ABSTRACT

PURPOSE: Dry eye disease (DED) is one of the most prevalent conditions at an ophthalmology office which is didactic classified as two forms that exists as a continuum: aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE). In EDE patients Meibomian Gland Dysfunction (MGD) is the major etiology and its treatment can be very challenging in cases where clinical approach are not sufficient. We propose a new treatment for refractory MGD patients with plasma jet to remove the hyperkeratinization layer from lid margin to unblock terminal gland ducts and use thermal stimulation to enhance meibum delivery and describe its results in four Caucasian patients from Hospital São Paulo.

METHODS: A retrospective, interventional clinical safety and efficacy trial with 4 Caucasian patients (2 male and 2 female) from Ophthalmology Department at Escola Paulista de Medicina (UNIFESP) to determine the efficacy and safety of the treatment of refractory MGD patients with plasma jet on both upper and lower lids. Patients were submitted to an ophthalmology workup with best corrected visual acuity (BCVA) (ETDRS chart), dry eye questionnaires (DEQ-5 and OSDI), tear film osmolarity, meibomian gland expression and Marx line assessment. Corneal topography, bulbar redness, tear meniscus height, noninvasive breakup time (NIKBUT) and meibography under infrared light were measured with Keratograph 5M. All exams were performed before and 30 days after plasma jet application.

RESULTS: 30 days after the plasma jet all patients had a significative improvement in DEQ-5 score, bulbar redness, tear meniscus height and upper lid meibography. BCVA has not changed.

CONCLUSIONS: Our case series findings suggest that use of plasma jet application as a new therapeutic option to free gland ducts and recover meibum secretion in patients with refractory MGD could be considered safe without any ophthalmological side effects up to 30 days follow-up. In order to reduce the need of lids hygiene and lubricants use and provide a better quality of life for MGD with DED.

INTRODUCTION

Dry eye disease (DED) is one of the most prevalent conditions at an ophthalmology office that may reach 15 to 40% of prevalence in the population. It is didactic classified as two forms that exists as a continuum: aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE). In EDE patients Meibomian Gland Dysfunction (MGD) is the major etiology in which the insufficient meibum secretion can be decreased by cicatricial (trachoma, ocular pemphigoid,

erythema multiforme) and non-cicatricial causes (skin disorders such as acne rosacea and atopic dermatitis, blepharitis)[1].

MGD pathophysiology can be explained by hyposecretion or ducts obstruction, resulting in low delivery of phospholipids and cholesterol that grant stability to the tear film[2]. Hyposecretion of the sebaceous glands can result from intrinsic (age, ethnicity, hormonal profile) and extrinsic factors (chronic blepharitis, *Demodex folliculorum* infestation, contact lens wear, topical drops)[3]. Furthermore the duct obstruction occurs in consequence to cicatricial rearrangement of the terminal ducts or by non-cicatricial hyperkeratinization of the lid margins, leading to increased duct pressure, dilatation and disuse atrophy of the glands[1].

Questionnaires such as Ocular Surface Disease Index (OSDI) and Dry Eye Questionnaire-5 (DEQ-5)[4] that evaluate the grade of severity of DED and assessment of MGD by noninvasive tear breakup time (BUT) evaluation that measures tear film stability and by meibography under infrared light[5] that analyses gland vitality are central when dealing with any EDE patient.

The treatment of MGD can be very challenging in cases where clinical approach with non-preserved ocular lubricants, lid hygiene and warm compresses are not sufficient[6]. Oral tetracyclines can be a good alternative in cases of evident lid inflammation to reduce bacterial colonization and inhibit collagenase action although long term use intolerance limits its use[7].

Thermodynamic treatment with a device that perform a controlled local heating and massage of the ducts showed clinical improvement and symptoms reduction whereas multiple sessions are necessary[8]. Mechanical debridement of gland ducts terminals with scalpel blade also improved ocular symptoms and gland function of patients with EDE with MGD[9]. Combination of intense pulsed light (IPL) therapy and gland expression has been shown to be an effective treatment to MGD with increases in BUT and improvement of ocular symptoms related to DED[10].

Plasma jet has been successfully used in Dermatology and is an increasingly popular method for smoothing wrinkles, blunt blepharoplasty, as well as performing thermal ablation for superficial skin layers. [11]

We propose a new treatment for refractory MGD patients with plasma jet with a device used in Dermatology to remove the hyperkeratinization layer from lid margin to unblock terminal gland ducts and use thermal stimulation to enhance meibum delivery.

