Intravitreal Triamcinolone Acetonide for the Treatment of Diabetic Macular Edema

Diabetik Makula Ödemi Tedavisinde İntravitreal Triamsinolon Asetonid

Fatih ÖZCURA[1], Sema ORUÇ DÜNDAR[2], Erkin KIR[3], Sayime AYDIN[1]. Turgay AKTUNÇ[2]

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ABSTRACT

Purpose: The purpose of this study is to evaluate the effectiveness and complications of intravitreal triamcinolone acetonide (IVTA) injection in the treatment of diabetic macular edema (DME).

Materials and Methods: Twenty-eight eyes of 26 DME patients who were resistant to laser photocoagulation treatment were enrolled in the study. Triamcinolone acetonide (TA) was injected intravitreally under topical anesthesia. The patients were evaluated at the first week, and the first, third and sixth months, in terms of visual acuity (VA), intraocular pressure (IOP), presence of TA crystals in vitreous, and regression of macular edema and hard exudates in the fundus photographs and fundus fluorescein angiography.

Results: The VA of the patients were 1.31±0.44 LogMAR unit before injection and improved significantly at the first week and the first and third months while there was no difference the sixth month (1.15±0.46, 1.01±0.51, 1.01±0.50, and 1.07±0.56 LogMAR units respectively). The IOP of the patients were 14.25±3.35 mmHg before injection and increased significantly at the first week and the first and third months while there was no difference the sixth month (16.07±4.27, 16.82±3.73, 17.32±6.08, and 15.35±3.15 mmHg respectively). Regression of macular edema in fundus fluorescein angiography detected in 22 (79%), 16 (57%), and 8 (31%) eyes the first, third, and sixth months respectively. TA crystals were observed in the vitreous in 26 (93%), 11 (39%), and 2 (8%) eyes the first, third and sixth months respectively. The hard exudates were regressed in 15 of 19 eyes (79%) end of the six months. One eye exhibited cataract progression.

Conclusion: IVTA injection in the treatment of refractory DME was found to be effective especially for 3 months.

Key Words: Diabetic macular edema, hard exudate, triamcinolone acetonide.

ÖZ

Amaç: Bu çalışmada diabetik makula ödemi (DMÖ) tedavisinde intravitreal triamsinolon asetonid (İVTA) enjeksiyonunun etkinliğini ve komplikasyonlarını değerlendirmek amaçlandı.

Gereç ve Yöntemler: Çalışmaya lazer fotokoagülasyon tedavisine dirençli DMÖ olan 26 hastanın 28 gözü alındı. Triamsinolon asetonid (TA) topikal anestezi altında intravitreal olarak enjekte edildi. Olgular birinci hafta, birinci, üçüncü ve altıncı ayda görme keskinliği, göz içi basıncı (GİB), vitreusta TA kristallerinin varlığı ve fundus fotografları ile fundus flöresein anjiografide makula ödemi ile sert eksudaların gerilemesi açısından değerlendirildi.

Bulgular: Hastaların enjeksiyon öncesi görme keskinliği 1.31±0.44 LogMAR unite olup birinci hafta, birinci ve üçüncü ayda anlamlı olarak artarken altıncı ayda anlamlı farklılık yoktu (1.15±0.46, 1.01±0.51, 1.01±0.50, 1.07±0.56 LogMAR ünite). Hastaların enjeksiyon öncesi GİB'i 14.25±3.35 mmHg olup birinci hafta, birinci ve üçüncü ayda anlamlı olarak artarken altıncı ayda anlamlı farklılık yoktu (16.07±4.27, 16.82±3.73, 17.32±6.08, 15.35±3.15 mmHg). Fundus flöresein anjiografide birinci, üçüncü ve altıncı ayda sırasıyla 22 (%79), 16 (%57) ve 8 (%31) gözde makula ödeminde gerileme saptandı. Birinci, üçüncü ve altıncı ayda sırasıyla 26 (%93), 11 (%39) ve 2 (%8) gözde vitreusta TA kristalleri izlendi. Enjeksiyon öncesi sert eksuda olan 19 gözün, altı ay sonunda 15'inde (%79) sert eksudaların gerilediği görüldü. Bir gözde katarakt ilerlemesi görüldü.

Sonuç: Lazer fotokoagülasyonuna dirençli DMÖ tedavisinde İVTA enjeksiyonunun özellikle ilk 3 ay için etkili olduğu bulunmuştur.

