Comparison of the Safety and Efficacy of Loteprednol Etabonate 0.5%/Tobramycin 0.3% with Dexamethasone 0.1%/Tobramycin 0.3% Following Strabismus Surgery

Şaşılık Cerrahisi Sonrası Loteprednol Etabonat %0,5/Tobramisin %0,3 ve Deksametazon %0,1/Tobramisin %0,3 Etkinlik ve Güvenliğinin Karşılaştırılması

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ABSTRACT

Objective: To compare the anti-inflammatory efficacy and safety of 0.5% loteprednol etabonate/0.3% tobramycin (LE/T) and 0.1% dexamethasone/0.3% tobramycin (DM/T) ophthalmic suspensions following strabismus surgery.

Materials and Methods: The records of 40 patients who were treated with either LE/T or DM/T following strabismus surgery were retrospectively reviewed. The recorded signs and symptoms of inflammation and intraocular pressure of the patients at 1 day, 1 week, and 3 weeks after the surgery were evaluated and compared between the groups.

Results: In both groups, reduced inflammation was noted during the follow-up visits. There was no statistically significant difference between the LE/T and DM/T groups with regard to the postoperative scores or measurements, including discomfort, chemosis, secretion, conjunctival hyperemia, and conjunctival gap size ($p>0.05$), during the follow-up visits. Allergic reactions to the medications were not reported in any patient. Intraocular pressures were within normal limits in both groups.

Conclusion: LE/T was found to be as effective as DM/T in reducing inflammation after strabismus surgery. LE/T, as a new-generation steroid combination product, could be used as a safe and effective anti-inflammatory agent for the treatment of inflammation following strabismus surgery.

Keywords: Loteprednol etabonate, dexamethasone, tobramycin, zylet, tobradex, strabismus surgery, corticosteroids, ocular inflammation

ÖZ

Amaç: Şaşılık cerrahisi sonrası loteprednol etabonat %0,5/tobramisin %0,3 (LE/T) ve deksametazon %0,1/tobramisin %0,3 (DM/T) oftalmik solüsyonlarının antiinflamatuar etkinlik ve güvenliğinin karşılaştırılması.

Gereç ve Yöntem: Şaşılık cerrahisi sonrası, LE/T veya DM/T ile tedavi uygulanmış 40 hastanın kayıtları retrospektif olarak gözden geçirildi. Hastaların cerrahi sonrası 1. gün, 1. ve 3. haftalarda kaydedilen göz içi basınçları, enflamasyona ait semptom ve bulguları değerlendirildi ve gruplar arasında karşılaştırma yapıldı.

Bulgular: Her iki grupta, takiplerde enflamasyonun azaldığı değerlendirildi. Operasyon sonrası, LE/T ve DM/T grupları arasında, rahatsızlık hissi, kemozis, sekresyon, konjonktival hiperemi skorları ve konjonktiva açıklık değerleri açısından istatistiki olarak anlamlı bir fark tespit edilmedi. ($p>0.05$) Hastaların hiçbirisinde alerjik reaksiyon rapor edilmemişti. Göz içi basınçları her iki grupta da normal sınırlar içerisindeydi.

Sonuç: LE/T'nin, DM/T kadar şaşılık cerrahisi sonrası inflamasyonun azaltmasında etkin olduğu; yeni jenerasyon steroid kombinasyon ürünü olarak, güvenli ve etkili olarak kullanılabileceği kanaatine varıldı.

Anahtar Kelimeler: Loteprednol etabonat, deksametazon, tobramisin, zylet, tobradex, şaşılık cerrahisi, kortikosteroid, oküler inflamasyon

Introduction

Dexamethasone (DM), an early-generation corticosteroid, is frequently prescribed after strabismus surgery for the treatment of ocular inflammation [1-3]. Loteprednol etabonate (LE), a new-generation corticosteroid, has been shown to be an effective anti-inflammatory agent with lesser side effects in anterior segment inflammatory conditions [4-6]. Recently, topical combination products of 0.5% LE/0.3% tobramycin (LE/T) or 0.1% DM/0.3% tobramycin (DM/T) are commonly used in the treatment of steroid-responsive ocular inflammation, and a risk of bacterial ocular infection exists [7-13]. LE/T has been found to be similar to DM/T in its anti-inflammatory effects for cataract surgery [8, 14]. However, there are no published reports on

