



WRESP-RC
Warfighter Refractive Eye Surgery Program & Research Center at Fort Belvoir



Tear Lacritin and Implications in Dry Eye After Photorefractive Keratectomy

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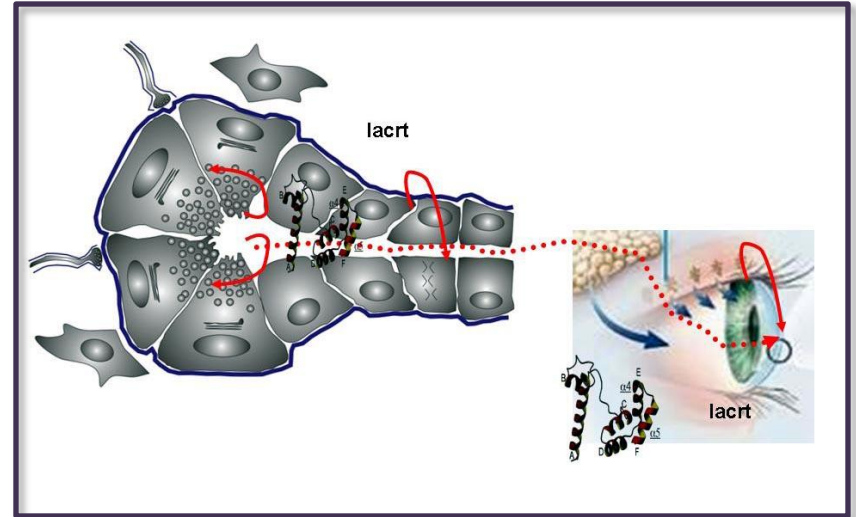
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Purpose

- Lacritin is a tear glycoprotein secreted from the lacrimal gland.
- It is said to be essential in regulating basal tearing and is selectively downregulated in dry eye.¹⁻³
- Decreased lacritin has been reported in patients with blepharitis² and contact lens-related dry eye³.

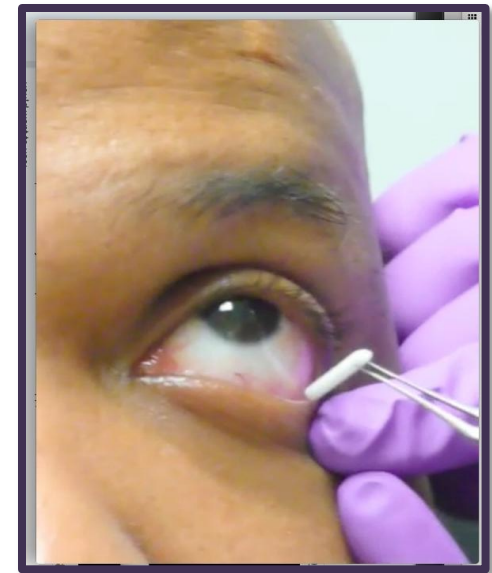


From the lacrimal acinar cells secretory granules, lacritin is released via lacrimal ducts to the surface of the eye.⁴

This purpose of this study was to determine whether levels of tear protein lacritin correlate with signs and symptoms of dry eye after photorefractive keratectomy (PRK).

Methods

- We enrolled 52 patients with myopia or myopic astigmatism undergoing photorefractive keratectomy (PRK).
- Tear samples were collected preoperatively and postoperatively on day 1, week 1, months 1, 3 and 6:
 - A drop of proparacaine 0.5% was instilled in the left eye
 - After 2 minutes, tears were collected at the lower conjunctival cul-de-sac using polyester fiber wick (Filtrona, Richmond, VA)



Methods

The following dry eye tests were performed preoperatively and at 1, 3 and 6 months postoperatively:

- Ocular Surface Disease Index (OSDI)
 - ❖ To evaluate dry eye symptoms; a score of ≤ 15 was considered normal⁵
- Schirmer test with anesthesia
 - ❖ To determine basal tear secretion; wetting >5 mm per 5 minutes was considered normal
- Tear break up time (TBUT)
 - ❖ To determine tear film stability; TBUT ≥ 10 seconds was considered normal
- Lissamine green (LG) staining
 - ❖ To determine ocular surface damage; Areas of staining in the cornea and conjunctiva will be scored on a scale of 0 to 3 (0=no staining, 1 = mild staining, 2 = moderate staining, 3 = severe staining) for the nasal conjunctiva, temporal conjunctiva, and cornea. A score of 0-1 was considered normal.

