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Original Article

Intraocular Pressure Elevation After Posterior Subtenon Triamcinolone Acetonide Injection in Pediatric Non-Infectious Uveitis

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Abstract

Objectives: The objectives of the study were to evaluate non-infectious pediatric uveitis patients developing elevated intraocular pressure (IOP) and glaucoma following posterior subtenon triamcinolone acetonide (PSTA) injection.

Methods: The data of 26 pediatric (<18 years) patients with active uveitis were retrospectively evaluated. Exclusion criteria were patients with a previous IOP >21 mmHg and previous subtenon or intraocular steroid injection. The IOP values of the patients before and after the PSTA injection and the treatments administered were recorded.

Results: PSTA injection was used in a total of 40 eyes. The mean IOP was 14.0±2.3 (12–19) mmHg before PSTA. The IOP was elevated (≥21 mmHg) in 19 eyes (48%) after PSTA with a mean IOP of 32.9±11.7 mmHg (22–55). The mean interval time to IOP elevation was 3.3±1.9 weeks (1–8). The IOP was controlled in 15 eyes (79%) with topical anti-glaucomatous and these patients were considered as having transient IOP elevation. Trabeculectomy with mitomycin C was required in 4 eyes (21%) in whom the IOP could not be controlled despite the use of maximum topical medication and oral acetazolamide at a mean duration of 9.7±3.6 months (4–19). Subtenon deposit excision was performed in 2 eyes (11%). The mean IOP at the last follow-up was 16.0±2.4 mmHg (12–20).

Conclusion: In our study, an IOP elevation rate as high as 47% was found in pediatric non-infectious uveitis patients following only a single PSTA injection. Steroid-induced IOP elevation and resistant glaucoma can develop even after the first PSTA administration in pediatric uveitis. Filtration surgery and the excision of subtenon triamcinolone deposits, when present, are important in glaucoma management. The risk/benefit ratio must be carefully considered when administering steroid injections to children with uveitis.

Keywords: Glaucoma, intraocular pressure, pediatric uveitis, subtenon injection, triamcinolone acetonide

Introduction

The incidence and prevalence of uveitis are lower in children than in adults. Pediatric uveitis cases make up 5–10% of all uveitis patients and 75–95% of these patients have non-infectious uveitis (1). Pediatric uveitis is difficult to manage due to the difficulties in diagnosis and treatment, the high complication rate, and the potential for visual loss if not treated.

Corticosteroids are among the important medication groups that are used through the topical, periocular, intravitreal, or systemic routes to control ocular inflammation in pediatric noninfectious uveitis cases, as in adults (2). Subtenon

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steroid injections have been shown to be effective in non-infectious uveitis. They are usually used as an adjuvant treatment in refractory cases or to support systemic treatment to minimize the related adverse effects (3). Triamcinolone acetonide (TA) is a water-soluble steroid and is preferred for subtenon injections as it supplies steroids intraocularly for a long period (4). The most commonly reported complications of subtenon TA administration include elevated intraocular pressure (IOP) and increased cataract progression (5). Periocular depot steroid administration creates a risk of IOP elevation due to the long-term steroid exposure of the trabecular network. This risk is further increased in young uveitis patients (6,7).

The aim of this study was to evaluate the treatment approaches in active non-infectious pediatric uveitis patients with no previous IOP elevation who had undergone posterior subtenon triamcinolone acetonide (PSTA) injection and developed IOP elevation and glaucoma afterward.

Methods

The records of patients (<18 years) who had been followed up with a diagnosis of non-infectious pediatric uveitis between 2004 and 2020 in the Uveitis Unit of the University of Health Sciences Ulucanlar Eye Training and Research Hospital were retrospectively evaluated.

A total of 26 patients who had undergone a single PSTA administration as an adjuvant to newly started or ongoing systemic treatment for noninfectious uveitis were included in the study. The study was conducted according to the Helsinki Declaration principles. Ethics approval was obtained from the Ankara Training and Research Hospital Ethics Committee (E-21-821).