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Table 1. Postoperative scores of the groups at the follow-up visits

	1 day		1 week		3 weeks	
Parameters	LE/T	DM/T	LE/T	DM/T	LE/T	DM/T
Discomfort	0.90±0.72	1.20±1.11	0.20±0.41	0.10±0.31	0.00±0.00	0.00±0.00
Chemosis	1.60±0.94	2.30±1.45	0.70±0.92	1.30±1.07	0.00±0.00	0.00±0.00
Secretion	0.60± 0.50	0.70±0.80	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Hyperemia	2.80± 1.28	2.30±1.30	1.60± 0.94	0.80± 0.89	0.00±0.00	0.00±0.00
Conjunctival gap	0.30±0.66	0.20±0.41	0.10±0.31	00.10±0.30	0.00±0.00	0.00±0.00
Intraocular pressure	14.40±1.67	14.60±2.16	14.30±1.59	14. 50±2.16	14.30±1.35	14.54±1.37

the use of an LE/T ophthalmic solution in the treatment of postoperative inflammation following strabismus surgery.

The aim of the present study was to retrospectively compare an LE/T ophthalmic solution (Zylet; Bausch & Lomb) with a DM/T ophthalmic solution (TobraDex; Alcon) for anti-inflammatory efficacy and safety following strabismus surgery.

Materials and Methods

Data on operated strabismus patients admitted to The Ophthalmology Clinic of Atatürk University School of Medicine between May 2015 and May 2016 were retrospectively evaluated. According to the postoperatively applied ophthalmic suspensions, the patients were divided into two groups: LE/T and DM/T. Patients with neurological disorders, systemic abnormalities, intraocular pathologies, and a history of allergic reactions to drugs were excluded in regard to their medical reports. Twenty randomly selected patients who had regular follow-up visits at 1 day, 1 week, and 3 weeks after the surgery were assigned to each group.

A limbal conjunctival incision and conjunctival incision made on the bulbar side of the conjunctiva close to the fornix had been used in the rectus and in the inferior oblique muscle surgeries, respectively. All conjunctival incisions had been closed with 8-0 vicryl sutures.

Postoperative treatment included one drop of each study medication three times a day for 3 weeks. At follow-up visits 1 day, 1 week, and 3 weeks after the surgery, the patients were examined by the same investigator. The efficacy of the treatment was assessed with regard to the decreased severity of inflammatory signs and symptoms, including conjunctival hyperemia, chemosis, and secretion, which was graded on a 0–3 scale (0, absent; 1, mild; 2, moderate; and 3, severe) by a slit-lamp biomicroscope in each group. The conjunctival gap size was measured in millimeters, perpendicular to the incision line, with a slit-lamp beam. The intraocular pressure (IOP) was measured by an air-puff tonometer. The patients were subjectively graded for comfort (0, total comfort; 1, mild discomfort; 2, moderate discomfort; and 3, severe discomfort) by asking them or their parents in younger ages [15].

This study was approved by the Ethical Committee of Atatürk University School of Medicine.

Statistical analysis

Data were analyzed with Statistical Package for the Social Sciences Statistics, version 20 (SPSS IBM Corp., Armonk, NY, USA) Student's t or Mann-Whitney U tests were used, depending on the distribution of variables. Values are presented as mean±standard deviation. A p value below 0.05 was accepted to be statistically significant.

Results

The mean±standard deviation ages of the patients were 18.66±10.73 years and 17.10±8.40 years in the LE/T and DM/T groups, respectively (p=0.302). The male/female ratio was 15/5 in the LE/T group and 11/9 in the DM/T group (p=0.173).

Strabismus surgery was performed on 36 muscles of 28 eyes and 38 muscles of 26 eyes in the LE/T and DM/T groups, respectively (p=0.441). In total, 22 recession/2 resection and 20 recession/6 resection operations to the horizontal rectus muscles were noted in the LE/T and DM/T groups. In each group, 12 inferior oblique muscle myectomies were reported.

Inflammatory signs, subjective discomfort scores, and mean IOPs of the groups are presented in Table 1.

