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Comparative study between intravitreal ranibizumab and triamcinolone treatment of diabetic macular edema as regard to optical coherence tomography changes and visual acuity

Estudo comparativo entre o tratamento intravítreo com ranibizumabe e triancinolona do edema macular diabético quanto às alterações na tomografia de coerência óptica e na acuidade visual

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Abstract

Objectives: *To compare the effect of intravitreal Ranibizumab (0.3mg) and Triamicinolone (4mg) on different parameters in spectral domain OCT and their relation to visual acuity of patients with diabetic macular edema.* ***Methods:*** *This study is designed as a prospective randomized study. Patients were randomly divided into 2 groups receiving either Pro re nata intravitreal Ranibizumab (0.3mg) or Triamicinolone acetonide (4mg), to whom Spectral Domain OCT was done as well as best corrected Log MAR visual acuity.* ***Results:*** *40 patients were included in this study. Comparison and correlation of mean BCVA and mean CMT among and within treatment groups of our study revealed strong and significant relationship between both parameters and showing equal effect of both treatment types regarding them with the consideration that Triamicinolone acetonide treated group (Group B) showed statistically significant lower CMT compared to Ranibizumab treated group (Group A) at three and six months. Also both showed equal effectivity regarding improvement of the photoreceptors integrity and in turn the improvement of the BCVA. Meanwhile the association of CMT and IS/OS integrity was found to be significant only at six months in both groups (p =0.009 in Group A; p =0.031 in Group B). The fading initial effect of a single ranibizumab injection on macular edema can be augmented by following that one injection with two injections of the loading dose. Triamicinolone effect after single injection began to fade at 3 months.* ***Conclusion:*** *Both treatment types had good effect on reduction of CMT and improvement of BCVA and the IS/OS junction with difference in sustainability of their effects due to difference in their pharmacokinetics and need for repeated injections.*

Keywords: *Macular edema, Diabetic retinopathy; Tomography, optical coherence anti-VEGF, Triamicinolone*

Resumo

Objetivos: Comparar o efeito do ranibizumabe intravítreo (0,3mg) e triacmicinolona (4mg) em diferentes parâmetros do domínio espectral da OCT e sua relação com a acuidade visual de pacientes com edema macular diabético. **Métodos:** Este estudo foi concebido como um estudo prospectivo randomizado. Os pacientes foram divididos aleatoriamente em 2 grupos que receberam Ranibizumab Pro rata intravitreal (0,3mg) ou acetonido de Triamicinolona (4mg), a quem foi realizada a Spectral Domain OCT, bem como a melhor acuidade visual de Log MAR corrigida. **Resultados:** Quarenta pacientes foram incluídos neste estudo. A comparação e a correlação da acuidade visual média e CMT média entre e dentro de grupos de tratamento do nosso estudo revelaram uma relação forte e significativa entre ambos os parâmetros e mostrando um efeito igual de ambos os tipos de tratamento, considerando que o grupo tratado com acetonido Triamicinolona (Grupo B) apresentou significância estatística. menor CMT comparado ao grupo tratado com Ranibizumab (Grupo A) aos três e seis meses. Também ambos mostraram igual efetividade em relação à melhoria da integridade dos fotorreceptores e, por sua vez, a melhora do BCVA. Enquanto isso, a associação de CMT e IS / OS integridade foi significativa apenas aos seis meses em ambos os grupos (p = 0,009 no Grupo A; p = 0,031 no Grupo B). O efeito inicial enfraquecido de uma única injeção de ranibizumabe no edema macular pode ser aumentado seguindo-se aquela injeção com duas injeções da dose de ataque. O efeito triamicinolona após injeção única começou a diminuir aos 3 meses. **Conclusão:** Ambos os tipos de tratamento tiveram bom efeito na redução da CMT e melhora do BCVA e da junção IS / OS com a diferença na sustentabilidade de seus efeitos devido à diferença em sua farmacocinética e necessidade de injeções repetidas.

Descritores: Edema macular; Retinopatia diabética; Tomografia de coerência óptica; anti-VEGF; Triancinolona

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Introduction

Diabetic Mellitus (DM), a chronic metabolic disorder, is a major public health problem due to its associated complications.[1] One of the major complications of DM is diabetic retinopathy (DR), which is an important cause of preventable blindness. DR is characterized by the progressive damage in the retinal microvasculature. It can be classified into non proliferative DR (NPDR) and proliferation DR (PDR).[2, 3] In most cases, DR is featured with increased vascular permeability, leading to fluid accumulation and retinal hemorrhages in the macula, all of which referred to DME. [4-6] The two most important causes of visual impairment secondary to DR are diabetic macular edema (DME) and proliferative DR (PDR). The prevalence of DME is 3% in mild non proliferative retinopathy and rises to 38% in eyes with moderate-to-severe non proliferative retinopathy, eventually reaching 71% in eyes with proliferative retinopathy.[7]