The demographic data, age, gender, follow-up duration, detailed ophthalmic examination findings, and the treatment administered were evaluated from the patient charts. Patients with chronic uveitis-related vitreous haze or cystoid macula edema (CME) and who had undergone PSTA treatment for the 1st time were included in the study. The follow-up and treatment approach to patients who developed IOP elevation of ≥21 mmHg after PSTA injection was evaluated. Exclusion criteria were patients with previous ocular surgery, previous IOP elevation over >21 mmHg, and previous subtenon, or intraocular steroid injections. IOP values during the follow-up before and after the PSTA injection were recorded.

The injections were administered by the same physician (PCO) and under topical or general anesthesia according to the age and treatment compliance of the patient. For the topical route, local anesthetic drops (Alcaine, 0.5% proparacaine hydrochloride ophthalmic solution, Alcon) were administered at least 5 times before the injection. 20 mg/0.5 ml TA was injected slowly into the subtenon space at the upper temporal region with a 25G needle advanced posteriorly toward the macular region.

Optical coherence tomography-retinal nerve fiber layer thickness analysis (OCT-RNFL) and/or visual field tests were used in addition to optic disk photography in the follow-up of all patients who developed IOP elevation. Young children who could not adapt to the visual field test were evaluated and followed up with the OCT-RNFL test which is an easy-to-perform, non-invasive, and non-contact method. In addition to the OCT-RNFL thickness analysis, the visual field test was evaluated in all children who could adapt. If the IOP is above 21 mmHg despite anti-glaucomatous treatment and one or more of the following findings were present, glaucoma surgery was decided. These findings were increased optic nerve head cupping on fundus examination, observation of a new notch in the optic nerve head (not existing before), monitoring progression in OCT-RNFL analysis, and monitoring progression in the visual field test.

Statistical Analysis

The data were analyzed with the Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, ABD) software. Qualitative data were expressed as percentages and quantitative data as mean ± standard deviation.

Results

There were 13 (50%) females and 13 (50%) males with a mean age of 11.3±4.3 years (4–17). The mean follow-up duration was 94.5±41.6 months (21–144). PSTA was administered for pars planitis in 24 cases (92.3%) and juvenile idiopathic arthritis associated uveitis in 2 cases (7.7%). A total of 16 patients (61.6%) were receiving concomitant systemic immunosuppressive treatment at the time of PSTA administration while 10 patients (38.4%) had been started systemic immunosuppressive treatment simultaneously with the PSTA injection. Ten patients (38.4%) used varying doses of systemic steroids during PSTA injection. Almost all (92.3%) patients in the study group had pars planitis, and these patients had no or minimal anterior segment inflammation. Therefore, patients generally used low-dose (≤3 drops/day) topical steroids. Before PSTA, only 9 (34.6%) of all patients had a history of topical steroid use, and the mean duration of topical steroid use before PSTA was 1.7±0.6 (1–3) weeks. After PSTA, topical steroid doses were reduced according to the patient's clinical condition and discontinued in an average of 2.5±1.0 (1–4) weeks.

PSTA was administered to a total of 40 eyes in 26 patients, to treat CME in 15 eyes (37.5%) and ≥3+ vitreous haze in 25 eyes (62.5%). No complications developed during the PSTA administration in any of the eyes. The mean IOP before PSTA administration was 14.0±2.3 (12–19) mmHg.

Following PSTA administration, IOP elevation (≥21 mmHg) was detected in 19 eyes (47.5%) and the mean IOP was 32.9±11.7 mmHg (22–55). The mean interval time to IOP elevation was 3.3±1.9 (1–8) weeks. The trend of IOP changes in affected eyes with elevated IOP is shown in Figure 1. Only 7 (53.8%) of the patients who developed increased IOP after PSTA used systemic steroids. Four of the patients (30.7%) who developed increased IOP after PSTA was using topical steroids before and after PSTA. The mean duration of topical steroid use in these patients before and after PSTA was 2.2±0.9 (1–3) and 1.7±0.9 (1–3) weeks, respectively.

