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### Editorial: Normal Tension Glaucoma
Amjad Akram

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### Effect of Panretinal Photocoagulation On Macular Thickness in Patients with Proliferative Diabetic Retinopathy
Rabia Sharif Bhatti, Aunaza Maqbool, Muhammad Usman Arshad, Zamir Iqbal, Sohail Zia, Masud ul Hasan

This quasi experimental study was performed to determine the mean change in macular thickness after panretinal photocoagulation in eyes with proliferative diabetic retinopathy. Total 126 adult patients affected by PDR and having sufficiently clear media to perform Optical Coherence Tomography were included. All patients underwent Panretinal photocoagulation (PRP) and macular thickness was measured pre and 3-month post PRP.

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### Evaluating the Successful Outcome in Dacryocystorhinostomy by External Approach with Mitomycin C Versus Standard Procedure Alone
Adnan Ahmad, Mohammad Farhan, Jawad Humayun, Mubbashir Rehman, Hamid Rehman

This trial evaluated the efficacy of intraoperative adjunctive mitomycin C (MMC) in external dacryocystorhinostomy (DCR) surgery and compared this procedure with the standard DCR procedure. In group A, intraoperative adjunctive MMC 0.2 mg/mL was applied to the osteotomy site & flaps for 30 minutes while group B underwent standard DCR procedure only. The success of surgeries was assessed using objective findings and subjective symptoms.

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### Outcomes of Intravitreal Bevacizumab Injections as Primary Treatment for Diabetic Macular Edema
Lubna Adeeb, Nadeem Ishaq, Zamir Iqbal, Farah Akhtar, Muhammad Aamir Arain

A Quasi Experimental Study was performed to evaluate change in visual acuity and decrease in central macular thickness after using Intravitreal Bevacizumab (IVB) in primary treatment of diabetic macular edema (DME). Diagnosed diabetic patients and no history of any previous treatment for DME were included. Efficacy of treatment was compared in terms of change in BCVA and CSFT on OCT. Intravitreal injection of 1.25 mg of IVB was given on Day 0 and then monthly for next two months. Follow up was done after 04 weeks of third injection.

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Management of Visual Malingering with Placebo Drugs
Muhammad Mateen Amir, Farah Tariq, Minahal Mateen, Muhammad Rizwan Ullah

This prospective study was conducted to evaluate the efficacy of placebo drops in the management of visual malingering. In cases of partially blind patients; neutralizing cylinder and plano glasses were used for diagnosis of malingering. Patients not diagnosed with above method and patients with complete visual loss were treated with placebo drops. Patients were advised to visit after one week for reassessment and any change in visual acuity was recorded.

Postoperative Refractive Outcome and Accuracy of Biometry in Pediatric Cataract with Primary Intraocular Lens Implantation
Muhammad Kashif Habib, Adnan Aslam Saleem, Nighat Jabeen, Maryam Ghuncha, Maryam Najam, Furqan Ahmed Khan

This study was conducted to report the refractive outcomes, accuracy of intraocular lens power selection in post-operative patients of cataract surgery beneath 8 years of age. Dilated objective refraction was performed by retinoscopy on all the post-operative patients fulfilling inclusion criteria to observe whether they achieved the target post op refraction or not. Information regarding pre-operative biometry and power of intra ocular lens implanted was taken from patients’ data. The collected data was analyzed using SPSS 19.0.

Correlation of Apparent Diffusion Co-Efficient Mapping of Visual Pathways with Glycosylated Haemoglobin Levels in Diabetic Patients Presenting with Blurring of Vision
Sarah Nisar, Lubna Sarfraz

This research has been done to study the impact of diabetes on Visual pathway using diffusion weighted magnetic resonance imaging (DW MRI) and calculating the Apparent Diffusion Co-efficient (ADC) values. Conventional MRI and Diffusion-weighted imaging (DWI) of the brain of diabetic patients were obtained and DW/ADC values of optic nerve, optic tract, thalamus and visual cortex were calculated by drawing regions of interest (ROI) of these regions. HbA1c was done using chemiluminescent technique.

Carotid Cavernous Sinus Fistula
Muhammad Rizwan Aziz, Paula Chattington, Faisal Saleem Khan

75 Years old male previously investigated for pulsatile tinnitus was admitted with six to eight weeks history of double vision and headache associated with red, painful left eye. Clinical examination confirmed 3rd, 4th and 6th cranial nerves palsies. Urgent ophthalmology referral was made, arranged for contrast intracranial and carotid CT scans and diagnosed as Carotid Sinus Fistula.
“Normal Tension Glaucoma” (NTG) is a baffling disease entity and can be a diagnostic challenge even for the most seasoned clinician. I have extensively reevaluated already “diagnosed” cases of NTG over the past 30 years only to discover mimicking underlying disease with only very few cases which could be labelled as NTG. Strict diagnostic criteria have been laid down by various authorities on glaucoma all over the world and I have found the criteria laid down by Roger Hitchings of Moorfields Hospital London quite practical and useful.

The biggest mimicker of NTG is Primary open angle glaucoma (POAG) itself. There are so many variables and pitfalls in intraocular pressure (IOP) measurement that I always view an IOP of less than 21mmHg with suspicion when dealing with patients from a glaucoma perspective in presence of typical disc changes and field loss.

As a matter of routine in every patient with glaucomatous cupping and corresponding field loss with “normal” IOP, I make it a point to perform an old-fashioned water drinking test only to witness a dramatic rise in IOP in many if not all cases. If water drinking test is negative, it is prudent to perform MRI scan of the brain and visual pathways. In one patient who was being treated for unilateral NTG, MRI revealed “aneurysm of the anterior cerebral artery compressing upon the left optic nerve”.

Do keep in mind that NTG is a systemic disease so resist making a diagnosis of unilateral NTG, you will probably be wrong most of the times.

“Cupping” of the disc is not unique to glaucoma alone and there are dozens of lesions which may produce cupping, so make sure you train your eye to differentiate neurological and glaucomatous cupping. Occasionally optic disc colobomas can be misinterpreted as a glaucomatous cupping and to add to the confusion is the fact that there is no specific test to diagnose a disc coloboma with absolute certainty. Therefore, in case of doubt you may have to resort to the very basics which is

“When in doubt, demonstrate progression in cupping and field loss by regular follow up of the patient i.e. No progression no glaucoma”. Its always wise never to make a diagnosis of NTG on the very first visit of a patient. If NTG is considered a diagnosis of exclusion, the chances of making a diagnostic blunder is greatly minimized.

If the doctor works hard enough, most of the NTG patients can be correctly ascribed to another disease. It is a fact that some patients have true glaucoma at a statistically normal range. However, it is even more likely as I have discovered that many of the patients diagnosed as NTG are having congenital disc anomalies, other neuropathies, other types of undiscovered glaucomas or non-progressive neuropathies which mimic glaucoma.

Last but not the least, this quote of Sir Stewart Duke Elder should always be
sounding alarm bells in your ears “When an ophthalmologist fails to account for the cupping and field loss, he labels it as NTG”.

References:
Effect of Panretinal Photocoagulation On Macular Thickness in Patients with Proliferative Diabetic Retinopathy

Rabia Sharif Bhatti, Aunaza Maqbool, Muhammad Usman Arshad, Zamir Iqbal, Sohail Zia, Masud ul Hasan

ABSTRACT

Objective: To determine the mean change in macular thickness after panretinal photocoagulation in eyes with proliferative diabetic retinopathy

Study design: Quasi experimental

Setting and Duration of Study: Retina Clinic of Al-Shifa Trust Eye Hospital, Rawalpindi between September 2014 to March 2015 for six months.

Methodology: Total 126 adult patients between age 45-65 years, irrespective of gender with eyes affected by PDR in which media was sufficiently clear to perform Optical Coherence Tomography (OCT) were included in the study. All patients underwent Panretinal photocoagulation (PRP). Macular thickness was measured pre and 3-month post PRP by OCT.

Results: About half of the (65, 51%) of patients were males and 48.4% (n=61) of patients were females. The mean macular thickness was noted as 205.9 um ± 18.2 SD pre PRP. After 3 months mean macular thickness was found to be 214.1 um ± 14.2 SD (P<0.05).


1. Al-Shifa Trust Eye Hospital Rawalpindi
2. Islamic International Medical College, Rawalpindi
3. Abbottabad International Medical College, Abbottabad
4. Bashiran Umer Eye Hospital, Islamabad

Introduction:

Diabetic retinopathy is the most common complication of diabetes mellitus. It is the leading global cause of visual morbidity.1 The incidence of diabetic retinopathy is estimated to be between 2-3/100 persons-years in diabetic patients and 4.5% for patients on insulin.2

Diabetic retinopathy is predominantly a microangiopathy in which blood vessels are vulnerable to damage from hyperglycemia. Hyperglycemia leads to multifocal cascades of physiological processes like increased permeability, altered blood flow and hypoxia.3

Early Proliferative diabetic retinopathy (PDR) is identified by the presence of new vessels on less than one-disc diameter without preretinal sub hyaloid and vitreous hemorrhage.4 Macular edema is the most
common cause of visual loss in proliferative diabetic retinopathy. Although Fundus fluorescein angiography (FFA) is typically used to assess vascular leakage qualitatively in patients with macular edema, assessment of actual macular thickness correlates better with visual acuity. Traditional methods of evaluating macular thickness like slit lamp ophthalmoscopy and stereoscopic fundus photographs are insensitive to small changes in macular thickness. Optical Coherence Tomography (OCT) is an imaging modality that helps in qualitative and quantitative assessment of macular thickness. Panretinal photocoagulation (PRP) appears beneficial for PDR and is the mainstay of treatment. PRP is an effective method of preventing progression of PDR and is standard care for patients with PDR. Nevertheless, studies have shown that PRP causes macular edema and serous retinal detachment.

In early treatment diabetic retinopathy study (ETDRS) which was performed prior to advent of OCT, 18% eyes that underwent full PRP were noted to have increased thickness of macula on standard fundus photography. OCT has superseded retinal thickness analysis to become the predominant technology for measuring macular thickness. Visual loss due to PRP induced edema occurs in 25-35% of treated. Exact mechanism has not been elucidated yet destruction of blood retinal barrier by laser causes edema and some cytokines such as Interleukin-6 (IL-6) and Interleukin-8 (IL-8) related to tissue inflammation appear to play contributory role. Studies have shown that central foveal thickness increases significantly from pre-treatment value 222.5± 59.1 µm at 1 month (p=0.01) to post treatment value 256± 101.38 at 3 months (p=0.04).

Despite the apparent improvement in the treatment of diabetic retinopathy, the management of progressive changes is associated with substantial morbidity among postoperative patients. The previous studies have been inconsistent regarding the impact of PRP on macular thickness. Moreover, there is limited data on the subject from Pakistan hence, the current study was undertaken. The goal of the study was to highlight the increase in macular thickness in patients who underwent Pan retinal photocoagulation (PRP).

