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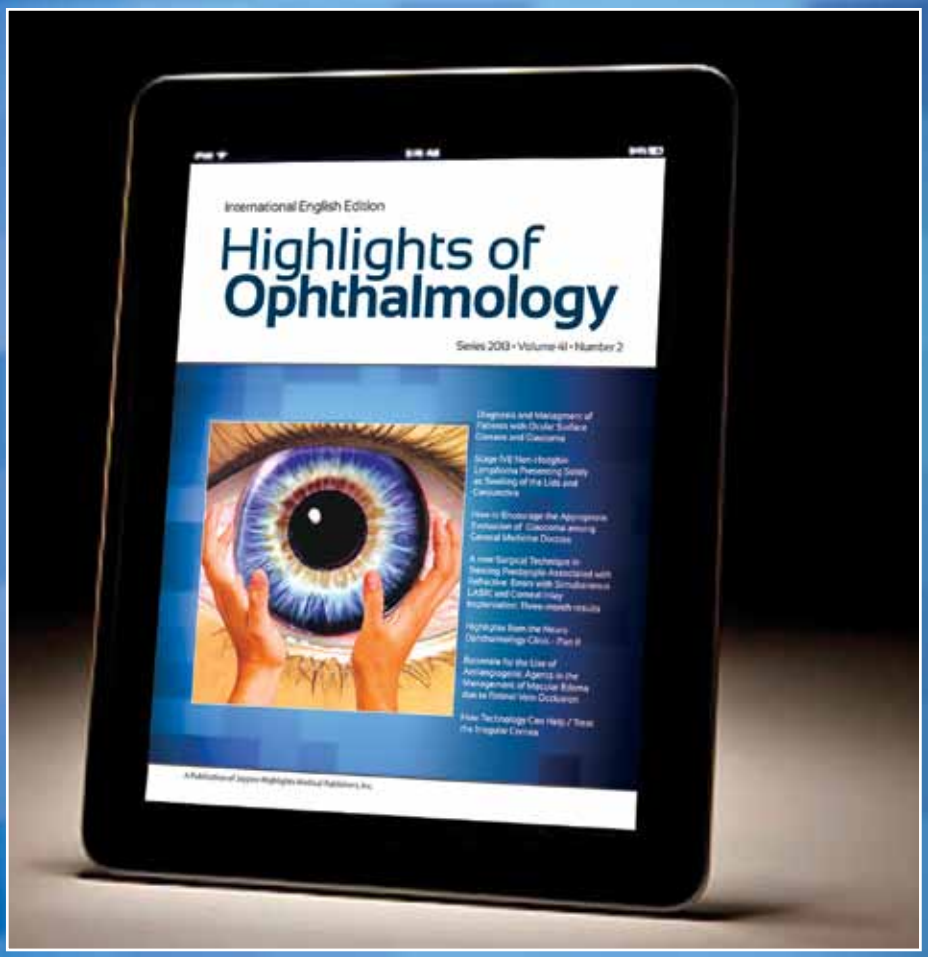

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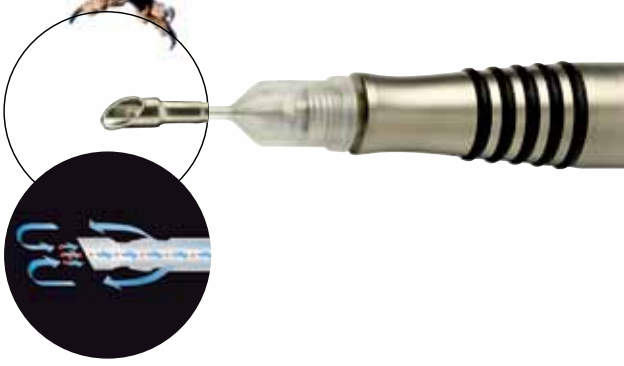

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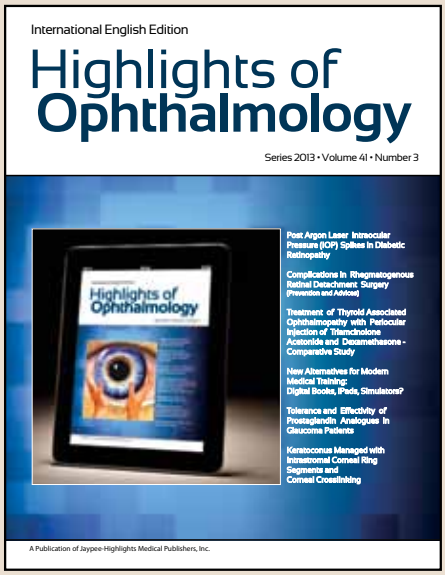

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Post Argon Laser Intraocular Pressure (IOP) Spikes in Diabetic Retinopathy

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Abstract

Purpose
To study the variation in IOP following argon laser photocoagulation in the treatment of diabetic retinopathy.

Material and Methods

Forty patients with proliferative and non-proliferative diabetic retinopathy requiring laser treatment were included in the study. These also included patients with coexisting glaucoma. All patients underwent argon laser photocoagulation. IOP was taken pre-treatment, post treatment at hourly interval for 2 hours on the day of treatment, on 1st and 2nd post treatment day and then on monthly intervals for three months. The data was analyzed using SPSS software version 16.

Conclusion
There was a significant rise ($p<0.005$) in IOP after 1-2 hours which lasted for 2-3 days after Argon laser photocoagulation.

Keywords: Intraocular pressure, laser photocoagulation, diabetic retinopathy.

Introduction
Diabetic retinopathy is the leading cause of blindness in industrialized countries. A vast majority of diabetic individuals lose their vision just due to delay in seeking medical attention. Successful management of diabetic retinopathy includes a combination of blood sugar control, laser therapy and vitrectomy. According to the indications of, Early treatment retinopathy study (ETDRS), the risks of severe visual loss are less than 5%, if the patient gets appropriate laser treatment .[1]

The goal of Pan Retinal Photocoagulation (PRP) is to arrest or to cause regression of neovascularization, by converting hypoxic areas into anoxic areas.[2] Laser therapy can evoke certain complications which includes decreased visual acuity due to increasing macular edema or causing macular pucker,[3, 4] transient increase in intraocular pressure (IOP) and worsening of colour vision and dark adaptation which are already impaired.[5] It is often found that there is a transient intraocular pressure (IOP) rise following PRP, the exact cause of which is unknown. This might be due to swelling of ciliary body or outpouring of fluid from choroid to vitreous with subsequent forward displacement of iris- lens diaphragm. [6-11] Few studies have been done regarding this subject, the studies available are on few patients with short study duration, and hence this study was undertaken.

Purpose
To study the variation in IOP following argon laser photocoagulation in the treatment of diabetic retinopathy.

Material and Methods
Forty patients with proliferative and non-proliferative diabetic retinopathy requiring laser treatment were included in the study, these also included patients with coexisting glaucoma. Patients with ischemic diabetic retinopathy, with other systemic and endocrine disorders, and myopics were excluded from the study.

The patients gave a detailed history, including type of diabetes mellitus. History of coexistent neuropathy, nephropathy and medication was recorded. These patients underwent uncorrected and best corrected visual acuity evaluation, slit lamp examination, Goldman applanation tonometery, direct and indirect ophthalmoscopy, slit lamp biomicroscopy with a 90 dioptre lens, gonioscopy, fundus fluorescein angiography and perimetry.

Patients ranged from 30-70 years, all had type 2 diabetes mellitus, were on full anti diabetic treatment. They were investigated for fasting and post prandial blood sugar levels. All patients underwent argon laser photocoagulation and IOP was taken pre-treatment, post treatment hourly interval for 2 hours on the day of treatment, on 1st and 2nd post treatment day and then on monthly intervals for three months.

Results (Tables 1 and 2)
34 patients were male and 6 were female out of which 32 (80%) were below 50 years of age and the rest were above 50 years.

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TABLE 1		
Age group (years)	**No. of Cases**	**Percentage**
<50	32	80.0
>50	8	20.0
Total	40	100%
Sex	No. of Cases	Percentage
Male	34	85.0
Female	6	15.0
Total	40	100%

History	No. of Cases	Percentage
Type II DM	32	80.0
Type II DM+ Associated hypertension	4	10.0
Type II DM+ Associated nephropathy	2	5.0
Type II DM + Associated neuropathy	2	5.0
Total	40	100

Pre-Laser angiography	No. of Cases	Percentage
BDR with maculopathy	2	5.0
PPDR	10	25.0
PDR	28	70.0
NPDR	-	-
Total	40	100

Pre-Laser angle	No. of Cases	Percentage
Open	36	90.0
Closed	4	10.0
Total	40	100

Here 36 had open angle and 4 had angle closure due to angle neovascularisation.

