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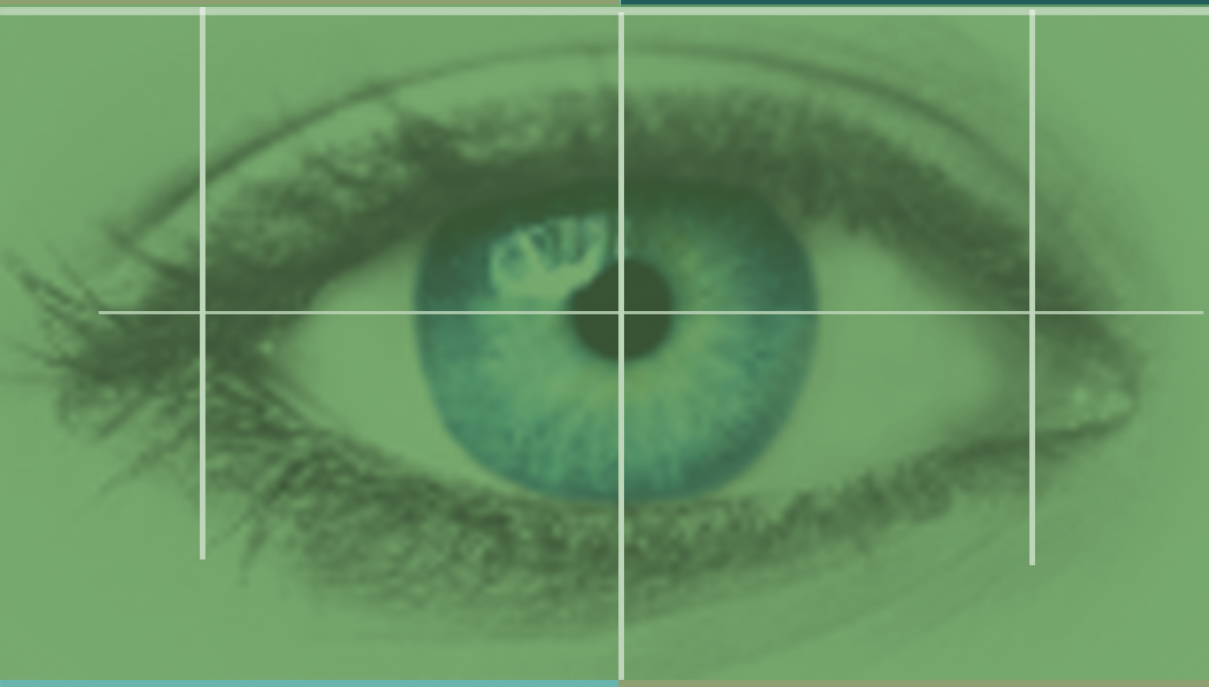

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Editorial

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Research and Its Importance

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Everyone has heard of research, but what exactly comprises research is often misunderstood. This word encompasses a large area of intervention and observation aimed at improving the quality of life of populations.

WHAT IS RESEARCH?

Research has been defined as a "systematic investigation, including research developments, testing and evaluation, designed to develop or contribute to generalizable knowledge". It also aims to establish facts and reach new conclusions. The Cambridge English dictionary defines research as a "detailed study of a subject, especially in order to discover (new) information or reach a (new) understanding". However, research often goes beyond the subject, going from the sub-molecular level to the study of gigantic structures, in order to develop new ideas, confirm or reject old theories and search for hypotheses. The basic tenet of research includes the gathering of data, information and observations to advance our knowledge. The evolution of the human race and technological advancement seen over the last couple of decades is a direct consequence of our increasing interest and dependence on research. While the human race is estimated to be 200,000 years old, most of our progress has occurred in the last 10.000 years. This advancement can be attributed to a better understanding of research methodologies.

TYPES OF RESEARCH

Medical research can be classified as:

1. Basic (experimental)
2. Clinical
3. Epidemiological

Medical research can also be "primary", wherein data is gathered; or "secondary", a process involving review or meta-analysis of the primary data. The primary research is a type of basic research, including experiments on animals or other models; biochemical, genetic, physiological, pharmacological, biotechnological, methodological and other investigations; population based studies or surveys and finally, development or improvement in analytical procedures. These primary studies generate the raw data required to make hypotheses or test-re-test theories.

Clinical research can be either "interventional (or experimental)" or "non-interventional (or observational)". Interventional studies are also called "clinical trials". Here, human volunteers (also called participants) are subjected to a rigid standard protocol designed by the investigators.

The clinical trial may compare an untested medical approach with a standard mode of practice, placebo or no intervention. The trial may also be a comparison of 2 arms of interventions already available. The ultimate aim of such research is to determine the safety and efficacy of the intervention.

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In an observational study, investigators assess the health outcomes in groups of patients according to the research plan or protocol. The participants continue to receive the standard healthcare practice without assigning to specific interventions. The different outcomes in comparable groups are then analyzed to gain further insight.

Epidemiological studies investigate the distribution and historical changes in the frequency of diseases and the causes for these. Interventional epidemiological studies can be "field studies" (sampling from an area) or "group studies" (samples obtained from a specific group). Observational epidemiological studies can be cohort studies (follow-up studies), case-control studies, cross-sectional studies (prevalence studies) and ecological studies (correlation studies or studies with aggregated data).

IMPORTANCE OF RESEARCH

Medical research is necessary to increase our knowledge regarding treatment, diagnosis and prevention of diseases or conditions. Research is required in order to fight against diseases, reduce the economic cost of illness, extend life and improve health. Overall, research is aimed at improving the quality of life of the general population and specially the vulnerable groups. It is fundamental in lowering the morbidity and mortality of patients.

CONCLUSION

Clinicians, non-clinicians and para-medical allied health personnel are in an unenviable position to conduct research. This is a process geared to improve the quality of life of the general population, leading to a healthier gene pool.

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Editorial

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Preferential Hyperacuity Perimetry: Perspectives of Self-Monitoring of Neovascular Activity in Patients with Age-Related Macular Degeneration

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The socio-economic burden of age-related macular degeneration (AMD) has strongly increased in public health importance due to the aging of the general population, and in clinics because of the world-wide use of anti-vascular endothelial growth factor (anti-VEGF) drugs in patients with neovascular AMD (NV-AMD).[1-5] In all health care services of the developed countries, a large portion of NV-AMD burden is related to the growing human resources employed to carry out those frequent monitoring visits required to verify the necessity of anti-VEGF repetition. In view of recent findings in earlier diagnosis of AMD-related choroidal neovascularization (CNV) by means of the self-monitoring with preferential hyperacuity perimetry (PHP) device,[6-8] possibilities and limitations of this innovative self-monitoring approach, whose rationale exploits the human "Vernier acuity" visual function,[9,10] should be investigate to verify its ability in detecting the need for anti-VEGF retreatments among patients with NV-AMD, and to prospectively reduce the costs for the clinical governance of this sight-threatening disease.

AMD is the leading cause of irreversible vision loss and legal blindness in the developed countries.[5,11] Before the large-scale utilization of intravitreally injected anti-VEGF drugs in the everyday clinical practice, NV-AMD accounts for more than 80% of the cases of severe visual deterioration caused by AMD.[12,13] At present, appropriate anti-VEGF utilization makes possible an outstanding reduction of patients eligible for legal blindness certification,[14-16] maintaining or improving their vision-related quality of life.[17-19] However, none of these benefits can be obtained without scheduling periodic anti-VEGF retreatments, whose correct decision-making process is practicable only after the execution of frequent monitoring visits because of: i. the limited intravitreal duration of the administered anti-VEGF drug; ii. the unpredictability of individual NV-AMD response to all different anti-VEGF regimens. In fact, considering the lack of a validated best clinical practice for anti-VEGF therapy in NV-AMD[20] and the risk of dramatic vision loss related to the protraction of follow-up intervals,[21] an intensive clinical monitoring of NV-AMD patients is currently mandatory to maintain the best outcomes possible, with consequent exponential growing of Medicare costs for the management of anti-VEGF injections regardless of the drug utilized during these interventional invasive procedures. The comprehensive appraisal of these aspects strongly recommends the realization large and independent clinical studies in view of the fact that PHP devices might also be an effective self- monitoring strategy to assess CNV activity in NV-AMD patients, allowing a substantial reduction of the socio-sanitary burden due to the great number of monitoring visits required for a correct application of anti-VEGF regimen, without risk of irreversible visual loss and legal blindness for an unmonitored extension of the monthly follow-up intervals. However, the appropriate utilization of PHP device for patient's self-monitoring in real-world setting could be feasible only after the acquisition of well-detailed data regarding its potential and limitations in a large population of NV-AMD patient. In particular, future investigations should be aimed to: i. assess the ability of a self-monitoring test based on PHP to detect the need for retreatment with intravitreal anti-VEGF drugs in NV-AMD patients using, as gold standard, the

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ophthalmologist's yes/no therapeutic decision after monitoring visits performed in accordance with good clinical practice; ii. verify whether the PHP monitoring data are influenced by individual demographic, clinical and ocular characteristics, which might be able to decrease the reliability of the test as a consequence of inadequate learning capacity, functional ability and/or compliance of each different NV-AMD patient treated with PRN anti-VEGF regimen.

Although the large-scale utilization of anti-VEGF drugs has made possible a reduction of up to 50% in incidence of legal blindness, the growing burden related to the appropriate monitoring of NV-AMD candidates for these treatment courses is becoming unsustainable for health care services. This emerging public health issue is currently faced without be aware of the potential applications of the innovative self-monitoring PHP device which, in turn, has been successfully utilized for the earlier detection of AMD-related CNV occurrence.[6] Considering the lack of large, population-based, studies assessing the accuracy of PHP device in patient's self-recognition of anti-VEGF retreatment necessity for NV-AMD, specific observational health care researches is recommended to provide those real-world clinical data helpful to maintain the best outcomes possible, yet rationally reduce the management cost of a chronic disease that reduces our accessibility to others in need.

NV-AMD represents a major burden to the modern society, and its all-inclusive cost for National Health Systems is continuously growing in terms of prevention, diagnosis, treatment, and rehabilitation. Diagnostic strategies for appropriate check of NV-AMD patients periodically treated with anti-VEGF injections are very expensive, posing a big translational emphasis on those innovative self-monitoring approaches developed to improve the methodological strategies for the surveillance of chronic sight-threatening diseases. However, although some pilot studies have shown that PHP device is a very promising tool to improve the early diagnosis of NV-AMD,[22-24] large-scale outcomes research programs will need to demonstrate that unconventional procedures for NV-AMD monitoring are methodologically robust and, thus, applicable in the real-world practice, also considering their tele-diagnostic potential if integrated into modern data transaction systems.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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Editorial

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Elbendary AM. Glaucoma diagnosis: past, present and future. *Ophthalmol Open J*. 2015; 1(1): e6-e8. doi: 10.17140/OOJ-1-e003

Glaucoma Diagnosis: Past, Present and Future

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Glaucoma diagnosis is one of the most challenging situation in ophthalmology. In daily clinical practice, many of glaucoma patients are missed on diagnosis and a lot of those receiving antiglaucoma therapy may not have the disease. This difficulty may be attributed to sensitivity and specificity of the diagnostic tools as well as the nature of disease in its early stages. In the past, subjective clinical evaluation of optic nerve head and Retinal Nerve Fiber Layer (RNFL) photography enabled diagnosis but with wide variability even among expert observers. Visual field analysis is a major subjective beneficial test, but requires patient cooperation, frequently shows fluctuation. Even tests with reliable indices should be repeated several times to ensure a reproducible defect.