**Methods and Materials:**
A quasi experimental study was conducted at Retina Clinic of Al-Shifa trust eye hospital, Rawalpindi which is a tertiary care hospital. The study was conducted from September 2014 to March 2015 for a duration of six months.

The sample size was calculated using open EPI, with confidence level 95%, Power 90%, Pre PRP macular thickness as extracted from the previous study was 222.05 ± 59.1 µm while the Post PRP macular thickness was 256 ±101.38 µm. A sample size of 126 was obtained. Patients were enrolled in the study using non-probability consecutive sampling techniques. All patients with diagnosed proliferative diabetic retinopathy (PDR) in which media was sufficiently clear to perform Optical Coherence Tomography (OCT), aged between 45 to 65 years irrespective of gender with diabetes duration of greater than 5 years whether type 1 and type 2 were included in the study. All patients with clinically significant macular edema on fundoscopy, intravitreal anti VEGFs, steroids or periocular steroids had been administered during the last 6 months, had focal laser treatment in last three months, or had a history of corneal opacity, uveitis, cataract, glaucoma, and reduced visual acuity due to any other cause were excluded from the study. The study was conducted after approval has been accorded by the hospital.
An informed written consent was taken from all the patients included in this study. Baseline readings of the sample included macular thickness of the involved eye of the recipient measured by optical coherence tomography. The study variables that were seen included macular thickness as measured by optical coherence tomography using Stratus OCT model-3000 S/no 3000-8637. PRP was performed with an Argon laser using a Vitra quantal medical machine. Patients were re-examined in one month and 3 months following Panretinal photocoagulation. Macular thickness measured to document any change. Patients were examined in the retina clinic pre-operatively. Macular thickness was measured before laser and repeated after laser at one month and three months. Final outcome measured at 3 months post PRP. Follow-up was ensured by taking contact no of patients. Verification of pre and post-laser readings was done by a senior consultant. All the observations along with the demographic information of patients were noted on pre-designed structured proforma.

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 24. Mean and standard deviation was calculated for numerical variables i.e. age, macular thickness pre-PRP and 3 months post-PRP. Paired sample t-test was used to compare pre and post-PRP mean macular thickness. P-value <0.05 considered significant. Frequency and percentages were calculated for qualitative variables like gender. Effect modifiers like age, gender, duration of diabetes and type of DM (I & II) were controlled by stratification. Post stratification independent sample t-test was applied keeping p value less than 0.05 as significant.

Results:
A total of 126 patients were enrolled in the study with a mean age of 55.6 ± 6.8 years. About one-half of the patients were male with a mean age of 55.3 ± 6.7 years and 61 (48.4%) of the patients were females with mean age of 56.1 ± 6.9 years (Table 1).

There were 67 (53.2%) of patients who were in age group 45-55 years and 59 (46.8%) were in age group 56-65 years. There were 53 (42.1%) of patients who had type-I diabetes and 73 (57.9%) had type-II diabetes. Duration of diabetes was between 6-10 years in 89 (70.6%) of patients and 37 (29.4%) had diabetes duration of more than 10 years (Table 2).

The mean macular thickness was noted as 205.9 um ± 18.2 SD pre PRP. Three months post PRP mean macular thickness was found to be 214.1 um ± 14.2 SD. The difference was statistically significant (P= 0.001). Macular thickness was significantly increased at 3 months post PRP (Table 2).

Older age was significantly associated with increment in the mean macular thickness pre- and post-therapy with p=0.004. Both in male and female patients there was a statistically significant increase in macular thickness post-therapy stage with p=0.001 and p=0.04, respectively. In patients with type-I diabetes (n=53), mean macular thickness was noted as 206.6 um ± 18.6 SD pre PRP. Three months post PRP mean macular thickness was found to be 215.7 um ± 14.1 SD. The difference was statistically significant (P= 0.006). In patients with type-II diabetes (n=73), mean macular thickness was noted as 205.5 um ± 17.9 SD pre PRP. Three months post PRP mean macular thickness was found to be 212.8 um ± 14.2 SD. The difference was statistically significant (P= 0.007) (Table 3).

In patients with diabetes duration of 6-10 years (n=89), mean macular thickness was noted as 206.9 um ± 18.1 SD pre PRP. 3 months post PRP mean macular thickness was found to be 214.7 um ± 13.6 SD. The difference was statistically significant (P=
Table 1: Demographic Profile of the study Population (n=126)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency(%age)</th>
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<tbody>
<tr>
<td>Male</td>
<td>65 (51.6%)</td>
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<tr>
<td>Female</td>
<td>61 (48.4%)</td>
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<table>
<thead>
<tr>
<th>Age Group</th>
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<tr>
<td>45-55</td>
<td>67 (53.2%)</td>
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<tr>
<td>56-65</td>
<td>59 (46.8%)</td>
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<table>
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<tr>
<th>Diabetes Mellitus</th>
<th>Frequency(%age)</th>
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<tbody>
<tr>
<td>Type 1</td>
<td>53 (42.1%)</td>
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<tr>
<td>Type 2</td>
<td>73 (57.9%)</td>
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<table>
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<tr>
<th>Duration of Illness</th>
<th>Frequency(%age)</th>
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<tbody>
<tr>
<td>6-10 years</td>
<td>89 (70.6%)</td>
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<tr>
<td>&gt; 10 years</td>
<td>37 (29.4%)</td>
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Table 2: Macular thickness pre and post therapy (in overall study sample) (n=126)

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<th>Variable</th>
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<th>P- value</th>
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<tbody>
<tr>
<td>Pre- PRP</td>
<td>205.9 ± 18.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Post PRP</td>
<td>214.1 ± 14.2</td>
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Table 3: Macular thickness pre and post therapy according to the patient characteristics (n=126)

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<thead>
<tr>
<th>Variable</th>
<th>Pre-PRP</th>
<th>Post-PRP</th>
<th>p-value</th>
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<tr>
<td>Age</td>
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<td>44-55 years</td>
<td>207.2 ± 18.3</td>
<td>214.3 ±13.5</td>
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<td>56-65 years</td>
<td>204.2 ± 18.2</td>
<td>213.7 ± 15.1</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>199.5 ± 16.7</td>
<td>210.2 ± 14.4</td>
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<tr>
<td>Female</td>
<td>212.9 ± 17.2</td>
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<td>Diabetes Type</td>
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<td>Type 1 Diabetes Mellitus</td>
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<tr>
<td>Type 2 Diabetes Mellitus</td>
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<td>Duration of Diabetes</td>
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<td>&gt; 10 years</td>
<td>203.6 ± 18.4</td>
<td>212.5 ± 15.5</td>
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Discussion:

Proliferative diabetic retinopathy (PDR) is a common complication of diabetes mellitus, which is characterized by neovascularization generating from the retina or in some cases the optic disk. The pathogenesis of the PDR is not well-understood however; evidence has shown that certain factors like the vascular endothelial growth factor (VEGF) are the main culprit behind the development and progression of PDR. Recently, Liu R and colleagues revealed that negative regulation of VEGF by MiR-126 increases the risk of occurrence of PDR. They noted that in patients with PDR, there was a higher expression of MiR-126(p<0.05) as well as concomitant increase in the expression of VEGF (p<0.05) compared to the controls who did not have PDR. There is an established link between VEGF expression and macular thickness.
The present study aimed to determine the mean change in macular thickness after panretinal photocoagulation in patients with proliferative diabetic retinopathy and to find the associated factors. The study findings revealed that the mean macular thickness after procedure was significantly enhanced. Moreover, the present study also concluded that age, gender, type of diabetes, and the duration of diabetes were all independently correlated with post-therapy macular thickness in patients.

Panretinal photocoagulation helps in reducing the incidence of severe visual loss almost by fifty percent especially in patients with high-risk features including neovascularization from optic disc with more than one-third in diameter or neovascularization with hemorrhage. Older patients also benefitted from the panretinal photocoagulation. However, it should be noted that the visual regain or potential is dependent upon many factors such as the pre-therapy and post-therapy condition of the macular region, retinal perfusion, and the status of the optic nerve.

The literature review indicated limited data from Pakistan, highlighting the impact of PRP on macular thickness in patients with PDR. Rationale of current study was to gather evidence about increase in macular thickness post PRP in our setting to improve the management of these patients by early initiation of adjunct therapy to reduce this side effect of treatment. This would also improve the overall outcome of management of our future patients. Our main objective was to determine the mean change in macular thickness after panretinal photocoagulation in eyes with proliferative diabetic retinopathy. 126 adult patients between age 45-65 years, irrespective of gender with eyes effected by PDR in which media is sufficiently clear to perform Optical Coherence Tomography (OCT) were included in the study. All patients underwent Panretinal photocoagulation (PRP). Macular thickness was measured pre and 3-month post PRP by OCT. 51.6% (n=65) of patients were males and 48.4% (n=61) of patients were females. In overall study sample of 126 patients, mean macular thickness was noted as 205.9 um ± 18.2 SD pre PRP. Three months post PRP mean macular thickness was found to be 214.1 um ± 14.2 SD (P<0.05).

The findings of the current study reinforce the previous study findings highlighting the macular thickening associated with the treatment. For instance, Watanachai N et al determined the changes in central subfield (CSF) macular thickness after a single session of PRP in recently diagnosed proliferative diabetic retinopathy patients. The authors reported a statistically significant increase of twenty-four micrometers in mean CSF thickness (P = 0.001) which progressed to 17.4μm from baseline to 12-week follow-up (P = 0.002). However, they found that only a minority of the patients had macular edema 2 (5%) at 12-week follow-up.

A prospective cohort study conducted by Lee SB to determine the difference in macular thickness in patients who underwent PRP. The authors concluded that significantly increased with a mean macular thickness of 199.0 (20.9) micrometer at baseline to 220.4 (17.3) at 12 months. However, they found that the thickening of macula reduced overtime with a mean macular thickness of 223.3 (40.6) micrometer at day 1 to 220.4 (17.3) at 12-month follow-up.

Certain morphological changes have been observed in patients on post PRP examination including spongy macular edema, cystoid macular edema, vitreomacular traction, epiretinal membrane, and subfoveal serous detachment.

In conclusion, we recommend that clinicians should be well aware of the
association between visual potential, macular edema and eventual thickness caused by PRP. It is advisable to use certain drugs such as intravitreal injection of triamcinolone prior to PRP which may be helpful in reducing the neovascularization and macular thickening among patients\textsuperscript{19-20}.

Conclusion:
Panretinal photocoagulation causes a significant increase in macular thickness at three months post-treatment in eyes with proliferative diabetic retinopathy. It is advisable to use certain drugs such as intravitreal injection of triamcinolone prior to PRP which may be helpful in reducing the neovascularization and macular thickening among patients.