TABLE 2: INTRAOCULAR PRESSURE (IOP) RANGES IN THE VARIOUS LASER PROCEDURES

Time interval	IOP Range in mmHg	Laser		χ^2	p-value
		Grid (n=14)	PRP (n=26)		
0 hr	≤10	-	-	1.134	0.287
	11-21	14 (100%)	24 (92.3%)		
	>21	0	2 (7.7%)		
Immediate Post Laser	≤10	0	7 (26.9%)	8.725	0.013*
	11-21	13 (92.9%)	12 (46.2%)		
	>21	1 (7.1%)	7 (26.9%)		
1 hour Post Laser	≤10	0	7 (26.9%)	12.627	0.002*
	11-21	13 (92.9%)	9 (34.6%)		
	>21	1 (7.1%)	10 (38.5%)		
2 hour Post Laser	≤10	0	7 (26.9%)	12.627	0.002*
	11-21	13 (92.9%)	9 (34.6%)		
	>21	1 (7.1%)	10 (38.5%)		
3 hour Post Laser	≤10	0	7 (26.9%)	12.627	0.002*
	11-21	13 (92.9%)	9 (34.6%)		
	>21	1 (7.1%)	10 (38.5%)		
1 day Post Laser	≤10	0	3 (11.5%)	4.412	0.110
	11-21	11 (78.6%)	12 (46.2%)		
	>21	3 (21.4%)	11 (42.3%)		
2 day Post Laser	≤10	0	3 (11.5%)	4.412	0.110
	11-21	11 (78.6%)	12 (46.2%)		
	>21	3 (21.4%)	11 (42.3%)		
3 day Post Laser	≤10	0	3 (11.5%)	3.033	0.219
	11-21	11 (78.6%)	14 (53.8%)		
	>21	3 (21.4%)	9 (34.6%)		
1 month Post Laser	≤10	0	0	1.746	0.186
	11-21	14 (100%)	23 (88.5%)		
	>21	0	3 (11.5%)		
2 month Post Laser	≤10	0	0	1.746	0.186
	11-21	14 (100%)	23 (88.5%)		
	>21	0	3 (11.5%)		
3 month Post Laser	≤10	0	0	0.552	0.457
	11-21	14 (100%)	25 (96.2%)		
	>21	0	1 (2.8%)		

*p<0.05

IOP rise is seen after argon laser photocoagulation and statistically significant p value was noted immediately (p=0.013), 1hour later (p=0.002), 2 hours later (0.002) and 3 hours later (p=0.002).

Discussion

In our study we have found that transient IOP rise occurs following retinal green laser photocoagulation except in few cases where IOP fall was noted. In some cases, after laser photocoagulation anterior chamber angle was closed, this remained so for about 2-3 days. The results are quite similar to results shown by Blondeau et al in 1981. Here is a comparison between three relevant studies: **(Table 3).** From the above comparison between Blondeau and our study, it is seen that a number of patients

TABLE 3

Variables	Mensher et al (1977)	Blondeau et al (1981)	Our Study (2010)
Number of patients	30	18	40
Before laser	30 patients with open angle and normal IOP	18 patients with open angle and normal IOP	36 patients with normal IOP and open angle. 4 patients with closed angle and high IOP
Immediately after laser		14 patients with open angle and high IOP 1 patient with open angle and normal IOP 3 patients with closed angle and high IOP	6 patients with open angle and high IOP 24 patients with open angle and normal IOP 6 patients with closed angle and high IOP 4 patients with open angle and IOP fall
Hours later	10 patients developed angle closure and 20 patients developed narrow angle IOP in closed angle group: 10-27 mmHg and in narrow angle group: 20-29 mmHg	Among 14 patients of open angle with high IOP, 5 developed angle closure	Among 6 patients of open angle with high IOP, 1 patient developed angle closure
p-value of IOP		Immediate = <0.005 1 hour later = <0.005 2 hours later = <0.005 3 hours later = <0.01	Immediate = 0.013 1 hours later = 0.002 2 hours later = 0.002 3 hours later = 0.002

were higher in our study and also 4 patients with angle neovascularization were included in our study. Immediately after laser, 24 patients with open angle and normal IOP were found in our study in contrast to 1 patient in Blondeau study. Moreover, 4 patients with open angle and IOP fall were also noted in our study. Hours after laser photocoagulation only 1 patient developed angle closure in our study in contrast to 5 patients in Blondeau study. P-value in our study is also significant up to 3 hours after laser photocoagulation but it was significant only up to 2 hours after photocoagulation in Blondeau study. In the Mensher study 30 patients were included in which, 10 developed angle closure and 20 developed narrow angle hours after laser photocoagulation.

We suggest the most probable reason of angle closure following PRP to be a rise in vitreous volume and pushing of lens iris diaphragm anteriorly, the reason for high IOP in open angle glaucoma could be due to post laser inflammation of angle structures.

Conclusion

We can conclude that after extensive laser photocoagulation in diabetic retinopathy patients, elevation in IOP may appear immediately for 1-2 hours or 1-2 days later and this lasts for 2-3 days. Angle closure may be a possibility and may add to outflow obstruction.

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Complications in Rhegmatogenous **Retinal Detachment Surgery** (Prevention and Advices)

Elena Rodriguez Neila, MD [1,2]
J. Carlos Pastor-Jimeno MD, PhD[2,3]

Introduction

Rhegmatogenous retinal detachment (RD) is a serious ocular disorder that may result in severe visual loss. Its prevalence among general population is around 1 new case per 8.500 eyes per year. Cataract surgery is the most important risk factor, and after intraocular lens (IOL) implantation its frequency multiplies by 10.[1] Also myopia is an important risk factor and some series have shown that 20% of highly myopic young patients develop RD in 10 years after cataract surgery.[2]

Anatomical success is now achieved in more than 90% of non-complicated cases of RD by surgery.[3] There are basically three procedures: pars plana vitrectomy (PPV), scleral buckle techniques (SB) and pneumatic retinopexy.[4]

The latter is only indicated for selected cases.[5] Phakic patients, with single peripheral superior breaks, localized RD (less than 4, 5 clock hours), no vitreous hemorrhage and others. In these selected cases anatomical outcomes are similar to other techniques, but complications include: cataract development, new breaks generation and failures derived from the incorrect selection of candidates.[6] Therefore this technique has not been generalized in Europe although it is popular in USA.

Among the two other techniques, PPV and SB, and despite that both showed similar results either anatomical or functional[7-9] the current situation is that most of the surgeons are increasing the indication of PPV which is now offered as primary option in the 80% of RD.[10] In pseudophakic RDs [3, 11] is preferred over SB. In some cases both techniques are associated. Surgeons prefer this association in younger patients, those with posterior or unidentified breaks, phakic eyes, eyes with posterior vitreous detachment and extensive RDs.[12]

Also, it is important to emphasize the current increase in the so named sutureless or microincision vitrectomy for the treatment of RD. These techniques (23 G and 25 G) have become popular among the vitreoretinal surgeons for reasons such as reduced surgical trauma, improved patient comfort after surgery, faster postoperative healing, faster visual recovery, shorter operating times, and reduced postoperative astigmatism when compared to traditional sutured procedures.[13, 14]

The following paragraphs on complications of RD surgery do not try to be an exhaustive list but only to point out the commonest complications and to provide some advices to avoid them, based on the authors' experience.

Intraoperative Complications

SB techniques are associated to several complications: inadverted perforation, complications derived of the sub-retinal fluid drainage, excessive compression of the band, incorrect positioning of the buckle, excessive retinopexy by cryo, and others. Some of them can be minimized by using the surgical microscope [15] such as the inadverted perforation which is commonest in myopic eye with a thinner sclera, and when sutures are located behind the extraocular muscles or in staphilomatous eyes. This complication arises up to 5% of SB procedures and can be minimized by using adequate sutures and performing them under the microscope. The most potentially serious complications are derived from the drainage of subretinal fluid. Complications include intraocular hemorrhage, retinal incarceration, retinal breaks, and others. They can be present up to 8% of the drainages and can be minimized by an adequate technique or avoiding drainage.

Choroidal hemorrhage is one of the most feared complications when transscleral draining of subretinal fluid is performed. If dark red bleeding appears, it is urgent to close sclerotomies as soon as possible and try to increase intraocular pressure above systolic pressure. The pressure on the area of the sclerotomy also tends to diminish the bleeding. It is advisable to place the eye so that no breakthrough bleeding toward the fovea occurs. For that reason are preferable nasal sclerotomies to perform the drainage. If choroid bleeding is massive, deferred vitrectomy is recommended.

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After 10 to 15 days, once it is found clot liquefaction by ocular ecography, transscleral draining can be performed associated to vitrectomy. In some cases, silicone oil can be used as a temporary tamponade. Pompt surgery is recommended if retinal detachment or kissing choroidal detachment is present **(Figure 1).**

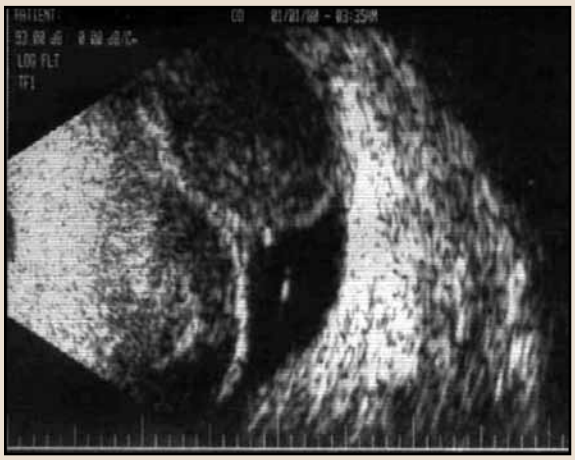

Figure 1: Ocular ecography showing the so named "kissing" hemorragic cahoroidal detachment.

Retinal incarceration is the major complication after drainage.Typically occurs by pressure fluctuations during drainage of subretinal fluid **(Figure 2)**. In these cases the scleral procedure should be repositioned to cover incarceration, if possible, but a vitrectomy can be considered because of the high risk of developing a postoperative proliferative vitreoretinopathy (PVR). Keep in mind that this maneuver (drainage) is not mandatory in all cases. It is highly recommended in aged patients, with chronic or extended RD. But in young patients with localized RD can be avoided. Healthy retinal pigment epithelium (RPE) is able to absorb subretinal fluid if favorable conditions are created by surgery.[16]

Excessive constriction of the encircling procedures is also a non-rare complication. It is a source of serious problems such as choroidal effusions, radial folds of the retina, distortion of the retinal tear causing a fish-mouth phenomenon preventing its posterior closure, and above all, anterior segment ischemia. With a non-elastic material, in a normal size eye-ball, a shortening of 12 mm of the band induces an indentation of 1 mm. This "shortening" can be taken as a reference but it must be "customized" for each patient. Anyway it is important to visualize the optic nerve head at the end of the procedure and to release the band in case of doubt. Induced myopia and some other refractive errors are consequences of SB and must be discussed with the patient. SB induces a myopic shift of around 2.75 diopters.[17] Also diplopia is reported in 5% of SB.

