RESEARCH ARTICLE

Effect of Autologous Eye Drops in Ocular Surgery

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Received: 03rd October,, 2021; Revised: 26th October, 2021; Accepted: 17th November, 2021; Available Online: 25th December, 2021

ABSTRACT

Aim of the Study: To evaluate the effects of the autologous eye drops with conventional treatment in patients with ocular surgeries.

Method: This is a single center prospective and interventional study evaluating the effects of 20% autologous eye drops after Corneal collagen cross-linking with riboflavin; It was conducted on sixty patients were recruited from Ibn AL-Haithem Teaching Eye Hospital from study included patients with keratoconus who were previously diagnosed and suitable for cross-linking surgery. All patients with keratoconus had accelerated corneal collagen cross-linking surgery and received conventional treatment, Patients were randomized into two groups. (study group n = 30) who received autologous eye drops as a 20% and (control group n=30) who received artificial tears drops. All patients had been seen in first, third, fifth, and seventh day of surgery to evaluated the following parameters: epithelial closure time, fluorescein test, pain score, visual acuity, postoperative opacity.

Result: The study includes 60 patients (30 autologous serum group as a study group, 30 artificial tears group as control). Mean ages were 23.83 ± 5.08 years in the autologous group and 25.47 ± 4.99 years in the artificial tears group (p = 0.214). There was no significant difference in sex between control and study, in comparison visual acuity between two groups; autologous patients had a best corrected visual acuity. Mean pain scores was statistically significantly difference,autologous group show lower mean pain scores in all the days of follow-up. On the 5th day, 28 (93.3%) patients in the study group had a complete closure, and in control group 7 (23.3%) patients with complete epithelial closure. On the first day after surgery, two patients in the autologous serum group and four in the control group had ocular haze.

Conclusion: After corneal collagen cross-linking, using autologous serum eye drops speeds up epithelial healing, lowers postoperative discomfort and pain, improves visual acuity. Shortening the time it takes for epithelial closure to close might be useful in terms of decreasing complication and infection risk.

Keywords: Autologous serum, Collagen cross-linking, Epithelial closure, Keratoconus, Pain score.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.4.50

How to cite this article: Al-Saadi TKAM, Al-Atrakji MQYM, Al-Taiyawi KAJ. Effect of Autologous Eye Drops in Ocular Surgery. International Journal of Drug Delivery Technology. 2021;11(4):1417-1421.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Corneal collagen cross-linking (CXL) one of the most recent eye procedures that has proven to be the most efficient therapy option for stopping the growth of keratoconus.[1] Keratoconus (KC) is a slowly progressive bilateral non-inflammatory thinning and ectasia of the cornea with an occurrence in the general population of around 1 per 2,000.[2] Corneal collagen cross-linking is a one-time application of riboflavin solution is administered to the eye, and that is triggered by ultraviolet irradiation (UV-A) light for about 30 minutes. Since riboflavin cannot easily penetrate the intact corneal epithelium, the traditional treatment requires the removal of the central 7–9 mm of epithelium. (epithelium -off CXL), To ensure proper corneal absorption, riboflavin is allowed to permeate through the cornea and reapplied regularly throughout the procedure.[3] It acts as a photosensitizer for subsequent UV-A irradiation UVA light is absorbed approximately 30% inside the lamellae of the corneal stroma, but when combined with the photo mediator properties of riboflavin, this absorption is increased from 30 to 95%.[4]

After epithelium-off (CXL), the time of epithelial closure and postoperative pain is a major concern in terms of possible complications and patient comfort. The removal of epithelium provides better corneal collagen cross-linking effect; on the other side, it could cause complications.[5] Preservative-free artificial tears are commonly used in normal ophthalmic practice to speed epithelial healing. Dry eye and non-healing corneal ulcers have long been treated with autologous serum eye drops.[6] Recently, after refractive surgery, autologous serum and its derivatives have been utilized to treat dry eye.[7]

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The use of autologous serum to treat ocular surface illness can be traced back to 1975 when it was utilized to treat ocular alkali damage using a mobile perfusion pump.[8] Later, in 1984, Fox *et al.* reported on the successful use of autologous serum as an eye drop in dry eye patients.[9] Nevertheless; it was not until late 1990 that attention in the use of autologous serum eye drops established due to the research of Tsubota *et al.*[10] Following penetrating keratoplasty, the autologous serum has also been proven to be effective in encouraging graft re-epithelialization.[11-13] After vitreoretinal surgery, serum eye drops help corneal epithelial wounds heal more effectively and quickly than artificial tears.[14,15]