CASE SERIES

A retrospective, interventional clinical safety and efficacy trial to determine the efficacy and safety of the treatment of refractory MGD patients with plasma jet was conducted at

Ophthalmology Department at Escola Paulista de Medicina (UNIFESP) with 4 Caucasian patients (2 male and 2 female) with mean age of 52.7.

All patients were instructed about the study design and were given full access to the results in anytime of the protocol. All signed an informed consent form and had their identity protected in accordance with patient medical confidentiality. This case series was in accordance with Good Clinical Practices and the Declaration of Helsinki.

Patients were submitted to an ophthalmology workup with best corrected visual acuity (BCVA) (ETDRS chart), dry eye questionnaires (DEQ-5 and OSDI)[4], corneal topography, bulbar redness, tear meniscus height, noninvasive breakup time (NBUT), tear film osmolarity, meibography under infrared light, meibomian gland expression and Marx line assessment. All exams were performed before and 30 days after plasma jet application.

Patients were instructed about the procedure by the ophthalmologist and a nurse and procedure was performed after topical anesthesia with lidocaine 2.0%. Plasma jet was applied for 3 times on both superior and inferior terminal gland ducts in the lid margins with a 14.4mm tip and intensity of 5 on the device (0,9W) reaching only superficial epidermis (Figure 1). Patients received topical antibiotic and corticosteroid after procedure. During all period (45 days) patients were using sodium hyaluronate 0,15% and actinoquinol at the recommended dosage of twice a day.

Software program GraphPad Prim version 7.0 was used to conduct the statistical analyses. Continuous data distribution was verified by Kolmogorov-Smirnov normality test. Data were analyzed by Kruskal-Wallis test with Wilcoxon test considering 2 time points for nonparametric variables and paired t-test for parametric variables. All p values of < 0.05 indicated statistically significant differences.

RESULTS

We observed a significantly improvement in DEQ-5 score at day 30 (Wilcoxon single rang test, p=0.0218) shown in Figure 1. Corneal topography, tear meniscus height, bulbar redness, noninvasive breakup time (NIKBUT) and meibography under infrared light were measured with Keratograph 5M (Figures 2A, 2B and 2C).

30 days after the plasma jet on both upper and lower lids patients had a significative improvement in bulbar redness (Pair t- test, p=0.0493), tear meniscus height (Pair t- test, p=0.0078) and upper lid meibography (Pair t- test, p=0.0303) as shown in figure 3.

BCVA has not changed. OSDI and DEQ-5 score, lower lid meibography, tear film osmolarity and meibomian gland expression were not statistically significant.

DISCUSSION

Refractory MGD can be very challenging as patient discomfort finds no resolution with standardized EDE treatment. Additional approaches are needed to the use of lubricants, lids hygiene and warm compresses in order to provide a better quality of life for severe cases of EDE.

Korb et al (2010) found that a thermodynamic device after a single session of 12 minutes treatment improved MGD score, doubled BUT and reduced ocular symptoms[8]. Three years later, Korb at al (2013) reported a technique in which mechanical debridement of lid margin Marx line in 20 patients with EDE due to MGD that reduced surface symptoms and improved meibomian gland function 1 month after the procedure[9]. Following Arita et al (2018) showed in a multicenter study with 31 patients presenting refractory obstructive MGD that IPL was able significantly improve meibum grade, lid margin abnormality scores and fluorescein breakup time[10].

Herein, our case series had improved sight and symptoms by the reduction of the DEQ-5 score and bulbar redness as well as the increase in TMH and number of Meibomian glands on the superior lid. Additionally, plasma jet application to the terminal gland ducts on the ciliary margin produced no change on BCVA, OSDI questionnaire scores, NBUT, corneal fluorescein staining and tear film osmolarity.

These findings suggest that this procedure could be considered safe without any ophthalmological side effects up to 30 days follow-up. Also, by improving sight and symptoms after 30 days, the initial evidence is that it has benefited our participants.

Posed limitations in the present study are the restricted number of patients and short follow up. Moreover as all participants were Caucasian further studies could enlight the influence of melanin content in patient skins' regarding treatment outcomes.