Vitrectomy has become popular during the last 15 years, without a clear or significant advantage over the SB technique. Vitrectomy is associated to some specific complications such as endophthalmitis, elevated intraocular pressure, cataract development, retinal dialysis, and many others related to the maneuvers carried out during its performance (trauma to the lens, direct retinal injury, etc). Endophthalmitis is a rare event after PPV but it has been associated to the new sutureless techniques with 23G or 25G instruments, especially in cases of postoperative hypotony. A controversy exists on its real incidence and some modifications such as the tunnel incisions have been proposed to reduce its prevalence, although meta-analysis does not show a clear evidence of this higher frequency of endophthalmitis.[18] Sutureless vitrectomy–related hypotony is usually described as transient. It is important to emphasize the low tolerance for leakage, suturing any visible leakage at the end of the procedure.

Cataracts are very common after PPV. Its further development is clearly associated to the age of the patient and to the duration of the surgery. Thus many surgeons are offering the patient a combined surgery (phaco-vitrectomy) especially in elderly patients.[19]

During the performance of a PPV many complications could be frequent and surgeons should learn how to avoid and to manage them. Subchoroidal or subretinal infusion could be a serious problem. To avoid this complication

Figure 2: Retinal incarceration after scleral drainage causing a severe tractional retinal detachment. Anatomical and visual prognosis in those cases is very poor.

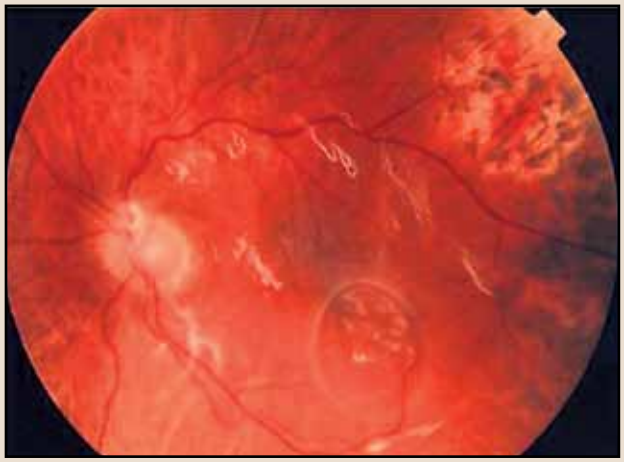

Figure 3: Posterior pole of a reattached retinal detachment showing a subretinal bubble of perfluorocarbon liquid inferior to the macula. Eye is fill with silicone-oil.

it is advisable to use long cannulas (4-6 mm) and always check the cannula position before opening the infusion line. This complication is more common in cases of hypotonia, trauma, proliferative vitreoretinopathy (PVR), and its frequency is declining since the 23G and 25G introduction. However, the very oblique placement of small size microcannulas, in order to reduce the risk of loss of the sclerotomy may increase the possibility of suprachoroidal or subretinal infusion placement.[20]

Another frequent problem is the appearance of corneal edema usually produced by changes in intraocular pressure or by mechanical trauma during intervention. This complication is possible in both techniques SB and PPV. The use of non-contact visualization systems, the adequate protection of the ocular surface by viscous material and short duration of surgery prevents it in many cases. If cloudiness of the cornea interferes with the surgical technique, epithelium can be removed by mechanical debridement. But this maneuver should be practiced only as last option, since reepithelialization in postoperative is usually troublesome, especially in diabetic patients, and because of the topical corticosteroids prescribed during the postoperative period. In these cases the use of artificial tears must be evaluated. Delayed epithelization is source of many problems including acute infections and also herpetic reactivation has been reported in prompt postoperative period.[21]

Miosis, secondary to hypotonia or surgical trauma is also a frequent problem. It can be reversed by mydriatics as adrenaline that can be administered directly into the anterior chamber or in the serum injected into the infusion. Some authors have advocated the preoperative use of topical non-steroidal anti-inflammatory drugs (NSAIDs) to minimize intraoperative myosis, but this practice has not been generalized.[22] In pseudophakic and aphakic eyes iris hooks can be used when necessary. [23]

There are also some other causes of poor visualization during PPV. Lens opacification is not rare and diabetes has a clear influence.[24] The use of osmotic substances has been advocated but none has been adopted in routine clinic.[25] Also during the air-fluid exchanges, intraocular lens could be a problem if fine drops accumulate on its posterior surface. The effect can be minimized by covering that surface with a viscoelastic.

The use of perfluorocarbon liquids (PFCL) is also a potential source of intraoperative problems. Fish egging phenomenon is very common and may result in the passage of PFCL into the subretinal space. This could be avoided by injecting the PFCL slowly inside of the initial bubble. It is essential also to achieve total relaxation of the traction on the retina so that PFCL does not move towards the subretinal space, which is frequent in those patients with a clear shortening of the retina, caused by intra-retinal PVR.[26,27] If PFCL gets into the subretinal space, more PFCL can be slowly inyected to displace up the subretinal bubble and aspirate it through an existing tear[28] or creating a retinotomy **(Figure 3)**.

Iatrogenic retinal break is the most frequent intraoperative complication of vitrectomy. Its incidence could be estimated at around 6%. To avoid this risk is needed to adjust parameters as cutting and aspiration rates when the vitrectomy cutter is near the retina.[29] The new small gauge vitrectomy devices with extra small cutter, very close to the tip, and the high speed cutting rate, allow more security when the surgeon gets near the retina. The use of PFCL in the posterior pole stabilizes retina and decreases the risk for the dissection of the vitreous base.

Incomplete posterior hyaloid dissection is especially frequent in young patients and after ocular trauma. To improve its visualization intraocular triamcinolone acetonide can be used.

Retinal displacement, also named slippage can occur after reapplication, in giant tears and in bullous superior RD. Meticulous removal of all aqueous from the subretinal space can eliminate this complication. Some "tricks" have been published to avoid this serious complication.[30]

Postoperative intraocular pressure (IOP) spike after RD surgery is relatively frequent.[31] There are several causes for IOP increase including gas tamponade, excessive constriction of the band, post-operative intraocular hemorrhage, excessive postoperative intraocular inflammatory reaction and the

topical use of corticosteroids. In our experience the most serious peaks are related to intraocular gas expansion. They could produce acute elevations of IOP and are related to many cases of low visual function after successful anatomical reapplication because of optic nerve atrophy. Correct dilution of gases is mandatory to prevent this complication. Prophylactic topical and systemic therapy is advisable.

Proliferative vitreoretinopathy (PVR) continues to be the main cause of failure of RD surgery, occurring in 5% to 10% of patients with RD.[32, 33] Most research has attempted to identify clinical risk factors for developing PVR; however, these variables do not completely explain the probability of its onset.[34] Also several efforts have been made to get an adequate prophylaxis but until now no effective treatment has been incorporated to the clinic. Recently the potential contribution of a genetic component to PVR has been described, suggesting that PVR is a complex disease resulting from the interaction between genetics and environmental factors.[35-37]

Even after the successful retinal reattachment, the postoperative visual function measured by best-corrected visual acuity, contrast sensitivity and low-contrast visual acuity, may be unsatisfactory in some cases. According to our data, 42% of patients with successful surgery obtain a visual acuity of 20/40 after 3 months of follow up, 37% between 20/40 and 20/100 and 20% below 20/100. Visual recovery after retinal reattachment is most dependent on macular involvement but in more than 15% of patients that have never had the macula involved lose visual acuity (personal non-published data). The mean best-corrected visual acuity is usually significantly lower if external retina lines show disruption on optical coherence tomography foveal findings at 6 months after surgery.[38-40] Nowadays, one of the challenges in RD treatment is how to preserve visual acuity by using different drugs which are under investigation. Thus, next generation of retinologists will get the goal of restoring the anatomy and above all the function of the detached retina.

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Treatment of Thyroid Associated Ophthalmopathy with Periocular Injection of **Triamcinolone Acetonide and Dexamethasone** – *Comparative Study*

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General Considerations

There is no gold standard treatment of thyroid associated ophthalmopathy (TAO) in the inflammatory stages of the disease. Corticosteroids reduce the transitory manifestation of TAO but their multiple side effects make the risk/benefit relation unsatisfactory.[1,2,3,5,6] The beneficial effects of steroids used locally (subconjunctival or retrobulbar injections) in the treatment of TAO have been reported in the literature. [7, 8, 9,16,17,18] In our study, we selected those cases in whom optic nerve was also involved as in previous studies, where some unfavourable results were found.[4]

Materials and Methods

A prospective randomized study was performed in a rural hospital on thirty patients diagnosed recently or less than six months, with TAO with mild proptosis and decreased vision with optic disc edema of 1-2 D, with partial restriction of ocular movements, with diplopia in extreme position of gaze. They were divided in two groups and compared at the end of six months after receiving treatment. Patients were randomized simply. In group A- fifteen patients (30 eyes) received periocular injection of triamcinolone acetonide 20 mg in each orbit every week for four weeks.

In group B- 30 eyes of fifteen patients received periocular injection of dexamethasone 8 mg in each orbit every week for four weeks.

All patients had undergone computed tomography **(Tables 2 and 3)** before **(Figures 1- 5)** and after receiving injections to know the size of extraocular muscles. Diameter perpendicular to the long axis of the muscle at the largest extent of the muscle belly (maximal diameter, Dmax) **(Figures 1 and 2)** was measured in coronal section for all muscles.

