ABSTRACT

Introduction: The objective of this pilot study was to determine the preliminary efficacy of a novel ophthalmic suspension containing povidone-iodine 0.4% and dexamethasone 0.1% in the treatment of adenoviral conjunctivitis. Methods: A prospective, open-label, single-armed, phase II clinical trial in humans. Eligible patients with the clinical signs and symptoms of acute conjunctivitis who tested positive for adenoviral antigen by Rapid Pathogen Screening (RPS) Adeno Detector were enrolled in a single treatment arm consisting of a combination povidone-iodine 0.4%/dexamethasone 0.1% sterile ophthalmic suspension given four times daily for a minimum of 5 days. RPS Adeno Detector testing was performed at baseline and at each follow-up visit along with ocular fluid sampling by conjunctival swabs. Subsequent analysis performed on all swabs included both adenoviral titer by quantitative polymerase chain reaction (qPCR) and cell culture with confirmatory immunofluorescence (CC-IFA). The primary endpoint was clinical resolution of conjunctival injection and discharge. Secondary measures included reduction of qPCR titers and eradication of infectious virus as determined by CC-IFA. Results: A total of nine eyes of six patients with clinical signs and symptoms of acute viral conjunctivitis and a positive RPS Adeno Detector test result were enrolled in the study. In eight/nine eyes enrolled in the study, clinical resolution was observed by day 3 or day 4. In six/six eyes with detectable adenovirus by qPCR, significant reduction in viral titer was seen by day 3, day 4, or day 5. In five/six eyes with infectious virus confirmed by CC-IFA at enrollment, elimination of infectivity was achieved by day 4 or day 5. One patient was lost to follow-up. Conclusions: An ophthalmic suspension
containing povidone-iodine 0.4% and dexamethasone 0.1% may be a useful agent in the treatment of acute RPS Adeno Detector-positive conjunctivitis. A further placebo-controlled study with a larger number of patients is warranted.

**Keywords:** adenovirus; conjunctivitis; cornea; ocular infection; pink eye; povidone-iodine; PVP-I; steroids

**INTRODUCTION**

External ocular infections caused by adenoviruses are among the most common eye infections seen worldwide. While typically self-limited, they can lead to highly infectious community epidemics, seasonal outbreaks, lost labor productivity, significant patient discomfort, and in some cases permanent visual compromise from long-term immune-mediated sequelae. Although several therapeutic agents have been evaluated for acute viral conjunctivitis in both animal models and human trials, none to date have been approved by the Food and Drug Administration for human conjunctivitis. Despite recent interest in the development of anti-viral agents by both industry and academic investigators, there are currently very few clinical trials evaluating anti-adenoviral ocular therapies in humans.

With no effective agents available to treat these common, highly symptomatic, contagious infections, many clinicians adopt idiosyncratic therapeutic regimens that include a mix of comfort measures (ie, artificial tears, cold compresses), topical antibiotics, and in many cases topical steroids. It is widely accepted that a short course of topical corticosteroids (and in some severe cases oral steroids) can limit patient discomfort and prevent some immune-related inflammatory complications of acute viral conjunctivitis. While this strategy may have some efficacy in the short-term amelioration of symptoms, studies in the New Zealand white rabbit model have suggested that even a short course of relatively low-potency corticosteroids without the addition of a suitable anti-viral agent can increase the duration of viral shedding and prolong the infectivity of affected patients. This in turn can potentiate the occurrence of community outbreaks and epidemic transmission in schools, places of business, and medical facilities.

Povidone-iodine (PVP-I) is a commercially available antiseptic with a long history of use in laboratory disinfection, general surgery, and ophthalmology. Dilute PVP-I solutions are toxic to viruses (including human immunodeficiency virus), fungi, parasites, and bacteria. Previous studies have demonstrated efficacy in active infections, endophthalmitis prophylaxis before and after ocular surgery, and in the prevention of neonatal conjunctivitis. Additionally, PVP-I has been described as an effective treatment for acute viral conjunctivitis in a variety of anecdotal reports. Dexamethasone is a well-tolerated, potent steroid with a long history of use as a topical ophthalmic anti-inflammatory alone and in combination with other agents.

It is our intention to investigate a safe, tolerable, efficacious combination agent that includes a powerful anti-viral and a potent topical steroid. In this way, we expect to be able to effectively treat both the inflammatory and infectious components of acute adenoviral conjunctivitis by decreasing the symptomatic period following infection, shortening the duration of viral shedding, and reducing the potential for infectious transmission.