Demodex Blepharitis Treated with a Novel Dilute Povidone-Iodine and DMSO System: A Case Report

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ABSTRACT

Introduction: Povidone-iodine aqueous solution is an antiseptic commonly used in ophthalmology for treatment of the ocular surface. Dimethylsulfoxide (DMSO) is a well-known skin penetration enhancer that is scarcely utilized in ophthalmic drug formulations. We describe here a low-dose formulation of 0.25% PVP-I in a gel containing DMSO for the treatment of Demodex blepharitis.

Case Report: A 95-year-old female presented with chronic blepharitis involving both the anterior and posterior eyelid margins. The anterior eyelid margins demonstrated pathognomonic features consistent with Demodex infection, and this diagnosis was confirmed with microscopy. Previous traditional therapies had been ineffective at controlling her signs and symptoms.

Conclusion: The topical PVP-I/DMSO system was effective at treating the signs and symptoms of Demodex blepharitis. Further investigation of the novel agent is warranted.

Keywords: Blepharitis; Demodex; Infection; Inflammation; Ocular surface

INTRODUCTION

Demodex is a well-recognized but often overlooked cause of chronic blepharitis and is implicated in ocular rosacea [1–7]. It is described as a translucent, eight-legged arachnid, and is the most common ectoparasite found on the human skin. Although prevalent in asymptomatic patients, rates of infestation with Demodex increase with age, nearing 100% by 70 years old [8]. Infection in humans is brought about by two distinct species, Demodex folliculorum and Demodex brevis. The former is typically found in lash follicles and manifests as anterior blepharitis, while the latter—which is smaller in size—more commonly infects the sebaceous glands, causing posterior blepharitis, meibomian gland disease, and keratoconjunctivitis. Besides the identifiable signs of
demodicosis, it has been reported that De-
modex-infested patients may experience dis-
turbing ocular surface symptoms which can be
enumerated by ocular surface disease index
scoring [9]. Both species of mite are capable of
inducing inflammation in a variety of direct
ways, including destruction of epithelial cells,
claw-related trauma, and mechanical obstruc-
tion of glands [10]. Indirectly, Demodex spp.
may serve as a vector transporting bacteria to
deep eyelid structures and a stimulant to the
host immune system. Also, reaction to the
chitin exoskeleton has been implicated in
granuloma and chronic chalazia formation
[11, 12]. Successful treatment of Demodex mites
has reportedly been achieved topically with tea
tree oil and systemically with ivermectin or
metronidazole [13–16].

Povidone-iodine (PVP-I) is a potent antisep-
tic that is commonly utilized in ophthalmology
for ocular surface pretreatment prior to invasive
surgical procedures [17–19]. It is lesser known,
however, that PVP-I has historic utility in the
treatment of camelid demodicosis [20]. We
previously reported that a dilute PVP-I and
DMSO system was useful in the treatment of
rosacea blepharoconjunctivitis [21]. We report
here the use of a dilute 0.25% povidone-iodine
gel in a DMSO solvent gel for the treatment of a
case of Demodex blepharitis.

CASE REPORT

Informed consent was obtained from the
patient prior to the publication of this case
report. A 95-year-old pseudophakic female pre-
sented to our clinic complaining of a long-s
standing history of ocular pruritus, dry eye,
irritation, and eyelid crusting, for which she
used only artificial tears and lid compresses
without improvement. Treatment with tea tree
oil or steroid/antibiotic combination medicines
was not attempted.

Slit lamp biomicroscopic examination
revealed mild bilateral anterior eyelid erythema
and multiple cylindrical collarettes found at the
base of the upper and lower lid eyelashes (Fig. 1a).
There was no lash breakage, madarosis,
poliosis, or misdirection. Inspection of the
posterior eyelid margins revealed mild meibo-
mian inspissation with capping. Secretions were
slightly thickened, but not turbid. There were
no mucocutaneous or marginal telangiectasias.
Conjunctival examination showed mild, diffuse
injection, and corneal examination was positive
for scattered inferior punctate corneal erosions
and a decreased tear break-up time. A diagnosis
of Demodex blepharitis was made. To confirm
the diagnosis, epilation of the affected eyelashes
was performed and examined with 25x micro-
scopy according to published protocols [22].
Visual confirmation of Demodex was achieved.

The patient was then prescribed a proprietary
formulation of a topical gel consisting of 0.25%
PVP-I in a dimethylsulfoxide (DMSO) vehicle
prepared by a licensed compounding pharmacy.
The treatment was administered twice daily and
administered by rubbing the gel with the finger
directly onto the lash line while the eye was
closed. The instructions were specific: to keep
the eye closed and apply the drug to the lash
surface from the skin side. At the first follow-up
visit, one week later, there were remarkable
improvements in both patient signs and symp-
toms. Most prominently, the seven foci of
cylindrical dandruff of the right eye and five
on the left eye were no longer present (Fig. 1b).
There was one remaining cylindrical dandruff
focus on the left lower eyelid. A few punctate
corneal erosions and a decreased TBUT
remained, but the patient reported a remarkable
improvement in ocular itching and irritation.
At one month, the changes to the anterior
eyelid were preserved, the corneal punctate
erosions were no longer present, and the pos-
terior eyelid meibum was less viscous. The
patient endorsed facile utilization of the medi-
cine with clear application instructions, and
there were no reported adverse events.

