

## Research Article

# Intravitreal Dexamethasone Implant (Ozurdex) for Ocular Toxocariasis

**Yongwei Zhou, Fangyuan Zhen, Jiahui Wu, Shasha Wang, Xiaoyan Lu, Ge Yang, Zhirou Hu, Fei Chen, Qiuming Li , and Shuqian Dong **

*Department of Ophthalmology, The First Affiliated Hospital of Zhengzhou University, Henan Provincial Ophthalmic Hospital, Zhengzhou, China*

Correspondence should be addressed to Qiuming Li; [liqiuming63@163.com](mailto:liqiuming63@163.com) and Shuqian Dong; [dongshuqian2006@163.com](mailto:dongshuqian2006@163.com)

Received 7 February 2023; Revised 13 June 2023; Accepted 2 February 2024

Academic Editor: Akio Oishi

Copyright © 2024 Yongwei Zhou et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

This study aimed to evaluate the efficacy and safety of intravitreal dexamethasone implants in the treatment of ocular toxocariasis (OT). A retrospective analysis was performed on 6 cases in which laboratory tests diagnosed OT. All patients were administered with intravitreal dexamethasone implants with or without vitrectomy. The average follow-up time was 19.7 months. All operated eyes achieved anatomic success, and all patients' visual acuity was improved. Five of these six had a visual acuity of 20/100, and three had final acuity of 20/40 or even better. Intravitreal dexamethasone implants can be used to treat different types of OT, which not only effectively control inflammation and improve the patient's vision but also reduce the use of systemic glucocorticoids.

## 1. Introduction

Toxocariasis is a manifestation of a parasitic infection caused by the roundworms *Toxocara canis* or *Toxocara cati* [1, 2]. They are the most prevalent gastrointestinal parasites in dogs and cats; when infected, these animals contaminate the environment through their feces [3]. Ocular toxocariasis (OT) is caused by people accidentally swallowing *Toxocara* eggs, which hatch in the small intestine and release parasitic larvae. These larvae then penetrate the intestinal wall, enter the circulation, and migrate to the eyes, where they cause an inflammatory response [4]. OT is usually unilateral, and its clinical manifestations are diverse, depending primarily on the number of parasites, the site of infection, the host's immune response, and the migration pattern of the larvae [5]. The typical fundus abnormalities are posterior pole granulomas or peripheral granulomas with vitreous traction cords, or moderate to severe vitreous inflammatory reactions with retinal inflammatory masses [6]. The main treatment methods include drug therapy (glucocorticoids and antiparasitic drugs) and surgical treatment [7–9].

Dexamethasone (DEX) is a powerful synthetic member of the glucocorticoid class of steroid drugs that has anti-

inflammatory and immunosuppressant activities, 30 times more effective than those of cortisol and 6 times more effective than those of triamcinolone [10]. In recent years, some scholars have proposed to apply the dexamethasone intravitreal implant to OT patients to reduce the use of systemic glucocorticoids [11]. The dexamethasone intravitreal implant (Ozurdex; Allergan, Inc., Irvine, CA) is an approved therapy for diabetic macular edema, retinal vein occlusion, and noninfectious posterior uveitis [12]. The efficacy was demonstrated by improvements in visual acuity and vitreous haze, as well as a decrease in retinal thickness [13]. In this study, we treated patients by injecting DEX implants with or without vitrectomy and studied the therapeutic effect of injection of Ozurdex on patients with ocular toxocariasis. As far as we know, this is the first systematic retrospective study on the treatment of OT with intravitreal DEX implants.

## 2. Materials and Methods

We retrospectively reviewed a case series of 6 patients diagnosed with ocular toxocariasis and treated with intravitreal DEX implants with or without pars plana vitrectomy (PPV) at

the First Affiliated Hospital of Zhengzhou University, China, between March 2018 and March 2021. Written informed consent was obtained from the patient or the guardian of the pediatric patient. This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University and was conducted in accordance with the Declaration of Helsinki (2021-KY-1241).

Patients underwent routine ophthalmic examination including best-corrected visual acuity (BCVA), intraocular pressure (IOP), a slit-lamp examination with a VOLK 90D lens, scanning laser ophthalmoscopy (Optomap 200Tx; Optos PLC, Dunfermline, UK), and optical coherence tomography (Spectralis OCT; Heidelberg Engineering GmbH, Dossenheim, Germany). Depending on their condition, they were tested with any of the following imaging methods: B-scan ultrasonography (Mylab 8ehd, Esaote, Genoa, Italy) and fundus fluorescein angiography (HRA2; Heidelberg Engineering GmbH, Dossenheim, Germany).