Anahtar Kelimeler: Diabetik makula ödemi, sert eksuda, triamsinolon asetonid.

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1- Dumlupınar Üniversitesi, Tıp Fakültesi, Göz Hastalıkları A.D., Kütahya, Yard. Doç. Dr.
2- Adnan Menderes Üniversitesi, Tıp Fakültesi, Göz Hastalıkları A.D., Aydın, Prof. Dr.
3- Adnan Menderes Üniversitesi, Tıp Fakültesi, Göz Hastalıkları A.D., Aydın, Doç. Dr.

1- M.D. Assistant Professor, Dumlupınar University Faculity of Medicine, Department of Ophthalmology Kütahya/TURKEY
ÖZCURA F., fatihozcura@yahoo.com
AYDIN S.,
2- M.D. Professor, Adnan Menderes University, Department of Ophthalmology Aydın/TURKEY
DÜNDAR S.O., orucs@hotmail.com
AKTUNÇ T.,
3- M.D. Associate Professor, Adnan Menderes University, Department of Ophthalmology Aydın/TURKEY
KIR E.,

Correspondence: M.D. Assistant Professor, Fatih ÖZCURA
Dumlupınar University Faculity of Medicine, Department of Ophthalmology
Kütahya/TURKEY

INTRODUCTION

Macular edema is the most important reason of visual disturbance in diabetes mellitus patients.[1] Today, the acknowledged treatment of diabetic macular edema (DME) is focal or grid laser photocoagulation. "Early Treatment Diabetic Retinopathy Study" (ETDRS) group has reported that the risk of vision loss in DME is reduced by laser photocoagulation.

ETDRS has compared clinically significant macular edema (CSME) patients who were under the treatment of laser photocoagulation for three years with those who did not receive this treatment. They have found out that the risk of moderate vision loss (the vision loss is declined half in the two consecutive check-ups done 4 months after one another) after three years of laser treatment, has declined 50%. While moderate vision loss was 15% in the treatment group, it was 30% in the control group.[2,3]

Today, it is known that laser photocoagulation causes a permanent damage in macula, and negative effects on patient's central vision area and color vision. Therefore, pharmacological ways of treatment that would not cause any damage on tissues are trying to be developed.[2,3] With this purpose in mind, there are some ways of treatment that are worked on, such as protein kinase, aldose reductase, advanced glycosylation inhibitors, and intravitreal injection of triamcinolone acetonide (TA), vascular endothelial growth factor (VEGF) inhibitors.[4]

