Research Article

Current Trends in Ophthalmology Intranasal Neurostimulation for Dry Eye: First Impressions

Faulkner WJ* and Granat S

Cincinnati Eye Institute, University of Cincinnati, USA

*Correspondence: William J Faulkner, Director Scott E. Burk Urgent Clinic, Cincinnati Eye Institute, Voluntary Assistant Clinical Professor, University of Cincinnati Department of Ophthalmology, 1945 CEI Drive, Cincinnati, Ohio 45242, USA, Tel: 513-984-5133; E-mail: WJFaulkner@CincinnatiEye.com

Received: January 07, 2019; Accepted: February 27, 2019; Published: March 04, 2019

Abstract

Although many new and helpful treatments for dry eye disease have been developed, there remains a subset of patients who continue to look for easier or more effective treatments. A consecutive group of 28 moderate to severe dissatisfied dry eye patients in one practice were surveyed after initial exposure to and trial with a novel intranasal neurostimulation technique. Results were overall positive. Seventy-one percent had a favorable impression. Average rating on 1-10 scale was 6.92. Twenty-five percent purchased the device immediately despite no insurance coverage. Of those who did not buy, 100% said they would consider purchase later. Time and experience will show how valuable this new technology is and how it fits in the dry eye armamentarium.

Introduction

Despite many treatment advances in recent years, dry eye disease remains a conundrum for both doctors and patients. After years of development, an innovative biotech team in the Silicon Valley (Oculeve) produced a minimally invasive intranasal neurostimulation device for treating dry eye. The product was purchased by Allergan, Dublin, Ireland, in August, 2015. FDA approval for True Tear was granted in April, 2017, "to provide a temporary increase in tear production during neurostimulation in adult patients." Initially introduced to a small group of physician investigators, it was later approved for prescription use in April, 2018 [1].

Neurostimulation for medical benefit is a concept at least several decades old. For years these techniques have benefited patients with multiple conditions such as chronic pain, post-herpetic neuralgia, complex migraines, and peripheral neuropathy. Ischemic pain from cardiovascular and peripheral vascular disease and visceral pain in interstitial cystitis have become treatable [2]. Patients with Parkinson's disease [3], intractable

epilepsy [4], and even obstructive sleep apnea [5], have also benefited from neurostimulation.

The True Tear device is a small handheld unit with two nasal prongs which the patient inserts into the nose. Low level electrical stimulation (adjustable from 1-5) stimulates the internal nares sending an afferent signal via the ethmoidal branch of the ophthalmic division of cranial nerve V to the brain. Then an efferent signal via cranial nerve VII results in stimulation of the lacrimal glands. The result is the production of physiologic tears with the delicate normal balance of lipid, aqueous, and mucous components [6]. Specifically, tear analysis post intranasal neurostimulation has shown an equivalent concentration of total lipid as compared to basal tears [7]. Also equivalent concentrations of total protein, lysozyme, and lactoferrin have been measured [8].

FDA approval was based on two studies. OCUN-009 studied 48 patients and noted a significant increase in Schirmer's test scores with the device vs. controls, cotton swab stimulation (> 25 mm vs < 10 mm). OCUN-10

involved 97 patients measured at baseline and after 7, 30, 90, and 180 days. Benefits were noted in OSDI scores, staining, and tearing. Patients were directed to use the device a minimum of two and up to ten times daily for a maximum of three minutes per application. Usage actually decreased with time so that the average at end of study was 1.7 times per day with an average time of 2.2 minutes per application [9].

Materials and Methods

Since this technology is brand new to our field and the method of use is quite novel, we felt it would be informative to gauge patients' reaction after first exposure. Specifically after discussion and consent, patients were screened for contraindications. Patients qualified as moderate to severe dry eye based on AAO Preferred Practice Patterns (Oct, 2013) for diagnosis: "Patients with moderate dry eye have increased discomfort and frequency of symptoms, and the negative effect on visual function may become more consistent. Patients with severe dry eye syndrome have an increasing frequency of symptoms that may be constant as well as potentially debilitating visual symptoms." Specifically, routine evaluation included OSDI, osmolarity, tear volume and breakup time, conjunctival and corneal staining, and meibomian expression. A consecutive group of patients (28) in the moderate to severe category of dry eye who met those criteria and who were usually on multiple treatments but were still dissatisfied became the study patients. Contraindications for use of the device include the presence of a pacemaker or other metallic device implanted in the head or neck, history of nosebleeds or bleeding disorder, and hypersensitivity to hydrogel in the nasal cannula. Instruction on the application and use of the device was given and the patient was allowed to self-administer the treatment. Patients were instructed to insert the device as directed and use until a result was produced or at the three minute limit if there were no effects. Patients were also instructed to remove the device if they experienced any discomfort. Twenty eight consecutive moderate to severe dry eye patients agreed to test out the device and answer a questionnaire. There were 22 females, average age 60, and 6 males, average age 66. Five patients (17.8%) had an established diagnosis of Sjogren's syndrome. All patients were established patients in this practice, and all had used or were continuing to use multiple traditional dry eye treatments. All were symptomatic and dissatisfied enough to have an interest in a new treatment. The questions surveyed were as follows: Was the treatment helpful? Rate your satisfaction on a 1-10 scale. Will you purchase the device

now or very soon? If not would you consider a purchase in the future? What did you like about this device? What did you dislike about this device?

