ISSN: 2641-2020
DOI: 10.33552/APPR.2022.03.000558
Archives of Pharmacy & Pharmacology Research
Iris Publishers

Review Article

Suprachoroidal Triamcinolone Injection for Noninfectious Uveitis Macular Edema Treatment

Lisa Kongrat[1,2] and Varanuj Chatsudthipong[3]*

[1]*Massachusetts Eye Research and Surgery Institution (MERSI), Waltham, Massachusetts, USA*

[2]*Department of Ophthalmology, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand*

[3]*Research Center of Transport Proteins for Medical Innovation, Faculty of Science, Mahidol University, Bangkok, Thailand*

***Corresponding author:** Varanuj Chatsudthipong, Research Center of Transport Proteins for Medical Innovation, Faculty of Science, Mahidol University, Bangkok, Thailand.

Received Date: December 12, 2022

Published Date: December 21, 2022

Introduction

Uveitis is inflammation of the uvea. The etiology of uveitis can be classified as infectious or non-infectious. Noninfectious uveitis can be an autoimmune process or due to idiopathic cause. Uveitis is one of the common causes of vision loss that accounts for about 5-20% of blindness in the US and Europe [1, 2]. In developing countries, uveitis is responsible for about 25% of blindness [3, 4]. The primary aim of noninfectious uveitis treatment is to control the inflammation and minimize complications. There are many complications from uveitis that can cause visual impairment, including macular edema, glaucoma, cataract or destruction of optic nerve or photoreceptor. Among these complications, macular edema happens the most common and the leading cause of visual loss in noninfectious uveitis (NIU) [5] and is present about 33% of patients with uveitis [6]. Macular edema is the accumulation of fluid in the retinal layers or the subretinal space. It is mostly associated with inflammatory processes which cause the release of various factors and result in breakdown of the blood-retina barrier. There are many treatment options in treating NIU, including corticosteroid, anti-vascular endothelial growth factor (VEGF) and immunomodulatory agents.

Corticosteroid

Corticosteroid is the mainstay and first line of treatment in NIU [7]. There are many routes of administration that can be utilized in the treatment of uveitis. The topical route has limited ocular penetration and is suitable for anterior uveitis [7]. Topical steroid drops can cause elevations in intraocular pressure (IOP) and cataract formation. Peribulbar and intravitreal steroid injections can target more posterior pathology. These routes can be used to treat anterior, intermediate, or posterior inflammation. However, the risk of complications limits their use, as IOP elevation and cataract formation are more frequently seen with injections compared to topical steroids [8]. Systemic corticosteroid is considered in more severe cases with posterior involvement. Systemic steroids can quickly decrease inflammation. However, careful monitoring is required, and systemic steroids are not recommended for long-term use as they can cause many adverse effects [9] including easy bleeding, electrolyte imbalances, cushingoid appearance, weight gain and adrenal insufficiency [8]. Steroid-sparing immunomodulatory agents are more suitable options in chronic cases. These conventional routes of steroid administration all have limitations. A novel route, suprachoroidal administration, provides superior benefits over the conventional route of steroid administration in uveitis management.

The suprachoroidal space

The suprachoroidal space is known as a potential space between the sclera and choroid, is closely proximate to the choroid

and retina. Since it is a potential space, it can be expanded without disrupting the adjacent tissue. The advantage of this novel mode of delivery is more targeted therapy. Drug administration via this approach can achieve chorioretinal drug concentrations 10 times higher than current intravitreal injections [10,11]. Furthermore, compartmentalization in the suprachoroidal space helps keep the drug away from non-targeted tissue. This delivery method can potentially be further applied to gene therapy and ocular oncology [12,13].

Suprachoroidal triamcinolone injection in treating noninfectious uveitis macular edema

Administration of triamcinolone acetonide (TA) into the suprachoroidal space provides greater concentrations of the drug in chorioretinal tissue which result in prolonged pharmacokinetic durability and therapeutic levels [14]. In preclinical studies, after suprachoroidal administration of 40 mg/ml TA in rabbit models, plasma levels of TA concentrations peaked at day 1 and decreased until no longer detectable at day 63 [15]. There was no TA level detected in the aqueous humor [15]. In the AZALEA study, an open-label trial, TA concentrations in plasma was < 1 mg/ml after injections, which highlighted the compartmentalization property of this delivery system [14]. The best-corrected visual acuity (BCVA) and central subfield thickness (CST) demonstrated moderate improvement in this trial [14]. In the previous PEACHTREE study, a 6-month trial of suprachoroidal triamcinolone injection in subjects with uveitic macular edema, showed improvement of ≥15 ETDRS letters from baseline with 47% of the treatment group compared to 16% of the control group [16]. This study also demonstrated a significant reduction of macular edema in more than 50% of patients. The CST reduction was greater in the treatment group, 153 μm, compared to the sham group, 18 μm (p <0.001) [16]. The efficacy was maintained for up to 9 months, according to an extended study, the MAGNOLIA study [17]. Another advantage of compartmentalization is a reduction in adverse events as previously mentioned. This route delivers therapeutic drug levels into the posterior segment with limited exposure to the anterior chamber. The ocular specific distribution of this method provides an IOP-sparing benefit. In the PEACHTREE trial, the rate of IOP elevation was 11.5% compared to 20% - 60% for intravitreal triamcinolone and intravitreal dexamethasone implants [18]. The rate of cataract progression was comparable, 7% in the treatment group vs 6% in the control group [16]. The therapy is well tolerated over 36 weeks.