Ophthalmological and systemic examinations were done in all patients. Every patient received four doses of 20 mg triamcinolone 40mg /ml in periocular region to the inferolateral region in four consecutive weeks in group A and in group B. All 30 eyes of 15 patients received four doses of 8 mg dexamethasone in periocular region to the inferolateral region in four consecutive weeks. Follow up was kept for six months in all patients.

Exclusion Criteria

Previous treatment for TAO with steroids or radiations, contraindications to steroids like DM, hypertension, peptic ulcer, pregnancy and psychosis. Patients included in the study were regardless their endocrine status.

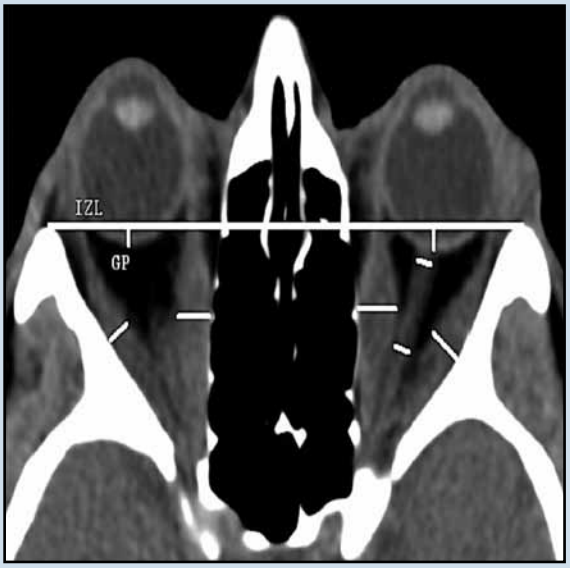

Figure 1: Axial CT scan at mid globe demonstrates length of the interzygomatic line (IZL), the distance between the interzygomatic line and the posterior margin of the globe (GP), width of the optic nerve-sheath complex (retrobulbar and waist diameter), and muscle diameter measurement for the medial rectus and lateral rectus.

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Figure 2: Coronal CT reconstruction of the orbit demonstrates measurement of the extraocular muscle.

Examination of Patients

Every week for four weeks patients were examined for best corrected visual acuity (BCVA) on Snellen's chart, intraocular pressure (IOP) in mm of Hg with applanation tonometry, exophthalmometry (Ex), optic nerve head examination (ON) graded as normal, disc edema or optic atrophy. Systemic systolic and diastolic arterial blood pressure was measured in each case. Ocular motility observed after a week, a month, after 3 months, and 6 months of last injection received. Patients undergone treatments were then compared within the groups at the end of six months.

Results were compared for both groups using Student's t test (paired and unpaired) and Chi-square test. Blood tests were defined as normal or abnormal, calculating the median for each value. Additional statistical analysis was performed (Dunnet T test, test of comparison of treatment versus control and analysis of log normal distribution).

Result

Total sixty eyes of thirty patients fourteen males/sixteen females. Age: 30-70 Average age: 45.7 years.

There was marked increase in vision from 1-3 lines of Snellen's chart. There was no change in SBP/DBP **(Table 1)**.

Visual acuity was taken after 1 month, 3 months, and 6 months.

Optic Nerve Heads

In all thirty cases optic nerve were appearing normal in colour with edema 1-2 disc dioptre (DD). After 24 weeks all optic nerve heads were appearing normal.

Mean (SD) initial sizes of muscles were SR -4.82 (0.5), IR-6.68 (0.75), MR-4.57 (0.46), LR-4.33 (0.48) in Group - A **(Table 2) (Figures 3, 4, 5)**.

We had taken follow up CT scan 24 weeks after treatment. Mean (SD) values of muscle sizes were given in **Table 2** and **Table 3** before and after the treatment. Study showed improvement in motility, reduction in the sizes of EOM, increase in vision and decrease in exophthalmos and absence of diplopia in extreme gazes in both groups.

Measurements of EOM showed the following differences after six months **(Table 2)**. For superior rectus muscles in Group-A percentage change mean (SD) was 22.31 (7.33) ($p<0.05$) and

Table 1: Visual Acuity in Both Groups .

BEFORE TREATMENT				AFTER TREAMENT (after 24wks.)			
GROUP A (n=30)		GROUP B (n=30)		GROUP A(n=30)		GROUP B(n=30)	
Visual acuity	No. of eyes(%)	Visual acuity	No. of eyes (%)	Visual acuity	No. of eyes (%)	Visual acuity	No. of eyes (%)
6/36	Nil	6/36	1 (3.3%)	6/36	Nil	6/36	Nil
6/24	1 (3.3%)	6/24	1 (3.3%)	6/24	Nil	6/24	Nil
6/18	6(20%)	6/18	7(23.3%)	6/18	Nil	6/18	Nil
6/12	15(50%)	6/12	13(43.3%)	6/12	Nil	6/12	2(6.6%)
6/9	3(10%)	6/9	2(6.6%)	6/9	10(33.3%)	6/9	8(26.6%)
6/6	5(16.5%)	6/6	6(20%)	6/6	20 (66.6%)	6/6	20(66.6%)

No statistically significant difference in visual acuity found in both groups.

Table 2: Muscle Parameters (Dmax) in Graves' Ophthalmopathy (n =30) and After Treatment in group A .

Muscle	Initial Value mean(SD) in mm	Changed Value mean(SD) in mm	Difference	Mean % change insize (SD) after 6 months	t-value	p-value<0.05
Superior rectus	4.82(0.5)	3.72(0.28)	1.10(0.51)	22.31(7.33)	6.79	0.0005
Inferior rectus	6.68 (0.75)	5.22(0.29)	1.46(0.59)	15.18(4.38)	7.71	0.0005
Medial rectus	4.57(0.46)	3.36(0.22)	0.71(0.27)	21.28(6.43)	8.11	0.0005
Lateral rectus	4.33(0.48)	3.58(0.37)	0.75(0.57)	16.41(13.21)	4.13	0.003

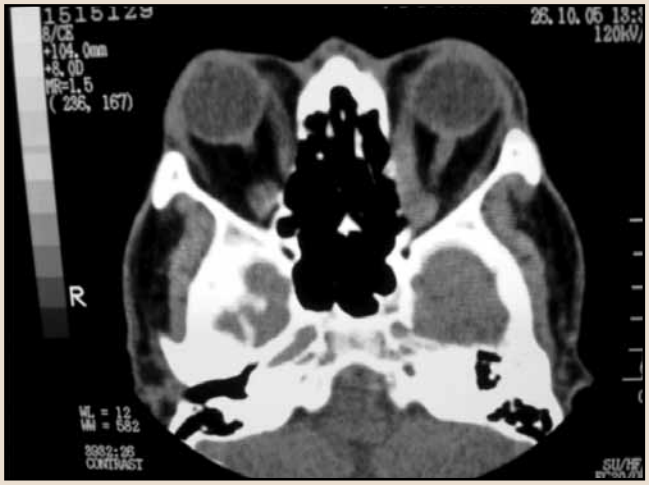

Figure 3: Transverse section on CT showing bilateral enlargement of EOM.

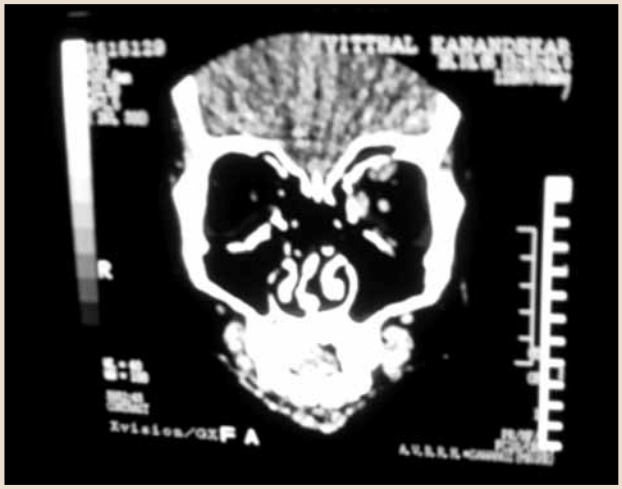

Figure 4: Coronal section showing muscles enlargement LE more than RE.

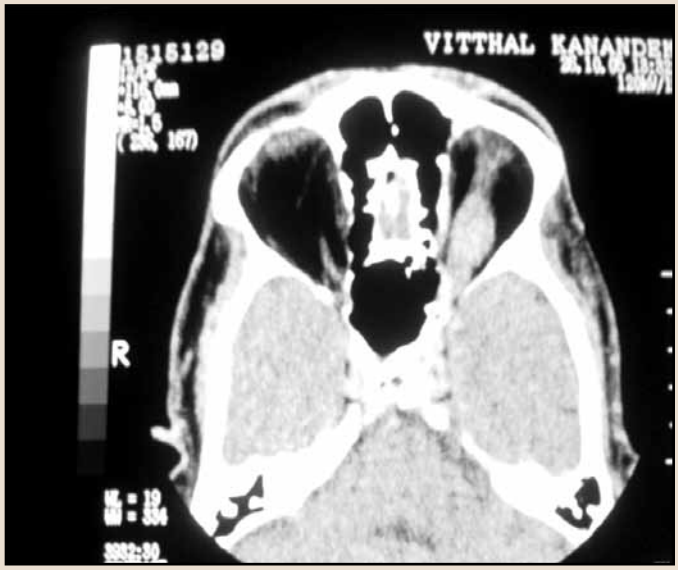

Figure 5: Transverse section showing enlarged muscles in LE.

Table 3: Muscle Parameters (Dmax) in Graves' Ophthalmopathy (n =30) and after Treatment in Group-B.