A single topical agent (beta-blocker with intrinsic sympathomimetic activity) was used in 4 eyes (21.0%), dual topical agents (fixed combination of non-selective beta-blocker and topical carbonic anhydrase inhibitor) in 7 eyes (36.8%), and triple topical agents (brimonidine with a fixed combination of non-selective beta-blocker and topical carbonic anhydrase inhibitor) in 8 eyes (42.1%) as an anti-glaucomatous treatment for high IOP. Patients using non-selective beta-blockers were recommended punctum occlusion immediately after the instillation. In addition, oral acetazolamide (3×125 mg) was used orally for 2 weeks in 3 patients (12%) with an IOP elevation of >50 mmHg. The mean duration of topical drug use was 5.5±5.3 months (1–19). The IOP was controlled with topical anti-glaucomatous drugs in 15 (79.0%) of the 19 eyes and these patients were considered to have transient IOP elevation. Trabeculectomy with mitomycin C was performed 9.7±3.6 months (4–19) after PSTA administration in 4 (21.0%) eyes with one or more progression findings where the IOP could not be controlled despite triple topical drug and acetazolamide use.

In addition, subtenon deposit excision was performed in 2 eyes (10.5%) (after PSTA at the 3rd and 4th week, respectively) that developed an IOP above 40 mmHg after PSTA administration. Following subtenon deposit removal, the existing topical anti-glaucomatous treatment was continued. The IOP of these patients was regulated after 3 months and the topical treatments were gradually discontinued (first the systemic acetazolamide, then brimonidine, and then the fixed combination of non-selective beta-blocker + topical carbonic anhydrase inhibitor). The mean IOP of the patients at the final examination was 16.0±2.4 mmHg (12–20).

Discussion

Corticosteroids are very effective in the treatment of noninfectious uveitis, and especially in the rapid control of inflammation. However, they should be used carefully, particularly in the pediatric age group due to the serious ocular and systemic side effects (1). With the use of periocular/intravitreal steroids, it is possible to decrease the systemic side effects of systemic steroids that may develop in children such as growth retardation, Cushing's syndrome, hypertension, hyperglycemia, and osteoporosis. PSTA administration can provide higher drug levels in the posterior segment through transscleral absorption than achieved with systemic administration (3,8). The efficacy of periocular steroids, especially in controlling unilateral intraocular inflammation and treating CME, has been shown in various studies (2,3,6,9).

Periocular steroid administrations are not as innocent as they seem and an increase in IOP and cataract development are the most commonly reported complications after steroid injections (2). Besides, complications such as upper eyelid ptosis, orbital fat prolapse, orbital infection, conjunctival ischemia or ulceration, capsular subtenon triamcinolone cyst, and globe perforation may develop after PSTA administration (8-10). In their study where they evaluated 173 pediatric uveitis patients, Sijssens et al. (11) reported that the development of IOP rise and secondary glaucoma were more common in those who underwent periocular steroid injections in children with uveitis. Kothari et al.'s multicenter, a retrospective study has reported that the risk for IOP elevation was 7–8 times higher with periocular corticosteroid injections in pediatric noninfectious uveitis (5). Authors have also shown that intravitreal steroid administration was as-