One day after the surgery, the mean±SD scores of secretion, chemosis, conjunctival hyperemia, and discomfort were 0.60±0.50, 1.60±0.94, 2.80±1.28, and 0.90±0.72, respectively, in the LE/T group and 0.70±0.80, 2.30±1.45, 2.30±1.30, and 1.20±1.11 in the DM/T group. The conjunctival gap size was 0.30±0.66 and 0.20±0.41 and the mean IOPs were 14.40±1.67 and 14.60±2.16 in the LE/T and DM/T groups, respectively. Statistical significance in the baseline scores for discomfort, chemosis, secretion, conjunctival hyperemia, conjunctival gap size, and mean IOPs was not found between the groups (p=0.525, p=0.118, p=0.905, p=0.115, and p=0.877, respectively).

Inflammation and discomfort were resolved at 1 week rather than at 1 day in both groups. Statistical significance was not observed between the groups in scores for discomfort, chemosis, secretion, conjunctival hyperemia, and conjunctival gap size (p=0.384, p=0.063, p=0.392, p=0.074, and p=1.000, respectively). Inflammatory signs and discomfort resolved at the third postoperative week in both groups.

An allergic reaction to the ophthalmic solutions was not reported in any patient. IOPs were within normal limits in both groups. There was no statistically significant difference in IOPs between the groups at 1 day, 1 week, and 3 weeks after the surgery (p=0.409, p=0.740, and p=0.758, respectively) (Table 1).

Discussion

Surgical trauma to the eye initiates the release of inflammatory mediators, resulting in hyperemia, pain, and scar formation (8, 14). By inhibiting the activation of phospholipase A2, corticosteroids prevent arachidonic acid formation which is the first step in the inflammatory cascade. In this way, they suppress cellular infiltration, capillary dilatation, fibroblast proliferation, collagen deposition, and scar formation (8, 14). Early-generation topical corticosteroids, such as DM, have been used for a long time for relieving ocular inflammation after strabismus surgery [1-3, 16]. Although they are effective in suppressing postoperative inflammation, they also have the potential to induce adverse effects, such as an increase in IOP, delay in wound healing, and decrease in resistance to infections [3, 14, 17].

Attempts were made to produce and use new-generation steroids with lesser adverse effects. LE is one of them and was produced using the retrometabolic design, in which an inactive and nontoxic metabolite of prednisolone is utilized as the starting point for conversion to a therapeutically active, metabolically labile compound. After exerting its effects, LE is rapidly metabolized by tissue esterases, limiting any potential adverse effects associated with its use. LE is reported to be highly lipophilic and has strong

binding affinity to glucocorticoid receptors [4, 17, 18]. Compared with DM, its lipophilicity was 10 times higher and its binding affinity to a glucocorticoid receptor was 4.3 times higher [4]. LE is indicated for the treatment of various ocular surface and anterior segment inflammatory conditions such as seasonal allergic conjunctivitis, blepharokeratoconjunctivitis, and uveitis [17, 4]. It offers a safe and proven management of postoperative pain and inflammation after cataract surgery [6, 14, 17].

Topical combination products of steroids and antibiotics are commonly used in the treatment of steroid-responsive ocular inflammation, and a risk of bacterial ocular infection exists after strabismus surgery. To date, there are no published reports on the use of an LE/T ophthalmic solution in the treatment of postoperative inflammation following strabismus surgery. In this study, DM/T and LE/T were found to be similarly effective in controlling postoperative inflammation. Both groups demonstrated resolved inflammation and discomfort at 1 week compared to 1 day. There was no statistically significant difference in any measurement of postoperative inflammation between the two groups during the follow-up visits.

Conjunctival hyperemia, burning, and stinging have not been noted in association with both combination products. Both medications have not demonstrated an adverse effect on IOP and the wound healing process.

This retrospective study suggests that following strabismus surgery, topical LE/T application is effective and well tolerated with regard to DM/T. An LE/T ophthalmic solution could be an option for the treatment of inflammation following strabismus surgery.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Atatürk University School of Medicine (date/no: May 31, 2016/01).

Informed Consent: Written informed consent was not obtained for this study due to its retrospective nature.

Peer-review: Externally peer-reviewed.