At present, diagnosis has been switched to objective computerized analysis techniques including Spectral domain-optical coherence tomography (SD-OCT). Given the fact that, structural changes precedes functional changes, peripapillary NFL thickness measurement is the most sensitive and discriminating parameter for glaucoma diagnosis up to the moment.[1,2] The ability of SD-OCT to differentiate between normal, glaucoma suspect and glaucomatous eyes is better for RNFL thickness than optic nerve head parameters.[3] With a specificity of 95%, Kuang, et al.[4] found that up to 35% of glaucoma suspect eyes had OCT- RNFL defects 4 years prior to perimetric glaucoma, and 19% of eyes had abnormal OCT results 8 years before visual field defects. Furthermore, application of OCT may revolutionize our knowledge about disease mechanisms. Based on OCT findings, Hood, et al.[5] found that the inferior arcuate bundle − though thicker − is narrower than the superior one at comparable locations. They suggested a crowding hypothesis for glaucomatous damage according to these OCT data.

Although, total macular thickness measured with OCT was found to decrease in glaucomatous patients. Its diagnostic power is much less than peripapillary RNFL thickness.[6] Total macular thickness measurement includes outer retinal layers which are spared in glaucomatous damage. So, researches had been focused on inner retinal layers that are specifically affected by glaucoma; namely: nerve fiber layer, ganglion cell layer and inner plexiform layer. These layers were collectively called the Ganglion Cell Complex (GCC) and proved to have high diagnostic power − that is − on par with and complementary to peripapillary RNFL thickness. The ganglion cell layer occupies about one third of the macular region. In this way, another anatomical area; the macular region had contributed to glaucoma diagnosis.[7]

Imaging of optic disc margin was tried and could illustrate border tissue of Elschnig. The latter is fibrous tissue that arises from anterior surface of sclera and fuses with termination of Bruch's membrane to separate axons of ganglion cells from choroidal circulation as they pass through the scleral canal. Its anatomy determines what structure is perceived clinically as the edge of the optic disc. According to their research, Reis, et al.[8] found that the clinically visible disc margin corresponds to border tissue of Elschnig or both Bruch's membrane with underlying border tissue. Less frequently, it corresponds to termination of Bruch's membrane. Therefore, the clinically visible disc margin differs from SD-OCT detected disc margin which is considered the termination of Bruch's membrane. This finding has important implication for the automated detection of the disc margin and estimates of the neuroretinal rim area.

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Still in the region of optic disc where OCT could clearly demonstrate the three dimensional structure of lamina cirbrosa (LC). It appears as highly reflective structure with distinct anterior and posterior boundaries that facilitate measurement of its thickness. The thickness of LC is reduced in glaucomatous patients and was found to correlate with mean deviation in ocular hypertensive, moderate and severe stages of glaucoma.[9] Laminar pores appear on enhanced depth imaging OCT as multiple small full thickness laminar perforations (<100 microns in diameter). In glaucomatous eyes, laminar defects were frequently seen and may be associated with focal retinal nerve fiber layer damage. Laminar defects should be more than 100 μ in diameter and 30 μ in depth.[10]

In the near future, OCT angiography my update our knowledge about pathogenesis, progression and management of glaucoma. Vascular dysfunction is one of the suggested mechanisms for glaucomatous damage. Reduced optic nerve head and peripapillary blood flow dynamics in glaucoma was shown by laser doppler flowmetry. Using the new Splits Spectrum Amplitude-Decorrelation Angiography (SSADA) algorithm on a custom swept-source OCT system, Jia, et al.[11] showed decreased optic disc perfusion in glaucoma. They showed attenuation of the dense peripapillary microvascular network and reduced disc flow index by 25% in glaucomatous eyes. The flow index value was highly correlated with visual field pattern standard deviation. In addition, different vascular beds including retinal, choroidal and sclera/lamina cirbrosa vascular networks were imaged and showed attenuation compared to normal subjects. Using OCT angiography, reduced peripapillary retinal perfusion in glaucomatous eyes could be visualized as focal defects and quantified as peripapillary flow index and peripapillary vessel density, with high repeatability and reproducibility.[12] Future researches will provide a deeper insight about role of disc perfusion in the course of glaucoma and possibly its progression. Lower flow index values may be added to risk factors that determine treatment strategy in preperimetric and perimetric glaucoma.

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Case Report

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Combined Trabeculectomy with Mitomycinc, Pars Plana Vitrectomy with Panretinal Photocoagulation, and Intravitreal and Intracameral Bevacizumab for Neovascular Glaucoma

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ABSTRACT

Purpose: To report the effectiveness of combined surgery for neovascular glaucoma.
Methods: Six eyes of six consecutive patients with neovascular glaucoma underwent the combined surgery: trabeculectomy with Mitomycin C, Pars Plana Vitrectomy (PPV), endolaserpanretinal photocoagulation, intravitreal and intracameral injection of bevacizumab.
Results: The intraocular pressure returned to normal range soon after operation. The neovascularization of iris regressed in a few days. Mild hyphema developed in three patients. All six patients had improved or stable visual acuity, and achieved normal intraocular pressure without antiglaucoma medications three months after operation.
Conclusions: This combined surgery may break the vicious cycle of neovascularglaucoma and preserve useful vision in these patients.

KEYWORDS: Neovascular glaucoma; Trabeculectomy; Mitomycin C; Pars plana vitrectomy; Endolaser photocoagulation; Intravitreal bevacizumab; Intracameral bevacizumab.

INTRODUCTION

Neovascular glaucoma (NVG) is a severe and rapidly progressive form of glaucoma associated with extensive retinal ischemia. Angiogenic factors, mainly Vascular Endothelial Growth Factor (VEGF), are released and result in Neovascularization of the iris (NVI) and the angle, and elevation of Intraocular pressure (IOP). The IOP elevation further reduces the ocular perfusion and aggravates retinal ischemia, which leads to a vicious cycle and a refractory glaucoma. Due to its rapid and devastating course, we suggest combined surgeries for NVG.

MATERIALS AND METHODS

A consecutive series of six eyes in six patients with uncontrollable NVG were enrolled. Informed consents were obtained for the off-label use of bevacizumab and the surgeries. All patients received the combined surgery including trabeculectomy with mitomycin C, pars plana vitrectomy (PPV), endolaser Panretinal photocoagulation (PRP), Intravitreal bevacizumab (IVB, 2.5 mg/0.1 ml), and Intracameral bevacizumab (ICB, 1 mg/0.04 ml)).

RESULTS

The outcome was illustrated in Table 1. In all six cases, the IOP returned to normal

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	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	80	63	55	36	62	63
Gender	Female	Female	Male	Female	Male	Male
Underlying disorder	CRVO	PDR	PDR + OIS	PDR	PDR	PDR
Previous ocular surgery	IVB*4	None	IVB*2, CC	None	PE+IOL	PRP, PE+IOL
At presentation						
Visual acuity	LP+	CF 30 cm	HM 10cm	HM	HM 50 cm	0.05
IOP (mmHg)	40	59	55	36	58	60
No. of medication	3	3	3	4	4	3
Neovascularization of iris	+	+	+	+	+	+
Hemorrhage Status of lens Postoperative bleeding	VH Brunescent Mild hyphema	Hyphema, VH Clear Mild hyphema	Hyphema, VH Nuclear cataract None	VH Clear None	Hyphema, VH PCIOL Mild hyphema	None PCIOL None
6 months after surgery						
Visual acuity	6/120	6/60	6/60	6/60	6/120	6/120
IOP (mmHg)	10	12	19	12	9	9
Recurrence	None	None	None	None	None	None

Recurrence indicates recurrence of neovascularization of iris and/or angle.
IOP: Intraocular pressure; CRVO: Central Retinal Vein Occlusion; PDR: Proliferative Diabetic Retinopathy; OIS: Ocular Ischemic Syndrome; IVB: intravitreous Injection of Bevacizumab; CC: Cyclocryotherapy; PE: Phacoemulsification; IOL: Intraocular lens; PRP: Panretinal photocoagulation; LP: Light Perception; CF: Counting Fingers; HM: Hand Motion; VH: Vitreous Hemorrhage.

Table 1: Patient characteristics and outcome.

range after surgery, and the NVI regressed completely in two weeks. All patients had improved or stable Visual Acuity (VA) for more than six months.

CASE REPORTS

Case 1

An 80-year-old woman was diagnosed with central retinal vein occlusion and had IVB four times. The VA was light perception. The IOP was 40 mm Hg with dorzolamide/timolol and brimonidine. Corneal edema, NVI, brunescent cataract, and Vitreous Hemorrhage (VH) were noted. She underwent phacoemulsification and the suggested combined surgery. Six months postoperatively, the best corrected VA of the left eye was 6/120, and the IOP was 10 mm Hg.

Case 2

A 63-year-old diabetic female had PDR, NVI, hyphema and VH. The IOP was 59 mm Hg and refractory to medication. The patient underwent combined surgery. The VA improved to 6/60 and IOP remained normal during the 4-year follow-up.

Case 3

A 55-year-old diabetic man was diagnosed as NVG and VH and had received Cyclocryotherapy (CCT) and IVB at another hospital but in vain. Combined surgery was carried out. Severe attenuation of retinal arteries and veins and whitening of the retina were noted. His ocular pain was resolved after the operation. Six months later, the IOP was 19 mm Hg and his VA improved to 6/60.

Case 4

A 36-year-old diabetic woman had NVG and VH in her right eye. The IOP was 36 mm Hg under full medication. The combined surgery was performed. The IOP was about 10 mm Hg during follow-up.

Case 5

A 62-year-old diabetic man had NVG in the right eye. The VA was HM at 50 cm. The IOP was 58 mm Hg with full medications. One week after operation, the NVI was completely resolved. At six-month's follow-up, his vision was 6/120, and IOP was 9 mm Hg with good bleb function.

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Case 6

A 63-year-old diabetic man was diagnosed with NVG in the right eye. The IOP was 60 mm Hg despite full medication. Gonioscopy revealed 360 degree peripheral anterior synechiae. One week after the combined surgery, the IOP decreased to 9 mm Hg and the NVI had resolved. The condition remained stable over a year of follow-up.

DISCUSSION

Medical treatment or separate procedure often leads to a disappointing visual result in NVG patients. This combined surgery provides prompt and adequate controlling of IOP.

NVG usually responds poorly to medication, and filtering procedure is mandatory. Failure rate of trabeculectomy alone is high in NVG eyes,[1] but decreases when adjunct with mitomycin C.[2]

PRP is important for ablation of the ischemic retina. When media opacity precludes complete PRP, more procedures are taken to make PRP possible, such as phacoemulsification for brunescent cataract (as in case 1), anterior chamber irrigation for hyphema (case 2, 3 and 5) or PPV for vitreous hemorrhage (in the first five cases).

PPV is indicated not only for clearance of the media opacity, but also of angiogenic factors. PPV eliminates the VEGF in the vitreous, and increases the clearance of VEGF that is produced afterward.[3-5]

The role of IVB in NVG has been verified,[6,7] but some reports suggested only for short term.[8,9] IVB is part of the surgery to reduce short-term complications. Increased level of VEGF is also noted in the aqueous humor,[10] and ICB is included in our surgery. In fact, with the existance of a filtering pathway, the drug might flow to the subconjunctival space, and subconjunctival bevacizumab has been suggested to reduce scar formation of the bleb.[11,12]

In conclusion, we suggest immediate combined surgery for NVG, which includes trabeculectomy with mitomycin C, PPV with endolaser PRP, IVB and ICB. This strategy has shown to be successful in controlling IOP and preserving useful vision.

