**Suprachoroidal Administration of Triamcinolone Acetonide Using a Microneedle for the Treatment of Posterior Ocular Inflammation**

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**ABSTRACT SUMMARY**

Administration of drugs to the suprachoroidal space (SCS) is a novel and emerging topic in ocular drug delivery to the back of the eye. This work describes a minimally invasive way to access this space with a microneedle and demonstrates the potential to treat inflammation in the back of the eye in two distinct animal models. Administration of triamcinolone acetonide (corticosteroid) leads to a reduction in the inflammatory response in these animal models and administration into the SCS did not lead to any significant adverse events.

**INTRODUCTION**

Local drug delivery to the back of the eye continues to be a challenging task both from a technical and clinical practice perspective. Currently, administration of drugs for treating many back of the eye diseases such as wet- age related macular degeneration and posterior uveitis is to administer drugs directly into the central chamber of the eye called the vitreous. These injections, called intravitreal injections, have become routine only within the last decade¹ and very few other options exist for clinicians to effectively deliver drugs to the back of the eye.

One novel alternative would be to administer drugs into the suprachoroidal space (SCS). The SCS is a virtual space that is located between the sclera and choroid of the eye and forms when fluid accumulates between these tissues. This space could be used as a route of administration for treating back of the eye diseases since it is located directly adjacent to diseased tissues and has the ability to hold a significant volume of drug formulation. This approach would allow more targeted delivery of the drug to the diseased tissues and may lead to a better safety profile of drugs such as corticosteroids. However access to the SCS has been limited to surgical techniques and tools². Microneedles have been shown to access this space in a non-surgical and minimally invasive way³ but very little work has been done to show the efficacy of drugs delivered into the SCS for treating diseases. This work shows in two animal models of posterior uveitis (inflammation) that administration of triamcinolone acetonide into the SCS is effective in mitigating the inflammatory response.

**EXPERIMENTAL METHODS**

The first experiment involved an acute porcine model of posterior uveitis. Twenty weanling pigs received intravitreal injection with balanced salt solution (BSS) or lipopolysaccharide (LPS) followed 24 hours later with injection of 0.2 mg or 2.0 mg of triamcinolone acetonide into the SCS or vitreous. The SCS was accessed using microneedles designed by Clearside specifically for pig eyes measuring approximately 850 µm in length. Clinical ocular inflammatory scores and intraocular pressure measurements were collected daily, while electroretinography, optical coherence tomography, and wide-field ocular fundus photography was performed on -1, 0, and 3 days after treatment. Pigs were then euthanized, aqueous and vitreous humor collected for cell counts and protein levels, and the eyes were processed for histopathology.

Treatment through the SCS was also tested in a second inflammatory model in the rabbit. On Day 1, female rabbits (4/group) received a
single unilateral injection of vehicle or 4 mg TA (Triesence®) into the suprachoroidal space (SCS) using a 750 µm microneedle, or a 4 mg TA intravitreal injection using a standard 30g needle. Intraocular pressure (IOP) was assessed prior to uveitis induction. On Day 6, each animal received a single unilateral subretinal injection of lipopolysaccharide (LPS) to induce ocular inflammation in the treated eye. Animals were monitored for 22 days following dose administration. Endpoints included body weights, ocular observations, slit lamp biomicroscopy with McDonald-Shadduck scoring and photography, indirect ophthalmoscopy, fundus photography, and histopathology.

RESULTS AND DISCUSSION

Preliminary results indicate that in the porcine model, delivery of TA to the SCS using microneedles was simple, effective, and not associated with adverse effect or toxicity. SCS injection of low (0.2 mg) and high doses (2 mg) of TA was as effective in the reduction of acute inflammation in the ocular posterior segment as high dose intravitreal injection. Low dose SCS TA was also effective in reducing inflammation, however low dose intravitreal TA was less effective. No adverse events were reported with any of the injections.

In the rabbit model, there were no test article or administration-related effects on mortality, body weights, ocular observations, or IOP. Following LPS injection in this endotoxin-induced uveitis model, eyes developed acute anterior and posterior segment inflammation with extensive fibrin formation in the anterior chamber and vitritis. Twenty-four hours following LPS injection, eyes that were administered by either SCS vehicle or intravitreal TA displayed greater panuveitis than SCS TA treated eyes. Vitritis, aqueous flare, and cellularity were substantially less severe in both SCS and intravitreal TA groups of eyes compared to SCS vehicle eyes. Iris vessel dilation and tortuosity was reduced in SCS TA animals and reduced to a lesser extent in intravitreal TA animals when compared with the SCS vehicle group. SCS TA caused a significant reduction in inflammatory endpoints when compared with the vehicle group throughout the study. There was a marked reduction in inflammation as assessed histopathologically in eyes administered either SCS or intravitreal TA when compared with the vehicle group.

CONCLUSION

Results from these two studies suggest that inflammation in the back of the eye can be treated with a SCS injection of triamcinolone acetonide. The injections performed with Clearside Biomedical’s proprietary microneedle technology did not lead to any adverse events and were performed without any surgical intervention.

REFERENCES

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