The Ocular Surface 16 (2018) 77–83

Contents lists available at ScienceDirect

The Ocular Surface

journal homepage: www.theocularsurface.com

Original Research

Randomized double-masked trial of eyelid cleansing treatments for blepharitis

Justin Sung, Michael T.M. Wang, Sang H. Lee, Isabella M.Y. Cheung, Salim Ismail, Trevor Sherwin, Jennifer P. Craig*

Department of Ophthalmology, New Zealand National Eye Centre, The University of Auckland, New Zealand

ARTICLE INFO

Article history:
Received 31 August 2017
Received in revised form
23 October 2017
Accepted 31 October 2017

Keywords:
Baby shampoo
Blepharitis
Conjunctival impression cytology
Eyelid cleanser
Eyelid hygiene
Meibomian gland dysfunction

ABSTRACT

Purpose: To compare the efficacy of a dedicated eyelid cleanser and diluted baby shampoo in the management of blepharitis.
Methods: Forty-three participants with clinical blepharitis signs were enrolled in a prospective, randomized, double-masked, paired-eye trial. A dedicated eyelid cleanser (TheraTears® SteriLid®) was applied to the eyelids of one eye (randomized) and diluted baby shampoo (Johnson's® No More Tears®) to the fellow eye, twice daily for 4 weeks. Tear film parameters, ocular surface characteristics, symptomology and cytology markers were assessed at baseline and day 28.
Results: Baseline measurements did not differ between treatments (all $p > 0.05$). The eyelid cleanser was preferred over baby shampoo by the majority of participants ($p < 0.001$). Improvements in the tear lipid layer, inferior lid wiper epitheliopathy (LWE), cylindrical collarettes, and MMP-9 expression were limited to the dedicated eyelid cleanser (all $p < 0.05$), and a greater decrease in SANDE symptoms score was also observed ($p = 0.04$). Meibomian gland capping and MUC5AC expression worsened with baby shampoo treatment (both $p < 0.05$). SPEED symptoms score, superior LWE, seborrhoeic lash crusting, and trichiasis decreased significantly following application of both treatments (all $p < 0.05$), but did not differ between treatments (all $p > 0.05$).
Conclusion: Clinical improvements in blepharitis occurred with both treatments. However, only the dedicated eyelid cleanser proved effective in reducing ocular surface inflammation, and was the preferred therapy. Long term impact of decreased goblet cell function secondary to baby shampoo treatment requires further exploration.

1. Introduction

Blepharitis is one of the most commonly encountered ophthalmic conditions in clinical practice [1,2] and is recognized to have a significant impact on ocular comfort and quality of life [2,3]. It is characterized by chronic eyelid inflammation and is frequently associated with symptoms of ocular surface irritation and dry eye [1,2,4,5]. The inflammatory process can involve both the anterior and posterior eyelid lamellae and affect the pericoular skin, eyelashes, lid margins, and meibomian glands [1,2].

The pathophysiology of blepharitis is multifactorial and has not yet been fully established. The over-colonization of eyelid bacteria observed in patients with blepharitis is thought to trigger hypersensitivity and inflammatory reactions of the ocular surface [1]. Bacterial lipolytic exoenzyme release may further promote such inflammatory responses and disrupt tear film homeostasis through the degradation of lipid layer constituents [6]. The potential association between *Demodex* infestation and blepharitis has also been recognized [7].

The management of blepharitis requires both the prevention and treatment of intermittent episodes of inflammatory exacerbation, which are associated with high bacterial loads [1,2,4,5]. Regular, ongoing eyelid hygiene regimens and warm compress therapy are commonly recommended for application in the longer-term for symptomatic relief [1,2,5]. An increasing range of dedicated eyelid cleansing formulations is becoming commercially available. Although greater subjective preference for dedicated eyelid cleansers has previously been reported [8,9], diluted baby shampoo continues to be frequently used [4,8,10]. However, an

* Corresponding author. Department of Ophthalmology, New Zealand National Eye Centre, The University of Auckland, Private Bag 92019, Auckland, 1142, New Zealand.
E-mail address: jp.craig@auckland.ac.nz (J.P. Craig).

https://doi.org/10.1016/j.jtos.2017.10.005
1542-0124/

animal study suggested increased ocular inflammation associated with diluted baby shampoo use [11], and a previous clinical study reported greater efficacy of a phospholipid-liposome solution than baby shampoo in improving clinical signs and symptoms of dry eye in contact lens wearers [9].

This randomized contralateral-eye trial sought to compare the efficacy of a dedicated eyelid cleansing formulation (TheraTears® SteriLid®) and diluted baby shampoo (Johnson's® No More Tears®) in blepharitis patients through the clinical assessment of ocular surface characteristics, tear film parameters, and symptomology, and through the quantification of inflammatory marker expression and goblet cell function via samples collected by impression cytology.

2. Materials and methods

2.1. Subjects

This prospective, 4-week, randomized, double-masked, paired eye trial, followed the tenets of the Declaration of Helsinki, was approved by the University of Auckland Human Participants Ethics Committee (UAHPEC-011255), and was registered as a clinical trial (ACTRN12616000545460). Subjects were required to be 16 years or older, with clinical signs of blepharitis on slit lamp examination (eyelash crusting, eyelid margin/eyelash abnormalities or meibomian gland capping), with no contact lens wear or use of topical/systemic medications known to affect the eye 48 h prior to baseline assessment or during the treatment period. Furthermore, eligibility required participants to report no history of major systemic, dermatological or ocular conditions, no ocular surgery in the previous three months, and no allergies or hypersensitivity to topical medications, cleansing formulations, or shampoos. Eligible participants were enrolled after providing written informed consent and were required to attend two visits, at baseline and day 28.