There are many different techniques for examining the macular area, including biomicroscopy, fluorescein angiography, and optical coherence tomography (OCT). Fluorescein angiography (FA) has played a central role in understanding the pathophysiology of various retinal diseases being used as an important clinical tool in the diagnosis and treatment of DME.[8-11] Fundamentally, the focal laser protocol in Early Treatment Diabetic Retinopathy Study (ETDRS) was based on speculating the pathogenesis of DME by FA.[12]

Subthreshold micropulse diode laser photocoagulation is a treatment that theoretically avoids damaging the inner neurosensory retina, thereby reducing potential complications such as paracentral scotomata and enlargement of post-treatment scars. This technique was first described in the late 1990s and since then there has been some randomized controlled trials (RCTs) comparing this technique to modified ETDRS laser treatment.[13,14] Vujosevic et al. found improvement of central retinal sensitivity in the micropulse group, but its deterioration in the modified ETDRS group.[15] Micropulse laser thus may offer a new, less aggressive laser approach in the treatment of clinically significant macular edema.

Structural modification of diabetic vitreous occurs secondary to enzymatic and non-enzymatic collagen glycation. [16] Accumulation of advanced glycation end products (AGEs) in the vitreous of hyperglycemic patients promotes collagen crosslinking and may be the cause of VMT in diabetic eyes. [17] AGE accumulates along the posterior vitreous cortex and the ILM, where it may cause structural alterations that promote vitreoretinal traction. Vitrectomy to remove the posterior hyaloid and ILM may be beneficial in two ways: (1) by removing AGE ligand-induced mechanical traction between the posterior cortical vitreous and the ILM of macula; and (2) removal of AGEs may also inhibit the activation of the RAGE axis and its pro inflammatory effects. Muller cells lie between the ILM and ELM and in close apposition with capillaries. In diabetic eyes, upregulation of VEGF in Muller cells may increase the vasopermeability of the retinal endothelial cells. The DRCR.net examined the role of vitrectomy and membrane peeling in the treatment of DME with a tractional component in a small, prospective cohort study(18) At six months postoperatively, VA improved by more than 2 lines in 38% of eyes. The mean decrease in macular thickness on OCT was approximately 160 μm, with 43% of patients having macular thickness of less than 250 μm.[19]

Methods

This study is designed as a prospective randomized study that involves a total of 40 diabetic patients with diabetic macular edema treated with intravitreal injections, to whom Spectral Domain OCT was done as well as best corrected Log MAR visual acuity.

The inclusion criteria

1. Type 1 or 2 diabetes mellitus with non-tractional diabetic macular edema with foveal thickness ≥300 μm

The exclusion criteria

1. Involve any patient with concurrent macular diseases as macular degeneration
2. Any significant media opacities (as cataract or vitreous haemorrhage) that hinder fundus examination &OCT imaging, any macular edema from other causes (including history of uveitis, retinal detachment, recurrent ERMs or vitreomacular traction)
3. Any type of previous macular treatment (macular laser photocoagulation, vitrectomy, intravitreal steroids &/or antiangiogenic drugs);
4. Any intraocular surgery at least 4 months before the study involvement
5. Ischaemic maculopathy

Pre-operative and post-operative evaluation:

Each patient underwent a complete ophthalmic examination, with determination of Best Corrected Visual Acuity (BCVA), anterior segment examination, indirect ophthalmoscopy & 90-D lens biomicroscopy. Thereafter, SD-OCT+/- Fundus fluorescein angiography was performed to every patient before treatment and after treatment at intervals of 1, 3 and 6 months from the injection. (Optovue RTVue-100; Optovue Inc, Fremont, CA) {RTVue scans used the three-dimensional (3D) macular scan protocol set to 6 6 mm containing 101 horizontal line scans each consisting of 513 A scans evaluated with Optovue analysis software version 4.0.5.39 or higher}

The injection was done in the operating theater in Research Institute of Ophthalmology under topical anaesthesia and full aseptic conditions which was made once with either Lucentis (ranibizumab injection) [Group A] or Triamcinolone Acetonide [Group B] (20 patients with Triamcinolone & The other 20 patients with Lucentis).

Triamcinolone acetonide in a single-use bottle (40 mg/ml, 1ml bottle), is drawn into a 1-cc tuberculin syringe after cleansing the top of the bottle with an alcohol wipe. A separate 27 or 26 gauge needle is placed onto the syringe, which is then inverted to remove air bubbles. The excess triamcinolone is discarded till 0.1 ml (4 mg) remains in the syringe. The injection site is usually the inferotemporal quadrant to avoid drug deposition in front of the visual axis. The stab is given 3-3.5 mm from the limbus (in aphakic and pseudophakic patients) and 3.5-4 mm from the limbus in phakic patients to ensure against passage of the needle through the vitreous base.