References:


Authors Contribution:
Concept and Design: Rabia Sharif Bhatti
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Evaluating the Successful Outcome in Dacryocystorhinostomy by External Approach with Mitomycin C Versus Standard Procedure Alone

Adnan Ahmad¹, Mohammad Farhan¹, Jawad Humayun¹, Mubbashir Rehman¹, Hamid Rehman²

ABSTRACT:
Objectives: To evaluate the efficacy of intraoperative adjunctive mitomycin C (MMC) in external dacryocystorhinostomy (DCR) surgery and to compare this procedure with the standard DCR procedure alone in the long term (1 year).

Study Design: Prospective, randomized controlled trial.

Methods: Patients with primary acquired nasolacrical duct obstruction were randomized into 2 groups i.e. A & B. In group A, intraoperative adjunctive MMC 0.2 mg/mL was applied to the osteotomy site & flaps for 30 minutes while group B underwent standard DCR procedure only. The success of the DCR surgeries were assessed using objective findings (e.g., irrigation of saline into lacrimal drainage passages and regurgitation test) and subjective symptoms (asking patients to describe the degree of tearing improvement).

Results: Total 139 eyes of patients were assessed and randomized to group A (38 women, 31 men; mean [SD] age, 49.0 [8.9] years) and group B (42 women, 28 men; mean [SD] age, 47.0 [8.9] years groups. The mean follow-up period was not significantly different between group A and B (12.1 vs 12.2 months). Significantly more eyes in group A than group B remained asymptomatic throughout the 1-year follow-up period (p= 0.005). Based on the patency of the drainage system, the success rate was significantly greater in group A than group B (p= 0.005). Based on irrigation of lacrimal drainage system, significantly fewer patients in group A than group B had an obstructed nasolacrical duct i.e. failed DCR (4/69 [5.8%] vs 12/70 [17.2%]). No adverse effects or any other surgical adverse events were observed with MMC.

Conclusions: It is advocated to use adjunctive MMC in external DCR surgery to enhance the success rate compared to standard DCR alone with minimal side.

Introduction:
Nasolacrimal duct (NLD) obstruction is a condition that results in the overflow of tears (epiphora) or infection of the nasolacrimal sac (dacryocystitis). The etiology of acquired NLD obstruction is multifactorial and is not fully understood. Dacryocystorhinostomy (DCR) is the surgical correction for NLD obstruction, which aims to establish a new drainage pathway between the lacrimal sac and the nose.¹

Various studies have reported an approximately 90% success rate of
dacryocystorhinostomy by an external approach in the management of NLD obstruction.\textsuperscript{2,3} However some studies have shown success rates that falls in the range from 82% to 100% with this procedure.\textsuperscript{4-6} The main cause of failure is the formation of granulation tissue at the site of osteotomy or common canaliculus in DCR by external approach.\textsuperscript{7,8} Others include technique of surgery or fibrous closure at the site of anastomosis.\textsuperscript{9,10} The main reason for surgical failure is the result of fibrocytes proliferation and granulation tissue formation that leads to narrowing of osteotomy and ultimately leads to non-patency.\textsuperscript{7,11} Various techniques should be utilized to prevent the granulation tissue formation at the osteotomy site and anastomosed flaps to enhance the success rate.

Mitomycin C (MMC), is an anti-cancer drug that acts on all the phases of cell mitosis via alkylating mechanism by inhibiting DNA-dependent RNA synthesis (alkylation of nucleic acid nitrogenous base pairs) and inhibits the proliferation of fibrous tissue at the osteotomy site and the anastomosed flaps.\textsuperscript{4} In trabeculectomy surgeries done for glaucoma, MMC has shown an improved success rate by inhibiting the fibrous tissue proliferation via alkylation of DNA in fibrocytes.\textsuperscript{12} Surgical success rate is increased in DCR done with MMC by its anti-proliferative property on fibrocytes which prevents the formation of fibrosis at osteotomy and common canaliculus.\textsuperscript{13-19}

As application of topical MMC is not without side effects, it is usually administered for brief durations i.e. 2-10 minutes at doses, ranging from 0.2 to 0.4 mg/ml. Studies have shown that 0.2 mg/mL MMC applied to an osteotomy site for thirty (30) minutes could enhance the success rate without significant increase in complication rates. The purpose of this study was to ascertain the effectiveness of intraoperative adjunctive MMC treatment in the management of external DCR surgery, in terms of successful outcome as compare to standard DCR procedure alone in the long term (1 year) follow up and to compare our local results with that of international studies done and if results were convincing, advocate this approach for successful outcome.

**Materials and Methods:**

The study was conducted at the Ophthalmology department of Qazi Hussain Ahmad Medical Complex, Nowshera, from 1\textsuperscript{st} Jan. 2018 to 1\textsuperscript{st} July 2019 (18 months duration), with total no. of 139 patients were recruited for this prospective, randomized (non-blinding) control study by consecutive sampling technique from an outdoor patient department (OPD).

All the patients recruited were suffering from primary acquired NLD obstruction, patients with other secondary causes of NLD obstruction, primary failed DCR, patients with age less than 18 years were excluded from the study. The recruited patients were divided into 2 groups almost equally with group A included those patients in whom external DCR was performed with adjuvant MMC, while group B included patients in whom standard external DCR surgery alone was done. An informed written consent was obtained from all the patients prior to randomization. All the cases were operated by a same surgeon with the same technique without silicon intubation under local anesthesia (LA).

In group A, intra-operative MMC was applied in a concentration of 0.2mg/ml for a duration of 30minutes with a 1*1cm cotton patty with long silk threads soaked with 1 ml of MMC in a dosage of 0.2mg/ml, it was placed over the anastomosed mucosal and lacrimal sac flaps and osteotomy site at middle turbinate. The silk threads were brought out from the nasal cavity and exposed at nostrils for later
removal, the flaps, muscle layer and skin were closed with 6/0 vicryl suture in separate layers respectively. The MMC soaked cotton was removed trans-nasally by pulling out the silk threads via nostrils in the recovery room after 30 minutes of application time.

In group B same surgical technique of external DCR was employed without using MMC. Post-operatively all the patients were prescribed topical tobramycin & dexamethasone combination eye drops (e/d) in quid regimen for 02 weeks, topical polyfax eye ointment over the wound twice daily along with oral antibiotics for 1 week each.

Follow up assessment was done at week 1, 2nd week, 01, 02, 03, 06 & 12 months respectively, skin stitches were removed on 7th day post-operatively in all patients, at each visit patients were asked about symptomatic improvement and objective evaluation was done by performing the regurgitation test and saline irrigation for patency of the lacrimal passages/ostium.

Success was defined in terms of symptomatic improvement by cessation of epiphora and objectively by the patency of lacrimal passages/ostium on saline irrigation, while failure was defined as being symptomatic with epiphora/discharge or consistency of the symptoms and non-patency of the lacrimal passages/ostium on saline irrigation. The independent sample t test and chi square test was applied to the data file, $p<0.05$ was considered statistically significant. The statistical analysis was performed on SPPS 20.

**Results:**
Total of 139 patients were recruited for the study and almost equally distributed to group A i.e. 38 women and 31 men with a mean age of 49 years and group B i.e. 42 women and 28 men with a mean age of 47 years. The mean follow-up period was not significantly different between group A and B i.e. 12.1 months vs 12.2 months. (Table 1)

The number of asymptomatic patients were significantly more in the group A than group B throughout the 1-year follow-up period (63/69 [91.3%] vs 50/70 [71.4%] of eyes; $p = 0.005$). Symptomatic improvement was attained in significantly fewer patients in group A than group B (2/69 [2.9%] vs 8/70 [11.4%]; $p<0.005$) at the end of 1-year follow-up. Fewer patients in the group A were symptomatic as compare to group B (excessive tearing) (4/69 [5.8%] vs 12/70 [17.2%]; $p = 0.005$). The success rate was significantly greater in group A than the group B, based upon the patency of the drainage system, (65/69 [94.2%] vs 58/70 [82.8%]; $p = 0.005$) respectively as shown in tab. 2. The remaining 4 patients in group A and 12 patients in group B had persistent nasolacrimal duct obstruction after surgery and they were subjected for repeat surgery.

No systemic and local side effects were observed due to MMC in group A patients i.e. delayed nasal mucosal bleed, mucosal flaps and tissue necrosis or post-operative infection etc.
Table 1. Study participants’ demography, symptoms & follow up duration (n = 139)

<table>
<thead>
<tr>
<th>Participants characteristic</th>
<th>Group A n= 69</th>
<th>Group B n= 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean(SD)</td>
<td>49(8.9)</td>
<td>47(8.9)</td>
</tr>
<tr>
<td>Range</td>
<td>34-64</td>
<td>32-62</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31(45)</td>
<td>28(40)</td>
</tr>
<tr>
<td>Female</td>
<td>38(55)</td>
<td>42(60)</td>
</tr>
<tr>
<td>Symptoms (mean (SD))</td>
<td>9.2(1.9)</td>
<td>8.5(1.7)</td>
</tr>
<tr>
<td>Follow up (mean(SD))</td>
<td>12.1(1.1)</td>
<td>12.2(1.4)</td>
</tr>
</tbody>
</table>

Table: 2. Success & failure rate in group A & B

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success rate %</td>
<td>94.2%</td>
<td>82.8%</td>
</tr>
<tr>
<td>Failure rate %</td>
<td>5.8%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Discussion:
Different studies were conducted to find out the success rate and complications with the use of adjunctive MMC in the treatment of acquired NLD obstruction.\(^5\) A prospective, randomized, controlled trail was conducted by Liao et al in patients with primary acquired NLD obstructions, he used 0.02% MMC which was applied to the ostium for 30 minutes duration in DCR surgery, he followed these patients for 10months, approx.\(^5\) 95% of patients in the MMC group were asymptomatic, while 70% of control group patients were asymptomatic.

The failure rate in the MMC group and the control group was approx. 4% and 11%, respectively. Similarly Ari et al.\(^19\) also investigated the efficacy of intra-operative MMC in external DCR with standard DCR alone by using 0.02% concentration with 30 min application at the osteotomy site and mucosal flaps with a neurosurgical cotton patty, that showed an increase in success rate in MMC group, 96% (48/50) vs 84% (42/50)(\(P<0.05\)) in control group with one year follow up, 4% (2/50) patients in MMC group & 16% (8/50) in control group showed non patency of NLD on saline irrigation test after 1yr. of follow up, his finding correlate with our study results.\(^19\)

In the same way Yeatts and Neves conducted a study by using 0.03% of MMC applied for 3 min. duration in patients who underwent external DCR, he reported improved results in a long term follow up period of approximately 15months. They also reported the efficacy of a single intraoperative use of MMC in redo DCR and suggested that adjunctive use of MMC increases the success rate of repeat DCR.\(^14\)

In another study of intraoperative MMC with DCR, Kao et al observed that in those patients where MMC was used showed an increase in ostium size as compared to controls, mean opening size in MMC group was about 27mm\(^2\) while in control group it was almost 10.5mm\(^2\), the concentration of MMC used was 0.02% with 30 min application time at osteotomy site.\(^11\) All the patients were examined post operatively for endonasal findings at one, three and six months in both groups. It was observed that intraoperative MMC was useful in maintaining a larger ostium diameter.