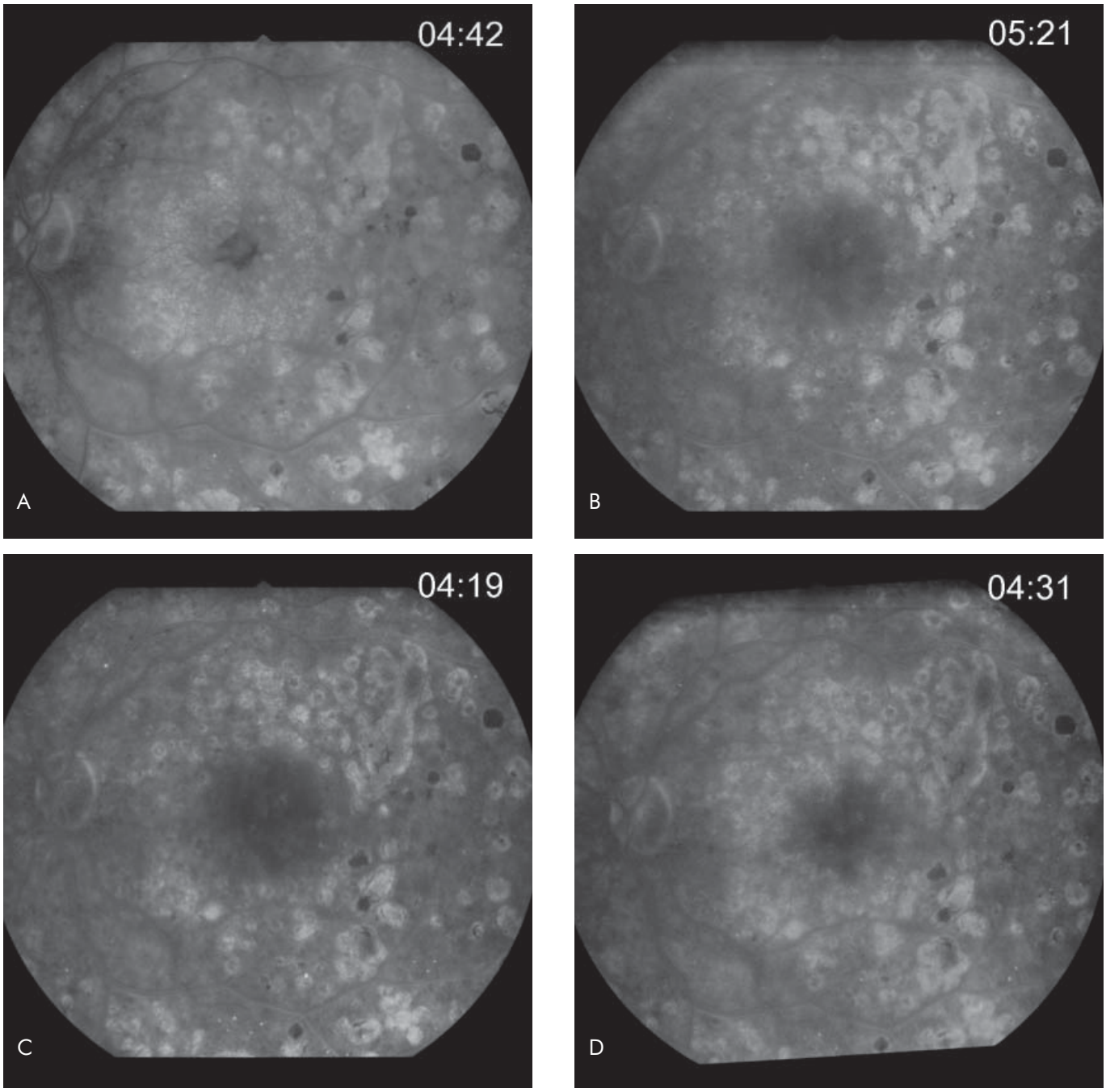

Figure 1: Late phase fluorescein angiography of a 54 year old man with clinically significant macular edema. (A) Before injection, (B) complete resolution, (C) complete resolution, and (D) recurrence of macular edema the 1, 3, and 6 months respectively after intravitreal triamcinolone acetonide injection.

Table 1: Visual acuity change after intravitreal triamcinolone acetonide injection.

Time	Number of eye	Mean visual acuity (LogMAR unit)	P Value
Before injection	28	1.31±0.44 (0.70-2.10)	
1 week	28	1.15±0.46 (0.40-2.10)	0.002*
1 month	28	1.01±0.51 (0.30-2.10)	<0.001*
3 months	28	1.01±0.50 (0.22-2.10)	0.001*
6 months	26	1.07±0.56 (0.22-2.10)	0.059

*Statistically significant ($p<0.01$)

Table 2: Intraocular pressure (IOP) change after intravitreal triamcinolone acetonide injection.

Time	Number of eye	Mean IOP (mmHg)	P Value
Before injection	28	14.25±3.35 (6-20)	
1 week	28	16.07±4.27 (9-29)	0.001*
1 month	28	16.82±3.73 (10-26)	0.001*
3 months	28	17.32±6.08 (11-42)	0.005*
6 months	26	15.35±3.15 (10-21)	0.258

* Statistically significant ($p<0.01$)

TA is a corticosteroid that has been used in periocular injection for uveitis and postoperative cystoid macular edema.[5] Positive effect of intravitreal TA (IVTA) injection on intraocular proliferation was firstly shown by Machemer et al. and then IVTA injection was initiated in experimental and clinical studies.[6] There are studies indicating that IVTA has been used in the treatment of proliferative vitreoretinopathy, retinal neovascularization, exudative age related macular degeneration, macular edema due to central retinal vein and branch retinal vein occlusion, postoperative cystoid macular edema, DME, uveitis, and proliferative diabetic retinopathy (DR).[7-15]

In this study, our aim is to evaluate the effectiveness and complications of IVTA injection in eyes with DME which were resistant to laser photocoagulation treatment.