Lucentis (ranibizumab) 0.3 mg (0.05 mL of 6 mg/mL LUCENTIS solution) is recommended to be administered by intravitreal injection once a month. It is withdrawn through a 5-micron, 19-gauge filter needle attached to a 1-cc tuberculin syringe. The filter needle should be discarded after withdrawal of the vial contents and should not be used for intravitreal injection. The filter needle should be replaced with a sterile 30-gauge x 1/2-

inch needle for the intravitreal injection. The contents should be expelled until the plunger tip is aligned with the line that marks 0.05 mL on the syringe.

Statistical methodology:

Data were analyzed using SPSSwin statistical package version 21 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation (Mean ± SD) or Median and range as appropriate according to Normal distribution curve and Histogram.

Qualitative data were expressed as frequency and percentage. Chi-square test or (Fisher's exact test) used to examine the relation between qualitative or categorical variables. Repeated categorical variables tested by Cochrane test.

For quantitative data, comparison between the two treatment groups were done using either student t-test or Mann-Whitney test (non-parametric t-test) as appropriate. Visual acuity at baseline & 1 month, 3 months or 6 months were analyzed using paired t-test. Repeated measure ANOVA analyze changes along time in VA & CMT. All tests are two tailed and a p-value ≤ 0.05 was considered significant.

Bivariate correlation analysis either by Pearson correlation or Spearman Rho correlation was done to examine the relationship between two numeric data or graphically summarized by Scatter dot diagram. It indicated:

- Strength of the relationship (strong or weak)
- Direction of the relationship:
  - Positive (direct): variables move in the same direction
  - Negative (inverse): variables move in opposite direction

The interpretation of correlation:

- From 0 to 0.25 (– 0.25): no or little relationship
- From 0.25 to 0.50 (- 0.25 to – 0.50) fair degree of relationship
- From 0.50 to 0.75 (–0.50 to – 0.75) moderate to good relationship.
- Greater than 0.75 (or – 0.75): very good to excellent relationship.

Results

Demographic data:

Age:

The mean age of our patients was 56.7 ± 6.182 years in Group A and 60 ± 5.487 years in Group B. Comparison between the two groups was insignificant with P = 0.082

Sex distribution:

There were 55% females and 45% males in Group A and 50% females and 50% males in Group B. Comparison between the two groups was insignificant with P = 0.752

Pre-operative examination:

Mean IOP (mmHg):

The mean IOP in our patients was 16.5+/- 2.05mm in Group A and in Group B 15.2+/- 2.931 mm.

Mean central macular thickness (CMT):

The Mean CMT in our patients was 525.95 ± 102.792 µm in Group A and 569.35 ± 177.447 µm in Group B.

Mean BCVA (Log MAR):

The Mean BCVA in our patients was 0.675 ± 0.1372 in Group A and 0.765 ± 0.230 in Group B.

The Inner segment / outer segment junction status (IS/OS):

The percentage of intact IS/OS on OCT was 35% vs 65% interrupted IS/OS in Group A and was the same in Group B.

Post-operative examination:

Mean IOP (mmHg):

IOP remained unchanged as compared to preoperative mean at one, three and six months in Group A. However, IOP revealed an increase in the mean IOP at one, three and six months as compared to baseline mean.

Comparison between both study groups was statistically difference at one month (p<0.002), three months (p<0.001) and six months (p<0.000). (Table 1)

Group B showed statistically significant higher mean IOP compared to Group A at all points.

Table 1
Comparison between study groups regarding IOP over time

Study Group	Preoperative	Postoperative		
		1 month	*3 months*	*6 months*
Group A	16.5+/-2.05	16.5+/-2.05	16.5+/-2.05	16.5+/-2.05
Group B	15.20+/-2.931	20.85+/-5.133	23.70+/-8.196	23.80+/-10.943

Mean Central macular thickness:

Since the main aim of the study is to compare the effect of Ranibizumab and Triamicinolone regarding their effect on OCT parameters in Diabetic macular edema patients and its correlation to Visual acuity and since the initial effect of Ranibizumab fade at 1 months it was necessary to reinject in patients with CMT above 300 um. At one month, All Ranibizumab patients but one received another injection. At three months only five patients in Ranibizumab group need another injection. On the other hand Group B need not receive another injection during study time.

Evaluation of postoperative CMT revealed a reduction in the mean CMT at one, three and six months in both groups compared with preoperative mean CMT (mean CMT at baseline).