Ugurbas et al explored the histopathological effects of MMC on DCR by transnasal approach, by applying MMC in a conc. of 0.05% for two and half min. intra-operatively.\(^15\) Examination of the specimens under light and electron
microscopy revealed diminished epithelial layer which were loosely attached to each other and looser, hypo-cellular sub-epithelial connective tissue in the MMC specimens as compared to controls. These evidences reflect the effectiveness of MMC application on the histological appearance of tissues. Yildirim et al in his study revealed that MMC being anti-mitotic agent effectively decreases cell population density in tissues hence when applied intra-operatively to mucosal flaps and osteotomy site it inhibits the fibrous and granulation tissue formation in DCR surgery.7

The study conducted by us, recruited the two (2) groups with almost identical distribution and characteristics. There was no statistically significant difference in the mean ages of the patients in the 2 groups. About 91% patients in group A and 71% patients in group B remained asymptomatic throughout the 1-year follow-up period. Based on the patency of the lacrimal drainage system, the success rate was significantly greater in group A (94%) than group B (83%). However, 4 patients in group A and 12 patients in group B had persistent NLD obstruction due to failure of primary intervention and all of them underwent repeat surgery.

You and Fang evaluated the effectiveness of intra-operative MMC application in DCR for that purpose they divided their study participants into 3 groups, among them 2 were given MMC in different conc. while the 3rd one without it in standard DCR surgery, the conc. of MMC used were 0.02% and 0.05% applied for 5 minutes and the results were compared with those of a DCR surgery alone, marked improvement in terms of patency rate and osteotomy size was observed between MMC groups vs control, but no remarkable difference was noted between the two MMC groups. Ugurbas et al. evaluated the role of MMC in a strength of 0.05% applied intra-operatively for 5 and 2 & half min. effectively prevented the formation of granulation tissue at the osteotomy site.15,16

We demonstrated in our trail, by using MMC in a conc. of 0.02% (0.2mg/mL) for thirty (30) minutes for sustained inhibition of fibrocytes which are responsible for fibrosis and granulation tissue formation, however no associated rise in adverse effects were observed. Ocular surgeries commonly employing adjunctive use of MMC like in pterygium excision and trabeculectomies, for improving the success rate, side effects are increased with its application.17, 18 However we didn’t encounter any side effect associated with MMC application in form of mucosal flap necrosis, altered nasal bleeding, and severe infections 3, 10

Our study has certain limitations including small sample size and absence of blinding in randomization of study groups. These issues need to be addressed in more refined study trails for obtaining better results.

**Conclusion:**
It is advocated to use adjunctive mitomycin C in external dacryocystorhinostomy surgery to enhance the success rate compared to standard DCR alone with minimal side effects from the antimetabolites use. However more randomized control trails are needed to elucidate further on this area of interest.

**References:**

Authors Contribution:
Concept and Design: Adnan Ahmad, Mohammad Farhan
Data Collection / Assembly: Adnan Ahmad, Mohammad Farhan
Drafting: Jawad Humayun, Mubbashir Rehman, Hamid Rehman
Statistical expertise: Mohammad Farhan
Critical Revision: Adnan Ahmad
Outcomes of Intravitreal Bevacizumab Injections as Primary Treatment for Diabetic Macular Edema

Lubna Adeeb¹, Nadeem Ishaq¹, Zamir Iqbal², Farah Akhtar¹, Muhammad Aamir Arain³

ABSTRACT

Objective: To evaluate change in visual acuity and decrease in central macular thickness after using Intravitreal Bevacizumab (IVB) in primary treatment of diabetic macular edema (DME).

Study design: Quasi Experimental Study

Place and Duration of study: Al Shifa Trust Eye Hospital Rawalpindi, from 01 June 2018 to 31 May 2019

Methodology: Only diagnosed diabetic patients were included. Exclusion criteria included patients having best corrected visual acuity (BCVA) better than 6/12 or worse than 6/60 or the central subfield thickness (CSFT) on spectral domain optical coherence tomography (OCT) less than 300 microns. No history of any previous treatment for DME was inclusion criteria. Efficacy of treatment was compared in terms of change in BCVA and CSFT on OCT. Intravitreal injection of 1.25 mg of IVB was given on Day 0 and then monthly for next two months. Follow up was done after 04 weeks of third injection.

Results: Total 130 eyes of 102 patients were included in the study. Mean age of patients was 60.2 years +/- 6.2 3. Male to female ratio was 2:1. Mean pre op LogMAR visual acuity was 0.60 +/- 0.15 and mean pre op CSFT was 421.10 +/-40.14 μm. Mean post op LogMAR visual acuity was 0.45 +/-0.23 and mean post op CSFT was 318.82 +/-35.22 μm. There was statistically significant difference in improvement of LogMAR BCVA and decrease in CSFT after treatment. (p=0.01 by paired t test)

agents became the primary therapy in DME patients and many recent clinical trials has supported that these treatments are better than laser photocoagulation in patients with DME.5-9

In Pakistan limited studies are available with smaller sample size on use of three IVB injections at monthly interval in treatment of DME.10,11 Moreover, the last paper published from Al Shifa Trust Eye Hospital on DME was in 2011 by Khan FA et al, was with single IVB injection using Time Domain OCT Stratus Zeiss.12 The rationale of this study was to assess the efficacy of three monthly injection of IVB in treatment of DME with larger sample size and by using Heidelberg Spectralis OCT. Efficacy of treatment was evaluated in terms of change in BCVA and CSFT on OCT.13

Materials and Methods:
The study was conducted at Al Shifa Trust Eye Hospital Rawalpindi, from 1 June 2018 to 31 May 2019. It was a Quasi Experimental Study. Non probability consecutive sampling was used. A total of 130 eyes of 102 patients were included in the study. Only patients diagnosed with diabetes and on oral hypoglycemic agents or insulin were included. Exclusion criteria included patients having significant cataract, glaucoma and other causes of macular edema like venous occlusion, epiretinal membrane, vitreomacular traction or age-related macular degeneration. Patients with previous history of macular laser, use of any anti VEGF injection or use of intravitreal steroids were also excluded from study. Those patients having baseline BCVA better than 6/12 or worse than 6/60 were excluded similarly those patients were also excluded if CSFT on OCT was less than 300 µm. [1]

The patient’s data was collected from Vitreo Retina OPD of Al Shifa Trust Eye Hospital Rawalpindi, keeping inclusion

exclusion criteria in mind. After a careful history, complete ophthalmic examination was carried out. Visual acuity was measured by Snellen’s chart and later converted to logarithm of the minimal angle of resolution equivalents (LogMAR visual acuity) for statistical analysis. OCT macula was done to document baseline CSFT. Before the injection all risks and benefits were explained to the patients and written informed consent was obtained. Intra vitreal injection 1.25 mg of Bevacizumab was given on Day 0 under aseptic conditions. The IVB injections were repeated after every 04 weeks for next two doses. A total of 03 IVB injections were given to every patient with a gap of 04 weeks. The injections were administered with an insulin syringe of 30G needle. The injection site was marked with caliper at 3.5mm in pseudophakic and 4mm in phakic patients in inferotemporal quadrant. 1.25 mg (0.05 ml) of Bevacizumab was taken into the syringe. 5% Povidone Iodine was instilled on ocular surface. Conjunctiva was grasped with Conjunctival Forceps and displaced toward limbus and 0.05 ml IVB was injected 3.5-4.0 mm behind the limbus. The needle is then removed and entry wound is pressed with a cotton bud for few seconds so that liquid vitreous does not escape. Again 5% Povidone Iodine was instilled on ocular surface and washed with Balanced Electrolyte Solution. Post operatively Ciprofloxacin eye drops (0.3%) were given QID for next 03 days as prophylactic therapy in all cases. Follow up was done at 4 weeks after third injection. On last follow up visit complete ocular examination was done including BCVA and OCT to evaluate CSFT and findings were recorded on proforma.

SPSS 20.0 was used for statistical analysis. Mean +/- SD was calculated for age. Male to female ratio was calculated. BCVA in LogMar and CSFT in µm are compared by paired t test at baseline pre operatively (pre op) and at one-month post operatively (post
op) after third injection of IVB. p value < 0.05 was taken as significant.

**Results:**
Total 130 eyes (n) of 102 patients were included in the study. Mean age of patients was 60.2 years +/- 6.23. Male to female ratio was 2:1. The data at baseline is shown in Table 1.

Mean pre op LogMAR visual acuity was 0.60 +/- 0.15 while mean post op LogMAR visual acuity was 0.45 +/- 0.23. There is a statistically significant difference of LogMAR BCVA in pre op and post op data comparison by paired t test (p = 0.01 by paired t test).

Mean pre op CSFT was 421.10 +/- 40.14 µm while mean post op CSFT was 318.82 +/- 35.22 µm. There is a statistically significant difference of CSFT in pre op and post op data comparison by paired t test (p = 0.01). The results are shown in Table 2. No case of endophthalmitis, vitreous hemorrhage or retinal detachment was noted. However, sub conjunctival hemorrhage was noted in 16 eyes and lens touch was noted in one eye. Phacoemulsification with intraocular lens implantation was done by Vitreoretinal Surgeon in that patient.

**Table 1: Patients Baseline Data**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>102 patients</td>
</tr>
<tr>
<td>Total number of eyes (n)</td>
<td>130 eyes</td>
</tr>
<tr>
<td>Gender</td>
<td>65 Male/ 37 Female</td>
</tr>
<tr>
<td>Mean Age</td>
<td>60.2 years +/- 6.23 (Range 47 – 69 years)</td>
</tr>
<tr>
<td>Insulin dependent</td>
<td>43 patients (42.1 %)</td>
</tr>
<tr>
<td>Non Proliferative Diabetic Retinopathy (NPDR)</td>
<td>72 patients (70.58 %)</td>
</tr>
<tr>
<td>Proliferative Retinopathy</td>
<td>30 patients (29.42 %)</td>
</tr>
<tr>
<td>Base line LogMAR VA</td>
<td>0.60 +/- 0.15</td>
</tr>
<tr>
<td>Base line CSFT</td>
<td>421.10 +/- 40.14 µm</td>
</tr>
</tbody>
</table>

**Table 2: Comparison of Pre Op And Post Op Data (n=130)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>LogMAR BCVA</th>
<th>CSFT (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Op</td>
<td>0.60 +/- 0.15</td>
<td>421.10 +/- 40.14</td>
</tr>
<tr>
<td>Post Op</td>
<td>0.45 +/- 0.23</td>
<td>318.82 +/- 35.22</td>
</tr>
<tr>
<td>p value (paired t test)</td>
<td>p=0.01</td>
<td>p=0.01</td>
</tr>
</tbody>
</table>

**Discussion:**
Riazi-Esfahani M et al evaluated the effect of IVB injection alone or in combination with intravitreal 1 mg triamcinolone acetonide in center-involved DME.\textsuperscript{14} He concluded that the mean CMT reduction was more significant in combination group at 2 weeks of follow-up (P < 0.001), but CMT changes were not significant between the groups at weeks 12th and 24th after injection. We concluded that CSFT was reduced from 421.10 +/- 40.14 micron to 318.82 +/- 35.22 micron at 04 weeks after third IVB injection. Our results are comparable with this study in short term follow up.
Bhayana S evaluated the effect of IVB and posterior subtenon triamcinolone (PST) as an adjunct to macular laser in diffuse DME.\textsuperscript{15} The mean change in maximum retinal thickness in IVB group and PST group was 177.8 ± 85.64 and 156.07 ± 102.86, respectively, which was significantly better than the baseline in both the groups and was comparable in both groups. In our study patients’ LogMAR visual acuity improved by 0.15 while CSFT reduced by 102.28 μm. Our results are comparable with his outcomes.