Paired intraocular fluid (IF) from aqueous humor (AH) and serum samples of each participant were also collected. The positive rate of *Toxocara canis*-specific IgG antibody in AH and serum of patients was detected by enzyme-linked immunosorbent assay (ELISA). Serum anti-toxocara IgG greater than 9 are positive, and AH anti-toxocara IgG greater than 3 are positive. All patients were confirmed to be infected by code-tection of aqueous humor and serum *Toxocara canis*-specific immunoglobulin G (IgG) antibody and were administered with intravitreal DEX implants for intraocular inflammation.

OT was divided into three types according to clinical manifestations and imaging examinations and references [14, 15]: endophthalmitis type, posterior pole granuloma type, and peripheral granuloma type. For the patients diagnosed as endophthalmitis type, our treatment plan was to inject Ozurdex into vitreous without surgery. For patients diagnosed with posterior and peripheral granuloma type, our treatment plan was vitrectomy combined with Ozurdex. We conducted a retrospective study on the visual acuity and fundus of the patients before and after treatment to analyze treatment methods, results, complications, and visual outcomes. All patients have been followed from 12 to 31 months.

### 3. Results

Six eyes of 6 patients were included in the study. The mean age of the study group was 15.7 years (range: 5–29 years), with gender distribution of two men and four women. All cases were affected unilaterally with three right eyes and three left eyes. A total of four children (<18 years) were featured in this study (range: 5–15 years). Diminution of vision was the most common presenting ocular symptom in both adults and children. All of our patients had an initial visual acuity of 20/100 or worse. Poor visual acuity  $\leq 20/200$  was noted in 5 eyes. The mean time from symptom onset to hospital visit was 10.5 months (range: 2 to 36 months). Results for the patients are given in Table 1.

Among the 6 patients, endophthalmitis type, posterior pole granuloma type, and peripheral granuloma type were 2 eyes, 2 eyes, and 2 eyes, respectively. We developed different treatment plans according to the clinical classification of the

patients. Of the six patients, one patient was treated only with DEX implant, one patient underwent surgery after DEX implant, and four individuals underwent vitrectomy with DEX implant. For the patients diagnosed as endophthalmitis type, our treatment plan was to inject Ozurdex into vitreous without surgery. Among them, one patient was reinjected with an intravitreal DEX implant 7 months after injection. One patient suffered from inflammation recurrence nine months after the first injection and was found to have retinal detachment with vitreous traction and macular epiretinal membranes. Subsequently, she underwent vitrectomy with membrane peeling. For patients diagnosed with posterior and peripheral granuloma type, our treatment plan was vitrectomy combined with intravitreal DEX implants, with additional scleral buckling in eyes with peripheral granuloma type. Of them, 2 patients received secondary surgery and intravitreal DEX implants. For one patient diagnosed with combined type, only an intravitreal DEX implant was administered because of the patient's heavy vitreous opacity and poor vision.

The 6 eyes that completed the treatment according to the guidance of ophthalmologists and recorded follow-up were considered for the final visual results. The average follow-up time was 19.7 months (from 12 to 31 months). By the end of the follow-up period, all the operated eyes achieved anatomic success (Figures 1 and 2), and all patients' visual acuity was improved. Five of these six had a visual acuity of 20/100, and three had final acuities of 20/40 or even better (Table 1). During the follow-up period, we did not find any side effects after injection of Ozurdex. The mean IOP was 14.1 mmHg (range 9.0–18.5) at baseline, and there is no increase in intraocular pressure (IOP >21 mmHg or an elevation of IOP of  $\geq 10$  mmHg from baseline) in the drug-injected patients. And none of the patients had cataract formation after treatment.

### 4. Discussion

Ocular toxocariasis is a rare worldwide parasitic infectious disease that occurs in both rural and urban areas [16]. It is the main cause of vision loss in children [3]. The most common causes of vision loss are traction retinal detachment, vitreous opacity, cystoid macular edema, and complicated cataract [6, 17]. Its incidence and case characteristics may be different in different areas. Relevant research reports have shown that in most countries such as the United States and in countries in Asia and Africa, the majority of OT patients are children and are related to the history of contact with pets (dog or cat); in South Korea and Japan, the majority of OT patients are adults and are mostly associated with a history of raw food intake [18–20].