The use of serum as a natural tear substitute depends on the discovery that serum encompasses essential ocular surface nutrients such as; growth factors, vitamins, cytokines, and bacteriostatic agents that are not present in artificial tears but are present in natural tears. Characteristics of serum also are similar to those of natural tears. Furthermore, the serum is free of preservatives, 1 stabilizers, and 1 chemicals.[16] Concentrations of epitheliotropic substances in serum and tear fluids, however, are not the same. To avoid this possibly detrimental effect, autologous serum eye drops are commonly made as a 20% dilution since TGF- has antiproliferative characteristics in a dose-dependent manner, and its level in serum level is about 5 times higher than that in that in tears.[17] Dilution, on the other hand, may diminish the concentration of other helpful substances, such as EGF and fibronectin, which have been shown to support corneal epithelial cell proliferation and migration.[18] Although most published studies have suggested using 20% autologous serum eye drops to treat a variety of ocular surface problems.[12]

PATIENT AND METHOD

A single center prospective interventional study evaluates the effects of 20% autologous eye drop after Corneal collagen cross-linking with riboflavin. It was conducted on sixty patients were recruited from Ibn Al-Haithem Teaching Eye Hospital from November 2020 to February 2021. The study included patients with keratoconus who were previously diagnosed and suitable for surgery. All patients with keratoconus had accelerated surgery and received conventional treatment. Patients were randomized into two groups (study group n = 30) who received 20% autologous eye drops and (control group n = 30) who received artificial tears drops. All patients underwent ophthalmic examination before surgery. Whole blood was drawn from patients in the same day before surgery, blood was collected into sterile tubes with clot activator. For complete clotting the tubes were left standing in an upright position for two hours at room temperature (18–25^{o}C). Then the blood was centrifuged at 3000 cycles per minute for fifteen minutes. The supernatant serum was transferred into a sterile tube in an aseptic manner diluted with 0.9 normal salines. Each 1-mL was added to 4 mL saline to produce a 20% autologous serum eye finally drops were transferred to, eyedropper bottles; The vials were sealed and labeled, with patient's name, date of manufacture, and the designation as a serum for topical treatment in the eye, as well as the dosage frequency. To retain freshness and slow the growth of hazardous bacteria, patients were told to keep all serum bottles in their freezer, ideally at 20°C, and thaw one bottle at a time in the refrigerator at 4°C. It should be used every 2 hours while awake it was kept in, the refrigerator (+4^{o}C) after each use. Since the eye drops are preservative-free, once opened, they should be used within three days of being thawed.

Assessment of Study Parameters

The data were collected in a prepared, printed personal interview formula. All patients had been seen on the first, third, fifth, and seventh day of surgery to evaluate the following parameters: epithelial closure time, fluorescein test, pain score, visual acuity, postoperative opacity. The ophthalmologist was noted the day of epithelial closure by ophthalmic examination. Epithelial healing was defined as the absence of fluorescein staining. The greatest pain level was inquired of all patients. The Wong-Baker, FACES Pain Rating Scale was used to assess pain, and the visual acuity obtained from the Snellen chart was transformed to logMAR units for statistical analysis.

Statistical Analysis

This is a case-control study in which continuous data were, expressed as mean ± standard deviation, and a comparison of means was done using unpaired t-test, and among more than two groups using analysis of variance (ANOVA). While categorical data were expressed as frequency and percentage, and comparison between frequencies of these data was made using Fisher exact test and Yates chi-square test. $p < 0.05$ is considered as significant. The software used was a statistical package for social sciences (SPSS) version 23 and Microsoft excel 2019.

RESULT

The study includes 60 patients; (30 autologous serum group, 30 artificial tears group as control). The mean age was 23.83 ± 5.08 years in the autologous serum group and 25.47 ± 4.99 years in the control group ($p = 0.214$) Results shown in Figures 1 and 2. There was no significant difference in sex between the groups (male, n = 11; female; n=19 in the study group, male, n=16; female; n = 14 in the control group, $p = 0.299$) as shown in Table 1.