Khan FA studied the effect of single intravitreal injection of IVB for treatment of clinically significant macular edema in his study at a tertiary care hospital of the same city in 2011.\textsuperscript{12} He reported improvement of BCVA from 0.967591±0.3705 logMAR to 0.65581±0.36078 at one month and 0.6319±0.3900 at two months. In our study mean pre op LogMAR visual acuity was 0.60+/−0.15 while mean post op LogMAR visual acuity was 0.45+/−0.23 at 4 weeks after 3rd injection of IVB. In his study mean pre op CSFT was 502.60±81.622 μm and reduced to 235.75±63.162 μm at one month and 237.58±64.230 μm at 2 months after single IVB. In our study mean pre op CSFT was 421.10+/−40.14 μm while mean post op CSFT was 318.82+/−35.22 μm. Our results are comparable with his results as both studies used IVB as monotherapy.

Talpur R et al studied the effect of IVB in diffuse diabetic macular edema at Sindh Institute of Ophthalmology and Visual Sciences, Hyderabad, Sindh in 2017. He injected three injections of IVB at monthly intervals in 50 eyes of 29 patients and reported significant increase in VA and decrease in CSFT after three months of third administration of IVB.\textsuperscript{10} Our study also reported improvement of BCVA and reduction of CSFT after three doses of IVB on monthly basis. Hence our study was comparable with his results.

Rafiq M et al studied the effect of 3 injections of IVB on monthly basis in DME at a private set up in Peshawar on 20 eyes and concluded the improvement in BCVA and reduction in CSFT after 3 months of last injection.\textsuperscript{11} Our study showed similar outcome at 04 weeks after three injection of IVB at monthly interval. Our results are comparable with his results as monotherapy with IVB resulted in improvement of BCVA and reduction in CSFT in both studies.

**Conclusion:**

Eyes with DME when treated with three injections of IVB at monthly intervals as primary treatment results in improvement of BCVA and reduction in CSFT at 4 weeks after third injection. However long term follow up studies are required to assess the long term effects of IVB injections in DME.

**References:**

4. Distefano LN, Garcia-Arumi J, Martinez-Castillo V, Boixadera A Combination of Anti-VEGF and Laser Photocoagulation for Diabetic Macular

Authors Contribution:
Concept and Design: Lubna Adeeb, Muhammad Aamir Arain
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Management of Visual Malingering with Placebo Drugs
Muhammad Mateen Amir¹, Farah Tariq², Minahal Mateen³, Muhammad Rizwan Ullah⁴

ABSTRACT
Objective: To evaluate the efficacy of placebo drops in the management of visual malingering
Study Design: Prospective study design
Place and duration of study: Al-Khidmat Teaching Hospital Mansoora Lahore
Methodology: A technique was developed for diagnosis and treatment of suspected cases of visual malingering. The technique was based on reassurance along with the instillation of placebo drops consisting of artificial tears. The study was conducted at Al-Khidmat Teaching Hospital Mansoora from February 2016 to October 2019. A total of 34 patients with age ranging from 7 - 25 years came with partial or complete loss of vision. In cases of partially blind patients; neutralizing cylinder and plano glasses were used for diagnosis of malingering. Patients not diagnosed with above method and patients with complete visual loss were treated with placebo drops. It was verbally mentioned that the next treatment option of placebo intraocular injection would be used if not cured with drops.
Result: Twenty patients (58%) have improved vision to 6/6. The remaining 42% improved vision from 6/12 to 6/36. After one week 23 patients was rechecked. Fourteen patients were 6/6 without glasses and the remaining 9 patients became 6/6 with glasses.

Introduction:
Malingering is the deliberate production of false or gross exaggeration of physical or psychogenic symptoms for a known external reward. Factitious disorder is a mental disorder with no clear cause while malingers exaggerate symptoms for personal gain.¹ Malingering may coexist with genuine psychosocial problems. Vision is of prime importance in everyday life because most occupations are essentially visual demanding in nature.² Decreased visual acuity is one of the most common non-organic complaints encountered in the practice of ophthalmology. It may be psychogenic or the result of malingering.³ Every now and then ophthalmologists are confronted with patients who have functional visual loss with complaints similar to those in patients who present with organic pathology. These include vision loss in one or both eyes,
ptosis, blepharospasm, and diplopia.\textsuperscript{4, 5} No recent explanation can be found in their ophthalmological or neurological condition for these complaints. There may be some legal issues behind. Even the most thorough examination and questioning do not reveal a plausible cause of the loss or its reported severity. The ophthalmologist may eventually suspect ocular malingering.\textsuperscript{4}

Determining real incidence or prevalence of malingering is difficult, because majority of cases are not reported. Strong suspicion of malingering arises when there is discrepancy between complaints and clinical findings.\textsuperscript{6} Few suspicion is aroused if the examinee reads fluently the first three lines of the sight-test and suddenly stops, as if he has decided beforehand how far down he will read.\textsuperscript{7} As far as malingering is concerned there is a battle of wits between the subject and his doctor, a struggle in which a clever and well-informed malingerer may come out on the top.\textsuperscript{2} Therefore, in today's world of ophthalmic practice, an ophthalmologist should have enough knowledge on simulation.\textsuperscript{7} The diagnosis is made when all possible contributory pathology of the visual system is excluded, and reassurance remains the cornerstone of management.\textsuperscript{8}

There is a long list of tests which are advised by different clinicians. Some of them are OKN, VEP, ERG, Binocular Tests, Prisms, Ishihara plates, Stereoaucity, Confusion test (polarized tests, red–green glasses, etc.) Preferential-looking acuity, Visual field testing with Goldmann Perimeter and Tangent screen field testing at 1 meter and then at 2 meters are the various tests used to diagnose malingering.\textsuperscript{9, 10, 11} Proprioception is normal even in the presence of severe visual loss if there is no Vitamin B12 deficiency or peripheral nerve dysfunction. A malingerer may not perform this test accurately by will. There is a list of various psychological tests used by psychiatrists to diagnose functional visual loss as well.\textsuperscript{12, 13, 14, 15} Over many decades the visual malingering was under discussion and various methods were suggested for diagnosis and treatment but in the last decade or more the work on this topic was not done. Still the cases are coming and the methods available for diagnosis such as Goldman perimetry, VEP etc. are not available in every hospital in our country. The method we adopted was simple and does not need any costly or non-available equipment such as Goldman Perimeter.

**Subjects and Methods:**
A simple observational study involving a different new technique was conducted at the Al-Khidmat Teaching Hospital Mansoora affiliated with University College of medicine and dentistry Lahore from February 2016 to October 2019 on patients suspected of visual malingering. A total of 34 cases were studied. The patients were examined and any evidence of organic pathology was first ruled out. A detailed history was taken. Optical disturbances, amblyopia, early stages of macula and optic nerve disease and cortical lesions were considered in differential diagnosis.

The patients suspected of visual malingering were examined quickly so as not to give time to the patient of thinking that what is happening. They were tested for malingering through neutralizing cylinder or plano glasses. In a trial frame, plano lenses were placed making the patient believe he was being corrected for his visual loss. Other technique used, was to place + 1.0 diopter cylinder axis 90 in posterior immobile compartment and corresponding -1.0 diopter cylinder axes 90 was placed in revolving compartment in front. If this method fails then some placebo drops were instilled, usually an artificial tear drop every 15-minute interval in the suspected eye only. An informed consent was taken before instilling the eye drops. The patients were informed of the side effects which are virtually none with artificial tears. Artificial tears eye drop was
used because it’s not the drug rather it is a psychological effect which causes reversal of blindness. At the same time the patients were told that if these drops do not cure, then we will go for intraocular injection.

The person responsible for putting the drops were expert enough to verbally communicate with the patient and their relatives in telling the efficacy of drops and in the meantime telling the alternative treatment of intraocular injections in case no improvement occurs with drops. It was carefully explained that the visual function can be expected to improve at any time. This treatment method proved very effective and the results were good enough to be recommended.

The patients were given a face-saving pathway to retreat from the symptom complex. Sufficient time was given for spontaneous recovery of vision in hospital. It was suggested that the instillation of artificial tears at home also for a week for the same reason. The parents were informed that “fortunately,” no organic disease was present. Careful questioning was done to discover the underlying causes. Often there were solvable problems such as excessive burdens experienced by students or not willing to continue further studies. For complex problems the parents were advised to consult some psychiatrist at their convenience afterward.

Results:
The patients were divided into two groups: Group A No Perception of light (Totally blind) and Group B (Partially blind) having VA between 6/36 to CF in one or both eyes. The average age of patients was 16 years and ranged from 7 to 25 years (Fig: 1). Female patients were more as compared to males. There were 22 females (65%) as compared to 12 males (35%) (Fig: 2). The number of patients presenting with unicoical or binocular visual loss is shown in the graph (Fig 3). Placebo drops are an effective way to diagnose and treat patients of malingering with visual loss. The results were good in that patients didn’t feel ashamed of telling the recovery of vision as they think of being the effect of the drops. Because the patients were misleading the physician and because of fear of being injected intraocular, they admitted visual improvement within 1-2 hours of treatment. Twenty patients (58%) improved VA to 6/6, 3 patients (9%) improved to 6/12, 4 patients (12%) improved to 6/18, 4 patients (12%) to 6/24, and 3 patients (9%) improved vision to 6/36 (Fig 4). The patients were advised to come for follow up after one week. Eleven patients did not report back. Out of 23 patients 14 patients were 6/6 without glasses and the remaining 9 patients became 6/6 with glasses.
Figure 2: Gender Distribution

Figure 3: Laterality of visual loss

Figure 4: Improvement in vision after instilling placebo eye drops
Discussion:
Vision is of prime importance in everyday life. A malingerer or a person with functional visual loss tries to mislead others in order to gain the desired end. A malingerer may present with partial or total blindness in one or both eyes. Functional visual loss is a common and challenging part of ophthalmological diagnosis. The diagnosis depends on detailed history and examinations. If a patient has some organic disease it should be treated first.