MATERIALS AND METHODS

In this study, 28 eyes of 26 DME patients who were resistant to focal or grid laser photocoagulation were reviewed retrospectively. The patients were treated with at least two session of focal or grid laser photocoagulation and DME duration was at least one year. Before the intravitreal injection, patients underwent a detailed ophthalmic examination including the visual acuity (VA), intraocular pressure (IOP) measurement with Goldmann applanation tonometer, anterior segment and fundus examination with a slit-lamp biomicroscope. VA was measured by Snellen and converted LogMAR equivalences in the statistical analysis. After the routine ophthalmic examinations, fundus photographs and fundus fluorescein angiography (FFA) were taken.

Apraclonidine HCL (Iopidine®) and ofloxacin 0.3% (Exocin®) were dropped 30 minutes before the injection, and ocular massage was performed 5 minutes before the injection. Proparacaine HCL 0.5% (Alcaine®) was used for the topical anesthesia. Eye circle was cleaned with 10% of povidone-iodine and eye surface was cleaned with 5% of povidone-iodine. Four mg TA (Kenacort-A® 40 mg/ml, 0.1ml) was injected into the eye from the inferotemporal quadrant. The injection was performed 3.5 and 3 mm behind the limbus in phakic and pseudophakic patients respectively. After the injection, the patients applied one drop of ofloxacin 0.3% (Exocin®) four times a day for a week.

Patients were controlled on the first day, at the first week, and the first, third and sixth months. In the control examinations VA, IOP, and whether any TA crystals remained in the vitreous, were followed. Regression of macular edema was evaluated by FFA the first, third, and the sixth months. Patients whose IOP exceed 21 mmHg, were treated with topical antiglaucomatous medication. Hard exudates were evaluated on fundus photographs end of the sixth month whether there was a regression or not. Cataract progression of the patients after the injection was graded according to Lens Opacities Classification System III.

The comparisons of the dependent groups were performed with Friedman and Wilcoxon tests. The significance was evaluated after the Bonferroni correction ($p<0.01$).