CONFLICTS OF INTEREST

All authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Research

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Air Cannula *Vs.* Weckcel Sponge in Manipulation of Corneal Flap and Incidence of SPK (Superficial Punctate Keratitis) after LASIK

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ABSTRACT

Aim: To compare the difference in early post-operative Superficial Punctate Keratopathy (SPK) in patients by using either blunt cannula or Weck-cel sponge intra-operatively to handle the corneal flap during Laser-assisted *in situ* keratomileusis (LASIK).
Materials and Methods: A randomized prospective comparative study comprising of 192 eyes of 96 patients undergoing LASIK in both eyes were selected for this study. Two groups were made. First group included 96 eyes using air cannula (group 1) and the second included 96 eyes using a Weck-cel sponge (group 2) to manipulate the corneal flap intra-operatively. Both the groups were later compared for different grades of SPKs.
Results: Out of total 192 eyes 51(26.8%) eyes showed Grade 4 SPKs of which 49(96%) belonged to the Weck-cel sponge group and 2(4%) eyes belonged to the air canula group.
Conclusion: In this study we found that group 2 associated with more SPKs and it affected the post-operative patient satisfaction compared to group 1 patients.

KEYWORDS: Superficial punctuate keratitis; LASIK; Weck-cel sponge.

ABBREVIATIONS: SPK: Superficial Punctate Keratopathy; LASIK: Laser-assisted *in situ* keratomileusis; DLK: Diffuse Lamellar Keratitis; UCVA: Uncorrected visual acuity.

INTRODUCTION

Laser-assisted *in situ* keratomileusis (LASIK) today is the commonest corneal refractive surgery performed around the world.[1] As with every surgical procedure the post-operative complications of LASIK affect the patient satisfaction and outcome of the surgery. Superficial punctuate keratitis (SPK) in the form of superficial punctuate epithelial erosions are one of the earliest complications noted within hours after surgery in the early post-operative period.[2-5] It not only affects the patient satisfaction but can be an early sign of forth coming complications after LASIK. Though the SPKs as a part of post-LASIK dry eye often develops at around 6 months post-operatively, the pathogenesis behind the early post-operative SPKs is likely to be different.[2] Damage to the epithelium in such cases is likely to be due to intra-operative methods used to handle the corneal flap. Various pre-operative patient related factors and different intra-operative techniques play an important role.

Pre-operative factors are like an age of more than 40 years, hyperopia, greater corneal thickness, and surface drying during the microkeratome's pass have shown greater risk of corneal epithelial defects after LASIK.[5] Certain intra-operative factors like, use of anaesthetic eye drops, site of hinge of corneal flap, use of microkeratome or Femto Second (FS) laser, thickness of corneal flap, affect the incidence of corneal epithelial defects.

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An epithelial defect can increase the patient's risk of developing Diffuse Lamellar Keratitis (DLK) 24-fold, with subsequent flap striae and epithelial in-growth.[6] Hence, early identification of epithelial abnormalities post-LASIK and finding intra-operative factors responsible for the same is important. In present, blunt air cannulas and specialized cellulose sponges like the Weck-cel sponge are being used to manipulate the corneal flap. Weck-cel sponge is commonly used to absorb irrigating fluids and quell the cells. The bed and flap are swept with such lint-free sponges to clear the interface of epithelial and other debris.[5] A 27-G blunt cannula is often used to put corneal flap back in position after laser ablation.[7] In our study, we found that by using air cannula instead of Weck-cel sponge the incidence of SPK in the form of epithelial erosions can be reduced. This is the first study as per our knowledge to show changes in incidence of SPK post-LASIK by comparing two alternative methods to handle the corneal flap intra-operatively.

MATERIAL AND METHODS

This is a randomized prospective comparative study comprising of 192 eyes of 96 patients undergoing LASIK for myopia or myopic astigmatism in both eyes. Patients were selected for this study after obtaining approval from the institutional review board and ethical committee. An informed consent was taken from the patients. LASIK with femto second laser was performed on both the eyes, in which air-canula was used for one eye and Weck-cel sponge used for the other eye respectively. Two groups, Air canula group and the Weck-cel sponge group were divided. Using simple randomization with SAS software a randomized numerical list was generated for 96 patients prospectively, distributing each eye (right or left) of every patient randomly into either of these 2 groups.

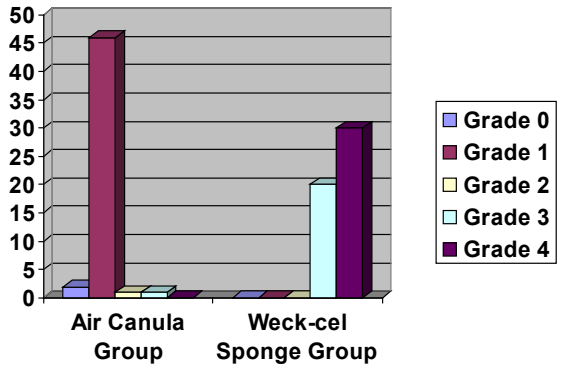
All patients underwent a thorough ophthalmic examination including Uncorrected visual acuity (UCVA), Best Corrected Visual Acuity (BCVA), slit lamp examination, dilated fundus evaluation using +90D and indirect ophthalmoscopy, corneal topography using the keratron scout analyser, wave front analysis using I-design (Abbot medical optics), Schirmers, tear film break-up time, pachymetry and specular microscopy. All patients were prescribed topical gatifloxacin 0.3% (Zymar, Allergan, USA) three times a day, one day prior to the surgery. All patient underwent a femtosecond assisted LASIK using the Intralase femto second (Abbott medical optics) and excimer laser (Abbott medical optics). No microkeratome was used. All the patients had a superior hinge and intra-operatively in the group 1 patients the flap was repositioned using the air canula and in group 2 patients the flaps was repositioned with the help of Weck-cel sponge. All patients were seen at the end of 2 hours after the procedure and the incidence of SPKs were noted and graded using the Oxford scheme as proposed by Bron, et al. by an independent observer who was not aware of the study protocol.[8] Patients were put on tapering doses of antibiotic and steroid combination for 15 days and lubricant for a month. All patients were followed up at the end of one week and one month.

STATISTICAL METHODS

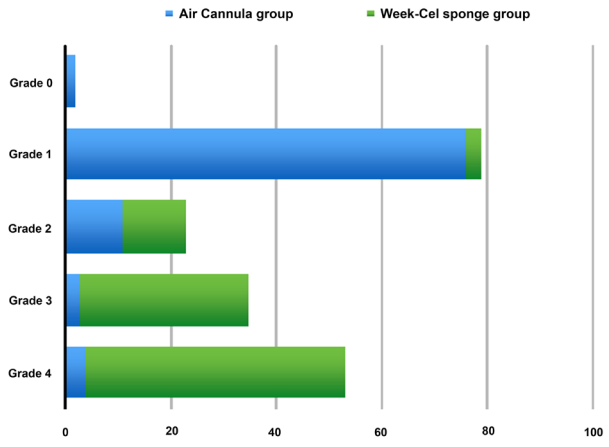
Statistical Analysis System (SAS) software was used for randomization of the eyes to either of the groups, Air canula group or the Weck-cel sponge group. The outcome measures in grades were expressed as percentage and compared. To find statistical association pertaining to clinical significance, the data was converted to a binary format as whether clinically significant (>or = grade 3 SPK) or not (<Grade 3 SPK). A Chi-square test was used with 1 degree of freedom to find which surgical technique had an association with higher grades of SPK.

RESULTS

The mean age of the study was 21+/-10 years. Out of total 192 eyes 51(26.8%) eyes showed Grade 4 SPKs of which 49(96%) belonged to the Weck-cel sponge group and 2(4%) eyes belonged to the air canula group. The number of eyes in Weck-cel sponge group with Grade 4 , Grade 3, Grade 2, Grade 1, Grade 0 SPKs were 49(51%), 32(33.3%), 12(12.5%), 3(3.1%) respectively. Similarly the number eyes in Air canula group with Grade 4 , Grade 3, Grade 2, Grade 1, Grade 0 SPKs were 24%), 4(4.1%), 11(11.45%), 76(79.1%), 2(2%) respectively. The number of eyes with clinically significant grades (Grade 4 and Grade 3) in Weck-cel sponge group was 81(84.3%) as compared with 7(7.2%) eyes of the Air canula group. (Graphs 1 and 2)



Graph 1: Incidence of SPKs in air cannula and Weck-cel sponge group.



Graph 2: Grades of SPK in both group.

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In order to study the association of both groups with clinically significant higher grades of SPK, Chi-Square test was used by considering the outcome as clinically significant if Grade 3 or Grade >3 (Figure 1). SPKs or clinically insignificant if Grade <3 (Figure 2) SPKs were present. The Chi-square test showed the Weck-cel sponge group was significantly associated with the clinically significant grades of SPK ($p<0.001$) at 1 degree of freedom. So the incidence of higher grades of SPKs in the Weck-cel sponge group is less probable to be due to a chance.

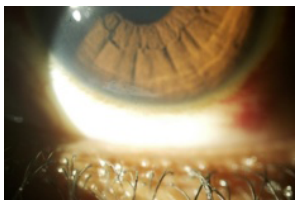

Figure 1: Showing grade 3 SPK.

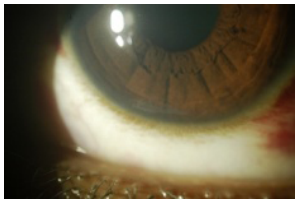

Figure 2: Showing grade 2 SPK.

DISCUSSION

SPKs occurring as a complication of LASIK have been previously described in context with post-LASIK dry eye and neurotrophic epitheliopathy.[9,10] Immediately after LASIK, 95% of patients report some dry eye symptoms.[11] The LASIK-induced change in corneal shape may affect the relationship between the eyelids and ocular surface and lead to abnormal tear distribution during blinking.[11-14] The main proposed cause of SPKs in post-LASIK dry eye is iatrogenic corneal nerve damage. LASIK disrupts both the dense sub-basal nerve plexus and stromal corneal nerves in the creation of the anterior stromal flap and excimer laser ablation of the cornea.[9]

Though with the use of femto-second laser the complications associated with the micro-keratome are reduced, an association of use of the laser with the early post-operative SPKs is yet to be determined. SPKs in such scenarios are mainly an outcome of chronic inflammatory environment of the cornea. Adding to which loss of corneal sensations for first few months can play a role in occurrence of late post-operative SPKs leading to a dry eye.[9] But whether any of these factors play any role in early pre-operative SPKs is yet to be proven. It is likely that mechanism behind the early pre-operative SPKs are related to immediate intra-operative events. In our case series, we found that SPKs can be found in early pre-operative stage in all LASIK operated cases but their severity differs based on type of instrumentation.