In Group A, a statistically significant difference was observed at One (p = 0.010), three (p< 0.001) and six months (p< 0.001) postoperatively. In Group B, a statistically significant difference was observed at one (p<0.001), three (p< 0.001) and six months (p = 0.025) postoperatively. (Figure 1)

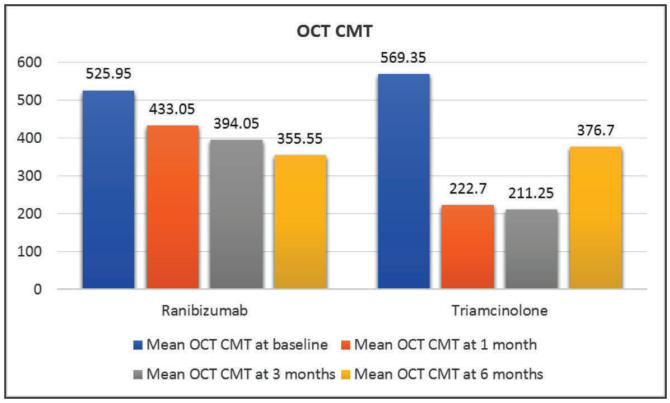

Figure 1: Mean OCT CMT in both treatment groups over time.

Comparison between the two study groups revealed statistically significant difference in mean CMT at three and six months only (p< 0.001) postoperatively. Group B showed statistically significant lower CMT compared to Group A at three and six months. (Table 2) (Figure 2).

Table 2
Comparison between study groups regarding CMT change on OCT over time

	Treatment type	N	Mean	Standard Deviation	P-value
OCT CMT at baseline	Ranibizumab	20	525.95	102.792	0.351
	Triamcinolone	20	569.35	177.447	
OCT CMT at 1 month	Ranibizumab	20	433.05	97.403	< 0.001
	Triamcinolone	20	222.70	45.978	
OCT CMT at 3months	Ranibizumab	20	394.05	90.612	< 0.001
	Triamcinolone	20	211.25	82.405	
OCT CMT at 6months	Ranibizumab	20	355.55	97.396	0.623
	Triamcinolone	20	376.70	163.825	

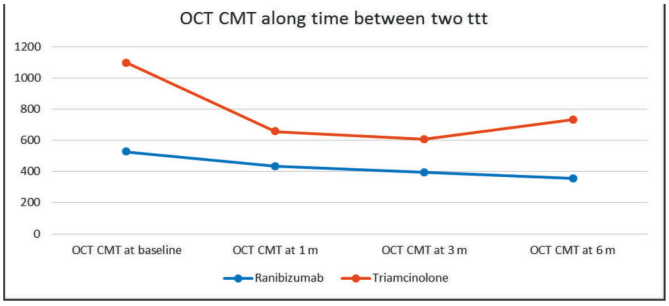

Figure 2: CMT on OCT along time in both treatment groups

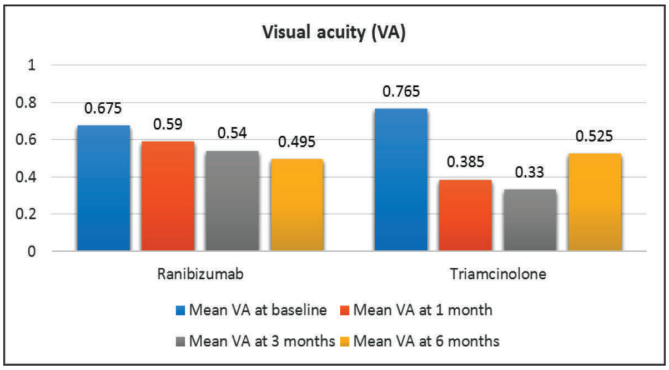

Figure 3: Mean VA in both treatment groups over time

Mean BCVA (Log MAR):

In Group A, There was a statistically significant improvement in the mean BCVA at three months (p =0.003) and six months (p =0.001). Group B showed significant improvement at one (p<0.001), three months (p<0.001) and six months (p =0.015). (Figure 3)

Comparison between the two study groups revealed statistical difference at one & three months (p < 0.001) but no significant difference at six months postoperatively. (Table 3) (Figure 4)

Table 3
Comparison between study groups regarding VA change on OCT over time

	Treatment type	N	Mean	Standard Deviation	P-value
Baseline Visual acuity	Ranibizumab	20	0.675	0.1372	0.143
	Triamcinolone	20	0.765	0.2300	
Visual acuity at 1 month	Ranibizumab	20	0.590	0.1210	< 0.001
	Triamcinolone	20	0.385	0.0813	
Visual acuity at 3 month	Ranibizumab	20	0.540	0.1353	< 0.001
	Triamcinolone	20	0.330	0.1129	
Visual acuity at 6 month	Ranibizumab	20	0.495	0.1099	0.557
	Triamcinolone	20	0.525	0.1970	