Many tests have been advised and in use today for an evaluation of malingering cases. Among those tests few are, Visual fields testing, Proprioception, Menace reflex, OKN test, ERG, VEP and Preferential looking method. The fields have sharp margins typically circular or spiral in shape and do not show the normal widening to the temporal side. Some tests are time taking, not available at the spot. Bilateral retrobulbar lesions, chiasmal lesions, bilateral disease of optic tracts, optic radiations or visual cortex may cause bilateral blindness with normal eyes but it does not happen suddenly and without any neurological signs. Hence advanced tests such as MRI or CT scan are not advisable.

Functional visual loss occurs most commonly in situations of conflict, excessive demands, or in personality disorders. The patients demand a compensatory gain: attention, care, considerate treatment etc. The symptom may become permanent if the problem is not resolved. The ophthalmologist then has an important responsibility to tackle the situation. We deal with such patients with a technique which is very convenient and gives us a quick result and releases the tension of parents as well as of patients without undergoing sophisticated tests. Visual field testing requires some vision and for patients denying any vision, instillation of eye drops, and verbally saying, if not cured then intraocular injection will be the solution helped in a great majority of patients. Visual improvement in 58% was 6/6 and in 79% of cases was 6/18 to 6/6 on the same day.

Conclusion:
A balanced mind is capable enough to successfully face emotional conflicts occurring in day to day life of an individual. Life being complex, sometimes results in such an emotional crisis that cannot be tolerated for long and various defensive mechanisms come into play creating symptoms. Visual malingering remains a clinical diagnosis which is made when the ophthalmologist demonstrates that the visual acuity is better than subjectively stated, and fails to find pathology of the visual system. Placebo drops work effectively and save the time of both patients as well as the clinician.

References:

Authors Contribution:
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Statistical expertise: Minahal Mateen
Critical Revision: Muhammad Rizwan Ullah
Postoperative Refractive Outcome and Accuracy of Biometry in Pediatric Cataract with Primary Intraocular Lens Implantation

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ABSTRACT:
Objectives: To show the refractive outcomes, accuracy of intraocular lens power selection.
Place & Duration of study: Paediatric ophthalmology department of Al-Shifa Trust Eye Hospital, Rawalpindi. 1st July 2014 to 31st December 2015.
Methodology: All post-operative patients of cataract surgery beneath 8 years of age. Patients with traumatic cataracts, with any other ocular illness were excluded. Dilated objective refraction was performed by retinoscopy on all the post-operative patients fulfilling inclusion criteria to observe whether they achieved the target post op refraction or not. Information regarding pre-operative biometry and power of IOL (intra ocular lens) implanted during the surgery was taken from patients’ clinical data. The collected data was entered in computer software SPSS (Statistical Package for Social Sciences) version 19.0 and analyzed with same software.
Results: The results of the study showed that a large number of the patients didn’t achieve the intended post-op target hyperopia. This study showed that the target post-op hyperopia was not achieved in a large number of patients (i.e. 17 patients out of 64 patients) with 13 patients becoming myopic and 04 patients becoming emmetropic after the surgery.
Conclusion: This study calls for an increase in the percentage reduction of the IOL power according to the age (in cases where percentage reduction method is implemented). Al-Shifa Journal of Ophthalmology 2019; 15(4): 174-180. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

Introduction:
The incidence of childhood cataract is estimated as 1 to 6 per 10,000 births.1 Aphakia after cataract extraction in children can cause problems like anisometropic amblyopia, glaucoma, strabismus and loss of binocular function. It is difficult for a child of less than 3 years of age to tolerate contact lenses and noncompliance can lead to amblyopia; IOL resolves these problems.2 Advances in surgical procedures, improvements in IOL designs & materials and improved understanding of paediatric eye, IOL is the most practical procedure for cataract removal and correction of aphakia.3

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Recent data suggests better visual outcome in unilateral cataract cases corrected with cataract extraction with IOL implantation vs. cataract extraction followed by contact lens correction. Different studies are done to show the efficacy and safety of IOL. After IOL implantation significant myopia is present that is why selection of IOL is done in such a way that it will produce under correction. Early surgery results in less likelihood of amblyopia and excellent visual acuity. The question is how much under correction should be performed according to the age. The two approaches used are percentage reduction or absolute value reduction from the calculated emmetropic power. The first one is more precise but second one is easy to perform. There is no consensus on ideal method of calculating IOL power in infants because of rapid growth of ocular dimensions after the surgery which can cause large refraction shifts.

There are different opinions regarding the age of implantation of IOL. There is risk of complications of IOL implantation in a very small child which includes inflammation and posterior capsule opacification after operation and it will lead to sequence of further surgeries. In children, eyes have steep keratometric values which cause difficulty in accurate IOL power calculation which can create problems for surgeon in long term care of child who is going to have a cataract surgery. As eye of a child is in growing process it puts surgeon in a fix, as to make a suitable decision regarding selection of power of the lens.

Recently, improvement in instruments helped a lot to take axial length and keratometry measurement more accurately. It became easy to calculate IOL power in adults but not in children. In children, implanting an IOL at the emmetropic power will lead to development of myopia when eye grows. Yet aiming for hyperopia may create difficulties in treating amblyopia. So both approaches have got pros and cons and there is no definitive solution. The IOL power calculation is affected the most because of the errors in AL measurement. In adults normally the error is of 2.5 D per mm but in children it increases up to 3.75 D per mm. To decrease the chance of error we have to take several readings and take an average of them. In this way an acceptable K value can be determined in children.

Usage of theoretical formulas is more preferable because of their accuracy for paediatric eyes and are much reliable than regression formulas. However, in children the main cause of post-operative refractive errors is the ongoing growth of eye instead of the errors in measurements. For long-term follow up in children, it is important to focus on how much under correction should be achieved depending on the growth of eye of that particular patient.

This was a descriptive study conducted at Pediatric Ophthalmology Department of Al-Shifa Trust Eye Hospital, Rawalpindi from 1st July 2014 to 31st December 2015 on 64 patients selected by non-probability purposive sampling. Every post-operative case of cataract surgery below 8 years old was included except for patients with traumatic cataracts, with any other ocular illness.

Dilated objective refraction was performed by retinoscopy on all post-operative patients fulfilling inclusion criteria to see whether they achieved the target post op refraction or not. Information regarding pre-operative biometry and power of IOL (intra ocular lens) implanted during the surgery was taken from patients’ clinical data.

The collected data was entered in computer software SPSS (Statistical Package for Social Sciences) version 19.0 and analyzed with same software.

**Results:**
The paired-samples t-tests were conducted to evaluate the difference between the
under correction in biometry values of patients before surgery and the spherical equivalent produced after surgery, in Myopic, Hyperopic and Emmetropic Patients. Among myopic patients, there was a statistically significant difference between the amount of under correction in Diopters from Biometric values of patients \( (M = 1.38, SD = 0.82) \) and the Spherical Equivalent of patients produced after surgery \( (M = -1.65, SD = 2.13) \), \( t (12) = 5.29, p <0.001 \) (two-tailed).

Among hyperopic patients, there was also a statistically significant difference between the amount of under correction in Diopters from Biometric values of patients \( (M = 2.79, SD = 1.53) \) and the Spherical Equivalent of patients produced after surgery \( (M = 2.22, SD = 1.65) \), \( t (46) = 2.98, p = 0.005 \) (two-tailed).

A statistically significant difference was also found among emmetropic patients, between the amount of under correction in Diopters from Biometric values of patients \( (M = 2.38, SD = 0.75) \) and the Spherical Equivalent of patients produced after surgery \( (M = 0.00, SD = 0.00) \), \( t (3) = 6.33, p = 0.008 \) (two-tailed).

### Table 1: Patient characteristics and target versus achieved post-operative refraction

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>N</th>
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<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
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### Table 2: Age of Patients

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Table 3: Target versus achieved post-operative refraction in different age groups

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Table 4: Target versus achieved post-operative refraction in males and females

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<td>Female</td>
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Table 5: Target versus achieved post-operative refraction in all three groups

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<td>Under Correction in Diopters (20% reduced from biometry for ≤ 2 yrs &amp; 10% for &gt; 2 yrs of age)</td>
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<td>5.29  (12)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hyperopia</td>
<td>Under Correction in Diopters (20% reduced from biometry for ≤ 2 yrs &amp; 10% for &gt; 2 yrs of age)</td>
<td>47</td>
<td>2.79</td>
<td>1.53</td>
<td>2.98  (46)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Spherical Equivalent in Diopters after Surgery</td>
<td>47</td>
<td>2.22</td>
<td>1.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emmetropia</td>
<td>Under Correction in Diopters</td>
<td>4</td>
<td>2.38</td>
<td>0.75</td>
<td>6.33  (3)</td>
<td>0.008</td>
</tr>
</tbody>
</table>
**Discussion:**

Many studies have demonstrated a better visual outcome with IOL implantation.\(^\text{10}\) McClatchy et al took data from seven centres, of 83 patients with IOL implanted eyes. Ages were between 3 months to 10 years were followed the patients up to 3 years and found that myopia developed more in the IOL implanted eye and it was due to effects of IOL in developing eye.\(^\text{11}\) Studies show that with increasing age of child, rate of development of myopia decreases and variation among patients also becomes less.\(^\text{12}\)

The ideal IOL power should be calculated by predicting the expected myopia and then under correct the eye accordingly. It will lead to less refractive errors when child grows and also helps to correct amblyopia in childhood. This selected power of IOL should be easily corrected by glasses or contact lenses and should help to treat amblyopia.

A child who has cataract or IOL in one eye, power of lens is selected to decrease the chances of aniseikonia. And if both eyes are undergoing surgery, it can be avoided by choosing same refraction for both eyes and even more hyperopia is accepted. Recent studies and advances suggest that future myopia is easily manageable as compare to amblyopia.

If patients or parents are less cooperative and their compliance regarding glasses, contact lenses or amblyopia therapy is less likely than wise decision is that refractive error should be less. Family history regarding high refractive error should be taken. Because if the parents have myopia, child eye will grow more so decision can be taken to leave more hyperopia. Generally, more undercorrection is needed, if the emmetropic IOL power is high. In children with abnormally small eye balls, highest possible power of the lens should be chosen because in such patients it is difficult to achieve the desired refraction.

The paired-samples t-tests were conducted to evaluate the difference between the under correction in biometry values of patients before surgery and the spherical equivalent produced after surgery, in Myopic, Hyperopic and Emmetropic Patients. Among myopic patients, there was a statistically significant difference between the amount of under correction in Diopters from Biometric values of patients ($M = 1.38$, $SD = 0.82$) and the Spherical Equivalent of patients produced after surgery ($M = -1.65$, $SD = 2.13$), $t (12) = 5.29$, $p<0.001$ (two-tailed).