Dry eye was defined as:

✓ LG staining score >1

Or a combination of two of the following:

✓ Schirmer score <5 mm

✓ TBUT <10 seconds

✓ OSDI score >15 .

Methods

Surgical Procedure

- The corneal epithelium was removed using a rotary brush (Amoils, Innovative Excimer Solutions, Toronto, Canada)
- Surface ablation was performed using the Wavelight Allegretto WAVE Eye Q Excimer Laser System (Alcon Surgical, Fort Worth, TX).
- Prophylactic mitomycin C (MMC) was used on eyes with central ablation depth of greater than 75 microns.
- After the surgery, bandage contact lenses were applied (Omafilcon A, Proclear, Proclear, CooperVision, Fairport, NY) and left in place until complete re-epithelialization.
- The following postoperative topical medications were used:
 - Moxifloxacin 0.5% 4x daily for 1 week or until complete re-epithelialization
 - Fluorometholone 0.1% 4x daily for 4 weeks followed by a 6-week taper
 - Preservative-free carboxymethylcellulose 0.5% 1 drop every hour for the first week, then at least every 2 hours or more for several months
 - Preservative-free ketorolac 0.5% up to 4x daily for 48 hours

Methods

Tear sample analysis

- Samples were sent to James Madison University for analysis.
- Lacritin levels were determined using enzyme-linked immunosorbent assay (ELISA)
- The samples from each patient were analyzed on the same microtiter plate with its own lacritin standard curve. Each sample is done in triplicate and the analysis is repeated on a second plate.

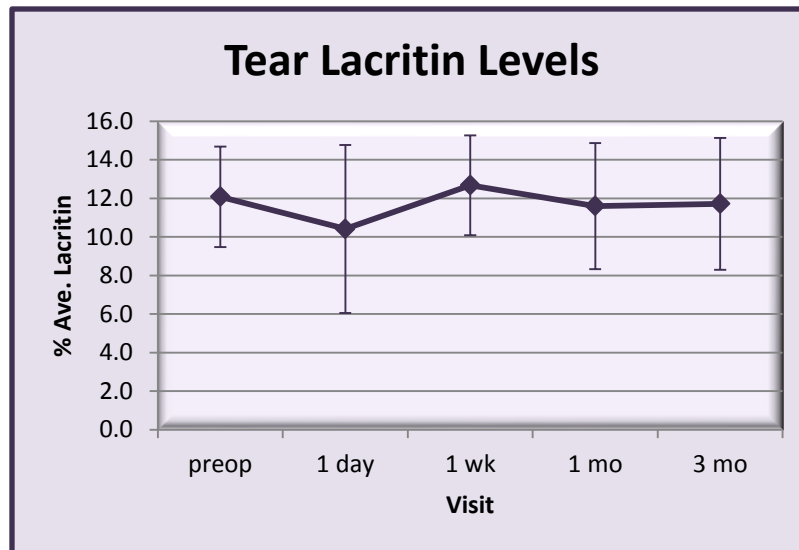
Data analysis

- Test results from left eye were used for data analysis.
- Repeated measures analysis of variance was used to compare post-surgical lacritin levels, dry eye signs and symptoms to pre-surgical baseline.
- Multivariate analysis of variance was performed to determine if lacritin had any significant correlation with signs and symptoms of dry eye.

Results

Demographic and preoperative clinical data (n=52)