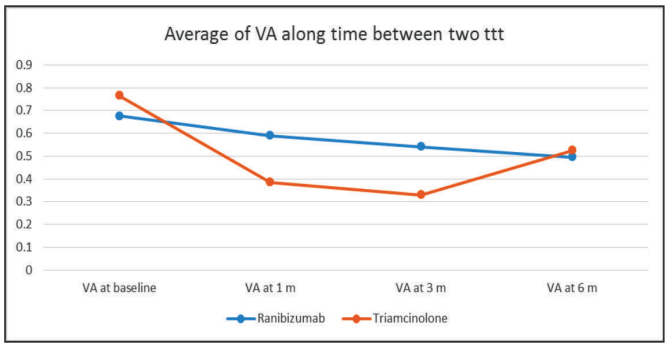

Figure 4: Log MAR VA along time in both treatment groups

Inner segment/Outer segment junction on OCT:

Within Group A the percentage of intact IS/OS was 35% and interrupted IS/OS was 65% at baseline. There was an improvement in IS/OS integrity at one month (Intact IS/OS were 70% and 30% were interrupted; but this improvement wasn't maintained at three months (Intact IS/OS were 55% and 45% were interrupted), and six month (Intact IS/OS were 80% and 20% showed interruption). The improvement at one and six months was found significant. (p =0.004)

Group B showed similar percentages at baseline. The improvement was observed in 1 month (45% Intact IS/OS vs 55% interrupted IS/OS) and 3 months (65% were intact vs 35% interrupted IS/OS); that wasn't found to be of significance, but

again this improvement began to fade at 6 months (50% were intact vs 50% interrupted IS/OS). Comparison between both groups showed no significant difference along time of the study. (Figure 5)

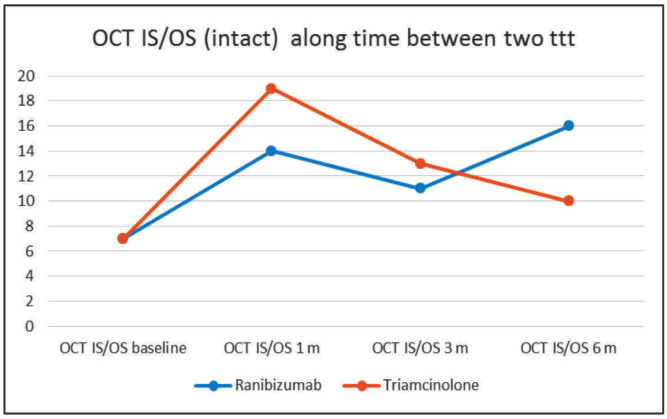

Figure 5: OCT intact IS/OS along time in both treatment groups

Correlation and association between different parameters in both treatment Groups:

In both treatment groups, there was a significant and strong correlation between VA and CMT at baseline (p<0.001) and at one (p<0.001 in Group A and p = 0.003 in Group B) (Figure 6, 7), three (p<0.001) and six months (p<0.001) of treatment.

