in contrast to a study undertaken in Alberton, Gauteng, which showed a male predominance in their 63 white patients with pterygia.[9] This difference in gender predominance between these two studies may be due to the genetic and environmental differences in the two sample populations.

Today, several methods for pterygium surgery are used – from bare scleral techniques to the use of medical and surgical adjunctives.[11,21,25] Pterygium surgery is commonly performed in this institution, using vicryl sutures to secure the autograft. This technique requires a high level of surgical expertise, and also has several disadvantages. These include: prolonged surgery time, the possibility of suture-related complications, such as suture granulomas (mass of granulation tissue), abscess formation, tissue necrosis (cell death), giant papillary conjunctivitis; and importantly, the patient may complain post-operatively of ocular irritation including foreign body sensation, pain, redness and itchiness.[13,14]

An upregulation in the inflammatory response around vicryl sutures in the conjunctiva seems to be responsible for these adverse events.[15] Therefore, by replacing the sutures with Tisseel fibrin glue; it would be expected that the graft would adhere and the post-operative discomfort and other complications associated with the suture material could well be alleviated.

Tisseel fibrin glue is registered with the Medical Control Council (Appendix F) as a blood fraction, which is used to achieve haemostasis, to seal or glue tissues, and to support wound healing. The use of ocular tissue adhesives was proposed in 1963; and in the late 1970s, fibrin adhesives became commercially available in Europe.[18] Their use in Ophthalmology included conjunctival wound closure, cataract surgery, oculoplastic and orbital surgery, repair of leaking blebs, lamellar keratoplasty and amnion patching. The "cut-and-paste" method used by Koranyi *et al.* comprises the use of Tisseel tissue glue to secure the autograft; and it was developed to reduce post-operative patient discomfort, and to reduce surgical time.[29]

Uy *et al.* later also found fibrin glue to be a safe and effective method for attaching autografts, as well as reducing surgical time and post-operative patient discomfort.[14] And more recently, Nieuwendaal *et al.* reported the use of Tisseel glue to be a safe, easy and effective technique for attaching the autograft with low recurrence rates.[17] There have been no studies prior to this one at St John eye Hospital regarding the use of adjunctives in pterygium surgery. The possibility of a safe, easy and effective surgical technique that could reduce patient discomfort, surgical time and costs in our institution was the driving force behind this prospective, randomized, comparative study.

Pterygium excision was performed using the technique described by Starck *et al*.[28] The autograft was adhered with either Tisseel fibrin glue or vicryl sutures. Overall, patients in

the Tisseel glue group on day-one and one-month following surgery were more comfortable than those in the suture group. The conclusion in this study that Tisseel glue significantly reduces post-operative discomfort is consistent with the literature.[13,14,15,17,19,20]

The size or grade of a pterygium is related to the extent to which it encroaches on the cornea; and it was thereby assumed that the greater the surface area of cornea involved in the procedure, the greater the post-operative discomfort. However, in this study, the grade of the pterygium did not impact on the amount of post-operative discomfort at any of the follow-up appointments. This observation was also noted in a study by Bahar *et al.*, where regression analysis failed to show any correlation between pterygium size and discomfort.[20]

Koranyi *et al.* reported no autograft losses or dislocations in their study that compared glue and sutures to attach conjunctival autografts in pterygium excision surgery.[29] In this study, autograft success was defined as a graft that was still adherent and intact at one-month follow-up. This study showed a 100% graft success in both groups of patients; and it highlights the fact that both techniques are effective for securing the autograft in pterygium excision surgery.

Recurrence is a common complication of pterygium surgery; and the success of this surgery is based on avoiding this complication. Recurrence rates vary in the literature, based on the surgical expertise, the surgical technique, and the adjunctives used. Conjunctival autografting, regardless of the material used, following pterygium surgery has been associated with lower recurrence rates of 2% to 9 %.[14] Hirst *et al.* reported a larger variability in recurrence rates of 2% to 39% when using glue-assisted conjunctival autografts.[11] In this study, recurrence was seen in seven (11.7%) patients: four (6.7%) patients in the glue group, and three (5%) in the suture group. These recurrence rates are

consistent with the literature. However, the small sample size and the duration of the follow-up need to be taken into consideration when interpreting the data.