Among hyperopic patients, there was also a statistically significant difference between the amount of under correction in Diopters from Biometric values of patients ($M = 2.79$, $SD = 1.53$) and the Spherical Equivalent of patients produced after surgery ($M = 2.22$, $SD = 1.65$), $t (46) = 2.98$, $p = 0.005$ (two-tailed).

Difference among emmetropic patients was significant, between the amount of under correction in Diopters from Biometric values of patients ($M = 2.38$, $SD = 0.75$) and the Spherical Equivalent of patients produced after surgery ($M = 0.00$, $SD = 0.00$), $t (3) = 6.33$, $p = 0.008$ (two-tailed).

There are different factors which affect the axial growth after IOL implantation and even few of them may affect the normal eyes such as gender and race. Further studies should be conducted to include all the factors that affect the growth of eye after surgery.

Surgeons should try their level best to achieve good outcome in future but at the same time they should be prepared for complications like myopia which their patient can develop later in adulthood which may lead to further surgeries for correction or exchange of implanted lens. And chances of such complications are high in patient who gets operated in early years. Studies should be conducted regarding long term outcome of the patients undergoing
IOL implantation so that we can make new formulas for calculation of power of the lens that is to be implanted.

Conclusion:
This study showed that the target post-op hyperopia was not achieved in a large number of patients (i.e. 17 patients out of 64 patients) with 13 patients becoming myopic and 4 patients becoming emmetropic after the surgery. This calls for an increase in the percentage reduction of the IOL power according to the age, if a surgeon wants to follow the percentage reduction method examined in this study.

References:

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Concept and Design: Muhammad Kashif Habib, Adnan Aslam Saleem
Data Collection / Assembly: Nighat Jabeen, Maryam Ghuncha
Drafting: Muhammad Kashif Habib, Adnan Aslam Saleem
Statistical expertise: Maryam Najam, Furqan Ahmed Khan
Critical Revision: Muhammad Kashif Habib
Correlation of Apparent Diffusion Co-Efficient Mapping of Visual Pathways with Glycosylated Haemoglobin Levels in Diabetic Patients Presenting with Blurring of Vision

Sarah Nisar¹, Lubna Sarfraz²

ABSTRACT:
Objective: This research has been done to study the impact of diabetes on Visual pathway using diffusion weighted magnetic resonance imaging (DW MRI) and calculating the Apparent Diffusion Co-efficient (ADC) values.

Materials and Methods: Conventional MRI and Diffusion-weighted imaging (DWI) of the brain of diabetic patients were obtained and DW/ADC values of optic nerve, optic tract, thalamus and visual cortex were calculated by drawing regions of interest (ROI) of these regions. HbA1c was done using chemiluminescent technique.

Results: Calculated ADC values were relatively found to be higher in the patients who had relatively raised HbA1C values and the duration of disease was longer, hence we can say value of HbA1c positively correlates with ADC values in the visual pathways. No difference was observed between women and men or between the hemispheres.

Conclusions: Thus we can say DWI can be a guide for follow-up and management of patients with potentially developing diabetic retinopathy and prevent blindness in them.

Introduction:
Diabetes mellitus is a multi-systemic disease causing multi-organ damage. Brain and retina being its important targets. Factors like reduced blood flow, oxidative stress, metabolic derangements, fluctuating blood glucose levels, and vascular disorders may cause changes in brain which can be both structural and functional.¹ MR imaging is used to investigate orbital conditions and helps in differentiating the orbital soft tissues and visual pathways.² Diabetic retinopathy is a major cause of blindness in adults. Micro-vascular changes in the retinas of diabetics can cause blurring or even blindness and this resultant visual impairment can also be a consequence of pathophysiological alterations in the visual pathway. In the quest to fully understand the pathophysiology of diabetic retinopathy resulting in vision loss, use of MRI techniques is a great tool. These are non-
invasive techniques and can map the changes in microstructure, white matter, metabolites, and anatomy and physiology of the brains of diabetic retinopathy individuals.³

Diffusion-weighted imaging (DWI) is a technique where strong magnetic gradients are applied to biological tissues and the water molecules in those tissues are quantitatively measured. Thus ADC (Apparent diffusion coefficients) can be calculated quantitatively. Tissue microstructure and micro dynamics affect the diffusion. Clinical application of DWI includes assessment in tumour, ischemia, infection and cysts. It can also be used in an emergency setting for screening for acute retinal pathology. Although it may not be specific for aetiology, but can be helpful in rapidly localising the retinal pathology and in early therapeutic interventions.⁴ An association between retinopathy and brain tissue damage is found by white matter lesions in the brain and on functional magnetic resonance imaging (f MRI) of these patients.⁵ The DWI image is created by the motion of water molecules in the extracellular, intracellular and intravascular space.

The vitreous also has changes through liquefaction in patients with DM, even in those without apparent Diabetic Retinopathy as shown in certain studies in different stages of DR using diffusion-weighted imaging technique.⁶ In addition to the micro-vascular complications of prolonged hyperglycaemia, it can produce cognitive dysfunction and is associated with decreased processing speed, mental flexibility and attention functioning.⁷

In this study, the aim is to highlight and quantify changes in visual pathway in brain by ADC mapping in diabetic patients presenting with blurring of vision, and correlating it with the HBA1C levels. To our knowledge, no such study has ever been conducted locally or in south Asian population to provide a baseline for a disease like diabetes which is so common yet disabling in these demographics. This study will not only help in early diagnosis and alternate treatment strategies and planning follow up of diabetic patients but also in preventing the complications leading to blindness.

**Materials and Methods:**

This observational study started in Nov 2018 and data collection was completed in Nov 2019. A total of 50 patients were selected by non-probability purposive sampling. After the approval by Research Ethics Committee, signed informed consent was obtained from the patients. This study was conducted by the radiology, pathology and eye departments of Bahawal Victoria Hospital, Bahawalpur. Known diabetic patients coming to Radiology department for MRI brain and orbit with complaints of blurring of vision were selected. Patients with orbital pathologies like glaucoma and other posterior chamber abnormalities were excluded from the study. Patient evaluation for study inclusion was done by ophthalmologist in EYE OPD. Time duration of the disease and hemoglobin A1c (HbA1c) levels were also recorded.

HbA1c was done in pathology Department, QAMC using chemiluminescent technique on Abbot’s Architect sr 1000. The MRI examination was performed on 1.5-Tesla GE machine (model: Optima MR 450w GEM (USA). T1-weighted images (TR=579ms, TE=14.1 ms) in the sagittal and axial planes. Fast spin-echo T2-weighted images (TR=4528 ms, TE=106 ms) in the axial and coronal planes. In DW, pulse sequence (TR=8000ms, TE=77.1 ms, with FOV24x24, matrix size of =128x128, slice thickness=5 mm and slice number=22. The slice orientation=axial plane, interslice gap thickness=1mm was used in all patients two different b values (0 and 1000s/mm²). With the help of available software, the ADC maps were drawn. Areas.
of optic nerve head, optic tract, thalamus and visual cortex were selected for analysis keeping in accordance with recent literatures that these areas are potentially thought to be affected in diabetic patients. Regions of interest (ROIs) drawn manually and ADC values were calculated from the ADC map (Figure I). A small ROI (20–40 pixels) was drawn to avoid vessel and CSF effect. The ROIs were drawn on each side and mean was used for analysis purpose (Fig 1).

For statistical analyses SPSS 23 for Windows was used. The data are presented as mean ± standard deviation (SD). ADC values obtained from the vitreous of each patient were analyzed and the three groups of patients were compared using one way using ANOVA. A p value less than 0.05 was considered to be significant.

**Results:**
Mean age is 65 years ± 24 years. 66% of the study participants were males as compared to 34% females (Table: 01). Calculated ADC values were found to be relatively higher in the patients who had raised HBA1C values (Table: 02) and the duration of disease was longer (Table III). Patients with HbA1C value ≤ 7.0% indicating good control had relatively lower ADC value as compared to patients having HbA1c values between 7.1-8.5% and poor glycaemic control (HbA1c values > 8.5%). Hence value of HbA1c positively correlated with ADC values of the visual pathways (p: 0.0001). No difference was observed between women and men or between the hemispheres.

The observed increase in ADC values indicates the neuronal loss especially in visual cortex by DWI in the poorly controlled diabetic patients. This result also supports the association between developing diabetic retinopathy and brain injury associated with uncontrolled HbA1C levels. This is really helping for the clinicians in terms of strategies applied in the treatment of visual impairment by knowing the injury in the visual cortex as well on DWI which may get missed otherwise.

<table>
<thead>
<tr>
<th>TABLE I: Age and sex distribution in study group</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE AND SEX DISTRIBUTION IN STUDY GROUP</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Age groups</strong></td>
</tr>
<tr>
<td>&lt;50</td>
</tr>
<tr>
<td>50-70</td>
</tr>
<tr>
<td>71-90</td>
</tr>
<tr>
<td>&gt;90</td>
</tr>
</tbody>
</table>
TABLE II: Severity of HbA1c and ADC Values

<table>
<thead>
<tr>
<th>HbA1C levels</th>
<th>ADC (Mean ±SD)x10^-6 mm2/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good control (≤7.0%)</td>
<td></td>
</tr>
<tr>
<td>n=13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optic nerve:845±15</td>
</tr>
<tr>
<td></td>
<td>Optic tract:660±28</td>
</tr>
<tr>
<td></td>
<td>Thalamus:709±12</td>
</tr>
<tr>
<td></td>
<td>Visual cortex:710±13</td>
</tr>
<tr>
<td>Fair control (7.1-8.5%)</td>
<td></td>
</tr>
<tr>
<td>n=21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optic nerve:899±45</td>
</tr>
<tr>
<td></td>
<td>Optic tract:690±12</td>
</tr>
<tr>
<td></td>
<td>Thalamus:722±31</td>
</tr>
<tr>
<td></td>
<td>Visual cortex:733±46</td>
</tr>
<tr>
<td>Poor control (&gt;8.5%)</td>
<td></td>
</tr>
<tr>
<td>n=16</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optic nerve:1098±48</td>
</tr>
<tr>
<td></td>
<td>Optic tract:704±18</td>
</tr>
<tr>
<td></td>
<td>Thalamus:759±17</td>
</tr>
<tr>
<td></td>
<td>Visual cortex:811±31</td>
</tr>
</tbody>
</table>

Table III: Disease Duration and ADC Values

<table>
<thead>
<tr>
<th>Disease duration (years)</th>
<th>No. of cases</th>
<th>Percentage</th>
<th>ADC value (Mean ±SD)x10^-6 mm2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>O.N</td>
</tr>
<tr>
<td>&lt;5</td>
<td>8</td>
<td>16</td>
<td>810±48</td>
</tr>
<tr>
<td>5-10</td>
<td>18</td>
<td>32</td>
<td>850±22</td>
</tr>
<tr>
<td>&gt;10</td>
<td>24</td>
<td>48</td>
<td>967±45</td>
</tr>
</tbody>
</table>

(O.N= Optic nerve, OT=Optic tract, TH= Thalamus, VC= Visual cortex)

Fig 1 (Nisar and Sarfraz.) ADC Mapping Showing ROI drawn at a) Left optic tract b) Right optic nerve c) Right Thalamus and visual cortex.