The most common symptoms in patients with OT are unilateral vision loss, strabismus, or leukocoria [3]. In our study, five patients came to the clinic with vision loss, including 4 pediatric patients. Three cases presented with retinal detachment, out of which two were children (5 and 15 years of age). This result is consistent with the report of related literature [18]. Compared to adult patients with OT, the symptoms and signs of were more severe in children. The

TABLE 1: Patient characteristics and outcomes.

Age	Sex	Symptom duration (mo)	Clinical feature	Eye	Laboratory tests (U)	Type	Intervention	Initial visual acuity	Visual outcome	Duration of follow-up (mo)	
1	15	F	2	Posterior granuloma, ERM, TRD	Left	Aqueous humor: 74.91 Serum: 44.89	Posterior pole granuloma	IV, PPV, membrane removal	20/200	20/100	31
2	22	M	36	Peripheral granuloma, TRD, peripheral traction band	Left	Aqueous humor: 43.86 Serum: 35.60	Peripheral granuloma	IV, PPV, membrane removal, SB	LP	20/100	17
3	12	M	5	Vitritis	Left	Aqueous humor: 66.78 Serum: 66.81	Endophthalmitis	IV, cataract operation	20/200	20/20	18
4	11	F	12	Peripheral granuloma, ERM, peripheral traction band	Right	Aqueous humor: 57.84 Serum: 41.60	Peripheral granuloma	IV, SB	CF	20/40	12
5	29	F	6	Vitritis	Right	Aqueous humor: 69.90 Serum: 45.66	Endophthalmitis	IV, PPV, membrane removal, oil	20/100	20/40	16
6	5	F	2	Posterior granuloma, ERM, TRD	Right	Aqueous humor: 31.07 Serum: 19.97	Posterior pole granuloma	IV, PPV, membrane removal, oil	HM	20/400	24

RD, retinal detachment; TRD, traction retinal detachment; ERM, epiretinal membrane; IV, intravitreal injection; PPV, pars plana vitrectomy; SB, scleral buckle; HM, hand motions; LP, light perception; CF, count fingers.

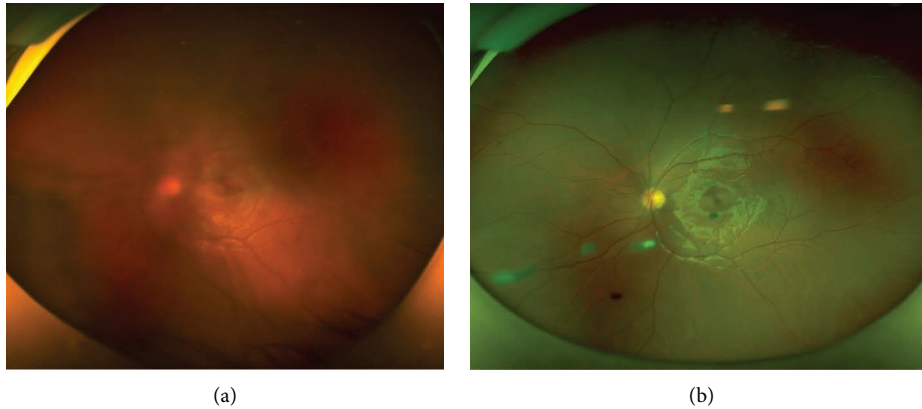


FIGURE 1: A 12-year-old male diagnosed with the endophthalmitis type. (a) The ultra-widefield fundus photograph showed opacity vitreous in the left eye and it was difficult to see the fundus of the eye. (b) The opacity vitreous improved after the injection, and the fundus was clearly visible. Patient's vision recovered from 20/200 to 20/20.