Further studies are needed to better understand potential use of plasma jet application to free gland ducts and recover meibum secretion on a larger scale of participants with EDE due to refractory MGD.

The use of plasma jet in refractory MGD evaporative DED patients in this case series was safe and effective after one month follow-up. Further investigation is needed, particularly comparing its outcome in other race and ethnicity, and longer follow-up times.

ACKNOWLEGMENTS

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Figure 1

Figure 2

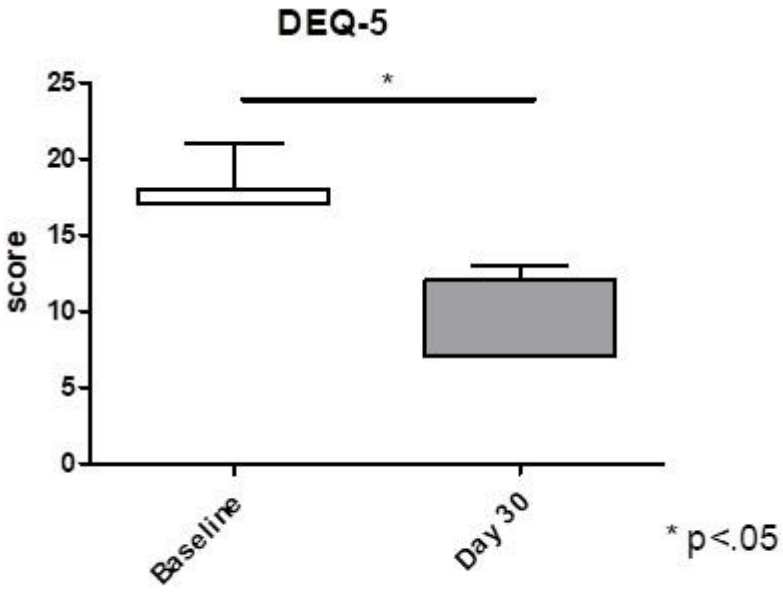

Figure 3A

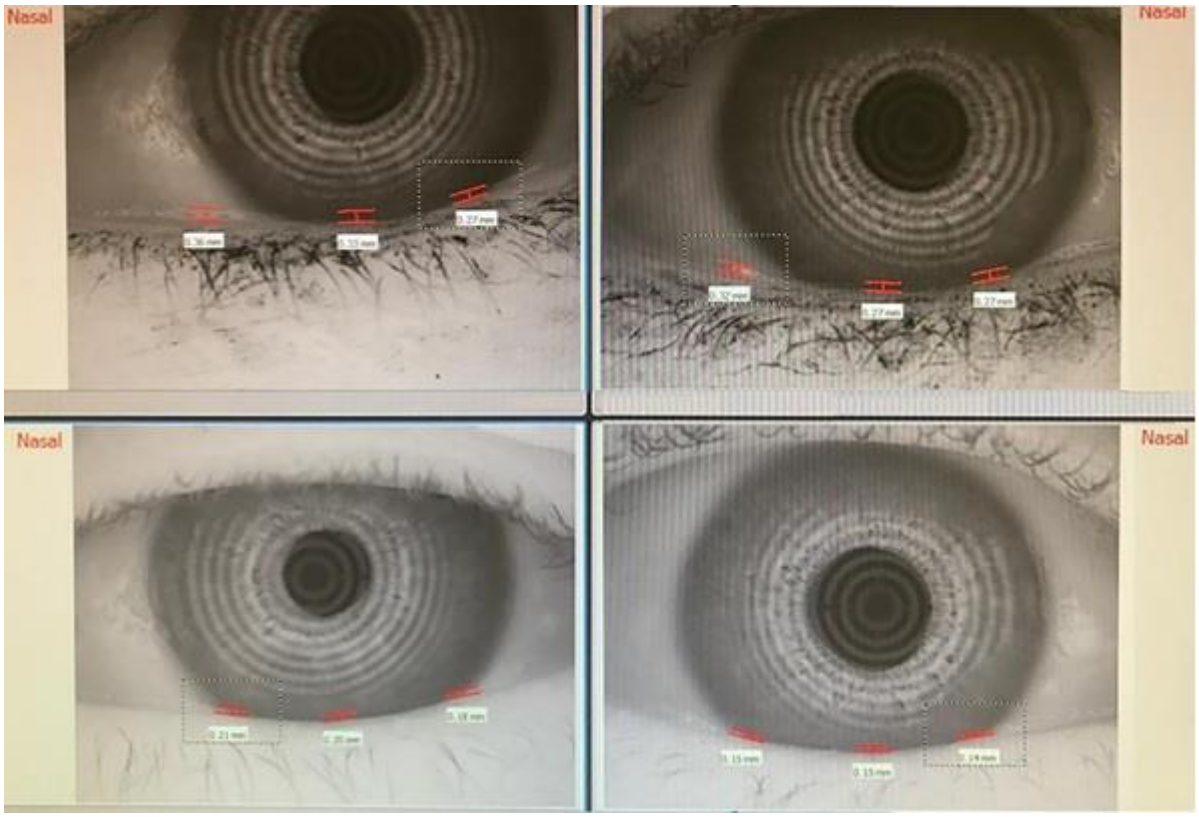

Figure 3B

Figure 3C

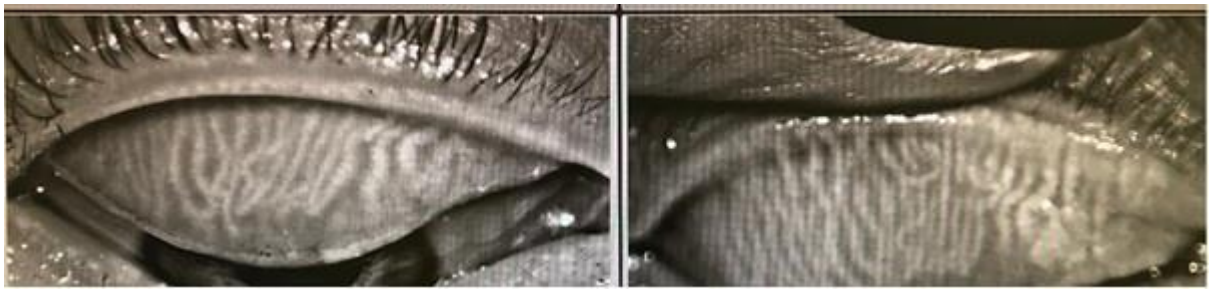

Figure 4

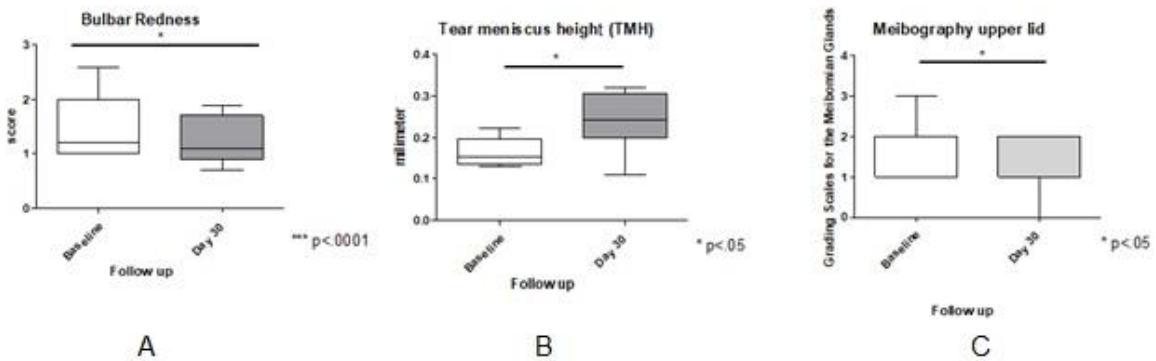

FIGURE LEGENDS

Figure 1. Plasma Jet applied to gland terminal ducts in the superior eyelid margin.

Figure 2. DEQ-5 questionnaire from baseline and 30 days after plasma jet application with a significantly improvement. (Wilcoxon single rang test, p=0.0218).

Figure 3 A. Tear Meniscus Height (TMH) from both eyes at baseline (bottom images) and 30 days after (upper images) evidencing the improvement.

Figure 3 B. Bulbar redness from Oculus Keratograph with a decrease from 2.9 to 2.2 30 days after the treatment.

Figure 3 C. Meibography from the upper eyelid before (left) and 30 days after the plasma jet (right).

Figure 4. Box plots presenting statistically significant improvement of bulbar redness (A), tear meniscus height (B) and meibography of the upper lid (C) from baseline and day 30 (paired t-test).