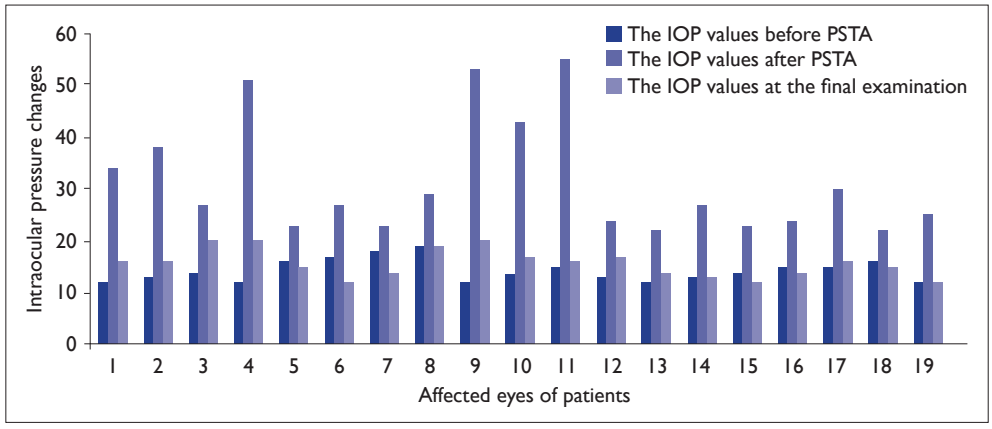

Figure 1. The trend of intraocular pressure changes in affected eyes.

sociated with the highest IOP rise risk, while periocular injections and the frequent use of topical steroids had similar effect (5). The prevalence of steroid-related IOP elevation in children with non-infectious uveitis who were treated with topical steroids, periocular/intravitreal injections, or systemic steroids has been reported to be 35% by Din et al. (7) Like other studies, periocular or intravitreal steroid injection was found to associate with a more severe IOP elevation compared to topical or systemic steroid use (7). However, unlike the studies mentioned above, patients who were previously administered periocular or intraocular steroids were excluded from our study. An IOP elevation rate as high as 47% was found in pediatric non-infectious uveitis patients following only a single PSTA injection. Particular care regarding IOP elevation and immediate treatment is required in children who underwent a periocular steroid injection.

The mechanism of IOP elevation due to steroids has not been fully elucidated. However, it is known that more than 1 mechanism may play a role, especially in uveitic eyes. Corticosteroids activate steroid receptors in trabecular cells and basically change gene expression and increase glycoprotein synthesis, resulting in accumulation in the intercellular matrix (11). This change in the microstructure and cellular activity of the trabecular meshwork is thought to lead to a gradual accumulation of cell particles and an increase in outflow resistance (12). The ocular hypertensive response occurring against steroids in children is more common, more severe, and more rapid compared to adults (6,13). This is thought to be associated with the anatomically and functionally immature trabecular meshwork in children (14). Besides different patients' related genetic and predisposing factors, variations in steroid receptors make the basis of steroid-induced IOP elevation (3,4). The number of periocular injections has been reported not to affect IOP elevation in certain studies (2,11). However, Iwao et al. (6) reported a higher (more severe) IOP elevation following repeated PSTA injections compared to the initial injection. In our uveitis practice, repeated injections are avoided in children. Our study included patients who were administered a single PSTA injection as an adjuvant to newly start or ongoing systemic treatment.

Typically, IOP elevation induced after periocular steroids occurs within weeks and continues for a long time (11,15). An IOP elevation of 5 mmHg or more was observed at a mean duration of 5.9 weeks after the PSTA injection in adult uveitis patients, and the IOP was reported to be taken under control in a mean duration of 2.9 months with medical treatment in all except two patients in a study by Jea et al. (4) In another study, IOP elevation was found to develop within a duration of 2–3 months following PSTA administration in adult (aged 19–81 years) uveitis patients and the IOP was reported to be taken under control with a single topical anti-glaucomatous drug in all eyes except one; the anti-glaucomatous drugs were stopped within 6 months (16). The IOP elevation in our patients was observed at a mean duration of 3.3 weeks after PSTA administration, and medical treatment was used for a mean duration of 5.5 months. IOP could be taken under control with multiple drug treatments in some cases. These results confirm that IOP increase is observed in a shorter time and can be controlled in a longer time in children than adults.