We came across that the incidence of Grade 4 and Grade 3 SPKs are higher with the use of Weck-cel sponge in the immediate post-operative period. Possible reason for the same could be the finely corrugated surface of the sponge which helps it in being porous and absorbing the excess fluid and keeping the corneal surface dry during surgery. Compared with the metal air cannula which happens to be smooth in its surface, handling of the corneal flap could yield lesser damage to the epithelial surface. Since the operative conditions and procedure undertaken were similar for both the eyes in all the cases, it is more likely that the structural properties of the surface of air cannula and the Weck-cel sponge plays important role in the incidence of early post-operative SPKs. Apart from SPKs, many patient related pre-operative risk factors have been associated with the post-operative epithelial defects.[15]

The intra-operative epithelial defects during LASIK have an association with the age of the patient and duration of use of contact lenses.[15,16] With age of the patient more than 40 years the chances of post-operative epithelial defects are more and the chances of the same are more in the other eye after occurrence in the fellow eye.[15,16] Intra-operative epithelial defects in the first eye is highly predictive of epithelial defects in the second eye of the same patient. Since this being a first study as per our knowledge to report difference in incidence of SPKs post-operatively after LASIK due to intra-operative factors, an association with pre-operative and patient related factors is what needs to be studied further. In this study, we found that using Weck-cel sponge to be associated with more SPKs in the immediate post-operative period and could affect the post-operative patient satisfaction. Instead an air cannula to manipulate the corneal flap intra-operatively could prevent SPKs with higher grades post-LASIK.

CONFLICTS OF INTERESTS

The authors declare that they have no conflicts of interests.

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Research

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Posterior Sub-Tenon Triamcinolone Injection for Chronic Macular Oedema Associated With Non-Ischemic Branch or Central Retinal Vein Occlusion

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ABSTRACT

Aims: To evaluate the effectiveness and safety of Posterior Sub-Tenon (PST) Triamcinolone Acetonide (TA) injection for persistent macular oedema associated with non-ischemic Central Retinal Vein Occlusion (CRVO) or Branch Retinal Vein Occlusion (BRVO) in non-vitrectomized eye.
Methods: Fourteen consecutive eyes of 14 patients characterized by macular oedema lasting more than 3 months and with a visual acuity of less than 20/40 were enrolled. Six eyes presented with BRVO, 8 eyes with CRVO. PST injection of 40 mg TA was performed in topical anaesthesia. All patients were phakic, and followed for at least 6 months. Snellen visual acuity converted to LogMAR units and anatomic responses were evaluated before, and at 1, 3, 6, and 12 (if required) months after injections and re-injection considered.
Results: In the BRVO group, mean foveal thickness was 548.2±49.50 µm preoperatively, and 452.8±56.2 µm and 280.8±62.5 µm at 1 and 12 month follow-up, respectively. Statistical analysis showed significant differences between preoperative and postoperative measurements ($p<.05$, paired t test) 3 months after injections. Improvement of visual acuity by at least 0.2 LogMAR was seen in 3(50%) of the 6 eyes. No re-injection was needed. In the CRVO group, mean foveal thickness was 543.7±34.4 µm preoperatively, and 283.0±29.0 µm and 234.8±23.6 µm at 1 and 12 month follow-up, respectively. Statistical analysis showed significant differences between preoperative and postoperative measurements ($p<.05$, paired t test). Improvement of visual acuity by at least 0.2 LogMAR was seen in 7 eyes (88%). Mean number of re-injection was of 2.1±0.3. Intraocular pressure elevation of 22 mm Hg or higher was found in 2/14 eyes (14%). Cataract progression was noted in 5/14 eyes (36%).
Conclusions: PST injection of TA appears to be as safe and effective treatment for chronic macular oedema associated due to both non-ischemic BRVO or CRVO, with a better efficacy in BRVO.

KEYWORDS: Branch/Central retinal vein occlusion; Chronic macular oedema; Triamcinolone; Posterior sub-Tenon injection.

ABBREVIATIONS: PST: Posterior sub-Tenon; TA: Triamcinolone Acetonide; CRVO: Central Retinal Vein Occlusion; BRVO: Branch Retinal Vein Occlusion; Anti-VEGF: Anti-Vascular Endothelial Growth Factor; IOP: Intraocular pressure; SEM: Standard Error of the Mean; ILM: Internal Limiting Membrane; LOCS II: Lens Opacities Classification System, version II.

INTRODUCTION

Macular oedema is the most common cause of visual loss among patients with Retinal Vein Occlusion (RVO).[1,2] The only proven treatment before the Anti-Vascular Endothelial Growth Factor (Anti-VEGF) intravitreal injection era consisted of grid pattern laser photoco-

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agulation which is based on the results of Branch Vein Occlusion Study (BVOS).[2] In the BVOS, patients received laser treatment when vision had been lower than 20/40 for at least 3 months and if there was no macular ischemia. The rationale for this waiting period was that one third of patients with retinal vein occlusion may have spontaneous resolution of macular oedema within this time span.[1-3] Grid laser treatment has also been advocated for macular edema in Central Retinal Vein Occlusion (CRVO). This therapy only had a positive effect on the edema, however not on visual acuity.[1]

Anti-VEGF intravitreal injection is nowadays widely considered as the first choice for retinal vein occlusion macular edema management with effective subsequent visual acuity improvement.[4,5] However the need of frequent administration, the risk of potential local and systemic complication and their high cost, unravelled the search of alternative treatment.[6]

Triamcinolone Acetonide (TA) is a corticosteroid that has been reported to be efficacious in the treatment of retinal vein occlusion induced macular edema when administrated intravitreally.[7,8] Nevertheless, intravitreal procedures may be associated with endophthalmitis, vitreous haemorrhage, retinal detachment, and high intraocular pressure. In some studies less invasive procedures such as Posterior sub-Tenon (PST) TA infusion[9] or TA injection in vitrectomized eyes[10] have been evaluated as a treatment for macular oedema associated with retinal vein occlusion.

In the present study we have evaluated the efficacy and safety of PST injection of TA in primarily non-vitrectomised eyes with severe macular oedema secondary to non-ischemic branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

MATERIALS AND METHODS

The study adhered to the tenets of Helsinki. We included 14 consecutive eyes of 14 patients, who had severe macular oedema secondary to non-ischemic branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) lasting more than 3 months after onset, with a visual acuity of less than 20/40 and without prior treatment. The patients were evaluated on the basis of central retinal thickness using a horizontal 5 mm Optical Coherence Tomography (OCT) scan through the macula (Stratus system, OCT Model 3000, software version 3.0; Carl Zeiss-Meditec, Dublin, CA, USA), Best Corrected Visual Acuity (BCVA), Intraocular pressure (IOP) and cataract progression as Lens Opacities Classification System, version II (LOCS II) classification system.[11] BCVA was obtained using Snellen charts and converted to LogMAR units. PST injection of TA injection (Kenacort A40, Dermapharm AG, Hünenberg, Switzerland) was performed in an outpatient setting. None of our patients had previous vitrectomy. After topical oxybuprocaine hydrochloride 4% had been instilled, a cotton tip soaked in 4% tetracaine was placed over the superotemporal quadrant for 1 minute as the patient was asked to look inferonasally. The upper eyelid was elevated manually and a 25 G needle was then passed through the conjunctiva and Tenon's capsule into the PST space, and 40 mg of TA was injected. Ofloxacin 3 mg/ml was instilled three times daily for 1 week. BCVA, central retinal thickness and IOP were assessed at 1, 3, 6, and 12 months after the injection or prior to these dates if the patient re-attended the clinic due to visual loss. Criteria for re-injections included worsening of macular oedema thickness on OCT defined as an increase of 100 microns or more coupled with worsening of the BCVA defined as a decrease of 2 or more lines after initial improvement following the first injection. These patients were then seen again after the second injection at the intervals described above to ascertain improvement both clinically and on OCT.

Third injections were performed if both BCVA and OCT worsened again during follow-up after the second injection. If patients showed no improvement after the first injection they continued to receive the standard treatment including anti-VEGF intravitreal injection and/or macular grid laser for BRVO patients *versus* clinical follow-up for CRVO patients.

Changes overtime in LogMAR visual acuity, central retinal thickness and IOP were compared using the *paired t test*. The differences between BRVO and CRVO groups in LogMAR visual acuity, central retinal thickness, IOP and other continuous variables were compared using the *Mann-Whitney U test*. Linear correlation between the number of required PST injections and cataract progression or IOP elevation, as well as with macular thickness and BCVA, was tested with the *Pearson correlation co-efficient*. Data were expressed with Standard Error of the Mean (SEM).

RESULTS

The patient characteristics of both groups are shown in Tables 1 and 2. Six patients were included in the BRVO group. The mean patient age was 64.3±4.2 years (range: 52 to 80 years) and the mean duration of the symptoms, according to patient history before TA injection, was 13.7±5.0 months (range: 3 to 24 months). Eight patients were part in the CRVO group. Mean age was 70.3±2.9 years (range: 59 to 81 years) and the mean duration of the disease was 7.6±2.6 months (range: 3 to 24 months). No statistically significant differences were found between groups regarding age *(P=0.15, Mann-Whitney test)*, or duration of the occlusion *(P=0.09, Mann-Whitney test)*.

BRVO Group

Data are summarized in Table 3. Patient 5 stopped attending our clinic 6 months after injection for personal reason. The mean follow-up period after injection was 9.0±3.3 months (range: 6 to 12 months). Mean foveal thickness was 548.2±49.0 µm preoperatively, 452.8±56.2 µm at 1 month follow-up,

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Patient	Age (years)	Duration (months)	Pre-VA (LogMAR)	Final VA (LogMAR)	Pre-OCT thickness (µm)	Final-OCT thickness (µm)	Follow-up (months)	Recurrence and date of re-injection
1	60	7	0.8	0.7	660	400	12	-
2	60	6	1.0	0.7	672	340	6	-
3	74	24	0.4	0.1	439	250	12	-
4	52	3	1.3	0.1	630	190	12	-
5	60	24	0.5	0.5	400	232	6	-
6	80	18	0.6	0.5	488	583	6	-

Table 1: Baseline and follow-up data for BRVO patients treated with posterior sub-tenon triamcinolone injection. Duration from onset of visual impairment to injection. VA: Visual acuity.

Patient	Age (years)	Duration (months)	Pre-VA (LogMAR)	Final VA (LogMAR)	Pre-OCT thickness (µm)	Final-OCT thickness (µm)	Follow-up (months)	Recurrence and date of re-injection
1	64	3	0.8	0.2	630	150	12	2 and 4 months
3	81	7	0.4	0.1	550	175	12	-
4	72	24	0.4	0.1	431	275	12	6 months
5	59	3	0.7	0.1	670	340	12	-
6	81	3	1.0	0.5	500	265	12	3 and 6 months
6	63	9	0.6	0.4	691	224	12	6 months
7	68	4	0.9	0.2	484	200	12	6 and 11 months
8	74	3	0.4	0.5	480	300	12	1 and 3 months

Table 2. Baseline and follow-up data for CRVO patients treated with posterior sub-tenon triamcinolone injection. Duration from onset of visual impairment to injection. VA: Visual acuity.

Time point	Foveal Thickness (µm)		Visual Acuity (LogMAR)		Pearson correlation		IOP (mm Hg)	
	Mean±SEM	*P* value	Mean±SEM	*P* value	R^2	*P* Value	Mean±SEM	*P* value
Baseline (n = 6)	548.2±49.0	NA	0.77±0.14	NA	0.66	0.05	16.2±1.3	NA
1 month (n = 6)	452.8±56.2	0.07	0.48±0.11	0.07	0.40	0.18	15.8±0.7	0.82
3 month (n =6)	340.0±5.8	0.01	0.42±0.13	0.05	0.25	0.67	20.0±5.1	0.44
6 month (n=3)	390.3±105.3	0.01	0.33±0.18	0.05	0.89	0.21	18.0±1.1	0.63
12 month (n = 3)	280.8±62.5	0.01	0.30±0.20	0.04	0.92	0.18	18.0±2.0	0.50

Table 3: Summary of changes in foveal thickness, visual acuity and intraocular pressure (IOP) for BRVO. Differences were analyzed with the paired *t* test and considered significant when $P<0.05$. Foveal thickness and visual acuity was correlated by the Pearson R^2 correlation test and considered significant when $P<0.05$.