DISCUSSION

It is understood that Demodex infestation plays
an etiologic role in chronic blepharitis.
Although the scope of blepharitis includes
anterior, posterior, and mixed phenotypes, only
the presence of cylindrical dandruff is consid-
ered pathognomonic for Demodex infestation
Other ocular manifestations of Demodex may include keratitis, marginal infiltrates, conjunctivitis, and blepharoconjunctivitis. Demodex is also isolated successfully from normal human subjects, and therefore a commensal role for the mite is plausible. The evidence supporting its importance in maintaining ocular ecology revolves around the ability of Demodex to control bacterial populations, impose its own bacterial microflora, and outcompete other mites [24]. The current preferred treatment agent for infection is tea tree oil or its active component, terpinen-4-ol. Both have demonstrated efficacy as a demodicidal agent in vivo and in vitro [13, 14, 25]. While these agents are useful, reports of local hypersensitivity reactions and persistent mite survival do exist [14, 26]. Other traditional mite therapies designed to trap or suffocate Demodex have been shown to be ineffective, perhaps due to the minimal aerobic requirements of the arachnid or the robust nature of its exoskeleton. In one report, Demodex was found to be resistant to both 75% alcohol and 10% PVP-I [14].

Our current understanding of Demodex and its relation to the human skin is evolving. Demodex has been implicated in not only chronic blepharitis but also other dermatological inflammatory conditions, including acne and rosacea. Patients with rosacea have been shown to have a higher density of Demodex infestation compared to controls [7, 27, 28]. Although there is no exact relationship of symptoms or manifestations of disease with the Demodex population, it is thought that factors such as age, genetics, immune status, and sebum content may play a role in disease expression. For instance, in those who harbor Demodex but show little inflammation, the deep, ensconced location of the mite within the eyelid may create a safe harbor from host innate immunity. An eventual inciting event, activating a delayed hypersensitivity cascade, may facilitate the development of inflammatory skin conditions such as rosacea. There is also a relationship between rosacea and the presence of Demodex mites carrying the bacteria Bacillus oleronius, a Gram-negative, nonmotile endospore-forming rod [29]. Studies have found that multiple antigenic proteins produced by the bacteria are particularly immunogenic and proinflammatory [28, 30]. Finally, Demodex may harbor other pathogenic bacteria such as Streptococcus and Staphylococcus spp., whose superantigens have also been implicated in rosacea [31].

We have reported the first successful treatment of mixed blepharitis secondary to Demodex with a dilute PVP-I/DMSO gel system. Similar success with a dilute PVP-I/DMSO agent in a case of rosacea blepharoconjunctivitis has been reported [21]. This is not surprising given the potential overlap between both conditions. The result is surprising given that more concentrated 10% PVP-I solutions reportedly failed to demonstrably eradicate Demodex during in vitro studies. To better understand this, there are certain advantages to our treatment that must be underscored. First, dilute PVP-I concentrations have a greater capacity to deliver free molecular iodine at infection sites [32]. This increased free molecular iodine is known to be...
the most antimicrobially active iodine species. We also may be seeing an anti-inflammatory effect of PVP-I, as the iodine is able to act as a reduction agent for superoxide generated in the host inflammatory cascade [33].

DMSO is a polar, aprotic solvent that has been employed as an inactive ingredient in several FDA-approved products. It has particular attributes that may enhance the efficacy of dilute PVP-I. Importantly, it is a skin penetration enhancer and exerts a concentration-dependent effect on cellular membranes. Modular dynamics simulations have shown that DMSO can partition the lipid bilayer, changing membrane fluidics, and at higher concentrations it can induce hydrophilic and hydrophobic water pores [34]. This pore formation is likely the means of enhancing the penetration of the dilute PVP-I.

In terms of potential mechanisms of action that are vital to the success of this treatment, it is likely that the PVP-I/DMSO system is able to reach the deep eyelid structures including the pilosebaceous units and the tarsal meibomian glands. As we have seen, it is in and around these structures that Demodex mites reside, often beyond the reach of conventional treatment agents that cannot penetrate into these locations. Once it has reached the target site, the strong solvating potential of the DMSO may have an effect on the permeability of the chitin exoskeleton, enhancing PVP-I penetration and contributing to the demodicidal effect.

The report of a single successful case is of course limited by the lack of confirmatory findings in additional cases, the lack of controls, and the lack of any study design intended to allow more rigorous evaluations of the therapy. Nonetheless, given our experience with PVP-I/DMSO systems in a variety of ocular and skin indications, we think that this promising initial report warrants additional study in expanded, controlled clinical trials.

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Disclosures. Jesse S. Pelletier is a founding member and employee of Veloce BioPharma. Jesse S. Pelletier also has a pending patent related to this work. Kara Capriotti is a founding member and employee of Veloce BioPharma. Kara Capriotti also has a pending patent related to this work. Kevin S. Stewart is a founding member and consultant to Veloce BioPharma. Kevin S. Stewart also has a pending patent related to this work. Joseph A. Capriotti is a founding member and employee of Veloce BioPharma. Joseph A. Capriotti also has a pending patent related to this work.

Compliance with Ethics Guidelines. Informed consent was obtained from the patient prior to the publication of this study.

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