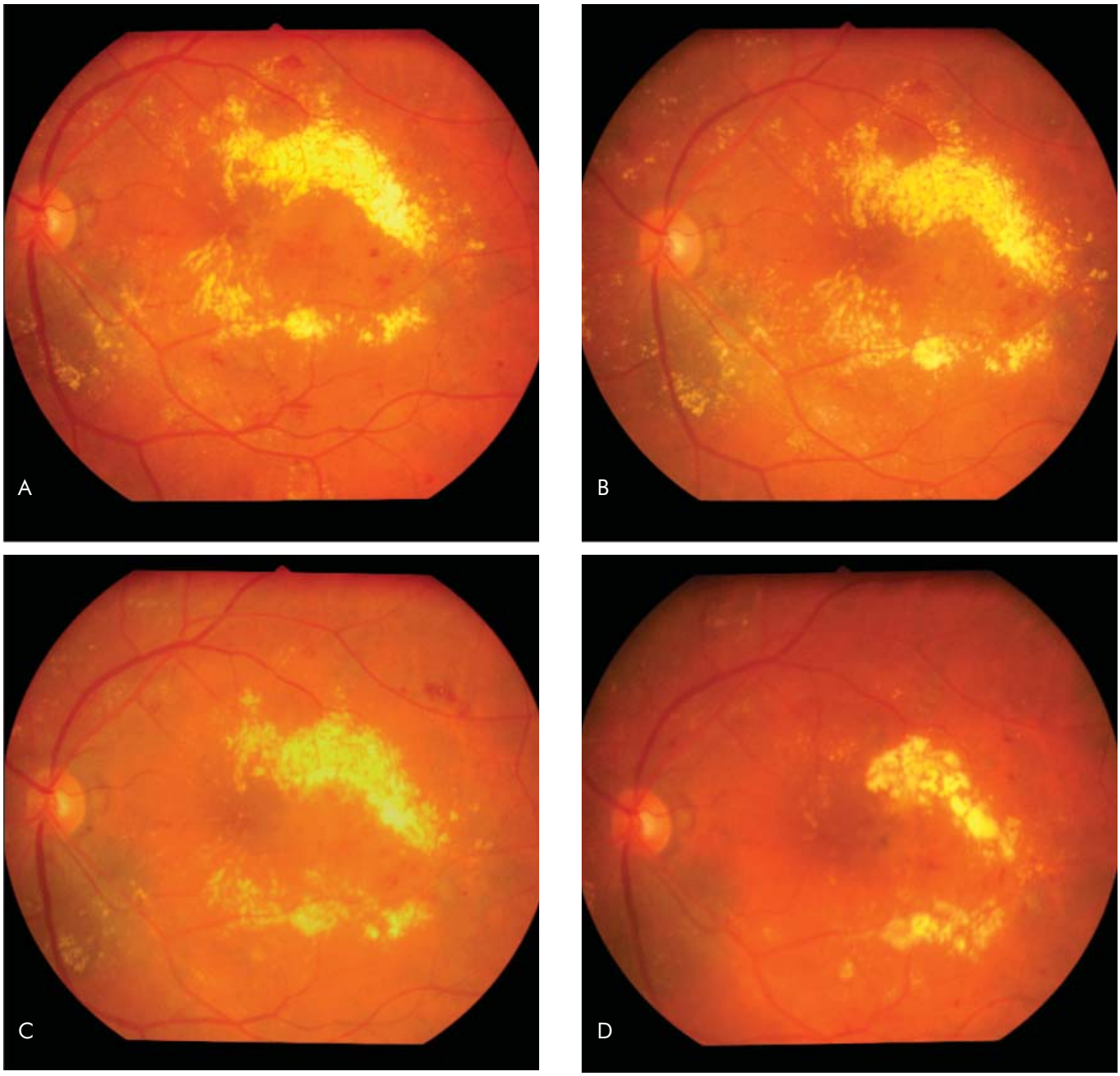

Figure 2: Fundus photographs of a 69 year old woman with hard exudates. (A) Before injection. (B), (C), (D) Progressive regression of the hard exudates the 1, 3, and 6 months after intravitreal triamcinolone acetonide injection.

RESULTS

Fifteen (57.7%) patients were female and 11 (42.3%) were male, and their mean age was 63.77±10.01 (ranging 34 to 82) years. All patients were followed for 6 months but only 2 patients did not come to the sixth month control examination.

Before IVTA injection, mean VA was 1.31±0.44 (ranging 0.70 to 2.10) logMAR units and the mean IOP was 14.25±3.35 (ranging 6 to 20) mmHg. Nine of the eyes were pseudophakic and 19 of them were phakic. Before the injection, fundus photographs and FFA were taken, and CSME were detected in all eyes. Nineteen of them had hard exudates. The VA and IOP of the patients increased significantly at the first week, and the first and third months compared to the baseline values ($p<0.01$). However, there were no significant differences between the sixth month and baseline values (Table 1 and 2). In all examinations, IOP was 21 mmHg or below in 21 eyes. On the other hand, IOP exceed 21 mmHg in 7 (25%) eyes. IOP elevation occurred in one patient at the first week, in 2 patients the first month, and in 4 patients the third month.

Those who had IOP elevation were treated with topical antiglaucomatous medication (timolol, dorzolamide, and brimonidine) and normotensive levels were achieved in all patients within one to three months. Antiglaucomatous medication was discontinued after one month when the IOP was normal. There were no patients who

had refractory IOP elevation or who had to use chronic antiglaucomatous medication. In the FFA examination, there was a regression of macular edema in 22 (79%), 16 (57%), and 8 (31%) eyes the first, third, and the sixth months respectively. There was no change in macular edema in 6 patients. A patients FFA samples were given in Figure 1. In the fundus examinations, TA crystals were observed in the vitreous of all eyes at the first week. TA crystals were observed in 26 (93%), 11 (39%), and 2 (8%) eyes the first, third, and the sixth months respectively.

In the fundus photographs, progressive regression of the hard exudates was noted in 15 (79%) of 19 eyes when compared to the state before the injection (Figure 2). Hard exudates locations were extrafoveal in 9 eyes, foveal in 1 eye and combined in 9 eyes. There was no change in the size of hard exudates in 4 eyes (21%) and those hard exudates were combined in 3 eyes and foveal in 1 eye. All extrafoveal hard exudates were regressed.

Five of the 19 phakic eyes developed cataract progression end of the sixth month. Four of these patients had the same rate of cataract progression in both eyes, although one of the eyes was treated with IVTA injection. When we take this into consideration, we can say that rapid cataract progression was developed only in 1 (5%) of the eyes that applied IVTA injection. None of the patients developed complications, such as endophthalmitis, vitreous hemorrhage and retinal detachment.