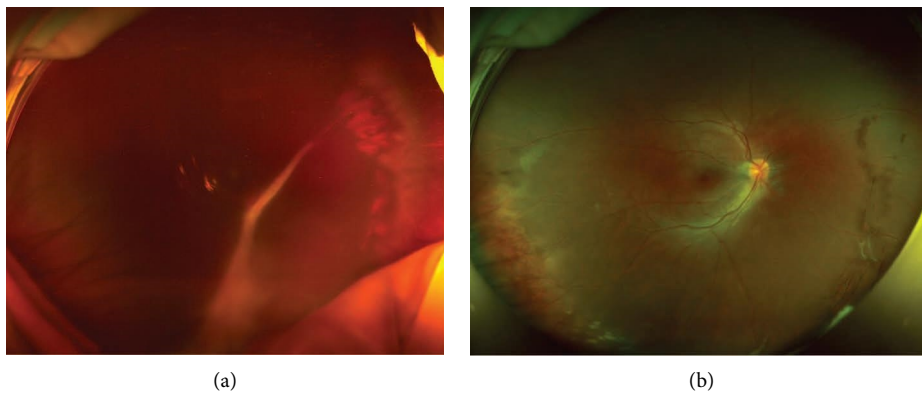


FIGURE 2: An 11-year-old female with a peripheral granuloma. (a) The ultra-widefield fundus photograph showed diffuse vitreous opacities with peripheral granuloma, a peripheral tractional band attached to the optic disc, and epiretinal membranes in the right eye. (b) After treatment, the anatomy of the retina of the patient's fundus was restored and the inflammation in the eye was reduced. Patient's vision recovered from count finger to 20/40.

reasons for this may be related to the long onset time of the disease, lack of early independent complaints and untimely discovery by the guardian, the combination of severe traction retinal detachment affecting the macular area, or severe vitreous opacity and lens opacity.

The main goals of the treatment of ocular toxocariasis are to control inflammation, reduce granuloma formation, and improve the patient's vision. It can be treated with medication and surgery. Medical treatment includes glucocorticoids and anthelmintic drugs. However, the use of anthelmintics may cause a strong immune response that, if not adequately controlled, can cause significant structural damage to the eye and more serious complications [21]. As a result, our treatment plan is primarily glucocorticoids combined with vitrectomy. Corticosteroids are used to control inflammation of the vitreous and anterior chamber. Systemic corticosteroids for treatment of ocular disease can cause significant toxicity because of the high concentrations of drugs needed to deliver enough drugs through the tight cellular junctions at the ocular surface or through the blood-

retinal barrier [22]. And long-term use of systemic corticosteroids can lead to cumulative complications in multiple major organ systems, such as hyperglycemia, hypertension, osteoporosis, higher susceptibility to infections, psychological problems, and growth suppression [13, 23, 24]. Compared with systemic administration, topical application of glucocorticoids, such as intravitreal triamcinolone, can theoretically provide higher drug concentrations to target tissues and avoid serious systemic complications. Therefore, local glucocorticoids can be used to treat OT to minimize systemic side effects of systemic steroids. Intravitreal injections of triamcinolone acetonide (TA) and sustained-release DEX are commonly used treatment plans for local application of glucocorticoids. TA is a suspension of fine particles, the half-life of it in nonvitrectomized patients was 18.6 days and that in a patient who had undergone a vitrectomy was shorter at 3.2 days, and it may be maintained at a level sufficient for clinical effect for only 3 days [25]. In addition, it has been shown that there are significant differences in the crystal size of TA, and these morphological

aspects may have a significant impact on the half-life of the drug [26]. Hence, we attempted to treat OT with the intravitreal dexamethasone implant (Ozurdex). Ozurdex, which contains poly (lactic acid-co-glycolic acid) (PLGA), is a completely biodegradable drug delivery device and can slowly and continuously release the active ingredient of the drug [22]. It can not only achieve adequate intraocular concentration but also greatly reduce the adverse reactions of systemic medication [27, 28]. Many studies have demonstrated the efficacy and safety of Ozurdex in clinical trials for a variety of retinal diseases, such as diabetic macular edema, retinal vein occlusion, and noninfectious uveitis [10, 13, 29].

In this study, we have reported on the efficacy of intravitreal DEX implants in different types of patients with OT. For 2 patients diagnosed with endophthalmitis type, we only injected Ozurdex into the vitreous. One of the patients had a second injection after 7 months and his vision returned to 20/20 after the injection. During the 11 months of follow-up, his vision remained stable. Another patient had a recurrence of inflammation and underwent a vitrectomy. The visual acuity returned to 20/40 after treatment. These results suggest that intravitreal DEX implants can be used as an alternative to systemic glucocorticoids for the treatment of OT patients diagnosed with endophthalmitis type. Because OT inflammation is prone to relapse and the duration of drug action is limited [30], a single injection may not completely control the inflammation. Therefore, we need to closely observe the changes in patient's condition, and if inflammation recurs, we should diagnose and treat it in a timely manner. For patients diagnosed with posterior and peripheral granuloma type, we performed vitrectomy combined with intravitreal DEX implants, with additional scleral buckling in eyes with peripheral granuloma type. Injection of Ozurdex at the end of vitreous surgery for OT can be done safely and simply, and the intravitreal DEX implant lasts longer and has a better safety profile compared to triamcinolone acetonide injections [12, 25, 30]. All of the surgical patients were considered successful, with improved visual acuity and an attached retina postoperatively. This indicates that the intravitreal DEX implant can effectively control inflammation and is an important supplementary therapy for OT patients who develop granuloma or other complications. Furthermore, for patients with peripheral granuloma type, scleral buckling can effectively alleviate the traction of granulomas on the retina and in combination with vitrectomy and Ozurdex injections may achieve better therapeutic results.