Muscle	Initial Value mean (SD) in mm	Changed Value mean (SD) in mm	Difference	Mean % change in size (SD) after 6 months	t-value	p-value <0.05
Superior rectus	4.85(0.5)	3.8(0.3)	1.0(0.51)	20.83(7.33)	6.47	0.0005
Inferior rectus	7.00 (0.7)	5.22(0.29)	1.8(0.6)	25.71(4.38)	7.71	0.0005
Medial rectus	4.6(0.5)	3.36(0.22)	1.3(0.27)	28.26(6.43)	8.53	0.0005
Lateral rectus	4.43(0.5)	3.58(0.37)	0.9.(0.57)	20.45(13.21)	4.42	0.0035

compared to Group B percentage change mean (SD) was 20.83 (7.33) ($p<0.05$). No statistically significant differences were detected between the two groups.

For inferior rectus muscles in the Group A percentage change mean (SD) was 21.28 (6.43) ($p<0.05$) and Group B percentage change mean (SD) was 25.71 (4.38) ($p<0.05$). No statistically significant differences were detected between the two groups.

For medial rectus muscles in Group A percentage change mean (SD) was 15.18 (4.38) ($p<0.05$) and in Group B percentage change mean (SD) was 28.26 (6.43) ($p<0.05$). No statistically significant differences were detected between the two groups.

For lateral rectus muscles in Group A percentage change mean (SD) was 16.41(13.21) ($p<0.05$) and in Group B percentage change mean (SD) was 20.45 (13.21) ($p<0.05$). No statistically significant differences were detected between the two groups.

In summary, there were no statistically significant differences between the two groups, there were decreases in muscles sizes significantly after treatment and there were no changes in IOP levels, systolic and diastolic blood pressure after treatment in both groups **(Table 4)**.

There were no variations in blood levels of calcaemia, glycaemia, and cortisol in both groups **(Table 5)**.

Discussion

Clinical manifestations of TAO reflect the enhanced orbital volume, due to an increase in retroocular fibroadipose tissue and swelling of extraocular muscles. Orbital tissues, including muscles, are infiltrated by inflammatory cells, including lymphocytes, mast cells, and macrophages. Proliferation of orbital fibroblasts and adipocytes, both in the retroocular space and in the perimysial space, is also associated with an increased production of glycosaminoglycans, which are the ultimate responsible for edematous changes both in the connective tissue and the muscles. Compressive optic neuropathy develops as there is swelling of EOM in TAO. As there is little space at the apex of the orbit, enlargement of the extra ocular muscles exerts pressure on optic nerve lying in the centre of the muscles. Pressure decreases vision because the function of the optic nerve is affected.[27,29] The judgment of therapeutic efficacy in Graves' ophthalmopathy rests to a large extent on improvement in the patients' clinical status.

Unfortunately, clinical activity scores based on symptoms fail to consistently provide reliable follow-up data for therapy monitoring, and their use is limited. Decreasing edema and volume of the orbital components is a more reliable sign of successful therapy.

Until the development of a simple, accurate method for automated volume measurement, clinicians need a parameter that can be measured quickly and that reflects changes in muscle volume. The usual approach to the enlarged eye CT is that the examiner evaluates one or two diameters of each muscle, and consecutive measurements of the same diameter(s) are performed during therapy for follow-up **(Figures 1 and 2)**.

Triamcinolone is a glucocorticosteroid with a potency that equals five times that of cortisol; it is metabolized in the liver and excreted as a soluble compound in the urine. It is fluorinated at position nine of the second ring giving it a marked glucocorticoid activity and a reduced mineralocorticoid activity due to OH substitution at C16.[16-19, 21] The administration of peribulbar injection in inferolateral quadrant of the orbit allows it's diffusion in the retrobulbar far to the EOM.[13] Multiple complications have been reported with periocular injections of steroids,[34-40] including globe perforation,[11] arterial occlusion,[12] toxic optic neuropathy[10] or atrophy of subcutaneous tissue in the face. [14]

Table 4: Muscle Parameters (Dmax) in Graves' Ophthalmopathy Group A (n = 30) and Group B (n = 30) Groups - Comparative Change After Treatment

Muscle	Group A mm, mean(SD)	Group B mm, mean(SD)	Difference in mm (SD)	t-value	p-value <0.05
SR	4.82(0.5)	4.85(0.5)	0.00(0.17)	6.77	0.0005
IR	6.68 (0.75)	7.00 (0.7)	0.02(0.25)	6.51	0.0005
MR	4.57(0.46)	4.6(0.5)	0.03(0.17)	1.81	0.012
LR	4.33(0.48)	4.43(0.5)	0.1(0.17)	3.79	0.0005

Table 5: Calcaemia, Glycemia,and Plasma Cortisol Level Variations in Groups A and B.

Laboratory test	Group A	Group B	p- value in treatment group
Calcaemia (mg/dl)			
Week 0			
Mean (SD)	9.16 (0.64)	9.06 (0.87)	0.11 (>0.05)
Range	(8.3–10.1)	(7.8–10.3)	
Number	5	5	
Week 10			
Mean (SD)	8.78(0.54)	9.58 (0.35)	_
Range	(8.1–9.7)	(8.2–9.9)	
Number	15	15	
Glycaemia(mg/dl)			
Week 0			
Mean (SD)	94.8 (15.3)	92.67(24.3)	0.52 (>0.05)
Range	(70.5–143.0)	(71.0–186.0)	
Number	15	15	
Week 10			
Mean (SD)	92.1 (16.7)	85.2 (8.3)	
Range	(65–135)	(71.0–102.0)	
Number	15	15	
Plasma Cortisol(µg /dl)			
Week 0			
Mean (SD)	17.21 (5.3)	20.86 (10.7)	0.04(<0.05)
Range	(6.4–32.7)	(6.2–35.4)	
Number	15	15	
Week 10			
Mean (SD)	16.20 (5.0)	24.40 (16.8)	
Range	(6.4–24.8)	(6.3–72.1)	
Number	15	15	

We did not have any of these complications in our series in both groups. Trobe et al[9] have reported unfavourable outcomes in compressive neuropathy. Bhisitkul RB, Lee OT, Wong J, reported neuroprotective effect of triamcinolone in a rabbit model. [15]

We included patients with TAO who had ONH edema of 1-2 DD in our study and did not found any unfavourable outcome in both groups. Sergott, Glaser, Lee and Brazis warn against their use.[4] They were concerned by the increase in volume produced by an injection in the congested orbit. In our study we didn't measure the area of binocular single vision without diplopia and only focused on decreasing the orbital volume.[20, 32] We used triamcinolone and dexamethasone injected intraorbitally and showed improvement in motility, reduction in the sizes of EOM, increase in the vision and exophthalmos. There were no change in IOP levels, systolic and diastolic blood pressure after treatment in both groups.

Conclusion

Triamcinolone and dexamethasone administered as a periocular injection were equally effective in reducing the sizes of EOM and equally effective in compressive optic neuropathy of recent onset and improves vision. No adverse effect and complications of the drug were seen locally as well as systemically in both the groups. Therefore, both drugs can be a substitute for each other.

Abbreviations:
BCVA - best corrected visual acuity
IOP - intraocular pressure
ONH – optic nerve head
TAO - thyroid associated ophthalmopathy
MR - medial rectus
LR - lateral rectus
SR - superior rectus
IR - inferior rectus
IO - inferior oblique
SO - superior oblique.

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New Alternatives for Modern Medical Training: **Digital Books, iPads, Simulators?**

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Computers have inexorably gained an important role in medical care and less so in medical training. Newer technologies, such as smartphones, tablet computers, and surgical simulators appear destined to play a role in the training of medical students and residents, but the importance of that role is uncertain.

Smartphones and Tablet/ Mobile Computers

The advantage with these devices is in the constant availability of both information and documentation, and the very different interaction provided through a touch screen interface. Mobile devices bring reference materials, test results, certain vision testing, patient education materials, and documentation capabilities to the bedside or to the operating, emergency, and conference room(s). New applications, specifically developed for mobile computers, bring new capabilities, such as language translation, to the patient/doctor relationship. While advantages are apparent, there are clear obstacles and challenges that remain in the integration of mobile technology into patient care and medical education. A summary of some of the advantages and disadvantages of mobile technology are outlined in **Table 1**.

Literature Review

Little empirical data is yet available regarding mobile computing in either medical practice or medical education. Some studies have been done which support the potential advantages.

Patel BK, et al[1] recently studied the effect of mobile tablet computers on the efficiency of Internal Medicine residents. The users estimated time savings of one hour per day. Improved order placement before rounds and at the end of the day indicated more timely patient care and supported the impressions of the residents.

Tanaka PP, et al;[2] evaluated the experience of anesthesia residents in an orthopedics rotation comparing paper based instruction to iPad instruction. Material access through an iPad was rated significantly higher, although the materials made available were identical.

Other studies confirm the self-reported preference of medical students and residents for mobile technology[3,4] but empirical data demonstrating improved performance remains sparse and indicates a need for further evaluation.

In addition to the studies above, a survey of providers (attendings, fellows, and residents) at ACGME institutions (Tirrell TF, et al)[5] found that 39% owned a tablet and 46% used it in their clinical practice. 53% of institutions supported tablet use. Interestingly, the vast majority of those without tablets felt they should be institutionally supported. Overall, 75% of all respondents believed that tablet use allows them to be better physicians. This indicates a high acceptance rate for tablet use among physicians.

Patient acceptance of desktop computers is more studied than acceptance of mobile devices. It is difficult, however, to generalize the results of these studies since they can vary significantly in the way the computer was used. Entering extensive patient data into an EMR may be perceived very differently than using the computer to look up lab data or to write prescriptions only. A 2010 study on tablet computers in the exam room,[6] found a generally good reaction to their use. Of 99 randomly chosen patients who had just finished an exam where a resident had used a tablet, only 4.3% stated that they disliked the idea of a doctor using a tablet computer. In this study, doctors used the device for information acquisition, but did not use it to enter extensive exam data.