When assessing the cost-effectiveness of a procedure, it is conventional to distinguish between the direct costs and the indirect or productivity costs, associated with the intervention, as well as what are termed intangibles, which, although they may be difficult to quantify, are often consequences of the intervention, and should therefore be included in the cost profile.[27]

Direct Costs: Tisseel fibrin glue, sutures and theatre time.

Productivity Costs: the longer the surgical time, the fewer the number of patients that can be operated on.

Intangibles: Post-operative discomfort (foreign body sensation, tearing, itchiness, sensitivity to light)

Using these simple definitions and equations, it was initially proposed in the protocol for this study that the following equation, Incremental Cost-Effective Ratios (ICER), could be used to calculate the cost-effectiveness of the different techniques.

$$\text{ICER} = \frac{\text{Difference in costs between the 2 techniques}}{\text{Difference in health effects between the 2 techniques}}$$

Costs (numerator) would include the cost of Tisseel fibrin glue, sutures and theatre time; while health effects (denominator) would include post-operative comfort and graft adherence/success. However, retrospectively this is not something that statistics can do. This would involve an equation with various assumptions on how different variables

(objective elements, such as costs; and subjective factors, such as patient comfort) should be weighted, which is beyond the scope of this study.

Rather, each element should be evaluated separately, without combining them into a single best-measure, which would require some form of arbitrary weighting. Therefore, cost effectiveness could not be accurately assessed in this study; however, subjective and objective costs could be compared in a simplified manner. The subjective cost would be the patient's level of comfort following the procedure; while the objective costs would include Tisseel fibrin glue (Tisseel Kit 1.0H), suture material (vicryl 8-0), and theatre time.

As already mentioned, patients in the Tisseel glue group experienced significantly less post-operative discomfort on follow-up when compared with the suture group, which could translate into a reduced subjective cost. Tisseel Kit 1H cost R1850 and the product could be shared between four and ten patients over a period of 4 hours from the time of glue preparation. It would be ideal to operate on ten consecutive patients, in order to reduce material costs; however, this is not always possible; as either there may be too few patients booked on the list, or there would be a need to use the theatre for more urgent surgeries. In this study, the Tisseel glue was shared among four patients. This equates to a cost of R462.50 per patient to use glue to secure the autograft.

The alternative material in this study was vicryl 8-0 sutures single arm at a cost of R204, which could only be used for one patient. Therefore, the cost of the product to secure the autograft in the suture group was R204 per patient. Other consumables were used during the surgery; but these are consistent with both techniques; and therefore, would equally affect the cost of both procedures. This demonstrates how objective costs can be reduced if Tisseel glue is shared amongst several patients.

The average surgical time for the Tisseel glue group was 7 minutes, and 12 minutes for the suture group. This compares to Bahar *et al.* who in their study reported a mean operating time of 16 minutes in the fibrin-glue group and 20 minutes in the suture group.[20] As previously noted, pterygia were graded, based on the size of the growth. In both the Tisseel glue group and suture groups, the size of the pterygium did not impact on the time of the procedure. Bahar *et al.* also failed to show any correlation between pterygium size and surgery time.[20] Most institutions bill per minute that the patient is in the operating room. Therefore, the shorter the procedure, the less costly it is. The average private institution charges approximately R200 per minute that the patient is in theatre. It follows that using Tisseel glue to secure the autograft would reduce this objective cost.

This prospective, randomized comparative study was small in size, and not double-blinded, which could have impacted on the statistical analysis. The evaluation of discomfort was expected to be problematic, as patients may have had variable sensitivities to the same stimulus; and they would, therefore, have reported their experience and level of discomfort differently. However, by categorizing discomfort into four simple dimensions, this variability in reporting was most probably limited.