IOP elevation following periocular steroid administration can generally be controlled with medical treatment, however, glaucoma surgery may be required in certain refractory cases (2,3). In their study including 109 eyes, Salek et al. (3) reported that glaucoma surgery was required in 2% of the eyes with uveitis where IOP developed after periocular injection. However, this study evaluated patients aged 6–71 years and did not specifically highlight the results in children (3). In another study of pediatric uveitis where IOP elevation due to oral, intravitreal/periocular, and topical steroids developed, multiple topical anti-glaucomatous drugs were required in 55%, and glaucoma surgery was required in 30% of the eyes (18/61) (7). Furthermore, in 13 eyes with an IOP <28 mmHg and monitored without medication, although the topical treatment was switched to less potent steroid (rimexolone instead of dexamethasone or prednisolone acetate), it was reported that an additional anti-glaucomatous agent was required in 10 eyes (7). In our study population, glaucoma surgery was required in 10% of the eyes that developed IOP elevation after only one PSTA administration. The results of our study also supported the fact that the IOP increase occurring with steroids is more common, more severe, and develops earlier in children.

Exposure of the trabecular meshwork to steroids is increased with the continuous release of steroid deposits that accumulate in the subtenon area following a PSTA injection. This causes a further increase in the resistance to the outflow and results in resistant IOP elevation (17,18). Okka et al. (17) have reported that the excision of subtenon TA deposits in resistant ocular hypertension cases after PSTA injections provides IOP normalization within 1 month, but this study consisted of 11 men and 3 women whose ages ranged from 27 to 82 years (mean 57 years). In the present study, IOP regulation was achieved within 3 months by gradually decreasing medical treatment after the excision of subtenon deposits in 2 eyes (10.5%) that developed an IOP above 40 mmHg after PSTA administration. This result supports that control of IOP increase in pediatric patients is more difficult than in adults.

A stepladder treatment approach including steroids, immunomodulatory agents, and biological agents is accepted in pediatric noninfectious uveitis (18). However, the long-term

use of steroids and repeated administrations are known to cause severe systemic and ocular morbidity in children (1,13,19). The management of pediatric uveitis patients is quite difficult due to the difficulties experienced in the diagnosis as well as in the treatment and the high complication rates. Ocular complications such as IOP elevation, glaucoma, or cataract that may occur in relation to the treatment also make the therapeutic process difficult. A study evaluating the risk of IOP elevation in pediatric noninfectious uveitis patients has reported that topical and periocular steroids and especially intraocular steroids increased the risk of IOP elevation, while systemic immunosuppressive drugs did not (5). The immediate start of appropriate immunosuppressive or biologic agents is very important to provide the remission in patients with chronic recurrent inflammation (19,20). PSTA injection should be performed in selected pediatric non-infectious uveitis cases and it should not be forgotten that a careful and close follow-up is required afterward.

The strengths of our study are that it had a long follow-up period (mean 94.5 months) and was conducted in a tertiary referral center. However, this study had some limitations. The most important limitation of our study was the use of systemic steroids at varying doses according to the clinical findings of each patient before and after PSTA in some patients. Therefore, it was not possible to isolate the effect of systemic steroids on IOP in patients receiving concomitant steroids. Other limitations were the retrospective design of the study and the low total number of patients.

Conclusion

IOP elevation and steroid-induced resistant glaucoma can develop even after the first PSTA administration in pediatric uveitis patients. This IOP elevation is observed at a very high rate in pediatric uveitis, and it can be controlled with difficulty. Filtration surgery with antimetabolites when required and excision of subtenon triamcinolone deposits when present are required to prevent the development of glaucomatous optic disk damage in cases developing medical treatment-resistant IOP elevation after PSTA administration. While deciding on periocular steroid injections in children, the benefit/loss ratio should be considered very carefully and injections should be used as an adjuvant treatment method in addition to systemic treatment in severe cases or as an alternative treatment in cases where systemic treatment cannot be administered. It is now possible to ensure remission and prevent steroid-related complications in pediatric uveitis with the use of non-steroidal new systemic drugs with proven effectiveness and reliability in children. The need for periocular steroid injections in pediatric uveitis cases has decreased significantly with the introduction of biological agents in our uveitis practice.

Disclosures

Ethics Committee Approval: Ethics approval was obtained from the Ankara Training and Research Hospital Ethics Committee (E-21-821).

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Conflict of Interest: None declared.

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