Results

Twenty participants (71.4%) said the device was helpful. Four (14.3%) said it was not helpful and four (14.3%) were unsure if it helped. Satisfaction scores ranged from 1 (two patients) to 10 (three patients) with an average score of 6.92. Seven of twenty-eight (25%) purchased the device after the trial. Of those who did not purchase, thirteen said they would definitely consider a purchase in the near future and eight said they would consider future purchase. No one ruled out future use despite four reporting it did not seem helpful on initial trial. Positive comments centered on immediate results, an innovative idea, and ease of use. The overriding objection was cost. Of note is the fact that intranasal placement did not seem to be a significant negative factor, though this was mentioned by a few.

Discussion

Dry eye is complex, multi factorial, multidimensional, and persistent. Addressing multiple contributing factors such as environmental modification, allergy, medication use, poor blink, autoimmune issues, tear film instability, hyperosmolarity, inflammation, meibomian gland disease, bacteria, and nutritional deficit may all be helpful [10], but sometimes still not enough or perhaps just too complicated. In a single dry eye clinic it did not prove difficult to recruit 28 dissatisfied patients to trial a new technology addressing a different component of the problem: the neurologic aspect. Prior to FDA approval, submitted data supported positive results without significant local or systemic side effects and no tachyphylaxis [1]. All device-related events were mild, including nasal pain, discomfort or burning (10.3%) transient electrical discomfort (5.2%), and nosebleed (5.2%) [1]. The purpose of this study was to gauge first impressions and initial reactions to trial use of the device. Seventy-one percent felt the technique was helpful and 25% purchased it immediately after brief exposure. The biggest objection was cost. The device may be purchased from the manufacturer for \$950 and disposable cannulas cost \$50 per month [1]. Lack of insurance coverage influenced the decision of many. Of the 75% of participants who did not request a prescription immediately after the demo, 100% said they would consider it in the future. Many mentioned they wanted to wait until it was on the market longer to see if insurance would eventually cover it.

Despite being a small study, results were encouraging. Since patients were using the device less often after time in the second clinical trial, which lasted 180 days, this may signify that the ocular surface was beginning to heal. Whether or not long term benefits remain or improve will be of interest to many patients and ophthalmologists. While perhaps not a panacea, this new technology appears to hold great promise to relieve intractable dry eye disease.

Acknowledgement

Conflict of interest

No conflict of interest
Neurostimulation in Dry Eye

Funding

No funding assistance

References

1. Allergan, Dublin, Ireland, Proprietary information.
2. Mekhail NA, Cheng J, Narouze S, Kapural L, Mekhail MN, Deer T. Clinical applications of neurostimulation: forty years later. *Pain Pract.* 2010;10(2):103-112. Doi: <http://dx.doi.org/10.1111/j.1533-2500.2009.00341.x>
3. Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for parkinson's disease with early motor complications. *New England Journal of Medicine.* 2013;368(7):610-622. Doi: <http://dx.doi.org/10.1056/NEJMoa1205158>
4. Heck CN, King-Stephens D, Massey AD, et al. Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive neurostimulation: final results of the RNS System Pivotal trial. *Epilepsia.* 2014;55(3):432-441. Doi: <http://dx.doi.org/10.1111/epi.12534>
5. Randerath WJ, Galetke W, Domanski U, Weitkunat R, Ruhle K-H. Tongue-muscle training by intraoral electrical neurostimulation in patients with obstructive sleep apnea. *Sleep.* 2004;27(2):254-259.
6. Berdahl J. Neurostimulation offers new approach to dry eye. *CRS Today.* <https://crstoday.com/articles/2017-apr/neurostimulation-offers-new-approach-to-dry-eye/>. Accessed February 13, 2019.
7. Green K, Kamat M, Franke M, Holdbrook M, Senchyna M. Tear total lipid concentration in patients with dry eye following intranasal neurostimulation. *Univ Florida, ARVO poster, Baltimore, 2017; Session 315/ Board 2693-A0283.*; 2007.
8. Woodward A, Senchyna M, Franke M, Holdbrook M, Argueso P. Effect of intranasal neurostimulation on total tear lipid and total protein concentrations in subjects with dry eye. <https://www.aaopt.org/detail/knowledge-base-article/effect-of-intranasal-neurostimulation-on-total-tear-lipid-and-total-protein-concentrations-in-subjects-with-dry-eye>. Accessed February 13, 2019.
9. Krader C. Intranasal neurostimulator shows benefit for increasing tear production. *Ophthalmology Times.* <https://www.opthalmologytimes.com/opthalmologytimes/news/intranasal-neurostimulator-shows-benefit-increasing-tear-production>. Accessed February 13, 2019.
10. Sullivan D et al. Conclusions and recommendations of the TFOS DEWS II announced. *Eyewire News.* <https://eyewire.news/articles/conclusions-and-recommendations-of-the-tfos-dews-ii-announced/>. Accessed February 13, 2019.

Copyright: © **Faulkner et al.** This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.