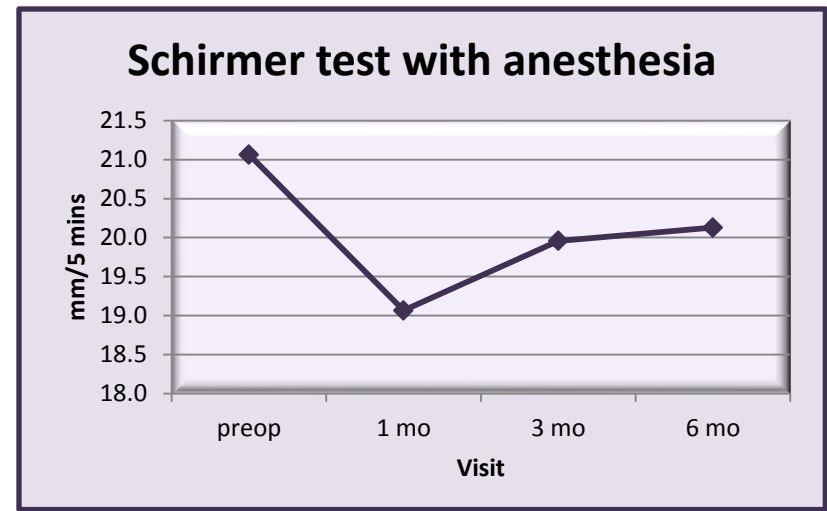
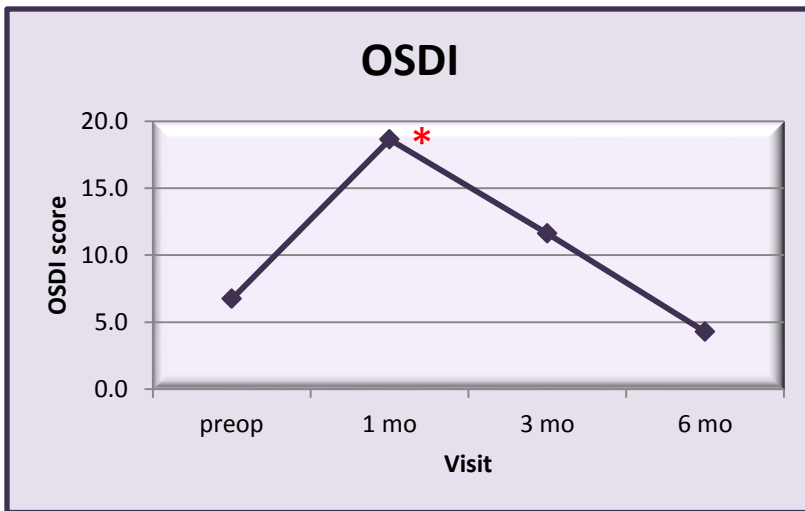
Age (years)	30.5 \pm 6.7
Male/Female (n)	34/18
Mitomycin C use (n)	9 (17.3%)
Manifest Sphere (diopters)	-2.59 \pm 1.72
Manifest Cylinder (diopters)	-0.55 \pm 0.55
Manifest Spherical Equivalent (diopters)	-2.86 \pm 1.70



- % Average lacritin decreased significantly from preop at day 1 postop ($p=0.03$). Lacritin concentration returned to baseline level at 1 week postop ($p=0.71$)

Results

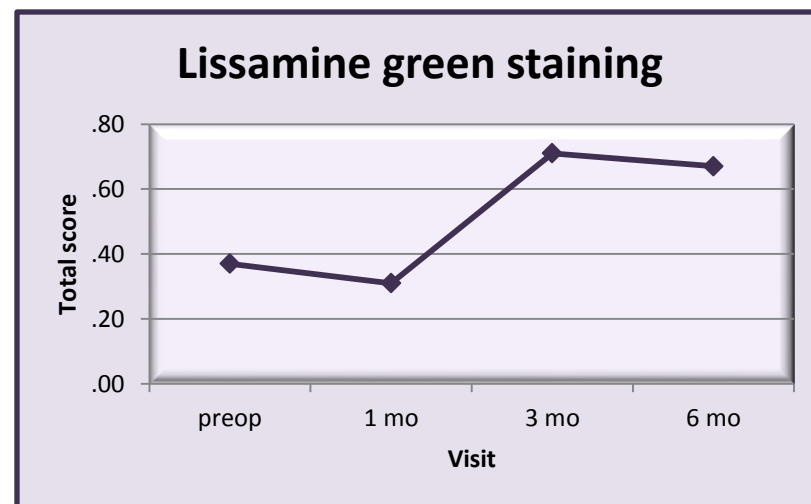
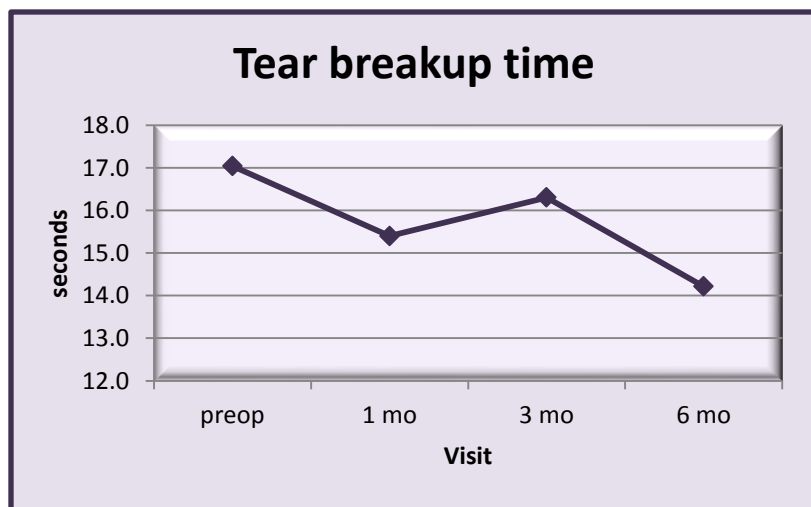
Dry eye test results over time



- OSDI scores were significantly higher from preop at 1 month postop* ($p < 0.01$).
- Postoperative Schirmer test scores were not significantly different from preoperative baseline values.