Conclusion

Corticosteroid is the gold standard in NIU management. It is crucial in early treatment since it can rapidly control the inflammation process. It can be given via topical drops, periocular injections, intravitreal injections, or systemically. Each route has benefits and risks as previously described and can be used according to the location and severity of the inflammation. The current delivery methods of local steroid therapy can provide good efficacy but risk complications such as cataract formation and glaucoma. The novel method, suprachoroidal triamcinolone injections, enhance delivery of therapies in more precise anatomical distribution which result in higher efficacy and safety compared to current modes of delivery.

Acknowledgement

We gratefully acknowledge Professor Stephen Foster for giving Dr. Lisa Kongrat an opportunity to obtain an excellent training at MERSI. Dr. Lisa Kongrat is supported by Thammasat University Hospital Fund for training at MERSI. We also thank Dr. Jonathan Lorgunpai for his critical comments of the manuscript and Dr. Supinda Leeamornsiri for her valuable advice.

Conflict of Interest

There is no conflict of interest

References

1. Suttorp-Schulten MS, Rothova A (1996) The possible impact of uveitis in blindness: a literature survey. Br J Ophthalmol 80(9): 844-848.
2. Thorne JE, Suhler E, Skup M, Tari S, Macaulay D, et al. (2016) Prevalence of Noninfectious Uveitis in the United States: A Claims-Based Analysis. JAMA Ophthalmol. 134(11): 1237-1245.
3. Rao NA (2013) Uveitis in developing countries. Indian Journal of Ophthalmology. 61(6): 253-254.
4. London NJS, Rathinam SR, Cunningham ET (2010) The Epidemiology of Uveitis in Developing Countries. International Ophthalmology Clinics. 50(2): 1-17.
5. Rothova A, Suttorp-van Schulten MS, Frits Treffers W, Kijlstra A (1996) Causes and frequency of blindness in patients with intraocular inflammatory disease. Br J Ophthalmol. 80(4): 332-336.
6. Joanne H Lee, Helen Mi, Rachel Lim, Su Ling Ho, Wee Kiak Lim, et al. (2019) Ocular Autoimmune Systemic Inflammatory Infectious Study - Report 3: Posterior and Panuveitis. Ocul Immunol Inflamm. 27(1): 89-98.
7. LeHoang P (2012) The gold standard of noninfectious uveitis: corticosteroids. Dev Ophthalmol. 51: 7-28.
8. Valdes LM, Sobrin L (2020) Uveitis Therapy: The Corticosteroid Options. Drugs. 80(8): 765-773.
9. Rothova A (2002) Corticosteroids in uveitis. Ophthalmol Clin North Am. 15(3): 389-394.
10. Patel SR, Lin AS, Edelhauser HF, Prausnitz MR (2011) Suprachoroidal drug delivery to the back of the eye using hollow microneedles. Pharm Res. 28(1): 166-176.
11. SR Patel, DE Berezovsky, BE McCarey, V Zarnitsyn, HF Edelhauser, et al. (2012) Targeted administration into the suprachoroidal space using a microneedle for drug delivery to the posterior segment of the eye. Invest Ophthalmol Vis Sci. 53(8): 4433-4441.
12. Ding K, Shen J, Hafiz Z, Hackett SF, Silva RLE, et al. (2019) AAV8-vectored suprachoroidal gene transfer produces widespread ocular transgene expression. J Clin Invest. 129(11): 4901-4911.

13. C Rei Wan, Leroy Muya, Viral Kansara, TA Ciulla (2021) Suprachoroidal Delivery of Small Molecules, Nanoparticles, Gene and Cell Therapies for Ocular Diseases. Pharmaceutics. 13(2): 288.

14. Henry CR, Shah M, Barakat MR, Dayani P, Wang RC, et al. (2022) Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA). Br J Ophthalmol. 106(6): 802-806.

15. Edelhauser HF, Verhoeven RS, Burke B, Struble CB, Patel SR, et al. (2014) Intraocular Distribution and Targeting of Triamcinolone Acetonide Suspension Administered into the Suprachoroidal Space. Investigative Ophthalmology & Visual Science. 55(13): 5259.

16. Yeh S, Khurana RN, Shah M, Henry CR, Wang RC, et al. (2020) Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial. Ophthalmology. 127(7): 948-955.

17. Khurana RN, Merrill P, Yeh S, Suhler E, Barakat MR, et al. (2022) Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). Br J Ophthalmol. 106(8): 1139-1144.

18. Thorne JE, Sugar EA, Holbrook JT, Burke AE, Altaweel MM, et al. (2019) Periocular Triamcinolone vs. Intravitreal Triamcinolone vs. Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Edema: The PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) Trial. Ophthalmology. 126(2): 283-295.