DISCUSSION

DME is the most important cause of vision loss in diabetic patients. Pathogenesis cannot be clarified; therefore deterioration occurs in inner blood-retinal barrier.[1] ETDRS has reported the benefits of laser photocoagulation in CSME patients; however laser photocoagulation treatment may have some adverse effects, such as foveal burn, choroidal neovascularization, retinal hemorrhage, subretinal fibrosis, formation of scotoma in the visual field, and anomaly of color vision.[2,3] In the study of Lee et al. only 14.5% of the patients were able to preserve the gain of vision in the long term after grid laser photocoagulation.[16]

Laser photocoagulation treatment is used widely because it has more advantages than disadvantages. However, there is still research on alternative treatment methods. IVTA injection has been used in the treatment of DME patients since 2001 and has been carried out successfully.[13]

Although there were benefits of corticosteroids in the treatment of DME, its influences have not been clarified yet. By inhibiting arachidonic acid metabolism, corticosteroids decrease the formation of prostaglandin and also inhibit the production of VEGF. The most common opinion in DME pathogenesis is that there is an increase in the vascular permeability due to the blood-retinal barrier deterioration. Experimental and clinical studies have shown that improvement of blood-retinal barrier deterioration is in accordance with IVTA injection.[17,18]

Martidis et al. reported that the mean VA of the patients increased 2.4 Snellen line the first and the third months, and 1.3 Snellen line increased the sixth month in laser resistant CSME patients with IVTA injection.[19] We treated similar patients with IVTA and we detected an increase in the VA for the first 3 months. VA was higher compared to the baseline values; however there was no statistically significant difference end of the sixth month. Jonas et al. reported that VA improved significantly, from 0.12 ± 0.08 at baseline to a maximum of 0.19 ± 0.14 during six months and Sutter et al. reported that 18 of 33 eyes (55%) treated with triamcinolone gained 5 or more ETDRS letters compared with 5 of 32 eyes (16%) treated with placebo end of the third month in DME.[20,21]

It was reported that as the mean VA increased, the fluorescein leakage decreased which was observed in the FFA before the injection. Jonas et al. also reported that there was a significant decline in the fluorescein leakage as a result of the IVTA injection.[20] We have detected that regression of macular edema was noted in 22 (79%), 16 (57%), and 8 (31%) eyes the first, third, and the sixth months respectively in the FFA but there was no change in macular edema in 6 patients. Those had worse baseline VA and possible poor systemic factors such as glycemic control, blood pressure, and nephropathy. These factors may affect macular thickness. We could not consider into systemic factors initiation of the study because of retrospective nature of the study.

Ciardella et al. reported that progressive reduction in the number and size of the hard exudates was noted after IVTA in all patients with DME.[22] Avci and Kaderli reported that intravitreal TA appears to be a valuable treatment in DME with severe foveal hard exudates. In all eyes in this study the hard exudates were completely resolved or decreased after IVTA.[23] In our study, progressive regression of the hard exudates was noted in 15 (79%) of 19 eyes when compared to the state before the injection.

The fact that the effect is temporary and the observation of recurrence is related to the elimination of TA from the vitreous is confirmed by the positive results achieved from repeated injections.[19,24] Audren et al. reported that the average maximum effect time was 140 days with 4 mg IVTA injection.[25] Another important point is that as the elimination of TA increased, the effect time decreased in patients who were treated with vitrectomy.[26] Kogure et al. reported that 4 mg intravitreal TA retention time was 115 days in DME patients, and patient age and retention time were negatively correlated. Kogure et al. concluded that biomicroscopic examination of intravitreal TA is useful for evaluation of its efficacy.[27] In our study, we clinically observed whether there were TA crystals in vitreous. At the first week, all the eyes had TA crystals. TA crystals were observed in 26 (93%), 11 (39%), and 2 (8%) eyes the first, third, and the sixth months respectively. On the other hand, Jonas reported that the duration of the effect of a single IVTA is dosage dependent (about 6 - 9 months with 20 mg, and about 2-4 months with 4 mg).[28]

There was no record of retinal toxicity related to IVTA injection in the experimental and clinical studies.[19,22,29] On the other hand, complications can be attributed to the injection procedure or to the corticosteroid suspension. Potential injection-related complications include endophthalmitis, vitreous hemorrhage, and retinal detachment.[24] No such complications were experienced in our study group. Eight (0.87%) acute endophthalmitis cases were recorded after 922 IVTA injections in the multi-central, retrospective studies of Moshfeghi et al.[30]