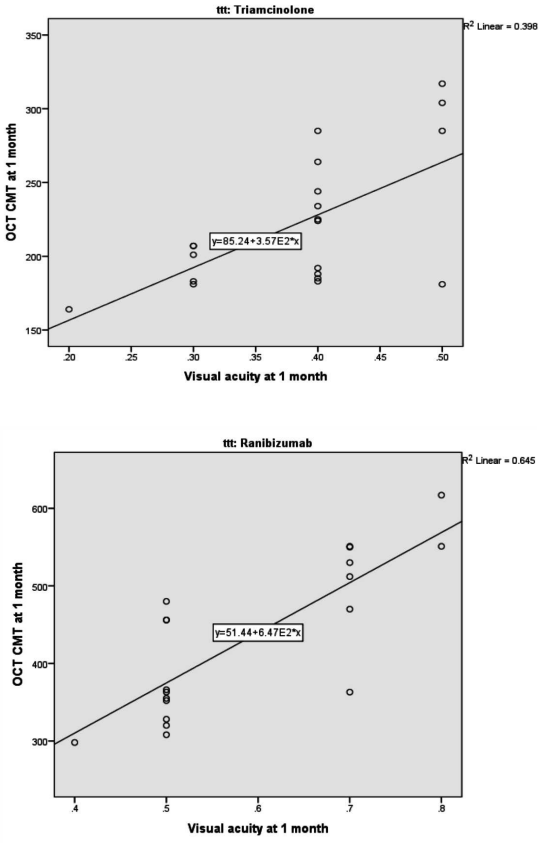

Figure 6 and 7: Correlation between CMT & VA in Group A and Group B at one month

Comparing VA to the integrity of IS/OS on OCT along time in both groups revealed significant association at three [mean BCVA was 0.473 in patients with intact IS/OS vs 0.622 in those with interrupted IS/OS in Group A; mean BCVA was 0.285 in patients with intact IS/OS vs 0.414 in those with interrupted IS/OS in Group B] (p =0.010 in Group A & p=0.045 in Group B) and six months [mean BCVA was 0.463 in patients with intact IS/OS vs 0.625 in those with interrupted IS/OS in Group A; mean BCVA was 0.440 in patients with intact IS/OS vs 0.610 in those with interrupted IS/OS in Group B] (p = 0.005 in Group A & p =0.051 in Group B). Group B also revealed significant association at baseline [mean BCVA was 0.629 in patients with intact IS/OS vs 0. 838 in those with interrupted IS/OS] (p =0.016)

Regarding CMT and IS/OS on OCT, Group B showed a significant association at baseline [mean CMT in patients with intact IS/OS was 459.71 µm while in those with interrupted IS/OS mean CMT was 628.38 µm] and six months [mean CMT in patients with intact IS/OS was 299.70 µm while in those with interrupted IS/OS mean CMT was 453.70 µm (p =0.010 & 0.031 respectively) while Group A showed significant association at three [mean CMT in patients with intact IS/OS was 334.73 µm while in those with interrupted IS/OS mean CMT was 466.56 µm] (p 0.001) and at six months [mean CMT in patients with intact IS/OS was 328.69 µm while in those with interrupted IS/OS mean CMT was 463 µm] (p =0.009).

Example to a case treated with intravitreal Triamicinolone acetonide (Group B): (Figure 8)

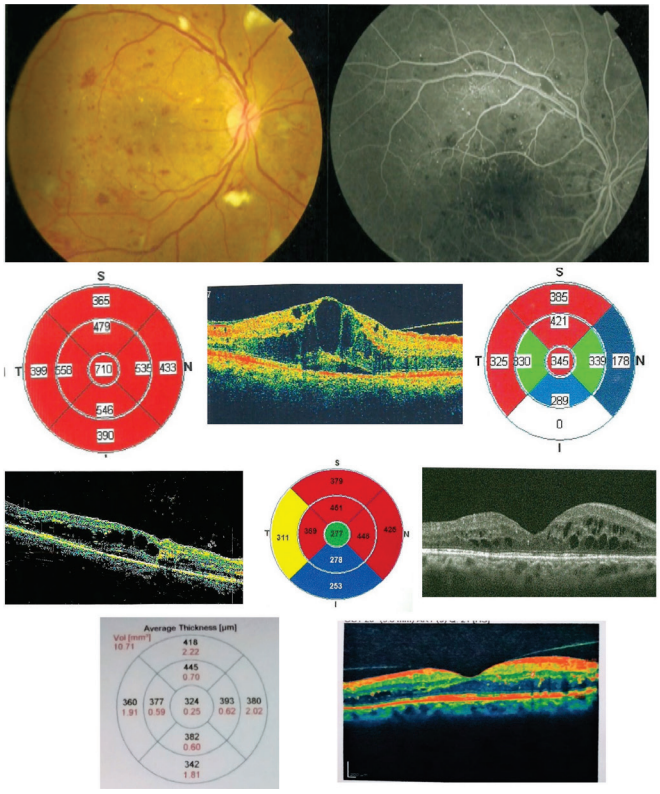

Figure 8: A case treated with triamicinolone acetonide. OCT at baseline, 1-3-6 months

Example of a case treated with intravitreal Ranibizumab (Group A): (Figure 9)