340.0±5.8 µm at 3 month follow-up, 390.3±105.3 µm at 6 month and 280.8±62.5 µm at 12 month follow-up. Statistical analysis showed significant and sustained decreased in foveal thickness between preoperative and postoperative measurements from the third months after PST injection ($p>.05$, at 1, 3, 6 and 12 months, paired *t* test) without need of further injection. Visual acuity improved also significantly 3 months after injections from preoperative 0.77±0.14 LogMAR (range: 1.3 to 0.4) to 0.30±0.20 LogMAR (range: 0.7 to 0.1; $p=0.04$, paired *t* test) at 12 month follow-up. Improvement of visual acuity by at least 0.2 LogMAR was seen in 3(50.0 %) of the 6 eyes. Time of injection (duration of the disease) did not influence final visual acuity

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(*Pearson correlation co-efficient, r^2=0.01, p=0.84*).

CRVO Group

Data are summarized in Table 4. The mean follow-up period after injection was of 12 months. Average re-injection number was 2.1±0.3. Mean foveal thickness was 543.7±34.4 µm preoperatively, 283.0±29.0 µm at 1 month follow-up, 372.0±60.1 µm at 3 month follow-up, 255.±22.4 µm at 6 month and 234.8±23.6 µm at 12 month follow-up. Statistical analysis showed significant differences between preoperative and post-operative foveal thickness measurements ($p<.01$, at 1, 3, 6 and 12 months, paired *t* test). Visual acuity improved significantly from preoperative 0.65±0.08 LogMAR (range: 1.0 to 0.4) to 0.26±0.06 LogMAR (range: 0.5 to 0.1; *p<0.01*, paired *t* test) after 12 months of follow-up with a non-significant value at 3 months which correspond to the mean interval 4.0±2.0 months before a second re-injection was needed. Improvement of visual acuity by at least 0.2 LogMAR was seen in 7(87.5%) of the 8 eyes.

Duration of the disease did not influence final visual acuity (*Pearson correlation co-efficient, r^2=0.14, p=0.18*).

No statistically significant differences were found between BRVO and CRVO groups regarding foveal thickness before and after treatment *(p=1.0, p=0.13, respectively, Mann-Whitney test),* or visual acuity before and after treatment *(p=0.55, p=0.16, respectively, Mann-Whitney test)*. In 6(0.75%) eyes of the CRVO group, additional injections were performed because of recurrent macular edema, and 4(50%) of those eyes required a third injection. Intraocular pressure elevation of 22 mm Hg or higher was found in 2/14 eyes (14%, CRVO group) but were not associated with the number of injections *(Pearson correlation co-efficient, r^2<0.01, p>0.97*). The IOP in those eyes could be controlled with topical low-pressure medication. All eyes were phakic and cataract progression was noted in 5 eyes (1 eye BRVO and 4 eyes CRVO), of which patient 3 of the CRVO group had cataract extraction 6 months after the injection. Cataract progression was not correlated with the number of injections *(Pearson correlation co-efficient, r^2=0.04, p=0.48*).

DISCUSSION

Several studies have suggested various invasive options to treat CRVO and BRVO including intravitreal tissue plasminogen activator,[12,13] radial optic neurotomy,[14] sheathotomy,[15] macular decompression using vitrectomy and Internal Limiting Membrane (ILM) peeling,[16] and laser induced chorioretinal anastomosis.[17] Intravitreal TA has been shown to be effective in treating macular oedema due to CRVO and BRVO.[8,9,18] However, intravitreal injections carry considerable risks, including acute infectious endophthalmitis[19] and pseudopendophthalmitis.[20]

PST injection seems to be less effective than intravitreal TA or grid laser photocoagulation for treatment of macular edema in BRVO.[21] However, PST of TA on the other hand may give rise to intravitreal TA concentrations comparable to the level achieved by intravitreal injection[22] without incurring the same risks. TA delivered *via* the posterior sub-tenon route has previously been widely used for treating macular edema due to Irvine-Gass Syndrome,[23] diabetes,[24] and uveitis.[25] Lin, et al. reported the clinical outcome of PST of TA in the early treatment of macular edema in CRVO lasting for not more than 15 days prior to the injection.[26] It was concluded that early injections are effective in reversing macular edema and improving visual acuity. However, since one third of patients with retinal vein occlusion may have spontaneous resolution of macular edema within the first 3 to 4 months,[1-3] we performed the sub-tenon injection of TA only after 3 months in the present study.

Our results showed that this form of treatment is effective in reversing macular oedema and improving visual acuity in retinal vein occlusion even after the presence of macular edema for several months. Those finding are in keeping with some recent reports.[27,28] However our study is the first one to compare PST injection between BRVO and CRVO patient. This treatment might be more effective in BRVO than CRVO patient, as only one injection was required in BRVO patients. In the CRVO group, while OCT and visual acuity values improved during the first months, patients often necessitated a second or a third injection after the transient effect of a PST. Compared to the CVOS data, where only 20% of the eyes with an initial VA ranging from

Time point	Foveal Thickness(µm)		Visual Acuity (LogMAR)		Pearson correlation		IOP	
	Mean±SEM	*P* value	Mean±SEM	*P* value	R^2	*P* value	Mean±SEM	*P* value
Baseline (n = 8)	543.7±34.4	NA	0.65±0.08	NA	0.02	0.36	15.8±0.7	NA
1 month (n = 8)	283.0±29.0	<.01	0.38±0.03	<.01	0.23	0.11	18.9±1.5	0.11
3 month (n = 8)	372.±60.1	<.01	0.43±0.15	0.11	0.34	0.06	17.6±1.5	0.40
6 month (n = 8)	255.0±22.4	<.01	0.34±0.07	<.01	0.27	0.12	15.3±1.0	0.69
12 month (n = 8)	234.8±23.6	<.01	0.26±0.06	<.01	0.25	0.16	17.9±1.3	0.27

Table 4: Summary of changes in foveal thickness, visual acuity and intraocular pressure (IOP) for CRVO. Difference were analyzed by the paired *t* test and considered significant when *P*<0.05.

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0.4 to 1.0 LogMAR improve to 0.4 or better, our results showed that 75% of the eyes (6/8) improved to that level.

Although the IOP rise in our study (2 eyes, 14%) is better compared to the IOP after intravitreal injections (20-33%),[3,7,18,24] it could be still argued that the incidence of intraocular pressure elevation is very high, and that TA injections should thus only be used in exceptional circumstances. However, in view of the devastating long-term effects of retinal vein occlusions on visual acuity we believe that these side effects can be managed either medically or surgically, and that this form of treatment should be evaluated further given the ease of injection, the low costs as well as the low risks of its application in an outpatient setting.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DISCLOSURE

The authors have no financial interest in the materials or methods used in this study.

CONSENT

The patient has provided written permission for publication of the manuscript.

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Mini Review

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Visual Perception: Scientific Lessons Learned From "The Dress" Phenomenon

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ABSTRACT

Our visual percept across the population is relatively similar with little or no ambiguity in what we perceive. A red flower on a green plant is still perceived as red flower by everyone. So when social media threw up a picture of a dress which was not agreed by everyone about the colour, it created an exception to our general perceptual stability and created an enigma for visual scientists to explain this apparent contradiction to relatively stable percept. This mini review aims to explain "the dress" phenomenon and provide theories explaining this illusion that has confounded many vision scientists.

KEYWORDS: Colour; Illusion; Visual perception.

INTRODUCTION

Our perception of colour is not a property of the visualised object, rather the consequence of the distribution of reflected light that the visual system interprets and assigns as a colour of the object. However, our percept of colour is remarkably stable, given the wide variation in luminance conditions. This phenomenon is called colour constancy[1] and is attributed to adaptation mechanisms within the visual system. This phenomenon is also the reason why the interpretation of the dress as interpreted through social media during a Scottish party became somewhat of a surprise when people started reporting the dress as being of two separate colours blue-black or white and gold. So how can the perception of a relatively simple coloured object be so different among members of the human population or in other words how the brain can get it so wrong? This mini review aims to review and explain this phenomenon.

How different is the perception of the dress amongst the general population. In an online experiment by Lafer-Sousa et al[2] conducted in 1401 subjects. The authors reported that 57% perceived the dress as blue-black, 30% saw white-gold, 10% brown-gold and the rest could switch between any combinations. However, when the same experiment was conducted in laboratory condition on calibrated monitor and the subjects were asked to match the colours of the dress to calibrated Maunsell chips, it was found that the percept is actually a continuum rather than just blue-black or yellow gold.[3] This leads us to our first question: are there fundamental differences in the make-up of our visual system that could result in this varied perception. The first stage of our perception of colour starts from the cone photoreceptors at the back of the eye. There are three types of cones: each selective for specific wavelengths and are names as red, blue and green cone photoreceptors. The numbers and the distribution of these photoreceptors vary between each individual,[4] however our perception of the colour is the same across the population as our brain weights the inputs coming from the photoreceptors and allocates them for a constant perception of colour. These differences are unlikely to provide an explanation for the dress phenomenon as there are rarely any differences in our perception of naturally coloured objects even though there are small variations in colour naming[5] amongst human population.

The second theory is based on how our sense of colour is influenced by other factors

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in particular the background. The picture of the dress is somewhat different from natural images. Our vision is calibrated to view within a very narrow band of wavelengths across the entire electromagnetic spectrum (approximately 380- 740 nm) available to us. Everything we view is within this spectrum. Our first clue about the percept comes from the image itself, the image in question is not from natural surroundings. It was taken using camera phone and appears to be a bleached image as evident from the background which is exceptionally bright. What does the background mean for our perception. Winkler et al[6] conducted experiments with photographs and what people perceived when the background information was filtered and overlayed onto the image. It is worthwhile noting that by applying a blue background, the percept shifted completely to white-gold in a majority of observers (95%) and to blue-black when the background was shifted to yellowish hues. This result points to the most likely explanation on why people perceive such a different colour.

Our visual system is designed to maintain a fair degree of consistency in its perception of colour, despite the myriad of change in the reflectance and illumination properties for e.g. we perceive a red apple as red whether it is a sunny day, cloudy day, inside or outside. This is achieved by factoring in the background illumination and the reflectance from the object. In the dress phenomenon, the unusually bright and ambiguous background means some people's brains allocate as the dress being viewed from a bluish background and hence a percept of white and gold, while others perceive it has blue-black as a result of the brain interpreting the background being from a bright day.

Although this seems like a valid explanation of the reported phenomenon, there are some unanswered questions that still remain. If the way we perceive is determined by how we interpret the background why should there be a continuum of percepts rather than a bimodal distribution of extreme case responses. More recently, there has been of MRI study[7] looking at brain activation regions with the dress phenomenon and asking if the varying percept is a direct result of activation of different networks within the brain. The yellow-gold responders had more activation in their middle frontal gyrus, inferior and superior parietal lobules and inferior frontal gyrus suggesting that there is significant involvement of top-down networks in the perception of this illusion. These networks are also involved in attentional mechanisms.

The dress phenomenon provides a rare case of discovery on how the human brain works as a result of viral social media observations. More scientific studies are warranted to determine how the brain interprets the background information and what the neurophysiological basis of such a phenomenon is.