The mean of pain was statistically different between study and control autologous patients showing a reduced pain score on all the days of follow-up. The mean pain score of control group n the first day was (9.0 ± 1.02), which was of high level compared to the mean of study group (4.07 ± 1.23) on first, third and fifth day. There was still a highly significant difference between the study and control groups on seventh day. The mean in the study group was (0.0 ± 0.0), while in control group (0.73 ± 0.98), on, the seventh postoperative day, no patient in the autologous serum group was in pain. In comparison of pain scores on 1st, 3rd, 5th and 7th days of follow up between control and study groups, there were statistically significantly difference ($p = <0.001$) as shown in Table 2.

Epithelial closure time was significantly shorter in the autologous serum group than in the control group; the numbers

Table 1: Age and sex distribution in the two groups (study group with autologous serum drop and control group with artificial tears drop)

Parameter		*Control N=30*	*Study N=30*	*p value*
Age (yr)	Mean ± SD	25.47 ± 4.99	23.83 ± 5.08	0.214*
	Range	18–35	18–35	
		N (%)	N (%)	
Sex	Female	14 (46.7%)	19 (63.3)	0.299**
	Male	16 (53.3%)	11 (36.7)	

* *p-value* by unpaired t-test, ** p-value by Fisher exact test

Table 2: Comparison of pain score in 1st, 3rd, 5th and 7th days of follow up between control and study groups

	Pain score			
Group	*1st day Mean ± SD*	*3rd day Mean ± SD*	*5th day Mean ± SD*	*7th day Mean ± SD*
Control	9.0 ± 1.02	6.13 ± 0.73	3.53 ± 1.14	0.73 ± 0.98
Study	4.07 ± 1.23	1.47 ± 1.04	0.07 ± 0.37	0.0 ± 0.0
P value	<0.001	<0.001	<0.001	<0.001

P value by unpaired ttest

Table 3: Comparison of epithelial closure time in 1st, 3rd, 5th and 7th days of follow up between control and study groups

Epithelial closure time	*1st day N (%)*		*3rd day N (%)*		*5th day N (%)*		*7th day N (%)*	
	Control	*Study*	*Control*	*Study*	*Control*	*Study*	*Control*	*Study*
Complete	0 (0.0)	0 (0)	0 (0.0)	22 (73.3)	7 (23.3)	28 (93.3)	28 (93.3)	28 (93.3)
Incomplete	30 (100)	30 (100)	30 (100)	8 (26.7)	23 (76.7)	2 (6.7)	2 (6.7)	2 (6.7)
P value	1.000		<0.001		<0.001		1.000	

p-value by Fisher exact test N= patient number %= percentage of patient

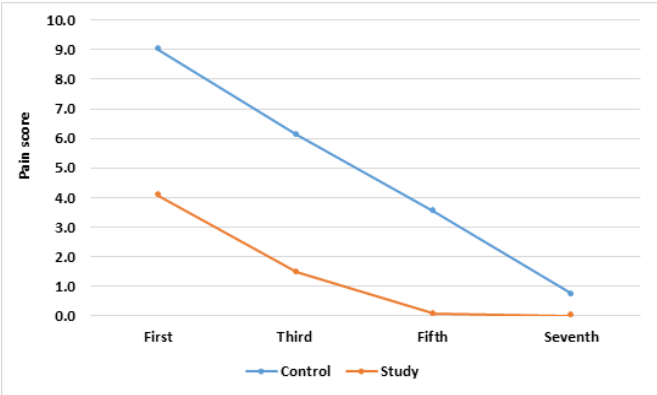

Figure 1: The pain score difference between control and study groups in 1st, 3rd, 5th and 7th days of follow up

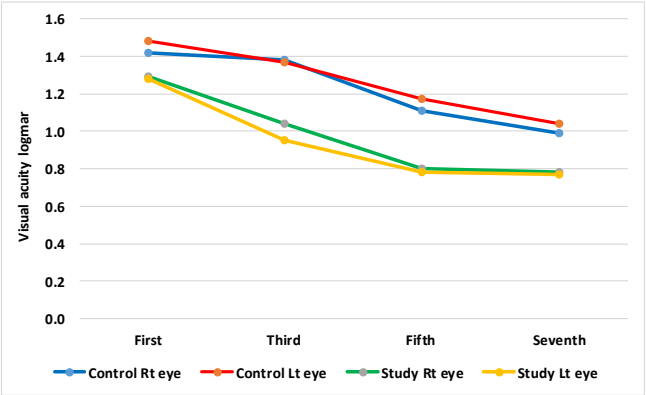

Figure 2: Logmar visual acuity difference between control and study groups of right and left eyes in 1st, 3rd, 5th and 7th days of follow up