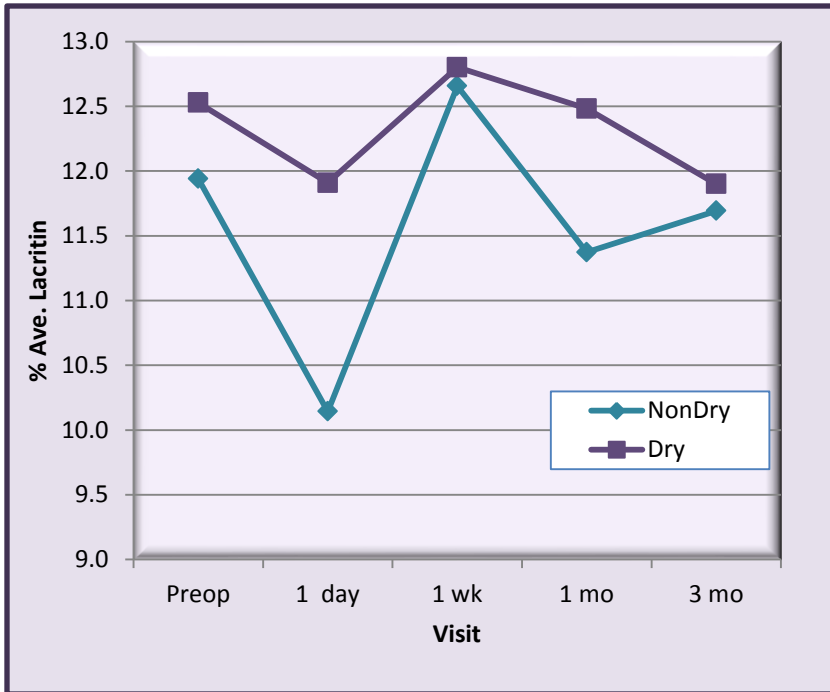
Results

Dry eye test results over time



- Postoperative TBUT and LG staining scores were not significantly different from preoperative baseline values.

Results



- There was no significant difference in % average lacritin between the participants who developed dry eye at 6 months post-PRK compared to the participants who did not have dry eye ($p=0.38$).

- Postoperative dry eye was observed in 25 (48.1%) participants at 1 month, 26 (50%) participants at 3 months and 11 (21.2%) participants at 6 months.
- Lacritin did not significantly affect dry eye markers at preop ($p=0.49$), at 1 month postop ($p=0.44$), or at 3 months postop ($p=0.08$).

Conclusion

- Lacritin concentration are significantly reduced on postoperative day 1 but why they are lower and the significance of the finding are still being explored.
- Initial results suggest there is no significant relationship between lacritin and selected clinical indicators of dry eye after PRK.
- Tear lacritin concentration in the early post-PRK period did not appear to be a significant factor in determining if a patient will develop chronic postoperative dry eye.
- A study examining association between LASIK and tear lacritin is underway.

References

1. Samudre S, Lattanzio FA Jr, Lossen V, Hosseini A, Sheppard JD Jr, McKown RL, Laurie GW, Williams PB. Lacritin, a novel human tear glycoprotein, promotes sustained basal tearing and is well tolerated. *Invest Ophthalmol Vis Sci*. 2011 Aug 5;52(9):6265-70.
2. Koo B, Lee D, Ha H, Kim JC, Kim CW. Comparative analysis of the tear protein expression in blepharitis patients using two-dimensional electrophoresis. *J Proteome Res*. 2005; 4: 719–724.
3. Nichols JJ, Green-Church KB. Mass spectrometry-based proteomic analyses in contact lens-related dry eye. *Cornea*. 2009; 28: 1109–1117.
4. Wang J, Wang N, Xie J, Walton SC, McKown RL, Raab RW, Ma P, Beck SL, Coffman GL, Hussaini IM, Laurie GW. Restricted epithelial proliferation by lacritin via PKC α -dependent NFAT and mTOR pathways. *J Cell Biol*. 2006 Aug 28;174(5):689-700.
5. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol*. 2000;118:615–621.