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Case Report

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Fine Needle Diathermy and Intraestromal Bevacizumab: A Combined Treatment for Corneal Neovascularization

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ABSTRACT

Purpose: The cornea is an avascular and transparent tissue due to a high level of anti-angiogenic molecules. Any alteration of the balance between angiogenic and anti-angiogenic molecules may cause corneal neovascularization which may lead to reduced visual acuity. Now-a-days there is a variety of treatments for corneal neovascularization. The aim of the present paper is to evaluate the efficacy and security of intraestromal bevacizumab combined with fine needle diathermy on corneal neovascularization.
Method: A 44-year-old patient presented with relapsing corneal ulcer and corneal inferior neovascularization resistant to conservative treatment, which led us to treat with fine needle diathermy and intraestromal bevacizumab.
Result: One week after the treatment, some intraestromal hemorrhages still remained but epitelial edema had solved, observing afterwards a complete resolution of hemorrhages and angioregression of treated corneal new vessels.
Conclusion: Fine needle diathermy associated with intraestromal bevacizumab should be considered as a simple, effective and low cost therapeutic option for corneal neovascularization.

KEYWORDS: Diathermy; Bevacizumab; Corneal neovascularization; New vessel.

INTRODUCTION

The cornea, supplied by the ophthalmic artery throught the ciliary arteries that come to an end near the limbus in the so called pericorneal plexus, is an avascular and transparent tissue. Under normal conditions, such transparency is due to the high level of anti-angiogenic molecules and thus a low level of angiogenic molecules. Any alteration of this balance may cause corneal neovascularization, defined as the growth of new blood vessels from previous capillaries and venules from the pericorneal plexus, which invade the cornea leading to inflammation and chronic corneal edema, lipidic exudation, estromal hemorrhage and corneal scarring. Subsequently, corneal neovascularization may lead to reduced visual acuity and worsening of penetrating queratoplasty prognosis after the alteration of the well-known immune privilege of the cornea.[1-4]

Prevalence of corneal neovascularization in the United States is known to be 4.14%, presenting 12% of the cases in association with visual loss.[1,2] The leading causes of corneal neovascularization are known to be infections, contact lens misuse and the vascular response associated to corneal transplantation.

Now-a-days there is a variety of treatments for corneal neovascularization such as topical corticoesteroids and non-steroidal anti-inflammatories, anti-angiogenic therapies such as bevacizumab, ciclosporine A, diathermy direct occlusion of vessels, topical ascorbic acid, criotherapy, photodynamic theraphy, laser photocoagulation and superficial queratectomy.[1,5]

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The aim of the present paper is to evaluate the efficacy and security of intraestromal bevacizumab combined with fine needle diatermy of corneal neovascularization.

CLINICAL CASE

A 44 year-old female presents with lagophtalmos in her right eye (RE) secondary to post-operative facial palsy after acoustic neuroma. Previously treated with hialuronic acid injections in the upper lid, lateral tarsorrhaphy and gold weight eyelid implant, the patient presented with relapsing corneal ulcer and corneal inferior neovascularization resistant to conservative treatment, which led us to treat with fine needle diathermy and intraestromal bevacizumab. Previous topic anaesthetic, intraestromal bevacizumab 2.5 mg/0.1 ml injections were performed with 30 gauge needle along corneal periphery between III and X hours followed by individual cauterization of new vessels located at VI, VII and IX hours with diathermy pencil for phacoemulsification equipment, coagulation mode and fine needle of 27 gauge and 40-50% power until light whitening of corneal estroma. Topic moxifloxacin drops were prescribed during 7 days. First day after, estromal hemorrhages and light epitelial edema on the sites of diathermy needle insertion were found (Figure 1). One week after, some intraestromal hemorrhages still remained but epitelial edema had already solved (Figure 2), observing afterwards a complete resolution of hemorrhages and angioregression of treated corneal new vessels (Figure 3) without ocular perforation.

DISCUSSION

Corneal neovascularization secondary to a disbalance tipped toward angiogenic factors is a vision threatening complication. The aim of corneal neovascularization treatment is to prevent vascular endothelial cells from proliferating and migrating in response to pro-angiogenic stimuli and thus, the regression of stablished vessels.

Choosing the best treatment depends on the maturation of new vessels. Mature or stablished vessels do not depend on angiogenic mediators and therefore require surgical intervention such as fine needle diathermy. Nonetheless, angiogenic mediators blockage help preventing new vessels to grow if the harmful stimuli persists. Other therapeutic options for mature new vessels are argon laser photocoagulation, photodynamic therapy and cryotherapy.[5]

First line therapy in every day practice for corneal neovascularization are topical corticosteroids, inhibiting the associated inflammation but not the underlying angiogenic stimuli, effect that was firstly reported in 1950.[1] Nevertheless, corticosteroids are mostly effective when administered within the first 24 hours after corneal injury.[1,5,6]

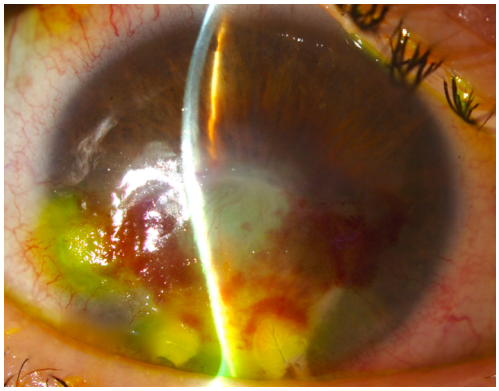

Figure 1: First day after treatment.

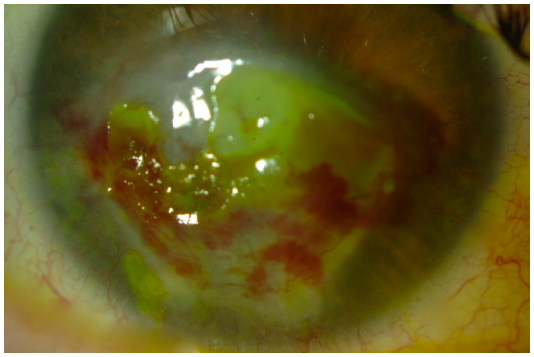

Figure 2: One week after treatment.

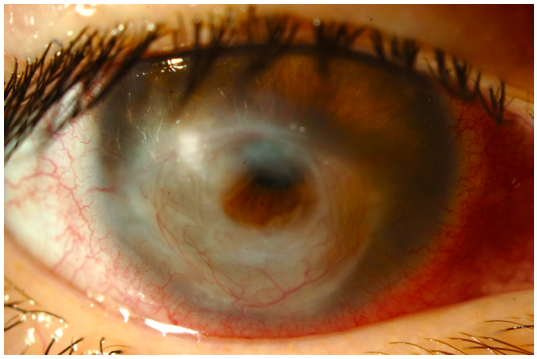

Figure 3: Complete resolution of hemorrhages and angioregression of treated corneal new vessels.

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Vascular endotelial growth factor (VEGF) plays an important part in pathological corneal neovascularization due to his role in the activation, proliferation, migration and vascular endothelial cells differentiation.[5] Isoform VEGF-A is known to be the most important hemangiogenesis mediator, playing also a significant role in linphangiogenesis.[1,3] Bevacizumab, initially approved by the US Food and Drug Administration (FDA) to treat metastatic colorectal cancer, is a humanized murine monoclonal antibody capable of blocking all VEGF-A isoforms and therefore inhibiting new vessels abnormal formation and diminishing vascular permeability.

Current anti-angiogenic therapy indications include corneal neovascularization, aggresive corneal neovascularization in recurrent pterygium and limbal stem cell deficiency, corneal and iris neovascularization secondary to neovascular glaucoma and corneal graft rejection. Reported Bevacizumab administration ways for corneal neovascularization are topical (5-25 mg/ml, 2-5 times a day), sub-conjuntival injection (1.25 mg/0.05 ml-5 mg/0.2 ml monthly and repetedly if necessary) and intrastromal injection (25 mg/ml: 100 ug per new vessel).[1]

Anti-angiogenic drugs such as Bevacizumab are known to be more effective in small and medium size vessels recently developed due to the more active release of VEGF and greater angiogenic stimuli. It might not be effective in patients where angiogenesis also depends on different citokines not blocked by Bevacizumab.[1]

Previous studies have shown the efficacy of topical and sub-conjunctival bevacizumab for corneal neovascularization. The disadvantages of these ways of administration are the diminished penetration and absorption of the drug through the intact corneal epithelium due to its high molecular weight (149 kDa) and the lacrimal clearance, the potential effects of sub-conjuntival administration such as thinning and erosion of the corneal epithelium, conjunctiva and sclera and the high costs of topical preparations.[2,5] Nevertheless, higher scientific evidence studies would be needed in order to determine the most efficient way of administration and the dose required to reach and adequate therapeutic concentration and the maximal effect of Bevacizumab for the treatment of corneal neovascularization. Compared to topical corticosteroids, studies do not report important side effects, otherwise bebacizumab tends to be used as adjuvant to corticosteroids rather than to replace them.[1]

Intrastromal bevacizumab for corneal neovascularization studies have shown hopeful results[5,7-9] due to its optimal intracorneal therapeutic levels and it also guarantees a better compliance compared to other ways of administration.[4] Nontheless should the security of intraestromal injection be studied. Side effects such as intracorneal hemorrhage, spontaneously absorbed and without sequelae[4,9] have been reported. Systemic side effects have not been reported.[5,7-9]

Few options for the treatment of corneal mature new vessels are available because its vascular wall covered by pericites do not depend of VEGF.[6] Fine needle cauterization of afferent and efferent vessels was described by Pillai et al[6] for the treatment of 14 patients with corneal neovascularization, obtaining the occlusion of all the vessels in 8 patients, 75% of the vessels in 4 patients and 50% in 2 patients. Four patients required to be retreated. Intraestromal haemorrhages in 3 patients and fine crystalline corneal deposits in one patient, all spontaneously resolved, were reported and no ocular perforation occured in any case.[6] Intraestromal haemorrhage is known to occur when the efferent vessel is cauterized before the afferent one, nevertheless diathermy allows the occlusion of both vessels if they are close one another. Fine needle diathermy is a useful, effective, safe and low cost technique for the treatment of stablished or mature corneal new vessels. This technique can also be performed under topical anesthesia.[6] Wertheim et al[10] showed in 2007 a modified technique using a finer and more flexible electrolysis needle which produces a direct thermic cauterization instead of diathermy. They showed the occlusion of all the new vessels in 3 patients with corneal neovascularization after 8 months of treatment but 2 of them required to be retreated without complications.[6]

Fine needle diathermy of corneal new vessels attract pro-angiogenic inflammatory cells. Therefore, our aim was to moderate the angiogenic stimulus caused by mature new vessels cauterization through the use of intraestromal Bebacizumab and acting simultaneously over actively growing new vessels. Koenig et al[5] reported a statistically significant regression of mature corneal new vessels treated with fine needle coagulation associated to topical bevacizumab (5 mg/mL) 5 times a day during at least 4 weeks in 14 of the 16 patients studied. They concluded that diathermy combined with topical anti-VEGF was a safe and well tolerated treatment for mature corneal new vessels.[5] Pillai et al[6] reported the occlusion of all mature corneal new vessels in 57.1% of patients using fine needle diathermy as single treatment while Koenig et al[5] obtained the occlusion of all new vessels in 68.8% of patients using topical anti-VEGF combined with diathermy.[5] This difference probably belongs to the additional use of bebacizumab.