Useful Mobile Apps and Web Sites

The usefulness of computers for furthering education is directly related to the information available electronically. Many web sites and/or mobile apps are often cited as very useful for both practicing ophthalmologists and residents in training **(Table 2)**. Some web sites/applications are specifically designed for educational purposes. An example is the ONE network, listed in Table 2, which contains the Resident Hub site, which provides educational content and assessments at an annual per resident cost. The site sends results of resident completion or performance directly to the Program Director for documentation. This site can be viewed and used on mobile devices such as the iPad or Android tablets. A large number of innovative homegrown ophthalmic applications are available on the iPad or Android devices; however the content of many of these have not been peer-reviewed and must be viewed cautiously.

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[2] Department of Mechanical and Industrial Engineering, University of Illinois at Chicago, Chicago
[3] Wilmer Eye Institute, Johns Hopkins University, Baltimore Maryland
[4] King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia

Table 1: Advantages and Disadvantages of Mobile Computers.

Advantages	Disadvantages
Continuous access to information Recording capability (audio, photos, videos) Handwriting recognition capability Compression of multiple textbooks, papers, and documents into a quickly accessible and easy to carry forms Real time reporting of resident activities (surgical logs, etc.) Multiple users in a space with limited or no desktops Mobile Applications specific for Ophthalmology Lower cost (typically) of electronic texts Can input data while facing the patient, as opposed to turning one's back to the patient when using a desktop	Cost of devices Potential loss or theft of device Greater privacy concerns with Wi-Fi Slower data input compared to physical keyboard Proprietary compatibility issues Dependency on devices, rather than learning the material; should be used as reference Can create negative perception in others (is the doctor texting or playing a video game?) Spread of infection (how does one disinfect a a screen?)

Table 2: Useful Websites and Mobile Applications.

Epocrates	Free version provides drug information designed for health care professionals. Includes drug interactions, calculators, and drug alerts. A subscription version includes infectious disease information, disease monographs, treatment guidelines, coding information and more	iPad, iPhone, Android, Blackberry, or online
British National Formulary	Provides information regarding pharmacology and prescribing medications in the national Formulary, but also medications outside the formulary. It is free to those in the United Kingdom and available through subscription outside the U.K.	Online web site
PubMed	Provides a free search engine to access the MEDLINE database of medical references and abstracts. Also provides access to older printed materials from other sources. PubMed offers a Mobile version. Multiple independent apps have been developed to interface with PubMed and promise an easier search experience.	iPad, iPhone, Android, Blackberry, or online
Wills Eye Manual	Quick reference guide for ocular conditions.	iPad, iPhone, Android, Blackberry, and others
Oxford Handbook of Clinical Medicine	General medical information in succinct, easy to read form. Classic reference source for medical students and residents.	iPad, iPhone, Android
ONE network	Sponsored by the American Academy of Ophthalmology, it is purported to be the largest online ophthalmic resource in the world. It provides free access to multiple peer review journals with AAO membership, and also contains courses, case studies, lectures, practice guidelines, resident training, and more.	Online web site
Medscape	Extensive medical information content with drug/formulary database, consistently updated disease reference for physicians, CME, patient information and illustrations.	iPhone, iPad, Android, Blackberry, Kindle Fire
Jibbigo Voice Translator	Bidirectional voice translator that works with over 20 languages. Free unlimited use with internet connection. Can buy download of individual languages for offline use.	iPhone, iPad, Android
Evernote	Cloud based application that allows categorization and storage of any type of electronic content. Categorizing and storing classic articles on a disease, selecting articles for a journal club, or saving notes from a lecture are some possible uses.	iPhone, iPad, Android, Blackberry, Windows Phone

Ophthalmic Surgery Simulators

Modern cataract surgery requires a fairly sophisticated level of training and expertise and there has been progress in the development of simulators to train residents in the different steps of cataract surgery.[7]

Surgical Simulator Devices

Commercially available ophthalmic simulators include The EYESI eye surgery simulator (VRmagic, Germany), PhacoVision (Melerit Medical AB, Sweden) and a more recently developed simulator, ImmersiveTouch-Sensimmer (ImmersiveTouch, USA) Virtual Phaco Trainer. Each of these simulators is based on either physical or virtual reality or a combination.

Literature Review

Ophthalmic surgical simulators use scoring techniques to track improvement and surgical skills. Using the EYESI simulator Selvander et al. demonstrated that medical student performance on a cataract simulator produced a short rapid initial improvement in performance, and suggested that both the capsulorrhexis and cataract module may be needed to achieve overall score improvement during training.[8,9] In a comparative study by Belyea et.al., residents who trained using a simulator had shorter phacoemulsification times, lower percentage powers, fewer intraoperative complications, and a shorter learning curve.[10] Another study suggested that virtual reality surgical simulator training mildly shortens the learning curve for the first 50 phacoemulsification cases.[11] The less experienced residents appear to benefit most from surgical simulator training.

Using a prototype version of the Virtual Phaco Trainer, various metrics were tested and compared between capsulorrhexis performance in live patients and the simulator capsulorrhexis module. Concurrent validity for the circularity metric for capsulorrhexis was established. Interestingly, the study noted high variations in metrics with residents at the same level of training between institutions, suggesting that large data sets may be needed to carefully study the effect of simulation training on performance.[12]

The issue of visual versus tactile feedback in cataract surgery simulation has been debated. Laurell et.al.[13] had initially predicted that phacoemulsification is a procedure that is largely dependent on visual input, with tactile feedback playing a minor role, and had suggested that these characteristics make phacoemulsification relatively easy to simulate. However these observations were later challenged by Hyunh et al 2008[14] where it was argued, after feedback from cataract and vitreoretinal surgeons, that a balance of visual and tactile feeback was essential. Hyunh et. al. also acknowledged that the lack of haptic feedback in current ocular surgery simulators parallels the drawback faced by robotic assisted surgery systems. They mention that like ophthalmic surgery simulators, robotic surgery enhances dexterity and precision and provides excellent visual feedback but lacks tactile input. The addition of tactile feedback enables better tissue characterization and suture approximation. Similarly, in a study of the EYESI simulator for vitreoretinal surgery, the need to incorporate tactile feedback was acknowledged; however, the relative importance of visual versus tactile feedback in retinal surgery is also unclear.[15]

Techniques to develop haptic interfaces in robotic surgical tools are currently underway. As the setup of a robotic surgery system is strikingly similar to computer-simulated ocular surgery models, these tools can potentially be applied to ocular surgery simulators. The EYESI simulator mainly incorporates visual feedback whereas the Sensimmer virtual phaco trainer incorporates a programmable haptic feedback in specific steps.

Summary

Mobile computing devices and computers are playing an increasing role in medical training. Increasing amounts of information available and novel applications are being developed for resident training and continuing education in ophthalmology. More studies focusing on the efficiency and value of electronic media in medical education and patient care are needed in ophthalmology. In addition, peer review of material content in innovative applications on mobile computing devices is highly recommended.

Ophthalmic surgical simulators are slowly playing an increasing role in training ophthalmology residents. Validation studies based on visual and tactile feedback from simulators is currently a topic of interest in ophthalmic surgery. While initial results seem to suggest that while the simulators are beginning to have an impact in improved training compared to the training methods without simulators, there are still a number of areas which need further study and development. Simulators which feature both high fidelity tactile and visual feedback in concordance with each other seem to offer the most in terms of real life reproducibility, there is still a long way to go before these features can be rigorously ascertained.

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Tolerance and Effectivity of Prostaglandin Analogues in Glaucoma Patients

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Reduction of intraocular pressure (IOP) is still the backbone of glaucoma treatment, either preventing or delaying the appearance or progression of damage to the ganglion cells and the subsequent visual field loss.[1,2] The efficacy of reducing IOP has proved to be useful even among patients with basal IOP within the normal range.[3] Therefore, the aim of most of the presently available drugs for glaucoma treatment is reducing IOP by modifying aqueous dynamics, reducing its production in the ciliary processes, reducing the outflow resistance at the trabecular meshwork and increasing the uveoscleral outfolw or by a combined mechanism.

Among the different commercially available drugs, prostaglandin analogues have shown the highest IOP reduction.[4] Therefore, they are presently considered first line drugs in the treatment of glaucoma and ocular hypertension.

At present the main prostaglandin analogues commercially available are latanoprost 0.005%, travoprost 0.004% and bimatoprost 0.03%. Latanoprost and travoprost are ester prodrugs of the prostaglandine F2α (PGF2α), whereas bimatoprost is an amide prodrug of 17-fenil-PGF2α, and is considered a prostamide. Active forms of prostaglandin analogues show a variable affinity for the FP receptor that is related to the agonist PGF2α effect; this affinity is highest for bimatoprost and lowest for latanoprost.[5]

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The mechanism of action of this group of drugs is by increasing aqueous outflow (mainly through the uveoscleral way and in a lesser degress through the trabecular meshwork). Increased aqueous outflow through these two ways is associated with a reordenation of the components of the extracellular matrix, with an overexpression of metalloproteinases in the trabecular meshwork, iris root, cilliary body, and nearby sclera, hydrolysing collagen fibres. These changes increase the interfibrillar space at the ciliary body and reduce the extracellular matrix of the trabecular meshworh, increasing aqueous outflow. The early hypotensive effect of thes drugs might be attributed to a FP receptors mediated relaxation of the cilliary muscle facilitating uveoscleral outflow.[5] It has been reported that prostaglandin analogues may increase blood flow and ocular perfusion pressure.[6]

Effectivity

Prostaglandin analogues became commercially available in the late 90's with latanoprost. Previously, ß adrenergic blockers, especially timolol maleate, were the 1st line drugs for the treatment of glaucoma and ocular hypertension. Therefore, the initial studies to prove the effectivity of prostaglandin analogues to reduce IOP compared latanoprost with timolol maleate.