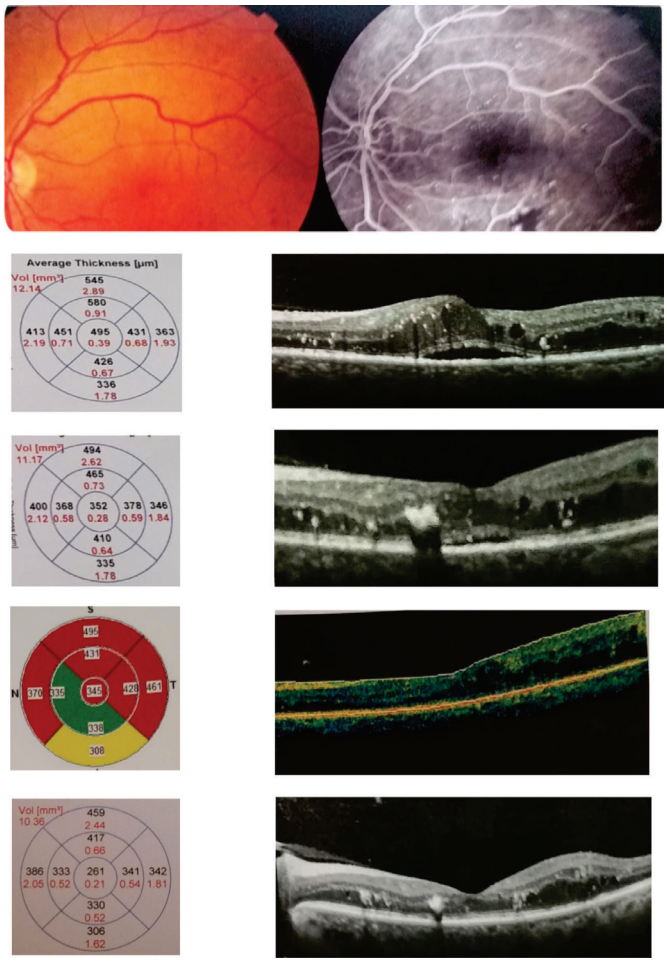

Figure 9: A case treated with Ranibizumab. OCT at baseline, 1-3-6 months

Discussion

DME is one of the main causes of visual impairment in patients with diabetic retinopathy. [20] A recent pooled analysis of 35 population-based studies in the United States, Australia, Europe, and Asia indicates that the global, age-standardized prevalence of diabetic retinopathy and diabetic macular edema (DME) in diabetic patients younger than 80 years of age is approximately 35% and 7.5%, respectively. [21] The existing burden of disease, high prevalence and incidence, life course characterized by development of chronic complications, decreased quality of life and increased cost of health care make diabetes one of the leading public health problems worldwide. [22]

Anti-VEGF drugs and corticosteroids have been proven, not only to suppress DME, but also to prevent or slow the disease progression of DR per se. [23] The fact that so many patients are proving to be resistant to treatment would suggest that different pathological mechanisms must be involved. [24] Also, Authors have found that some eyes with DME have poor visual outcomes despite complete resolution of edema. [25]

The SD OCT machines technology enhanced our ability to examine retinal microstructure and obtain more reliable measurements. [26] Several studies have found a modest correlation between OCT-measured retinal thickness and visual acuity. Central retinal thickness has a more significant effect on visual acuity than does the age, fluorescein leakage, hemoglobin A1c, perifoveal capillary blood-flow velocity, or severity of peri¬foveal capillary occlusion. [27,28] Several studies showed that many factors influence visual function in eyes with DME, including morphologic pattern of edema (cystic or diffuse retinal thickening), duration of retinal edema, retinal perfusion, total retinal volume, vitreomacular interface abnormalities [29] macular ischemia, photoreceptor dysfunction and accumulated subfoveal hard exudates. [30]

Despite the relevance, it is unknown whether the IS/OS line seen on OCT images truly corresponds to the histologic junction of the inner and outer segments. Spaide and Curcio speculated that this highly reflective band was located at the ellipsoid in the inner segments, considering the correlation between the microstructure on the SD-OCT images and the histologic findings. [31] The OCT reflectivity changed around the line after light exposure, which suggested that the line may represent photoreceptor function per se. [32,33] Many authors have found out that visual acuity has a positive correlation with the survival rate of ELM and IS/OS, [34] and that the postoperative status of the photorecep¬tors is related to the final visual function after restoration of normal retinal morphology following surgery for persistent DME [25] or epiretinal membrane. [35] Shin and associates reported that ELM disruption predicts poor visual outcomes after treatment with triamcinolone. [36]

To our knowledge, there have been limited trials that compared Triamicinolone acetonide to Ranibizumab in treatment of diabetic macular edema over short term and monitored their effects on visual acuity, CMT and IS/OS junction on SD-OCT. [37] One of the drawbacks of our study is that we could not give a percentage to the integrity of IS/OS layers in our classification, as assumed by some authors. [38] Any disruption of the inner segment/outer seg¬ment (IS/OS) line was searched for within the central 1 mm of the fovea. If the IS/OS line appeared to be complete at the fovea in all scans, we diagnosed it as an intact IS/OS. Any discontinuity or inter¬ruption of the IS/OS line in one scan or more was considered an interrupted IS/OS layer. Limitation to our study was the small sample size mainly.