Corneal neovascularization treatment and prevention is a challenge for ophthalmologists due to its significant impact in public health. Traditionally, the treatment of corneal neovascularization was based on corticosteroids, being its response variable. Fine needle diathermy associated with intraestromal bevacizumab allows corneal new vessels regression and should be considered as a simple, effective and low cost therapeutic option for corneal neovascularization. Prospective, double blind, randomized and controlled clinical trials would be needed in order to prove long-term efficacy and security of this therapeutic combination.

PATIENT CONSENT

The patient has consented to the submission of the case report

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entitled "*Fine needle diathermy and intraestromal Bevacizumab: A combined treatment for corneal neovascularization*" for submission to The Ophthalmology Open Journal.

CONFLICTS OF INTEREST

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in the manuscript entitled "*Fine needle diathermy associated with intraestromal Bevacizumab injection: A combined treatment for corneal neovascularization*".

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Research

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Microperimetry in Optic Neuritis

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ABSTRACT

Aim: To evaluate microperimetry as a tool for visual field assessment in optic neuritis and compare it with standard automated perimetry.
Methods: A case-control study was conducted at a tertiary eye care centre in India. Ten cases of unilateral optic neuritis and 10 healthy controls underwent a detailed ophthalmic evaluation and visual field testing at presentation and 1 month and 3 months follow-up. Visual fields were charted using both the standard automated perimeter (10-2 and 30-2 programs) and microperimeter (central 20 degree program) at each visit.
Results: The visual acuity at presentation of the affected eye, fellow eye and control eyes was 0.27±0.19, 0.93±0.14 and 0.94±0.17 respectively. The affected eye visual acuity improved significantly to 0.89±0.24 (p<0.001) at the 3 months follow-up visit. The mean sensitivity thresholds of 10-2 visual field test at presentation were 14.16±11.51, 30.40±1.98 and 31.04±1.95 respectively of which the affected eye showed a significant improvement over 3 months to 28.90±8.36 (p<0.001). The mean sensitivity thresholds of 30-2 visual field test at presentation were 12.88±10.32, 26.03±2.59 and 27.99±2.31 respectively of which the affected eye and fellow eye showed a significant improvement over 3 months to 26.02±7.54 (p<0.001) and 27.86±1.77 (p<0.03) respectively. The mean sensitivity thresholds of microperimetry 20 degree visual fields at presentation were 5.60±7.32, 16.54±1.46 and 17.30±1.64 respectively of which the affected eye showed a significant improvement over 3 months to 16.41±4.87 (p<0.001). Microperimetry fields did not improve completely at 1 month unlike the 10-2 fields and correlated strongly with visual recovery. The 30-2 fields were the most sensitive to determine subclinical affliction of the fellow eyes in optic neuritis.
Conclusion: Microperimetry is a sensitive test to evaluate visual fields in optic neuritis and corresponds with visual recovery. The larger 30 degree module is still indispensible for visual field assessment in optic neuritis.

KEYWORDS: Microperimetry; Optic neuritis; Visual fields; Perimetry; Microperimeter.

ABBREVIATIONS: IEC: Institutional Ethics Committee; ANOVA: Analysis of variance; HVF: Humphrey Visual Field.

INTRODUCTION

Optic neuritis negatively impacts various visual functions including visual fields. Varying patterns of field loss have been reported, ranging from altitudinal, arcuate and centrocaecal to diffuse and even unilateral hemianopic field defects.[1-8]

Nearly all studies on visual fields in optic neuritis have been done using the standard automated perimetry, which has inadequate compensation for eye movements and this is particularly important in cases of poor vision and central scotomas such as those seen in optic neuritis. Microperimetry is a novel diagnostic modality that overcomes this limitation by continuously tracking the patient's fundus during stimulus projection. Eye movement detected by the machine either causes a pause in stimulus projection, or alteration the position of stimulus

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projection to match the amount of eye excursion. Additionally, the microperimeter also overlays the sensitivity map on the fundus image providing a visually appealing result with good structural correlation.[9-23]

There are limited studies of microperimetry in optic neuritis and only one comparing it to the standard perimetry.[24,25] This study evaluates microperimetry as tool for visual field assessment in optic neuritis and compares it with the standard automated perimetry.

METHODS

A prospective case control study was conducted at a tertiary eye care hospital in India after prior approval from the Institutional Ethics Committee (IEC). Ten consecutive cases of optic neuritis and 10 controls were enrolled into the study after written informed consent. The inclusion criteria for cases was the presence of acute unilateral optic neuritis diagnosed clinically (sudden onset diminution of vision in one eye of less than 2 weeks duration with or without optic nerve head changes and/or pain on eye movements preceding the vision loss in the presence of relative afferent papillary defect) in the absence of any other ocular or neurological pathology likely to affect fields. Cases were excluded if they were bilateral, had a previous episode of optic neuritis, were aged less than 18 years and/or had a Snellen's visual acuity worse than 6/60. Controls recruited were healthy individuals aged above 18 years with no known ocular or neurological disease. Cases or controls were excluded if they did not consent to the study or were lost to follow-up.

The subjects underwent a comprehensive evaluation including a detailed clinical history and examination (neurological and ophthalmic) followed by visual fields and microperimetry. Visual acuity was assessed using the Snellen's chart, visual fields by the 10-2 and 30-2 protocols on the Humphrey visual field analyzer (Carl Zeiss Meditec AG, Germany) as well as the central 20 degrees algorithm on the MP-1 microperimeter (Nidek, Japan). The order of these field tests was selected randomly. Visual fields on the microperimeter were performed using a 4-2 threshold strategy with an initial attenuation of 10 decibel-milliwatt (Dbm) and Goldmann III sized stimulus of white color, projected for 200 ms with a red cross fixation target of 7 degrees diameter.

To negate the effect of learning curve on visual field assessment, visual fields were repeated daily in both eyes till two identical fields on two consecutive days were obtained. These fields were then chosen for the study.

Patients were followed at 1 and 3 months after the initial presentation for visual parameters and field testing. Controls also underwent the Humphrey 10-2 and 30-2 field tests and microperimetry using the same settings as cases.

Statistical analysis was performed using SPSS 13.0 software (IBM Corporation, Armonk, NY, USA). For the purpose of analysis, the study population was divided into 3 groups; A (Eyes clinically diagnosed to be affected by optic neuritis n=10), B (Fellow, apparently unaffected eyes in unilateral cases, n=10) and C (Eyes of normal healthy controls; n=20). Comparison of variables was done at all hospital visits between the three groups, and over time for each group. Independent and paired samples *t*-test, Analysis of variance (ANOVA), Pearson's chi square test, Mann-Whitney test and the Friedman test were used as appropriate. A $p<0.05$ was considered statistically significant.

RESULTS

The demographic details of the cases and control groups are summarized in Table 1. There was no statistically significant difference with regard to demography between cases and controls. The duration of optic neuritis at presentation was 6±2.6 days with a range of 1-10 days.

	Patients (n=10)	Controls (n=10)	*p*-value
Age (years) (Mean±SD) (Range)	25.7±2.8 (18-38)	27.8±2.4 (25-32)	0.48 (independent sample *t*-test)
Sex Male Female	4 (40%) 6 (60%)	7 (70%) 3 (30%)	0.134 (Pearson chi square test)

Table 1: Demographic profile of cases and controls.

Mean visual acuity was reduced in affected eyes at presentation, being significantly lower than that of fellow eyes and controls. Statistically significant improvement occurred at both 1 month and 3 month follow-ups. However, at 1 month follow-up, the visual acuity was still significantly lower than that of controls. Vision in fellow eyes was not significantly different from that of controls at any visit, and did not show any significant change over time (Table 2).

The mean sensitivity of the central visual field as measured by Humphrey visual field (HVF) 10-2 was significantly reduced at presentation in affected eyes when compared to fellow eyes and controls. This improved significantly by 1 month after presentation and reached near normal levels and did not improve significantly thereafter. The mean sensitivity of fellow eyes was comparable to that of controls at all visits (Table 3; Figure 1). The pattern deviation and change (within and between groups) for HVF 10-2 mean defect was similar to that discussed for HVF 10-2 mean sensitivity (Table 4).

On Microperimetry, the mean sensitivity (central 20 degrees of the visual field) of affected eyes was significantly lower at presentation as compared to fellow eyes and controls, and improved significantly by 1 month follow-up. However, at 1 month, the mean sensitivity was still significantly lower than that of controls. Further changes in mean sensitivity over time were not statistically significant. The mean sensitivity of fellow eyes was not affected at any visit in comparison to controls (Table 5;

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		At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (n=10)	Decimal scale (Mean±SD)	0.27±0.19	0.72±0.26	0.89±0.24	$p(A_0,A_1)$: <0.001 $p(A_1,A_3)$: 0.012
Group B (n=10)	Decimal scale (Mean±SD)	0.93±0.14	0.92±0.18	1.01±0.14	$P(B_0,B_1)$: 0.755 $p(B_1,B_3)$: 0.088
Group C (n=20)	Decimal scale (Mean±SD)	0.94 ± 0.17			
p value(for intergroup differences)		$p(A_0,B_0)$: <0.001 $p(A_0,C_0)$: <0.001 $p(B_0,C_0)$: 0.91	$p(A_1,B_1)$: 0.07 $p(A_1,C_0)$: 0.02 $p(B_1,C_0)$: 0.85	$p(A_3,B_3)$: 0.15 $p(A_3,C_0)$: 0.89 $p(B_3,C_0)$: 0.38	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 2: Visual acuity changes and trend.

	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean ± SD)	14.16±11.51	28.55±8.32	28.90±8.36	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.468
Group B (Mean ± SD)	30.40±1.98	32.04±1.61	31.56±1.76	$p(B_0,B_1)$:0.085 $p(B_1,B_3)$:0.344
Group C (Mean ± SD)	31.04±1.95			
p value (for intergroup differences)	$p\ (A_0,B_0)$: 0.001 $p\ (A_0,C_0)$: <0.001 $p\ (B_0,C_0)$: 0.328	$p\ (A_1,B_1)$: 0.084 $p\ (A_1,C_0)$: 0.158 $p\ (B_1,C_0)$: 0.373	$p\ (A_3,B_3)$: 0.212 $p\ (A_3,C_0)$: 0.545 $p\ (B_3,C_0)$: 0.475	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 3: HVF 10-2 Mean threshold sensitivity changes and trend.

	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean±SD)	-20.87±12.13	-6.06±8.71	-5.74±8.42	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.53
Group B (Mean±SD)	-4.02±1.72	-2.49±1.88	-3.04±1.82	$p(B_0,B_1)$:0.09 $p(B_1,B_3)$:0.19
Group C (Mean±SD)	-7.27±1.84			
p value (for intergroup differences)	$p(A_0,B_0)$: 0.002 $p(A_0,C_0)$: <0.001 $p(B_0,C_0)$: 0.109	$p(A_1,B_1)$: 0.192 $p(A_1,C_0)$: 0.071 $p(B_1,C_0)$: 0.650	$p(A_3,B_3)$: 0.250 $p(A_3,C_0)$: 0.148 $p(B_3,C_0)$: 0.871	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 4: HVF 10-2 Mean defect: changes and trend.