However, despite its remarkable role in the treatment of retinal diseases, its side effects should not be ignored. High intraocular pressure and cataracts are the main long-term sequelae identified in large randomized clinical trials [27, 31–33]. According to reports [27, 33], the increase of IOP after Ozurdex injection typically occurs within the first 2 weeks, reaches the peak roughly after 2 months, and then begins to decrease gradually, to reach the preinjection values usually within 6 months. In our study, we analyzed eye function and adverse reactions after Ozurdex injection. Overall, most patients, whether they had surgery or not, had

significantly improved visual function after the injections. During the follow-up from 12 to 31 months, we did not find that the patients had elevated intraocular pressure and complicated cataract, even after repeated injections. Although one patient underwent cataract surgery after 7 months of medication, this patient was diagnosed with cataract at the first visit, and his cataract was caused by long-term inflammation.

Our research has several limitations. First, the follow-up time is short. Long-term follow-up is needed to determine the final outcome of eye treatment. These patients should be followed up for a long period of time to observe whether they have recurrent inflammation and symptoms related to recurrent retinal detachment. Second, the sample size is small, so our research may not be representative of all patients with OT in the real clinical environment; we should expand the sample size and continue the research. Third, this study is a retrospective study, and the treatment and follow-up procedures are inconsistent. These limitations should be solved in future research.

## 5. Conclusions

In conclusion, our study provides a novel treatment option that intravitreal DEX implants can be used to treat different types of ocular toxocariasis, which not only effectively control inflammation and improve the patient's vision but also reduce the use of systemic glucocorticoids. Additionally, the slow and sustained release of the drug makes it safer. To the best of our knowledge, our study is the largest case series of OT treated with intravitreal DEX implants.

## Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

## Authors' Contributions

Yongwei Zhou and Fangyuan Zhen were responsible for conceptualization. Yongwei Zhou was responsible for data curation. Shuqian Dong was responsible for funding acquisition and resources. Yongwei Zhou, Fangyuan Zhen, Jiahui Wu, Shasha Wang, and Zhirou Hu were responsible for investigation. Fangyuan Zhen and Fei Chen were responsible for methodology. Qiuming Li and Shuqian Dong were responsible for project administration. Xiaoyan Lu, Ge Yang, Qiuming Li, and Shuqian Dong were responsible for supervision. Yongwei Zhou, Fangyuan Zhen, Jiahui Wu, and Shasha Wang were responsible for original draft preparation. Xiaoyan Lu, Ge Yang, Zhirou Hu, Fei Chen, Qiuming Li, and Shuqian Dong were responsible for review and editing.

## Acknowledgments

Thanks are due to the Beijing Giantmed Medical Diagnostics Lab for aqueous humor and vitreous fluid testing. This study was supported by the National Natural Science Foundation of China (no. 81800830) funded by the Chinese government, the Young and Middle-Aged Health Science and Technology Innovation Talent Training Project (Outstanding Young Persons) of Henan Province (no. YXKC2022025) funded by the Health Commission of Henan Province, and the Medical Science and Technology Project (the Key Project Jointly Built by the Province and the Ministry) of Henan Province (no. SBGJ202102167) funded by the Health Commission of Henan Province.