The major ocular side effects attributed to corticosteroids include IOP elevation, and cataract progression. In the recent studies, IOP elevation rate is detected 28 to 78% after IVTA injection. Almost all of the IOP elevations can be controlled with topical antiglaucomatous medication without any optic nerve damage; however there may be some refractory IOP elevation that require trabeculectomy, though very rare.[31,32] Vasconcelos-Santos et al. reported that 4 mg IVTA injection was associated with secondary ocular hypertension in 32% of eyes. The risk of IOP elevation was higher in eyes with previous glaucoma and higher baseline IOP.[33] In our study, the mean IOP for 3 months after the injection were significantly higher compared to the baseline IOP and IOP exceed 21 mmHg in 25% of eyes.

Gillies et al. reported that there was 24.2% cataract progression with IVTA after two years.[34] In the studies during 3 to 6 months of period, Martidis et. al., Sutter et al., and Ciardella et al. reported that there were 1/8 (13%), 1/27 (4%), and 2/30 (15%) cataract progression respectively; however, Massin et al. reported that there was no cataract progression.[19,21,22,35] In our study, we detected cataract progression in only 1 patient (5%). It should be taken into consideration that, with a longer period of following, these ratios may increase likewise in the studies of Gillies et al.[34]

As a conclusion, current approach for the treatment of DME and DR is to prevent and stop the pathogenetic process, but a medicine that prevent and stop the pathogenetic process cannot be found yet. IVTA injection can be an alternative treatment to especially laser photocoagulation resistant DME. In this study, 4 mg IVTA injection in the treatment of refractory DME was found to be effective especially for the 3 months. Nonetheless, a long term, prospective, randomised, and controlled studies are needed in order to find out the effects and side effects of the IVTA injection.