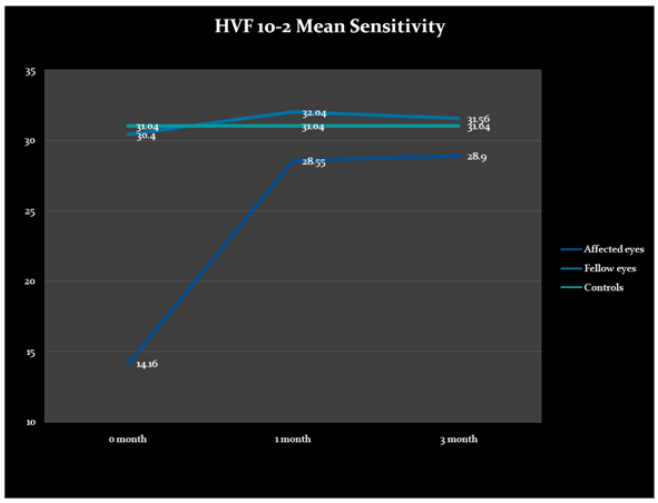

Figure 1: Graphical trend of change in HVF 10-2 mean sensitivity.

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Figure 2). The trend of affection and change of mean defect on microperimetry paralleled that of mean sensitivity (Table 6).

On the HVF 30-2 examination, the affected eyes showed a similar trend of affliction and recovery as the 10-2 though the fellow eyes differed. The mean sensitivity for fellow eyes was found to be significantly lower than that for controls at the time of presentation. This improved significantly by the first follow-up visit to match that of controls. No further statistically significant improvement was seen (Table 7; Figure 3). The results of mean defect on HVF 30-2 echoed those of mean sensitivity (Table 8).

The microperimetry mean sensitivity showed a strong and significant correlation with visual acuity and the mean sensitivity and mean defect on HVF 10-2 (Table 9).

DISCUSSION

Microperimetry has several advantages over standard automated perimetry. These range from greater accuracy to more aesthetically appealing results. Our study was designed to evaluate the sensitivity of microperimetry for visual field analysis in optic neuritis and compare it with HVF 10-2. In addition, we also compared the findings of HVF 30-2 to the above two field tests

	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean±SD)	5.60±7.32	15.34±4.59	16.41±4.87	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.058
Group B (Mean±SD)	16.54±1.46	16.67±1.52	16.93±2.16	$p(B_0,B_1)$:0.839 $p(B_1,B_3)$:0.699
Group C (Mean±SD)	17.30±1.64			
p value (for intergroup differences)	$p(A_0,B_0)$:0.002 $p(A_0,C_0)$:<0.001 $p(B_0,C_0)$:0.109	$P(A_1,B_1)$:0.437 $p(A_1,C_0)$:0.030 $p(B_1,C_0)$:0.214	$p(A_3,B_3)$:0.920 $p(A_3,C_0)$:0.849 $p(B_3,C_0)$:0.901	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 5: Microperimetrymean threshold sensitivity changes and trend.

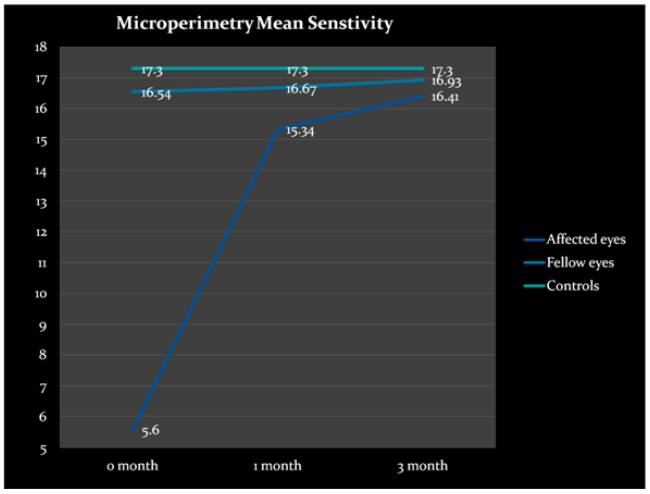

Figure 2: Graphical trend of change in microperimetry mean sensitivity.

	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean±SD)	-12.63 ± 6.80	-4.35±4.68	-3.31±4.96	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.083
Group B (Mean±SD)	-3.09±1.39	-3.04±1.46	-2.81±2.14	$p(B_0,B_1)$:0.930 $p(B_1,B_3)$:0.736
Group C (Mean±SD)	-2.42±1.70			
p value (for intergroup differences)	$p(A_0,B_0)$:0.004 $p(A_0,C_0)$:<0.001 $p(B_0,C_0)$:0.143	$p(A_1,B_1)$:0.664 $p(A_1,C_0)$:0.027 $p(B_1,C_0)$:0.169	$p(A_3,B_3)$:0.494 $p(A_3,C_0)$:0.796 $p(B_3,C_0)$:0.901	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 6: Microperimetry mean defect: changes and trend.

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	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean±SD)	12.88±10.32	25.73±7.72	26.02±7.54	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.60
Group B (Mean±SD)	26.03±2.59	28.58±1.50	27.86±1.77	$p(B_0,B_1)$:0.03 $p(B_1,B_3)$:0.26
Group C (Mean±SD)	27.99±2.31			
p value (for intergroup differences)	$p(A_0,B_0)$:0.004 $p(A_0,C_0)$:<0.001 $p(B_0,C_0)$:0.044	$p(A_1,B_1)$:0.636 $p(A_1,C_0)$:0.224 $p(B_1,C_0)$:0.914	$p(A_3,B_3)$:0.743 $p(A_3,C_0)$:0.259 $p(B_3,C_0)$:0.619	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 7: HVF 30-2 Mean threshold sensitivity changes and trend.

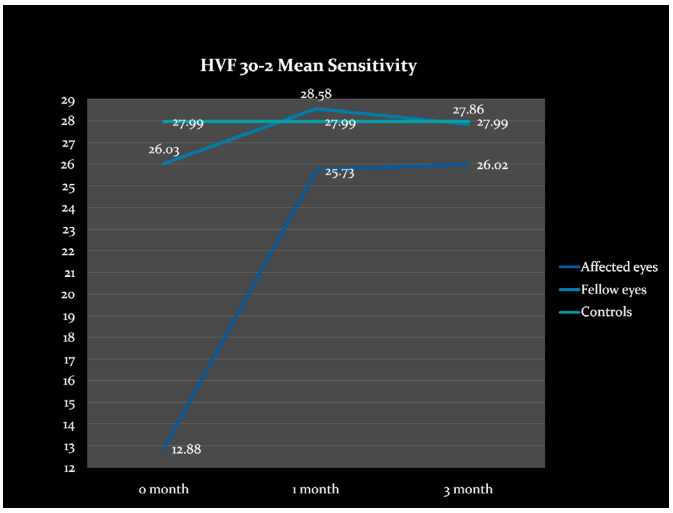

Figure 3: Graphical trend of change in HVF 30-2 mean sensitivity.

	At first visit (0 month)	At 1 month	At 3 months	*p* value (for change over time)
Group A (Mean±SD)	-19.32±11.38	-5.61±8.29	`-5.37±7.82	$p(A_0,A_1)$:<0.001 $p(A_1,A_3)$:0.63
Group B (Mean±SD)	-4.85 ± 2.06	-2.41±1.58	-3.14±1.53	$p(B_0,B_1)$:0.03 $p(B_1,B_3)$:0.19
Group C (Mean±SD)	-3.08±2.24			
p value (for intergroup differences)	$p(A_0,B_0)$:0.001 $p(A_0,C_0)$:<0.001 $p(B_0,C_0)$:0.031	$p(A_1,B_1)$:0.192 $p(A_1,C_0)$:0.29 $p(B_1,C_0)$:0.914	$p(A_3,B_3)$:0.341 $p(A_3,C_0)$:0.112 $p(B_3,C_0)$:0.502	

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 8: HVF 30-2 Mean defect: changes and trend.

	At presentation	**At 1 month**	**At 3 months**
Visual Acuity	*r=0.865* *p=<0.001*	*r=0.678* *p=0.008*	*r=0.715* *p=0.004*
Mean sensitivity 10-2	*r=0.917* *p=<0.001*	*r=0.965* *p=<0.001*	*r=0.970* *p=<0.001*
Mean defect 10-2	*r=0.914* *p=<0.001*	*r=0.963* *p=<0.001*	*r=0.969* *p=<0.001*

Group A: Eyes affected by optic neuritis; Group B: fellow eyes; Group C: eyes of controls.

Table 9: Correlation of microperimetry mean threshold sensitivity with visual acuity and 10-2 visual field parameters.

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in order to determine whether peripheral visual field testing provides any extra information than can be obtained from the central visual field alone.

Visual acuity in clinically affected eyes was found to be significantly lower than fellow eyes and controls. It improved incompletely over 1 month and needed a period of 3 months to reach normal levels, similar to the control group (p=0.89). This is consistent with previous studies that have reported delayed recovery of vision.[26-29] This delayed recovery in visual acuity was paralleled by the delayed recovery of central 20 degree sensitivity on microperimetry at 1 month but not the sensitivity of the 10-2 standard automated perimetry. This may imply that field testing by microperimetry is more sensitive to visual function changes. A similar result was reported by previous studies in literature.[24,25]

The finding that on microperimetry, at 1 month follow-up, the mean sensitivity in affected eyes was still lower than that of controls (p=0.03) suggests that subtle residual changes in macular sensitivity may persist in eyes with optic neuritis (atleast for the first month) even after apparent clinical resolution on the standard 10-2 perimetry (p=0.16).These results are in contrast to a recent report by Lima et al, [23] where in they suggested that microperimetry detects lesser sensitivity loss than standard automated perimetry in diseases involving the inner retina and optic nerve. However, their assumption is based on studies in glaucoma. Optic neuritis has a significant pathogenetic differences from glaucoma, and these may explain the difference in sensitivity patterns of the two tests in the two disorders. Acton et al[26] published a review highlighting the differences between microperimetry and standard automated perimetry and found adequate evidence to show the link between functional and structural changes in diseases pertaining to the retina as well as correlation between visual outcome and sensitivity on microperimetry. Whilst not strictly comparable to the current study, the review does concur with our study.

Another significant finding in our study was that the asymptomatic fellow eyes were found to have defects (compared to controls) on HVF 30-2, whereas they tested normal on HVF 10-2 and microperimetry. This suggests that though macular sensitivity may be unaffected in fellow eyes at the time of acute attack of optic neuritis, there are changes in the remaining visual field (central 60 degrees), which may affect the quality of vision and be a marker for subclinical damage. Thus, even though central visual field examinations like HVF 10-2 and microperimetry chart scotomas and other defects in much greater detail, testing a larger area of the visual field cannot be done away with. Likewise for cases of optic neuritis with unaffected visual acuity, peripheral field defects may be present which would get missed on a test such as the microperimetry and would require a full field evaluation. Nevalainen et al,[1] Fang et al[3], Rothova Z et al,[5] and Mienberg et al[30] agree with this view, but Keltner J et al[4] opine that in most cases, follow-up of optic neuritis eyes can be monitored by central visual field alone.

Among the central visual field tests, microperimetry appears to be superior to the standard automated perimetry. However there are potential drawbacks associated with this technology including the cost, requirement of technical expertise, and the long duration of the test (approximately 15 minutes per eye). The duration however can be reduced to a great extent (as low as 5 minutes per eye) by judicious selection of the test protocol and the testing strategy. Additionally, the inability to acquire peripheral visual fields prevents it from being a holistic perimetry testing system.

To conclude, the superior sensitivity of microperimetry and its greater correlation with vision as compared to HVF 10-2 put forward a case for the use of microperimetry as an alternative visual field examination in patients with optic neuritis. However, the standard HVF 30-2 examination remains indispensable in the work-up of optic neuritis.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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