These studies proved that latanoprost significantly reduced IOP compared with timolol maleate.[7] A higher response has been reported among Mexican and Asian patients in different trials.[8] Travoprost and bimatoprost have also shown a higher hypotensive effect than timolol.[9, 10]

Similarly, latanoprost showed a higher hypotensive effect than dorzolamide.[11] It has been established that latanoprost permits a better circadian control of IOP than timolol and dorzolamide.[12]

Latanoprost presents a higher hypotensive effect than brimonidine [13] as well as less IOP fluctuation.[14]

Those patients who were under treatment with timolol maleate showed a better additive effect with latanoprost than with dorzolamide.[15] The additive effect of latanoprost and pilocarpine has also been documented.[16]

A meta analysis study performed to compare the hypotensive effect of latanoprost vs. a fixed combination of timolol maleate and dorzolamide showed a higher IOP reduction among those patients treated with latanoprost who previously were under timolol therapy. However, IOP reduction was similar for both treatments among those patients who previously were not treated by timolol maleate.[17] In a similar way, bimatoprost induced a higher reduction of IOP among those patients who had been previously treated by timolol maleate, than a fixed combination of timolol/dorzolamide.[18]

The hypotensive effects of latanoprost, travoprost and bimatoprost were followed during 12 weeks by Parrish et al, who documented an IOP reduction with the 3 prostaglandin analogues. The IOP differences at different times of the day were not statistically significant, but a

lesser degree of conjuctival hyperemia was reported in eyes treated by latanoprost.[19] Conjunctival hyperemia starts during the first 2 days of the treatment and decreases within the following 2 to 4 weeks, even though it may persist longer.

A meta-analysis study performed by Aptel et al comparing IOP reduction in patients treated by latanoprost vs bimatoprost, documented a higher hypotensive effect of bimatoprost. This difference was statistically significant among different IOP determinations during the day. Comparing patients treated by bimatoprost vs travoprost, the hypotensive effect of the former was more marked; however the difference was statistically significant at certain times of the day. Comparing patients treated by latanoprost vs travoprost the differences were not statistically significant.[20]

It has been reported that the ocular hypotensive effect of travoprost is superior to latanoprost,[21] and bimatoprost is superior to travoprost.[22]

Orzalesi evaluated the hypotensive effect of latanoprost, travoprost and bimatoprost during the circadian cycle and found an adequate tonometric control with the three analogues, without significant differences. It is remarkable that according to his results, IOP control was superior during daytime and less marked in the early hours.[23]

An additional 1.4 mmHg reduction was found at three months among patients that had been previously treated by latanoprost, and was replaced by other prostaglandin analogues, when it was replaced by travoprost, and 2.1 mmHg when it was replaced by bimatoprost.[24] Fixed combinations of prostaglandin analogues with timolol maleate reduce IOP beyond the isolated effect of these components.[25-27]

Latanoprost is unstable to heat and sun ultraviolet B radiation.[28] Bimatoprost is the most thermally-stable prostaglandin analogue.[29]

Tolerance and Treatment Adherence

Inadequate treatment adherence is not uncommon among glaucoma patients,[30,31] especially among the younger and the aged patients.[32]

Patients' compliance depends on several factors such as the patients' own awareness of the disease and the treatment's benefits, physical and economical availability of the treatment, ease and comfort of instillation, as well as the appearance and severity of associated adverse events.

Prostaglandin analogues are administered once a day, increasing patients adherence to the treatment. It has been mentioned that those treatments that require a lesser number of daily administrations and prostaglandin analogues are associated with a better compliance.[33]

Adverse events lead to treatment interruption in 19% of patients.[34] Bimatoprost and travoprost are more frequently abandoned than latanoprost.[35]

Latanoprost is less frequently associated with conjunctival hyperemia than travoprost and bimatoprost **(Figure 1)**. Honrubia et al performed a meta-analysis study finding that the average number of patients who developed conjunctival hyperemia with prostaglandin analogues was 16.5% for latanoprost, 33% for travoprost and 40.2% for bimatoprost.[36]

Eisenberg compared the three drugs and found an adequate IOP control with the three agents and similiar side effects; however, the appearance of conjunctival hyperemia and eyelash growth was significantly more frequent for bimatoprost and travoprost than latanoprost.[37]

A direct correlation has been reported between conjunctival hyperemia severity and IOP reduction.[38] Conjuctival hyperemia increases treatment costs among patients treated with prostaglandin analogues; hyperemia is less frequent and costs are lower among patients on treatment with latanoprost.[39]

It has been shown that benzalkonium chloride-free travoprost

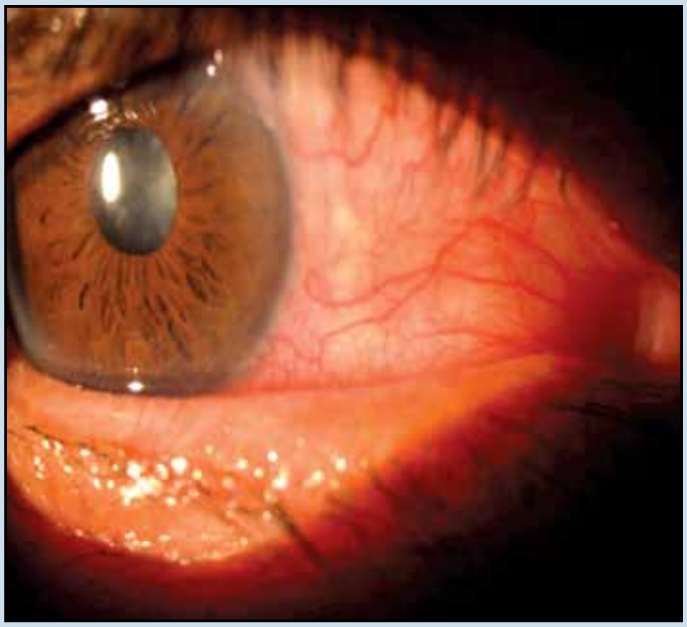

Figure 1: Conjunctival hyperemia induced by prostaglandin analogues.

is less frequently associated with ocular side effects, improving tear break-up time and reducing ocular surface alterations. [40, 41]

Other adverse effects of prostaglandin analogues are pigmentation changes in nearby tissues containin melanin such as eyelids, eyelashes and iris.[42]

Latanoprost and other prostaglandin analogues induce pigment changes of the iris, specially in mixed colour irides.[43] Iris darkening is related to an increased number and size of pre-existing melanin granules. Histological premalignant changes have not been observed in pigmented irides treated by prostaglandin analogues.[44]

Eyelashes growth and pigmentation has been documented **(Figure 2)** as well as the cheek hair following prostaglandin analogues administration.[45] Darkening of the periocular area has also been reported and is more frequent among bimatoprost users than in patients using latanoprost.[46]

A possible association between latanoprost and anterior uveítis has been reported; therefore, prostaglandin analogues are frequently contraindicated among patients with uveitic history.[47] Herpetic keratitis reactivation has also been reported following instillation of prostaglandin analogues.[48, 49]

Cystoid macular edema has been reported after the instillation of prostaglandin analogues, more frequently among aphakic eyes or posterior capsule ruptures;[50] however, these findings have not been consistent in other series.[51]

Conclusion

The selection of the more adequate ocular hipotensive drug for each patient can determine an adequate adherence and therapeutical response. Prostaglandin analogues achieve the highest IOP reduction and might be therefore considered as the most adequate drugs to treat glaucomatous or ocular hypertensive patients. However, local side effects might be associated with treatment intolerance and low adherence making our prescription ineffective. As a general rule, we may say from the literature evidence that among the available prostaglandin analogues, latanoprost is the best tolerated drug and bimatoprost shows the highest hypotensive effect, while travoprost lies in the middle of these drugs. In order to decide which prostaglandin analogue should be used in each case we have to balance desired IOP reduction and the possibility that the patient may not be willing to tolerate the side effects of the drug. These considerations will help us choosing the best option for our patients.

Figure 2: Eyelashes with increased size and pigmentation induced by prostaglandin analogues.

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Keratoconus Managed with **Intrastromal Corneal Ring Segments** and **Corneal Crosslinking**

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Keratoconus is a bilateral, non-inflammatory, progressive ectatic corneal disorder characterized by thinning and protrusion of the central cornea.[1] These corneal changes result in a mild to severe decrease in the best-corrected visual acuity (BCVA) as a result of progressive myopia, regular and irregular astigmatism, and apical scarring.[2] Most patients can be managed successfully with spectacles or contact lenses, especially in the early stages and with mild forms of the disease. However, when these measures fail to provide adequate vision or patients can no longer tolerate contact lenses, lamellar or penetrating keratoplasty or intracorneal ring segments are acceptable surgical alternatives with high success rates.[3-6]

Clinical Case

A 52-year-old male presented at our Eye Center with a complaint of variable visual acuity of several years duration. In the preoperative examination, his best-corrected visual acuity was 20/30 (distorted), with a manifest refraction of +1.50-10.00 x 85 in the right eye and +1.00-10.00 x 90 in the left eye. Slit-lamp examination and fundus examination were normal.

Keratometry was 44.10 / 51.40 D in the right eye and 38.00 / 48.70 D in the left. Preoperative central ultrasound pachymetry was 449 µm in the right eye and 495 µm in the left eye. He had no family history of ocular disease. Keratoconus presence was confirmed and documented by elevation-based tomography *(Pentacam; Oculus Optikgeräte, Wetzlar, Germany)*.

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Ophthalmological examination at presentation, **(Figure 1 A-B)** shows the curvature with central corneal steepening in both eyes. Using the Scheimpflug tomography (Pentacam Oculus Optikgeräte), and the on-line nomogram, we were able to dedide the location of the ring segments in both eyes through the curved astigmatism.