of patients who had complete epithelial closure in first day post-operation were 0 (0.0) in both groups, while the numbers of patients who had epithelial, closure in third day were 22 (73.3%) in the autologous serum group and 0 (0.0) in the control group.On the fifth day, 28 (93.3 %) patient in the study group had a complete closure, and in the control group 7 (23.3%) patients with complete epithelial closure, on the seventh day, the same number of patients with complete epithelial closure in two groups. In the comparison of epithelial closure time in 1st, 3rd, 5th and 7th days of follow up between control and study groups, there was a highly significant in third and fifth day $p<0.001$ as shown in Table 3.

Visual acuity, which converted to logmar for statistical show an improvement and significant difference in both groups (study and control) from first to seventh day of surgery ($p<0.001$) but in comparison between two groups show a highly significant difference in third and five days ($p<0.001$). All patients in both groups had improvement in visual acuity after surgery, but autologous group had a best corrected visual acuity.

On, the first postoperative day, two patients in the autologous serum group and four in the control group had ocular haze. In comparison of postoperative opacity in 1st, 3rd, 5th and 7th days of follow up between control and study groups there was no statistically significant $p = 0.671$.

DISCUSSION

Healing of epithelial takes time; for patients, this period is painful and uncomfortable. Even though UV exposure causes the release of inflammatory cytokines and damage to the corneal nerves, epithelial removal enhances postoperative pain and generates foreign body sensations, burning, and ripping until the epithelialization is completed.[19] Because of their epitheliotrophic concentration of growth factors, fibronectin, immunoglobulins, and vitamins that are not found in artificial tears, autologous serum eye drops promote corneal re-epithelialization.[20] It is a non-invasive method of healing (only requiring a needle stick to collect blood). There is little danger of illness transmission because the blood belongs to the patient; furthermore, the chance of contamination and eventual infection is minimal when prepared under aseptic conditions.[21] The efficacy of serum eye drops in treating ocular surface disease has been well documented in the literature for many years. However, the majority of these studies are retrospective and use different protocols for serum synthesis. In these trials, the concentration differed as well (from 20 to 100%). Previous studies have shown that the most favored concentration is 20%. The reason for diluting serum 1:5 is to lower the concentration of Transforming growth factor alpha (TGF-α) in serum to an amount equal to natural tear because the fivefold concentration of TGF-α possibly retarding epithelial wound healing.[10] In our study, the goal was to see how autologous serum eye drops affected corneal collagen cross-linking. We discovered that utilizing autologous serum eye drops after surgery expedited epithelial closure, reduced pain, and improved visual acuity. Chen *et al.*[11] used autologous, serum after penetrating keratoplasty found that it promotes graft re-epithelialization, particularly in diabetic patients. It has also been proven that autologous serum speeds up epithelial closure in epithelial erosions caused by vitrectomy surgery, which helps visualize.[14] previously, the use of autologous serum as an complementary therapy has been documented in the treatment of keratitis and subsequent corneal melting after corneal collagen cross-linking.[22] We have found that autologous serum statistically significantly lower the time required for epithelial closure there was a (73.3%) of autologous group patients had a complete epithelial closure on third day while no patient had in artificial tears group, in comparison with the previous study.[23] Another study indicates that using autologous serum after photorefractive keratectomy results in a mean epithelial closure time that was almost one day shorter in the group that received autologous serum than in the group that received artificial tears.[24] pain scores were significantly lower in patients with autologous serum eye drops in all days of follow-up compared with the artificial tears group. The mean in the autologous group was (4.07 ± 1.23) on first day, while the mean of the artificial tears group was (9.0 ± 1.02), $p < 0.001$ in the first, third, fifth, and seventh day of follow up. Patients with artificial tears had a high score of pain.

Compared with the previous study, Kirgiz *et al.,* 2020 showed that the autologous serum group had statistically significant pain scores on the first and second postoperative days (p=.001 and p=.02, respectively). This could be owing to substances in the autologous serum, such as neural growth factor and substance P, which can cause corneal nerve regeneration.[25-27]

CONCLUSION

After corneal collagen cross-linking, using autologous serum eye drops speeds up epithelial healing, lowers postoperative discomfort and pain, improves visual acuity. Shortening the time it takes for epithelial closure to close might be useful in terms of decreasing complication, and infection risk.

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