Of the 60 patients treated, 56 (93.3%) were black African patients. A census in 2011 reported that Soweto has a population of 1,271 628 million people; and 98.54 % were black Africans.[30] This shows that the sample population was a good reflection of the demographics of patients in this area; and that the surgical recommendations from this study could be used for patients at this institution and surrounding areas. Perhaps a study that included another region of South Africa, with different population demographics, might be useful in comparing these two surgical techniques

CHAPTER 5

CONCLUSION

This comparison of the use of Tisseel fibrin glue and vicryl sutures in pterygium excision surgery showed that patients post-operatively in the Tisseel glue group were significantly more comfortable than those in the suture group. Graft success was documented in all patients of both surgical groups. Tisseel fibrin glue is, therefore, considered an effective method for attaching conjunctival autografts; and it also offers the benefit of less post-operative discomfort, shorter operating times, and reduced overall costs for the procedure.

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APPENDICES

Appendix A: Information Sheet

Translations into your language of preference may be carried out by Sister Tshabalala, St John Eye Hospital.

A Comparison of Fibrin Glue with Sutures For Conjunctival Autografts In Pterygium Excision Surgery

Good day, my name is Dr Lara Sandri and I am specializing in eye surgery in the Department of Ophthalmology at the University of the Witwatersrand. As part of my training, I am required to do research in this field. Research is a process where we try and learn more about a question we don't have the answer for.

A pterygium is a triangular growth on the surface of the eye; and it is very common in our country. They are usually red and painful, and can affect your vision. It is believed that these growths are caused by exposure to high levels of ultraviolet -B rays from the sun, hot, dry and dusty climates; and they may possibly have a genetic component as well. It is believed that wearing a large hat and sunglasses when spending extended hours in the sun may prevent this condition in patients who are at risk of developing a pterygium. However, if a pterygium is present, most of these growths require an operation to remove them from the surface of the eye. You have been identified as having this growth on your eye; and I, therefore, ask you to consider the following invitation.

This is an invitation to participate in my study that will be carried out at St John Eye Hospital.

The study will involve the standard surgical procedure of removing this growth from your eye. During this procedure, the growth is removed superficially from the eye; and the bare area left behind is covered with a small piece of tissue (conjunctival graft). This conjunctiva lines the surface of the white part of your eye known as the sclera. A very small piece is taken from a different area on the same eye; and this is then used to cover the bare area where the mass was excised. At this point, this tissue is known as a graft; and it needs to be secured to the surrounding tissue. The study will be comparing two techniques, which are routinely used to secure this graft, namely: stitches and glue. The glue is a natural fibrin glue known as Tisseel; while the stitches are dissolving stitches. Both techniques are practised throughout the world, and have been proven to be safe and effective.

The reason why I have chosen this study is that I want to investigate which one of the techniques leaves you with less pain after the operation, and still keeps that area closed (allows the graft to stick). Regardless of which material is to be used on your eye, both are regarded as standard practice, and are considered safe and effective.

If you decide to take part in this study, you will be allocated randomly to one of the two groups, and receive either the glue or stitches during the surgery. The surgery will take place at St John Eye Hospital under local anaesthetic (numbing injection around the eye). During the procedure, you will be awake, but will have no pain at all. The operating time may vary between 16-40 minutes, depending on which technique is performed.

All the tissue that is removed will be sent for routine examination at our laboratory; and the results will be given to you at your follow-up visits. Standard follow-up includes an examination the day after the operation, as well as 1 month and 3 months, thereafter. On each follow-up visit, a brief routine examination will be carried out; and it would be

appreciated if a few questions regarding your level of comfort could be answered. These questions will include descriptions of how your eye feels; and they will be very brief. After each consultation, the necessary eye drops/medications will be supplied to you at no extra cost. If you are unable to attend these appointments, I would like your permission to contact you telephonically, so that another time can be rescheduled or another arrangement made.