ICRSs (Kerarings) were implanted in both eyes using the manual technique for tunnel creation. Two standard segment implant of 200 µm, 155 arc length (155 degree), were placed at axis 175, with a tunnel depth of 397 µm in the right eye and with a modification on the pachymetry of 400 µm for the left eye. The implants resulted with a good visual improvement, but the patient still experienced variabilities. Post-Kerarings topography is shown in **(Figure 2 A-B)**.

As reinforcement, 10 months after ICRS insertion, the both eyes were treated with combined ultraviolet radiation and riboflavin treatment to achieve collagen crosslinking. Seven months after treat-

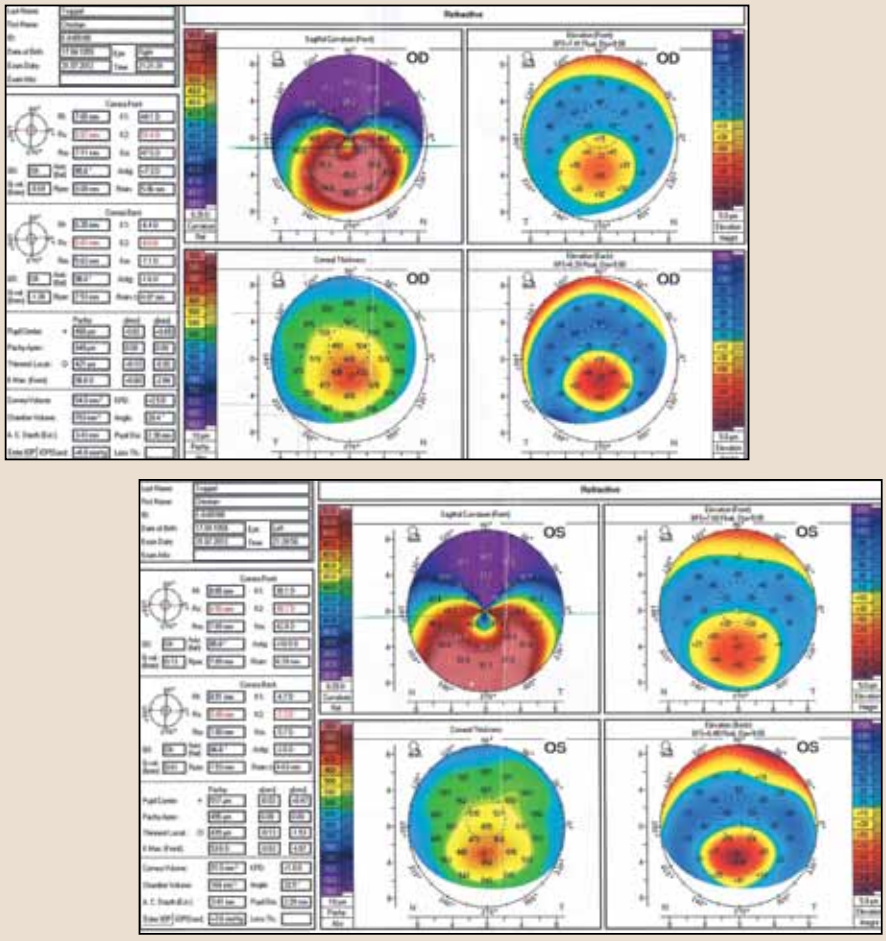

Figure 1 A- B: Corneal topography. Preop for ICSR.

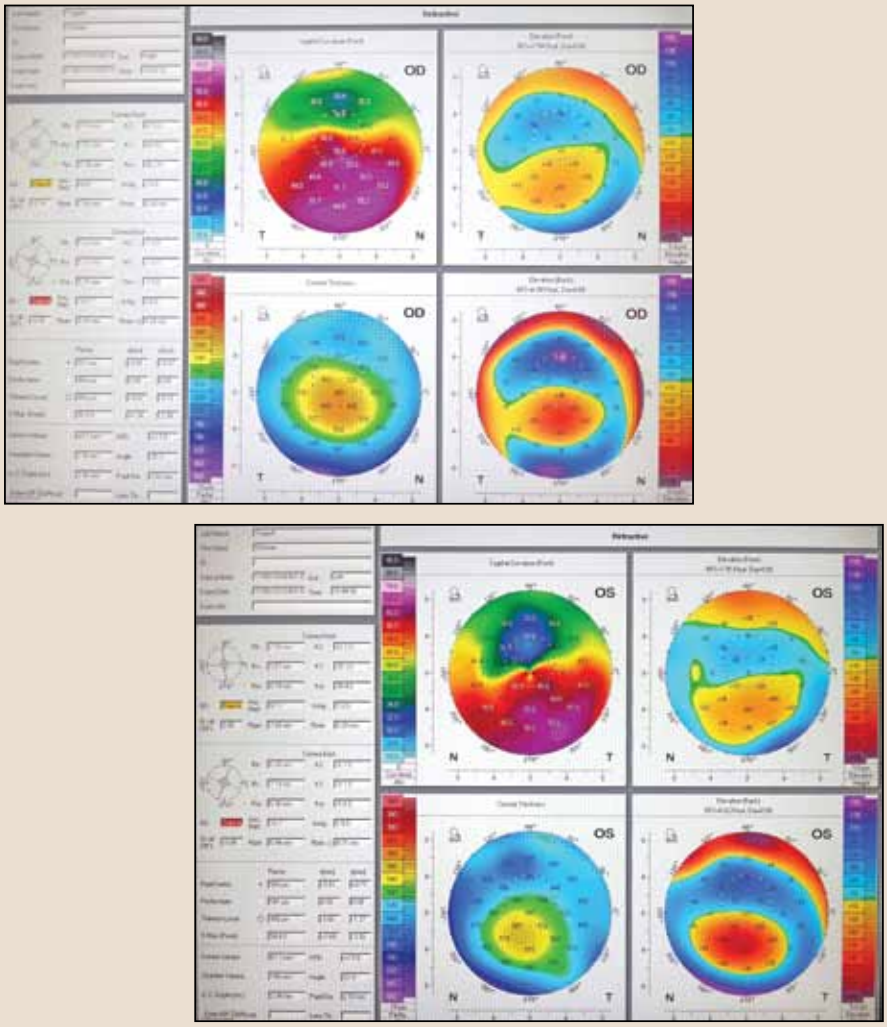

Figure 2 A-B: Corneal topography 9.5 months post-Kerarings implantation.

ment, his uncorrected visual acuity quality improved to 20/20-2 in each eye. His refraction changed to -0.50-3.00 x 56 (44.90/47.60) in the right eye and +0.25-3.50 x 95 (38.60/42.80) in the left eye.

Discussion

Keratoconus is one of the most challenged pathologies of refractive surgery.[7] This progressive corneal distortion can result in progressive myopia, irregular astigmatism, and visual impairment.[8] Rigid contact lenses are frequently required to achieve good functional vision, but progression can lead to intolerance of contact lenses, and ultimately the patients may require lamellar or penetrating keratoplasty.

The use of intracorneal segments (ICRS) for these cases has been previously reported with positive results.[9,10] Combined treatment adding crosslinking procedures has also shown promise.[11-13]

Combined ICRS implantation and collagen crosslinking produced a stable visual outcome in our patient. The efficacy of this approach is clearly limited, however now we would generally consider more aggressive strategies at the outset.

ICRS implantation in the corneal periphery flattens the central corneal apex,[3] while crosslinking induces additional covalent bonds between collagen molecules to increase corneal strength.[11] A patient receiving both treatments consecutively may receive the beneficial effects of improved corneal topography and stabilization of keratoconus.

We did not combine our treatment measures with photorefractive keratectomy (PRK), as described by Kanellopoulos in the Athens Protocol,[14] because we have no experience with this modality and also because the long-term results of further corneal thinning and destabilization remain to see.

The combination of these two minimally invasive therapies, ICRS and crosslinking, for the management of keratoconus appears to be a promising alternative to lamellar or penetrating lamellar keratoplasty. Longer follow-up and larger studies are needed to evaluate the refractive and topographic stability of these alternative and desirable treatment options.

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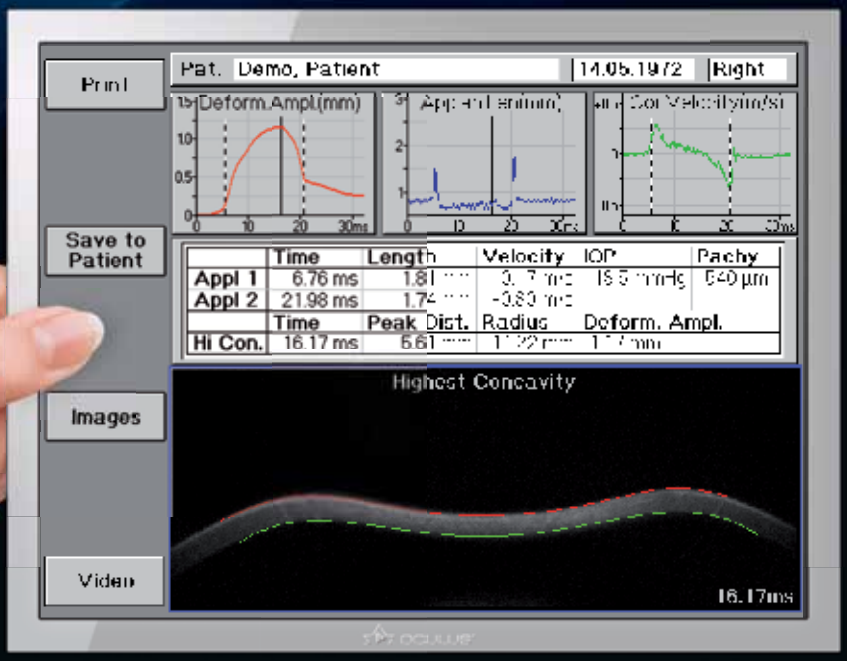

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