KAYNAKLAR/REFERENCES

1. Klein R, Klein BE, Moss SE: Visual impairment in diabetes. Ophthalmology. 1984;91:1-9.
2. Early Treatment Diabetic Retinopathy Study Research Group: Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Arch Ophthalmol. 1985;103:1796-1806.
3. Early Treatment Diabetic Retinopathy Study Research Group: Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 4. Int Ophthalmol Clin. 1987;27:265-272.
4. Bandello F, Pognuz R, Polito A, et al.: Diabetic macular edema: classification, medical and laser therapy. Semin Ophthalmol. 2003;18:251-258.
5. Suckling RD, Maslin KF.: Pseudophakic cystoid macular oedema and its treatment with local steroids. Aust N Z J Ophthalmol. 1988;16:353-359.
6. Machemer R, Sugita G, Tano Y.: Treatment of intraocular proliferations with intravitreal steroids. Trans Am Ophthalmol Soc. 1979;77:171-180.
7. Munir WM, Pulido JS, Sharma MC, et al.: Intravitreal triamcinolone for treatment of complicated proliferative diabetic retinopathy and proliferative vitreoretinopathy. Can J Ophthalmol. 2005; 40:598-604.
8. Antoszyk AN, Gottlieb JL, Machemer R, et al.: The effects of intravitreal triamcinolone acetonide on experimental pre-retinal neovascularization. Graefes Arch Clin Exp Ophthalmol. 1993; 231:34-40.
9. Jonas JB, Kreissig I, Hugger P, et al.: Intravitreal triamcinolone acetonide for exudative age related macular degeneration. Br J Ophthalmol. 2003;87:462-468.
10. Ip MS, Kumar KS.: Intravitreous triamcinolone acetonide as treatment for macular edema from central retinal vein occlusion. Arch Ophthalmol. 2002;120:1217-1219.
11. Chen SD, Lochhead J, Patel CK, et al.: Intravitreal triamcinolone acetonide for ischaemic macular oedema caused by branch retinal vein occlusion. Br J Ophthalmol. 2004;88:154-155.
12. Jonas JB, Kreissig I, Degenring RF.: Intravitreal triamcinolone acetonide for pseudophakic cystoid macular edema. Am J Ophthalmol. 2003;136:384-386.
13. Jonas JB, Sofker A.: Intraocular injection of crystalline cortisone as adjunctive treatment of diabetic macular edema. Am J Ophthalmol. 2001;132:425-427.
14. Degenring RF, Jonas JB.: Intravitreal injection of triamcinolone acetonide as treatment for chronic uveitis. Br J Ophthalmol. 2003; 87:361.
15. Jonas JB, Sofker A, Degenring R.: Intravitreal triamcinolone acetonide as an additional tool in pars plana vitrectomy for proliferative diabetic retinopathy. Eur J Ophthalmol. 2003;13:468-473.
16. Lee CM, Olk RJ.: Modified grid laser photocoagulation for diffuse diabetic macular edema. Long-term visual results. Ophthalmology. 1991;98:1594-1602.
17. Sakamoto T, Miyazaki M, Hisatomi T, et al.: Triamcinolone-assisted pars plana vitrectomy improves the surgical procedures and decreases the postoperative blood-ocular barrier breakdown. Graefes Arch Clin Exp Ophthalmol. 2002;240:423-429.
18. Wilson CA, Berkowitz BA, Sato Y, et al.: Treatment with intravitreal steroid reduces blood-retinal barrier breakdown due to retinal photocoagulation. Arch Ophthalmol. 1992;110:1155-1159.
19. Martidis A, Duker JS, Greenberg PB, et al.: Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology. 2002; 109:920-927.
20. Jonas JB, Kreissig I, Söfker A, et al.: Intravitreal injection of triamcinolone for diffuse diabetic macular edema. Arch Ophthalmol. 2003;121:57-61.
21. Sutter FK, Simpson JM, Gillies MC.: Intravitreal triamcinolone for diabetic macular edema that persists after laser treatment: three-month efficacy and safety results of a prospective, randomized, double-masked, placebo-controlled clinical trial. Ophthalmology. 2004;111: 2044-2049.
22. Ciardella AP, Klancnik J, Schiff W, et al.: Intravitreal triamcinolone for the treatment of refractory diabetic macular oedema with hard exudates: an optical coherence tomography study. Br J Ophthalmol. 2004;88:1131-1136.
23. Avci R, Kaderli B.: Intravitreal triamcinolone injection for chronic diabetic macular oedema with severe hard exudates. Graefes Arch Clin Exp Ophthalmol. 2006;244:28-35.
24. Ip MS: Intravitreal injection of triamcinolone: an emerging treatment for diabetic macular edema. Diabetes Care. 2004; 27:1794-1797.
25. Audren F, Tod M, Massin P, et al.: Pharmacokinetic-pharmacodynamic modeling of the effect of triamcinolone acetonide on central macular thickness in patients with diabetic macular edema. Invest Ophthalmol Vis Sci. 2004;45:3435-3441.
26. Beer PM, Bakri SJ, Singh RJ, et al.: Intraocular concentration and pharmacokinetics of triamcinolone acetonide after a single intravitreal injection. Ophthalmology. 2003;110:681-686.
27. Kogure A, Ohkoshi K, Kogure S, et al.: Efficacy and retention times of intravitreal triamcinolone acetonide for macular edema. Jpn J Ophthalmol. 2008;52:122-126.
28. Jonas JB.: Intravitreal triamcinolone acetonide for diabetic retinopathy. Dev Ophthalmol. 2007;39:96-110.
29. McCuen BW 2nd, Bessler M, Tano Y, et al.: The lack of toxicity of intravitreally administered triamcinolone acetonide. Am J Ophthalmol. 1981;91:785-788.
30. Moshfeghi DM, Kaiser PK, Scott IU, et al.: Acute endophthalmitis following intravitreal triamcinolone acetonide injection. Am J Ophthalmol. 2003;136:791-796.
31. Kaushik S, Gupta V, Gupta A, et al.: Intractable glaucoma following intravitreal triamcinolone in central retinal vein occlusion. Am J Ophthalmol. 2004;137:758-760.
32. Jonas JB, Kreissig I, Degenring R.: Intraocular pressure after intravitreal injection of triamcinolone acetonide. Br J Ophthalmol. 2003;87:24-27.
33. Vasconcelos-Santos DV, Nehemy PG, Schachat AP, et al.: Secondary ocular hypertension after intravitreal injection of 4 mg of triamcinolone acetonide: incidence and risk factors. Retina. 2008; 28:573-580.
34. Gillies MC, Simpson JM, Billson FA, et al.: Safety of an intravitreal injection of triamcinolone: results from a randomized clinical trial. Arch Ophthalmol. 2004;122:336-340.
35. Massin P, Audren F, Haouchine B, et al.: Intravitreal triamcinolone acetonide for diabetic diffuse macular edema: preliminary results of a prospective controlled trial. Ophthalmology. 2004; 111:218-224.