Discussion:
The neuronal loss observed in our study is also seen in study done by Wessels AM et al who applied voxel-based morphometry on MRI, it was a comparison of grey matter density (GMD) between three groups of participants and used it as a cortical atrophy marker. ADC change patterns differed among brain regions as shown in our study as well as in a study by Glaser et al, where in regions like
frontal cortex and thalamus, values were markedly raised during DKA treatment, compared to after recovery values. However, these trends are not evident in the occipital cortex.\textsuperscript{9}

The ADC values in the literature do not provide any definite baseline value, however the values in the study fall within the normal rough range available for each area, however in increasing order with the disease severity and duration. In normal brain, the ADC values in both grey and white matter were within a narrow range and beyond these may indicate disease making DW useful tool for tissue characterization.\textsuperscript{10,11}

In this present study, ADC values in optic nerve head, optic tract, visual cortex, and thalamus with blurring is seen to be higher in diabetic patients with poor glycaemic control and raised HBA1c. It is thought to be due to neuron cell death and gliosis, secondary to increase in interstitial fluid. Diabetic retinopathy triggers neuronal apoptosis and causes visual loss. The changes are not limited to retina only in these cases, they also cause neuronal loss in visual pathway.\textsuperscript{1} The stimulation of the visual centre is thought to be decreased by neuronal degeneration. In lieu of these, we can say that possibly due to long-term decreases in stimulation of cortical neurons, changes in entire visual pathway may occur.\textsuperscript{11}

Another study explains abnormal changes in these indices as a compensatory behaviour to reduce the cognitive impairments in patients with type 2 DM by mobilizing additional neural resources like excessive activation and prompt networking of various brain areas.\textsuperscript{12}

In brain, the ADC is relatively less as compared to free water diffusion in aqueous solution. Molecules displacement becomes limited as it reaches the boundaries of closed spaces and ADC lowers as seen in restricted diffusion. However, no evidence of clear restriction behaviour has been observed in vivo for water in the brain.\textsuperscript{13}

Furthermore, studies have also established that true compartmentation or restriction effects from cell membranes, any scattering or obstruction or tortuosity does not well explain the low diffusion of water. This suggests that the reduced diffusion coefficient in biological tissues is due to much smaller cellular components. Meaning that the permeable membranes are likely to hinder the diffusion process.\textsuperscript{14}

Another study shows that in diabetics with proliferative retinopathy, ADC values were found higher than that to non-proliferative type of retinopathy. It can be related to poor glycaemic control.\textsuperscript{15} Thus we can say Diffusion-weighted imaging can be used as a useful tool to predict the ‘at risk’ tissue fate with ADC values analysis.\textsuperscript{16}

Lu et al. and Çakmak et al measured ADC to be significantly lower in kidneys of patients with diabetic nephropathy. Significant negative correlation between ADC values and clinical stage of diabetic nephropathy was found. There is also a significant correlation between Renal ADC values with clinical stages of diabetic nephropathy.\textsuperscript{17} Being used in diffuse pathologies, DWI shows not only feasibility and reproducibility, it also highlights the need to standardize methods, additional validation and qualification.\textsuperscript{18}

In patient with symptoms of ischemia, follow-up MR revealed ischemia in the optic nerve and retina adding to an accumulating body of literature on restricted diffusion in brain tissues in severe ischemia.\textsuperscript{19} Chronic ischemia occurs in diabetes, leading to reduced cerebral perfusion, additionally long-term uncontrolled sugar levels lead to neuro-degeneration. There is decrease in intracellular volume in the brain and the ratio of the extracellular to the intracellular volume is increased, leading to increased ADC.\textsuperscript{20}
Diabetic retinopathy is a major complication and cause of blindness occurring in about 45% of diabetic patients. Blurred vision and abnormal appearance of the fundus are the late presenting manifestations. By the time a clinical diagnosis is made, vision loss or blindness is often the inevitable outcome. Results from clinical trials have documented that strict glycaemic control in the early stages is effective in reducing the risk of DR. Thus, an early identification of at risk diabetic patients of developing DR will enable timely intervention and treatment to minimize the risk of vision loss.

In this study an increase in ADC values was found that supports the possible neuron loss in patients with diabetic retinopathy. It also supports brain injury associated with diabetic retinopathy. Additionally, our findings in current study are helpful in terms of strategies that need to be applied by clinicians in treatment of visual impairment.

**Conclusion:**

We can conclude that DWI and ADC mapping can be a guide for treatment, follow-up and management of the patients presenting with early diabetic retinopathy.

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Carotid Cavernous Sinus Fistula
Muhammad Rizwan Aziz¹, Paula Chattington², Faisal Saleem Khan³

ABSTRACT
75 Years old male previously investigated for pulsatile tinnitus in the primary care was admitted with six to eight weeks history of double vision and headache that intensified during the day time, associated with four weeks history of red, painful left eye for which he was seen in the emergency department (ED). Clinical examination confirmed 3rd, 4th and 6th cranial nerves palsies. Urgent ophthalmology referral made, arranged for contrast intracranial and carotid CT scans, diagnosed as Carotid Sinus Fistula and referred to the Neurosurgical team for further management. Due to effective communication and early management steps taken such as involving specialist team, arranging important diagnostic investigations it was possible to establish diagnosis. Patient was referred to tertiary centre for definite management. The take home message is to highlight importance of appropriate history taking, clinical examination and to involve relevant specialist for the best management and outcome as in this case was helped by the Ophthalmology team. Al-Shifa Journal of Ophthalmology 2019; 15(4): 188-191. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

Introduction
Carotid sinus fistulas are vascular malformations. These are mostly acquired rather congenital malformations. Carotid-cavernous fistulas (CCFs) may arise spontaneously or from secondary causes. CCFs can present with a variety of signs and symptoms. Many lesions are associated with significant neuro-ophthalmologic morbidity and mortality.¹ The diagnosis is based on history, clinical examination and radiological investigations. It is classified into two subtypes, direct and indirect CSF.² Management depends on the clinical signs and symptoms, location of the lesion, local tissue involvement and complications associated with or without treatment.

Case Report
A 75 year old man with past medical history of epiglottitis, rheumatoid arthritis, hypertension and hypercholesterolemia currently taking amlodipine, atorvastatin, folic acid and methotrexate, was presented to the AED with bilateral dry, itchy eyes. He had 2-3 weeks history of blurred vision and headache that worsened throughout the
day. He reported that he had pulsatile tinnitus for several years that had been investigated by his GP in the past but unsure about outcome.

On examination the visual acuity was 6/5 on the right side and 6/6 on the left side. His pupils were reactive and equal with direct and consensual light reflexes preserved, 3rd, 4th and 6th cranial nerves were intact. He was discharged from the ED with chloramphenicol eye drops that did not resolve his symptoms. Four weeks after his first attendance to the AED he was admitted with left eye redness, outwards and downward deviation, with incomplete adduction and abduction. His pupil was marginally bigger on the left side although reactive to light. He had diplopia in his left eye in all directions of gaze and had clinical palsy of the 3rd, 4th and 6th cranial nerves. No other acute neurological deficits.

The plain CT scan head was normal and all base line blood tests were within normal limits. The case was discussed with on call ophthalmology registrar and after specialist review further investigations including carotid and cranial contrast angiogram carried out that confirmed diagnosis of carotid cavernous sinus fistula. He was referred to a tertiary neurosurgical centre for embolization of his fistula and treated successfully.

Discussion:
A carotid-cavernous sinus fistula (CCF) is an abnormal connection between carotid artery and the network of veins located in small spaces behind the eyes called cavernous sinuses. Sometimes an abnormal channel forms between these veins and one of the internal or external carotid arteries. This formation happens following a small tear in one of the carotid arteries. If the tear occurs near the veins in the cavernous sinus, an abnormal channel may form between the artery and the network of veins, through which blood may flow. This is called a fistula. Due to fistula, pressure in cavernous sinuses can rise that may cause compression of important cranial nerves around the cavernous sinuses leading to disruption in eye motor functions, facial sensation and also eye swelling and abnormal vision due to its effect on venous drainage system of eyes. Further discussion highlighting types, clinical presentation, key investigations, management and risks is provided in a separate table below.

Table 1: Types of CCF and their characteristics

<table>
<thead>
<tr>
<th>Type of Fistula</th>
<th>Direct</th>
<th>Indirect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>A connection between part of the internal carotid artery and the veins inside cavernous sinus. In this type of fistula, there is usually a high blood flow rate. This type is most common.</td>
<td>A fistula between the cavernous sinus veins and branches of the carotid artery in the membranes that enclose brain. The rate of blood flow in these fistulas is usually low. Indirect CCFs frequently arise without warning</td>
</tr>
<tr>
<td>Causes of Carotid-Cavernous Sinus Fistula</td>
<td>Motor vehicle accidents, Fights, Falls, Surgery</td>
<td>They have no known cause. However, risk is increased with: High blood pressure, Hardened arteries / ATH</td>
</tr>
</tbody>
</table>
| Clinical signs and symptoms | Red eye  
|----------------------------| Double vision  
|                             | Loss of vision  
|                             | Eye protrusion  
|                             | Headache  
|                             | Facial pain  
|                             | Epistaxis  
|                             | Ringing in ears  
|                             | Weak or missing eye movements  
|                             | Bulging eye which may be pulsate  
|                             | An audible swish or buzz coming from eye |
| Investigations | Cerebral angiography is considered the gold standard for diagnosing a CCF. Non-invasive imaging modalities such as computed tomography angiography and magnetic resonance angiography can help make a presumptive diagnosis of CCF, but do not definitively confirm its presence. |
| Treatment of Carotid-Cavernous Sinus Fistula | The goal of CCF treatment is to completely occlude the fistula while preserving the normal flow of blood through the ICA. Trans-arterial or trans-venous embolization is the first line treatment modality for the treatment of most CCFs. |
| Conservative management | Conservative management, consisting of external manual compression of the ipsilateral cervical carotid artery several times a day for 4–6 weeks, may be effective in the treatment of indirect, low-flow CCFs. However, this is ineffective in the treatment of direct, high-flow fistulas. Eye lubricants. Reduce I/O Pressure Close follow ups with ophthalmology team required. |
| Risks if untreated | A fistula can raise the pressure in cavernous sinuses, which may compress the cranial nerves located around the cavernous sinuses Facial numbness / pins / needles Abnormal vision Corneal ulcers Proptosis Headaches CN palsies |
References:

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Data Collection / Assembly: Muhammad Rizwan Aziz
Drafting: Muhammad Rizwan Aziz
Critical Revision: Paula Chattington, Faisal Saleem Khan
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