## References

- [1] S. Li, L. Sun, C. Liu et al., "Clinical features of ocular toxocariasis: a comparison between ultra-wide-field and conventional camera imaging," *Eye*, vol. 35, no. 10, pp. 2855–2863, 2021.
- [2] E. S. Sahu, B. Pal, T. Sharma, and J. Biswas, "Clinical profile, treatment, and visual outcome of ocular *toxocara* in a tertiary eye care centre," *Ocular Immunology and Inflammation*, vol. 26, no. 5, pp. 753–759, 2018.
- [3] D. Woodhall, M. C. Starr, S. P. Montgomery et al., "Ocular toxocariasis: epidemiologic, anatomic, and therapeutic variations based on a survey of ophthalmic subspecialists," *Ophthalmology*, vol. 119, no. 6, pp. 1211–1217, 2012.
- [4] S. J. Ahn, S. J. Woo, Y. Jin et al., "Clinical features and course of ocular toxocariasis in adults," *PLoS Neglected Tropical Diseases*, vol. 8, no. 6, Article ID e2938, 2014.
- [5] M. Badri, A. V. Eslahi, M. Olfatifar et al., "Keys to unlock the enigma of ocular toxocariasis: a systematic review and meta-analysis," *Ocular Immunology and Inflammation*, vol. 29, no. 7-8, pp. 1265–1276, 2021.
- [6] J. M. Stewart, L. D. P. Cubillan, and E. T. Cunningham, "PREVALENCE, clinical features, and causes OF VISION loss among patients with ocular toxocariasis," *Retina*, vol. 25, no. 8, pp. 1005–1013, 2005.
- [7] G. P. Giuliani, G. Ramirez, and R. T. Cortez, "Surgical treatment of ocular toxocariasis: anatomic and functional results in 45 patients," *European Journal of Ophthalmology*, vol. 21, no. 4, pp. 490–494, 2011.
- [8] T. Barisani-Asenbauer, S. M. Maca, W. Hauff et al., "Treatment of ocular toxocariasis with albendazole," *Journal of Ocular Pharmacology and Therapeutics*, vol. 17, no. 3, pp. 287–294, 2001.
- [9] A. J. Schneider and M. L. Durand, "Ocular toxocariasis: advances in diagnosis and treatment," *International Ophthalmology Clinics*, vol. 51, no. 4, pp. 135–144, 2011.
- [10] M. Scaramuzzi, G. Querques, C. L. Spina, R. Lattanzio, and F. Bandello, "Repeated intravitreal dexamethasone implant (ozurdex) for diabetic macular edema," *Retina*, vol. 35, no. 6, pp. 1216–1222, 2015.
- [11] Y. Cai, Y. Yang, and X. Zhong, "A case report of intravitreal dexamethasone implant with exudative retinal detachment for ocular toxocariasis treatment," *Korean Journal of Parasitology*, vol. 60, no. 2, pp. 133–137, 2022.
- [12] A. Hostovsky, R. H. Muni, K. T. Eng, D. Mulhall, C. Leung, and P. J. Kertes, "Intraoperative dexamethasone intravitreal implant (Ozurdex) in vitrectomy surgery for epiretinal membrane," *Current Eye Research*, vol. 45, no. 6, pp. 737–741, 2020.
- [13] M. Kim, S. A. Kim, W. Park, R. Y. Kim, and Y. H. Park, "Intravitreal dexamethasone implant for treatment of sarcoidosis-related uveitis," *Advances in Therapy*, vol. 36, no. 8, pp. 2137–2146, 2019.
- [14] M. Zhou, Q. Chang, J. A. Gonzales et al., "Clinical characteristics of ocular toxocariasis in Eastern China," *Graefes Archive for Clinical and Experimental Ophthalmology*, vol. 250, no. 9, pp. 1373–1378, 2012.
- [15] L. Huang, L. Sun, C. Liu et al., "Diagnosis of ocular toxocariasis by serum and aqueous humor IgG ELISA," *Trans Vis Sci Tech.*, vol. 10, no. 8, p. 33, 2021.
- [16] J. F. Arevalo, J. V. Espinoza, and F. A. Arevalo, "Ocular toxocariasis," *Journal of Pediatric Ophthalmology & Strabismus*, vol. 50, no. 2, pp. 76–86, 2013.
- [17] A. M. Maguire, W. R. Green, R. G. Michels, and Y. S. Erozan, "Recovery of intraocular toxocara canis by pars plana vitrectomy," *Ophthalmology*, vol. 97, no. 5, pp. 675–680, 1990.
- [18] D. Jee, K. S. Kim, W. K. Lee, W. Kim, and S. Jeon, "Clinical features of ocular toxocariasis in adult Korean patients," *Ocular Immunology and Inflammation*, vol. 24, no. 2, pp. 207–216, 2016.
- [19] D. Martinez-Pulgarin, M. Munoz-Urbano, L. Gomez-Suta, O. Delgado, and A. Rodriguez-Morales, "Ocular toxocariasis: new diagnostic and therapeutic perspectives," *Priamus*, vol. 10, no. 1, pp. 35–41, 2015.
- [20] M. Yoshida, Y. Shirao, H. Asai et al., "A retrospective study of ocular toxocariasis in Japan: correlation with antibody prevalence and ophthalmological findings of patients with uveitis," *Journal of Helminthology*, vol. 73, no. 4, pp. 357–361, 1999.
- [21] J. Martinez, G. Ivankovich-Escoto, and L. Wu, "Pediatric ocular toxocariasis in Costa Rica: 1998–2018 experience," *Ocular Immunology and Inflammation*, vol. 29, no. 7-8, pp. 1246–1251, 2021.
- [22] J. E. Chang-Lin, M. Attar, A. A. Acheampong et al., "Pharmacokinetics and pharmacodynamics of a sustained-release dexamethasone intravitreal implant," *Investigative Ophthalmology & Visual Science*, vol. 52, no. 1, p. 80, 2011.
- [23] H. Wang and Y. Tao, "Clinical features and prognostic factors in northern Chinese patients with peripheral granuloma type of ocular toxocariasis: a retrospective cohort study," *Ocular Immunology and Inflammation*, vol. 29, no. 7-8, pp. 1259–1264, 2021.
- [24] M. Oray, K. Abu Samra, N. Ebrahimiadib, H. Meese, and C. S. Foster, "Long-term side effects of glucocorticoids," *Expert Opinion on Drug Safety*, vol. 15, no. 4, pp. 457–465, 2016.
- [25] P. M. Beer, S. J. Bakri, R. J. Singh, W. Liu, G. B. Peters, and M. Miller, "Intraocular concentration and pharmacokinetics of triamcinolone acetonide after a single intravitreal injection," *Ophthalmology*, vol. 110, no. 4, pp. 681–686, 2003.
- [26] D. Veritti, A. Di Giulio, V. Sarao, and P. Lanzetta, "Drug safety evaluation of intravitreal triamcinolone acetonide," *Expert Opinion on Drug Safety*, vol. 11, no. 2, pp. 331–340, 2012.
- [27] C. Iovino, R. Mastropasqua, M. Lupidi et al., "Intravitreal dexamethasone implant as a sustained release drug delivery device for the treatment of ocular diseases: a comprehensive review of the literature," *Pharmaceutics*, vol. 12, no. 8, p. 703, 2020.
- [28] T. A. Ciulla, A. Harris, N. McIntyre, and C. Jonescu-Cuypers, "Treatment of diabetic macular edema with sustained-release