Pterygium surgery is carried out frequently at most eye centres worldwide; and it is well reported on in textbooks and articles. Most surgical procedures come with risks or complications; fortunately for this surgery, these are minimal. Complications for this procedure usually refer to whether the graft has remained stuck down or not, and whether the pterygium has grown back.

Complications of the suture material include allergic irritation and the formation of a bump at the surgical site; but these are uncommon. Some ingredients of the glue are made of animal products; and this carries with it an incredibly small risk of infection. Many of you may have had this surgery on the other eye before; and you will have an understanding of the procedure and the post-operative period.

The benefits of being included in this study include the following:

- Patient's eyes in one of the group may experience less pain post-operatively;
- The technique with a shorter surgical time may be identified;
- It may have a large impact on the number of pterygium surgeries performed at our institution; as one technique appears to be far less time-consuming. This will facilitate a higher turnover and a shorter waiting list for patients;

- One technique may be more cost-effective, thereby allowing a larger number of patients to be operated on;
- If abnormal results are found on the analysis of the tissue, these will be managed appropriately.

Other treatments for this condition include: moisturizing eye drops; however, this is only a temporary measure; and usually surgery alone is needed.

During and after the study, your identity will remain confidential, which means that all your personal details will not be shared. Your name will be assigned a study code, under which all your demographics, surgery details, examination findings and responses to questions will be collected. This information without your name will be seen by me, the statistician, and the medical fraternity (both national and international).

If at any point you choose to withdraw from this study, you may do so immediately, and without reason or consequence; and your withdrawal will not impact on your future health care at our facility.

Contact details of researcher:	REC Administrator and Chair
For further information, feel free to contact me on the following numbers	The study has been approved by the Wits HREC (Medical). Any queries or questions regarding your right as a research participant please contact
Lara Sandri (011) 933 9771 / (011) 463 0406	Prof. Peter Cleaton-Jones/ Anisa Keshav (011) 717 1234

Appendix B: Informed Consent

I, _____, the undersigned hereby consent to voluntarily participate in this study. Dr Lara Sandri has clearly informed me and pointed out the purposes of the research she will be conducting. I have read and understand the information sheet provided to me, which clearly explains the procedure and its risks.

- I am aware that I do have the right not to participate or to discontinue participation at any time, without prejudicing any treatment that is required for existing or future medical conditions.
- Patient confidentiality will be maintained at all times, meaning that information may be used from my file, as long as my name is not mentioned.
- The documents completed by Dr Sandri are the only records that will be used for data collection.
- If I have any queries, they will be directed accordingly.

ENROLLED PATIENT

_____	_____	_____
Full name and Surname	Date	Signature

STUDY DOCTOR:

I, Dr Lara Sandri, hereby confirm that I have fully informed the participating patient of the nature and purposes of my study.

_____	_____	_____
Full name and Surname	Date	Signature

Appendix C: Data-Capturing Sheet

Consent	Y / N	Race	B I C W
Patient study number	☐☐☐	Age ☐☐	Sex M / F
Occupation	_____		
Involved Eye	R / L	Family members with pterygia	Y / N
Hr's sunlight exposure/day	_____	Hat/sunglasses worn	Y / N
Grade of Pterygium	1 2 3	Pre-Op Visual Acuity	___ ___
Date of Procedure	☐☐☐☐☐☐		
Surgeon	_____	Procedure Time	☐☐:☐☐

Examination Day 1:

Visual Acuity	___ / ___					
Flap Adherent	Y / N					
Discomfort will be graded from 0-4 (1= none 2= mild, 3 moderate, 4= severe)						
Foreign Body Sensation		1	2	3	4	
Sensitivity to Light		1	2	3	4	
Tearing		1	2	3	4	
Itchiness		1	2	3	4	Routine Ointment/ Drops Y / N

Examination 1 Month:

Visual Acuity	___ / ___					
Flap Adherent	Y / N					
Recurrence	Y / N					
Patient discomfort:						
Foreign Body Sensation		1	2	3	4	
Sensitivity to Light		1	2	3	4	
Tearing		1	2	3	4	
Itchiness		1	2	3	4	Routine Ointments/Drops Y / N

Examination 3 Months

Visual Acuity	___ / ___					
Flap Adherent	Y / N					
Recurrence	Y / N					
Patient discomfort:						
Foreign Body Sensation		1	2	3	4	
Sensitivity to Light		1	2	3	4	
Tearing		1	2	3	4	
Itchiness		1	2	3	4	Routine Ointments/Drops Y / N

Appendix D: Ethics Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Lara Sandri

CLEARANCE CERTIFICATE	**M120242**
PROJECT	A Comparison of fibrin Glue with Sutures for Conjuctival autographs in Pterygium Excision Surgery
INVESTIGATORS	Dr Lara Sandri.
DEPARTMENT	Dept of Neurosciences/Div of Opthalmology
DATE CONSIDERED	24/02/2012
DECISION OF THE COMMITTEE*	

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr D Soma

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix E: Letter For Permission To Conduct Research

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 02 February 2012

TITLE OF PROJECT: A comparison of fibrin glue with sutures for conjunctival autografts in pterygium excision surgery

UNIVERSITY: Witwatersrand:

Principal Investigator: Dr L Sandri

Department: Ophthalmology

Supervisor (If relevant): Prof T Carmichael and Dr D Sama

Permission Head Department (where research conducted): Yes

Date of start of proposed study: March 2012

Date of completion of data collection: September 2012

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

.....

Recommended

(On behalf of the MAC)

Date: 02 February 2012

.....

Approved/~~Not Approved~~

Hospital Management

Date: 06 Feb 2012

Appendix F: Medical Control Council Registration of Tisseel

Registration number: *Registrasienommer:*	**31/30.3/0368.**
Name of medicine: *Naam van medisyne:*	**Tisseel kit 1,0 H.**
Dosage form: *Doseringsvorm:*	Powder for solution. Poeier vir oplossing.
Active ingredients: *Aktiewe bestanddele:*	Factor XIII/ Faktor XIII . . . 10,0 –50,0 U, Plasminogen\ Plasminogeen . . . 0,04 – 0,12 mg, Protein Hydrolysate/Proteienhidrofisaat equivalent to/ekwivalent aan: Fibrinogen/ Fibrinogeen . . . 70,0 – 110,0 mg Plasmafibronectin/ Plasmafibronektien . . . 2,0 - 9,0 mg per 1 mℓ solution/oplossing.
Conditions of registration: *Voorwaardes vir registrasie:*	1b, 2, 3, 4, 5a.
Applicant: *Applikant:*	Omnimed (Pty) Ltd.
Manufacturer: *Vervaardiger:*	Osterreichisches Institut fur Haemaderivate, Vienna, Austria.
Packer: *Verpakker:*	Osterreichisches Institut fur Haemaderivate, Vienna, Austria.
Laboratory: *Laboratorium:*	Osterreichisches Institut fur Haemaderivate, Vienna, Austria; Omnimed, Randburg, RSA.
Shelf-life: *Rakleeftyd:*	24 months. 24 maande.
Date of registration: *Datum van registrasie:*	23 July 1997. 23 Julie 1997.

Appendix G: Sponsorship Certificate from Adcock Ingram

30 August 2011

ST JOHN'S EYE HOSPITAL

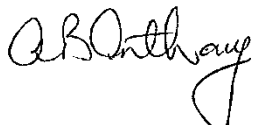
Att: Dr Lara Sandri

REQUEST FOR DONATION OF TISSEEL

Adcock Ingram Critical Care will sponsor the Tisseel required for your research project on Pterygium Surgery using a fibrin glue vs sutures.

Please contact me should you require further information.

Kind Regards,



AUDREY ANTHONY

Product Manager

Medicine Delivery

Tel: 011 494 8745

Cell: 082 561 5325