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References

1. Dadeya S, and Kamlesh. Comparative evaluation of diclofenac and dexamethasone following strabismus surgery. J Pediatr Ophthalmol Strabismus 2002; 39: 166-8.
2. Snir M, Siegel RA, Friling R, and Weinberger D. Efficacy of diclofenac versus dexamethasone for treatment after strabismus surgery. Ophthalmology 2000; 107: 1884-8. [CrossRef]
3. Khan HA, Amitava AK. Topical diclofenac versus dexamethasone after strabismus surgery: A double-blind randomized clinical trial of anti-infalmmatory effect and ocular hypertensive response. Indian J Ophthalmol 2007; 55: 271-5. [CrossRef]
4. Amon M, Busin M. Loteprednol etabonate ophthalmic suspension 0.5%: efficacy and safety for postoperative anti-inflammatory use. Int Ophthalmol 2012; 32: 507-17. [CrossRef]
5. Pflugfelder SC, Maskin SL, Anderson B, et al. A randomized, double-masked, placebo-controlled, multicenter comparison of loteprednol etabonate ophthalmic suspension, 0.5%, and placebo for treatment of keratoconjunctivitis sicca in patients with delayed tear clearance. Am J Ophthalmol 2004;138: 444-57. [CrossRef]
6. Lane SS, Holland EJ. Loteprednol etabonate 0.5% versus prednisolone acetate 1.0% for the treatment of inflammation after cataract surgery. J Cataract Refract Surg 2013; 39: 168-73. [CrossRef]
7. White EM, Macy JI, Bateman KM, Comstock TL. Comparison of the safety and efficacy of loteprednol 0.5%/tobramycin 0.3% with dexamethasone 0.1%/tobramycin 0.3% in the treatment of blepharokeratoconjunctivitis. Curr Med Res Opin 2008; 24: 287-96. [CrossRef]
8. Comstock TL, Holland EJ. Loteprednol and tobramycin in combination: a review of their impact on current treatment regimens. Expert Opin Pharmacother 2010; 11: 843-52. [CrossRef]
9. Bartlett JD, Holland EJ, Usner DW, Paterno MR, Comstock TL. Tolerability of loteprednol/tobramycin versus dexamethasone/tobramycin in healthy volunteers: results of a 4-week, randomized, double-masked, parallel-group study. Curr Med Res Opin 2008; 24: 2219-27. [CrossRef]
10. Holland EJ, Bartlett JD, Paterno MR, Usner DW, Comstock TL. Effects of loteprednol/tobramycin versus dexamethasone/tobramycin on intraocular pressure in healthy volunteers. Cornea 2008; 27: 50-5. [CrossRef]
11. Comstock TL, DeCory HH. Loteprednol Etabonate 0.5%/Tobramycin 0.3% Compared with Dexamethasone 0.1%/Tobramycin 0.3% for the Treatment of Blepharitis. Ocul Immunol Inflamm 2016; 20: 1-8. [CrossRef]
12. Comstock TL, Paterno MR, Bateman KM, Decory HH, Gearinger M. Safety and tolerability of loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension in pediatric subjects. Paediatr Drugs 2012; 14: 119-30. [CrossRef]
13. Chen M, Gong L, Sun X, et al. A multicenter, randomized, parallel-group, clinical trial comparing the safety and efficacy of loteprednol etabonate 0.5%/tobramycin 0.3% with dexamethasone 0.1%/tobramycin 0.3% in the treatment of Chinese patients with blepharokeratoconjunctivitis. Curr Med Res Opin 2012; 28: 385-94. [CrossRef]
14. Pleyer U, Ursell PG, Rama P. Intraocular pressure effects of common topical steroids for post-cataract inflammation: are they all the same? Ophthalmol Ther 2013; 2: 55-72. [CrossRef]
15. Akyol-Salman I, Leçe-Sertöz D, Baykal O. Topical pranoprofen 0.1% is as effective anti-inflammatory and analgesic agent as diclofenac sodium 0.1% after strabismus surgery. J Ocul Pharmacol Ther 2007; 23: 280-3. [CrossRef]
16. Wright M, Butt Z, McIlwaine G, Fleek, B. Comparison of the efficacy of diclofenac and betamethasone following strabismus surgery. Br J Ophthalmol 1997; 81: 299-301. [CrossRef]
17. Sheppard JD, Comstock TL, Cavet ME. Impact of the Topical Ophthalmic Corticosteroid Loteprednol Etabonate on Intraocular Pressure. Adv Ther 2016; 33: 532-52. [CrossRef]
18. Kuppermann BD, Zacharias LC, Kenney MC. Steroid differentiation: the safety profile of various steroids on retinal cells in vitro and their implications for clinical use (an American Ophthalmological Society thesis). Trans Am Ophthalmol Soc 2014; 112: 116-41.