glucocorticoids: intravitreal triamcinolone acetonide, dexamethasone implant, and fluocinolone acetonide implant,” *Expert Opinion on Pharmacotherapy*, vol. 15, no. 7, pp. 953–959, 2014.

- [29] J. Zarranz-Ventura, E. Carreño, R. L. Johnston et al., “Multicenter study of intravitreal dexamethasone implant in noninfectious uveitis: indications, outcomes, and reinjection frequency,” *American Journal of Ophthalmology*, vol. 158, no. 6, pp. 1136–1145.e5, 2014.
- [30] M. Dutra Medeiros, M. Alkabes, R. Navarro, J. Garcia-Arumí, C. Mateo, and B. Corcóstegui, “Dexamethasone intravitreal implant in vitrectomized versus nonvitrectomized eyes for treatment of patients with persistent diabetic macular edema,” *Journal of Ocular Pharmacology and Therapeutics*, vol. 30, no. 9, pp. 709–716, 2014.
- [31] J. M. Fassbender Adeniran, D. Jusufbegovic, and S. Schaal, “Common and rare ocular side-effects of the dexamethasone implant,” *Ocular Immunology and Inflammation*, vol. 25, no. 6, pp. 834–840, 2017.
- [32] K. Kishore, P. V. Bhat, P. Venkatesh, and C. C. Canizela, “Dexamethasone intravitreal implant for the treatment of macular edema and uveitis: a comprehensive narrative review,” *Ophthalmology*, vol. 16, pp. 1019–1045, 2022.
- [33] B. Rajesh, J. Zarranz-Ventura, A. T. Fung et al., “Safety of 6000 intravitreal dexamethasone implants,” *British Journal of Ophthalmology*, vol. 104, no. 1, pp. 39–46, 2020.