A total of 43 eligible participants were recruited, exceeding the sample size requirements for the desired study power. Power calculations were made with non-invasive tear film breakup time as the designated outcome, and showed that a minimum of 41 participants was required to detect a clinically significant difference of 5 s in pairwise comparisons, with 80% power ($\beta = 0.2$) at a two-sided statistical significance level of 5% ($\alpha = 0.05$). The SD of normal values was estimated to be 8 s [12]. Sample size estimates were determined using a uniform non-parametric adjustment, with NCSS PASS 2002 (Utah, USA).

2.2. Treatments

Participants were randomized to apply the dedicated eyelid cleanser (TheraTears® SteriLid®, Akorn, Illinois, USA) to one eye and the 1:10 diluted baby shampoo solution [11] prepared with distilled water in a sterile laboratory environment (Johnson's® No More Tears® Baby Shampoo, Johnson & Johnson, New Jersey, USA) to the fellow eye, twice daily, for a period of 28 days (Table 1). Participant masking was achieved by supplying the two treatments in identical 48 mL foam pump bottles that were labelled with the study allocated eye for application. Product application was demonstrated during the enrollment visit, and written instructions were also provided. Participants were instructed to apply and gently massage foam from one bottle onto the pericoular skin of the closed superior and inferior eyelids of the designated eye with clean fingertips for one minute before rinsing with water, and to take care to avoid the transfer of residual products to the fellow eye during cleansing and drying. Participants were also instructed to avoid direct contact with the ocular surface, and to clean their hands prior to using the second bottle for the fellow eye, in order to prevent cross contamination. Unused products were returned to the investigators at the end of the 28-day trial period, and weighed as a measure of participant compliance.

Table 1
Ingredients of the dedicated eyelid cleanser (TheraTears® SteriLid®) and baby shampoo (Johnson's® No More Tears®).

Eyelid cleanser	Baby shampoo
Water	Water
PEG-80 Sorbitan Laurate	PEG-80 Sorbitan Laurate
Sodium Trideceth Sulfate	Sodium Trideceth Sulfate
Cocamidopropyl Betaine	Cocamidopropyl Betaine
PEG-150 Distearate	PEG-150 Distearate
Sodium Chloride	Sodium Chloride
Sodium Lauroamphoacetate	Phenoxyethanol
Linalool	Glycerin
Sodium Laureth-13 Carboxylate	Citric Acid
Sodium Piperazinoethyl Acetate	Sodium Benzoate
Ethylsulfonate	Tetrasodium EDTA
Boric Acid	Polyquaternium-10
Sodium Perborate	Ethylhexylglycerin
Panthenol	Sodium Hydroxide
Allantoin	Potassium Acrylates Copolymer
Cocamidopropyl PG Dimonium Chloride	Yellow 6
Melaleuca Alternifolia Leaf Oil	Yellow 10
Trisodium EDTA	Parfum
Etidronic Acid	
Citric Acid	
Sodium Hydroxide	

2.3. Clinical measurements

The McMonnies dry eye questionnaire and Ocular Surface Disease Index (OSDI) were administered to grade the level of dry eye symptoms at baseline, while the Standard Patient Evaluation of Eye Dryness (SPEED) and Symptom Assessment iN Dry Eye (SANDE) questionnaires were administered for the purpose of comparing symptomology at baseline and day 28. The overall SANDE score was calculated as the square root of the product of the frequency and severity scores [13].

Clinical assessments were conducted at baseline and day 28 of the treatment period. The investigators conducting clinical assessments were masked to treatment randomization. All participants were assessed at the same location, with a mean ± SD room temperature of 20.8 °C ± 1.4 °C and a mean ± SD relative humidity of 52.4% ± 5.1%. The measurements were conducted in ascending order of invasiveness to minimize the impact on ocular surface or tear film physiology for subsequent tests: tear meniscus height, noninvasive tear film breakup time, tear film lipid layer grade, conjunctival hyperaemia, tear film osmolarity, slit lamp examination, ocular surface staining, meibomian gland expression, infrared meibography, and conjunctival impression cytology.

The lower tear meniscus height was assessed using high magnification digital imaging captured by the Oculus Keratograph 5M, and three measurements near the center of the lower meniscus were averaged. Noninvasive tear film breakup time and tear film lipid layer grade were also assessed using the Oculus Keratograph 5M. Breakup time was recorded as the time taken following a blink for the grid reflection to first show distortion, while the subject maintained fixation and was requested to refrain from blinking. Three breakup time measurements were averaged in each case [14]. Lipid layer grading was based on the modified Guillon-Keeler grading system: grade 1, open meshwork; grade 2, closed meshwork; grade 3, wave or flow; grade 4, amorphous; grade 5, colored fringes; grade 0, non-continuous layer (non-visible or abnormal colored fringes) [15,16]. Bulbar conjunctival hyperemia was assessed by automated objective evaluation of high magnification