The Differences between results and effect of both treatment groups may be attributed to the half-life of ranibizumab in the vitreous cavity 2.73 +/- 0.38 days [39] compared to the longer half -life of Triamicinolone, which is 18.6 days [40]

Maheshwary et al., in 2010 claimed a strong trend suggesting a relationship between macular volume and visual acuity, although borderline significance was found (P =0.07). They used macular volume instead of central retinal thickness as an indicator of edema severity. The Diabetic Retinopathy Clinical Research Network (DRCR.net) showed that total macular volume may be used when macular edema is more diffuse and represents a more global measurement of macular edema. [41] A statistically significant correlation between percentage disruption of the IS/OS junction and visual acuity was found (P =0.0312). The relationship between visual acuity and the percentage disruption held true in both treated and untreated eyes Also a relationship between macular volume and percent disruption of the IS/OS junction was found. Because IS/OS junction line integrity is an independent predictor of vision, Maheshwary and his associates recommended that clinicians may recall that for each percentage disruption, a decrease by 0.33 ETDRS letters can be anticipated. As noticed they used percent disruption as their indicator of IS/OS disease and not a simple grading of presence or absence of disruption.

Paccola et al. [42] reported that a single IVTA had more effect on reduction of CMT in patients with DME compared with one

intravitreal bevacizumab (IVB) during an eight-week period. Oh et al. [43] also reported that CMT reduction was maintained until three months after IVTA injection, while in the IVB group, CMT reduction was maintained until two months after injection.

Massin et al. [44] also demonstrated a significant reduction of CMT for at least three months. Although ranibizumab was used here instead of bevacizumab, however the results of Paccola and the other studies are in accordance with the conclusions here. Moreover the interrelationship between anti-VEGF drugs used in treatment of DME support using those studies to be compared to ours.

Similarly, according to Paccola and his associates, more favorable BCVA improvement was observed with IVTA compared with that of IVB as early as four weeks after treatment and persisting up to 12 weeks. Similarly, other reports have shown significant visual acuity improvements after IVTA. [45-47]

However this differs a little bit than the conclusions of Karst el al., specially regarding CMT. The CMT was found be thinner in the Ranibizumab treated group than the Triamicinolone treated ones at 3 months in Karst study. [37] But this can be explained by different dose and regimen used to inject Ranibizumab in their study (three monthly injections of 0.5 mg ranibizumab vs single injection of 0.3 mg ranibizumab in our study)

Sakamoto et al. in 2009 found postoperative IS/OS junction status to be related to the visual acuity after resolution of diabetic macular edema by vitrectomy. Retinal sensitivity, measured at 40 points within the central 10 degrees of the macula with the Micro Perimeter, was used by Kameda et al. to objectively assess the macular function beside analysis of best-corrected visual acuity (BCVA), central macular thickness (CMT), photoreceptor inner and outer segments (IS/OS) line. Their study found retinal sensitivity after IVTA for DME to show, albeit relatively slow, significant improvement than did BCVA or CMT. The nasal quadrant of the macula showed more improvement than did any other quadrant. In addition, cases with a discontinuous IS/OS line within 500 μm of the center of the fovea showed significantly worse BCVA and retinal sensitivity at 2 degrees. Those conclusions support the improvement of IS/OS noticed with the treatment by IVTA and the positive effect of its integrity correlated with the improvement of macular function clinically in the form of improvement of BCVA [48]

Fursova el al. investigated the morphological changes and visual acuity response to ranibizumab therapy in patients with different OCT types of diabetic macular edema (DME) as well as different state of the inner and outer photoreceptor segments (IS and OS) and the external limiting membrane (ELM); to study relationships between functional and morphological parameters before and after the treatment with ranibizumab. The most favorable type of DME in terms of preserving the integrity of photoreceptor segments and the ELM was sponge-like edema, while DME with neuroepithelial detachment and mixed-type DME were prognostically unfavorable. The last two types prevented any statistically significant improvement of the main clinical factor – VA –even after complete reduction of the edema. [49] This not only showed similar conclusions to our study but also tried to classify diabetic macular edema into categories according to the integrity of IS/OS and ELM and so their predictive clue to the final visual outcome.

Conclusion

In conclusion, our data on the overall treatment response assessed as a change in BCVA and CMT are in accordance with previous studies, which have proven the clinical efficacy of Ranibizumab and Triamcinolone for DME therapy. This study also found an association between IS/OS integrity on SD-OCT and visual acuity in both treatment types but especially in Ranibizumab group, it means that patients with DME having an intact IS/OS junction would have a better visual outcome and this may be used as a predictive factor for evaluating these cases. So, CMT and integrity of the photoreceptor IS/OS layer are significant predictors of VA in patients with DM, which may help to predict the outcome after treatment and to choose the best treatment modality. Further studies have to be held comparing Ranibizumab and Triamicinolone acetonide regarding their effect on different OCT parameters and their reflectance over the improvement of macular function in patients of DME in both short term and long term situations.

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