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EDITORIAL

Current Management Options and Future Trends in Diabetic Retinopathy

Sara Zafar, Tayyab Afghani

Diabetic Retinopathy is one of the leading causes of blindness in the world. It has emerged as an epidemic in developing countries. There is continuous focus on finding new strategies to prevent and control blindness from diabetic retinopathy.

Most important risk factors for the development and progression of DR are the type and duration of diabetes, hyperglycemia and hypertension. Others factors like microalbuminuria and dyslipidemia are also important risk factors for the progression of DR.

Several systemic drugs have been developed for the prevention and treatment of DR. The protein kinase C inhibitor, ruboxistaurin mesilate, administered orally was effective in halting DME and vision loss but not in preventing the progression of DR [1]. Another drug, long-acting somatostatin analogue, octreotide, given intramuscularly every 4 weeks in moderate-to-severe NPDR to low-risk PDR, was not effective in arresting DR progression. However recently two classes of drugs: renin-angiotensin system (RAS) blockers [2] and fenofibrate (a hypolipidemic drug) [3] have emerged as potential systemic treatments for DR. Furthermore, calcium dobesilate monohydrate (CaD) appears to be a promising treatment for DR, though it is not widely used in clinical practice [4].

Laser has remained the mainstay of treatment for quite sometime. Pan retinal photocoagulation and focal photocoagulation have been used in recent past. However recently Pattern scan laser (Pascal), Subthreshold diode micropulse laser (SDM), Retinal rejuvenation therapy (2RT) and Selective retina therapy (SRT) are new treatment options that promise reduced laser-induced side effects like constriction of visual fields, reduced dark adaption, and reduced color and contrast perception [5].

Anti-VEGF agents Pegaptanib (Macugen), Ranibizumab (Lucentis), Bevacizumab (Avastin), Aflibercept (Eylea) have been used effectively at different times. The new treatment options now include Anti-VEGF agents plus focal/grid laser therapy. Intravitreal anti-VEGF therapy is generally safer and visual acuity could be maintained with tapering the injection frequency over time [6].

There is also a recent interest in the use of steroid implants like Dexamethasone sustained-release intravitreal implant (Ozurdex) Fluocinolone acetonide implant (Retisert). These implant therapies tend to reduce the frequency of intravitreal anti-VEGF injections and less associated with cataract formation and increased intraocular pressure than the previous steroid agents[7].

Similarly transconjunctival sutureless 23- or 25-gauge vitrectomy has gradually taken over the conventional 20-gauge vitrectomy reducing surgical time and making the rehabilitation of patients faster [8].

What future holds for stem-cell therapy in diabetic retinopathy remains to be seen. Most studies so far have attempted to alleviate typical abnormalities of early retinopathy, including vascular

hyperpermeability, capillary closure and pericyte dropout. Success was reported with adult stem cells (vascular progenitors or adipose stem cells), as well as induced pluripotent stem cells from cord blood [9].

Regardless of the modern therapeutic options and novel preventive strategies being investigated for diabetic retinopathy, there is no alternative to tight glycaemic control, as well as comprehensive patient, professional and public health education and a strong networking between Diabetologists/physicians and Ophthalmologists.

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ORIGINAL ARTICLE

Visual and Angiographic Outcome of Oral Danshenform Compound (Tricardin) in Cases of Non proliferative Diabetic Retinopathy

Tehmina Nazir[1], Fariha Taimur[1], Badaruddin Athar Naeem[1]

ABSTRACT:
Objective: To determine visual and angiographic outcome of oral Danshenform Compound (Tricardin) in patients of non proliferative diabetic retinopathy & observe FFA changes
Study design: An Interventional case series.
Place of study: Department of Ophthalmology, Fauji Foundation Hospital Rawalpindi.
Subjects and Methods: The study included 30 eyes of patients diagnosed as cases of moderate to severe non proliferative diabetic retinopathy meeting the inclusion criteria. Duration of study was 0ne & a half year. Post medicine BCVA , slit lamp examination and fundoscopy was done on each visit. Wilcoxin signed rank test was applied at 5% level significance. P –values of 0.00 was statistically significant
Result: There was a marked improvement in post op visual acuity with P- value < 0.000 which is highly significant after the use of Danshenform Compound (Tricardin). FFA showed no changes.
Conclusion: Trial of Danshenform Compound resulted in marked improved visual outcome of almost all the patients with moderate to severe non-proliferative diabetic retinopathy with no angiographic changes. *Al-Shifa Journal of Ophthalmology 2016; 12(4): 178-182.* *© Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

Introduction:

Diabetic retinopathy is increasingly becoming a major cause of blindness throughout the world in the age group of 20–60 years.(1) Loss of productivity and quality of life for the patient with diabetic retinopathy lead to additional socio-economic burdens on the community.

1. *Fauji Foundation Hospital / Foundation Medical College Rawalpindi*

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Diabetic retinopathy usually affects both eyes. People who have diabetic retinopathy often don't notice changes in their vision in the disease's early stages. But as it progresses, diabetic retinopathy usually causes vision loss that in many cases cannot be reversed. Diabetic retinopathy is a predominantly a microangiopathy in which small blood vessels are particularly vulnerable to damage from high gulucose levels. (2) DM is the leading cause of cardiovascular diseases, which can lead to varied cardiovascular complications by aggravated atherosclerosis in large arteries and coronary atherosclerosis, thereby grows the risk for macro and microangiopathy such as myocardial infarction, stroke, limb loss and retinopathy.(3) Several forms of specific end organ damage including nephropathy, retinopathy, lacunar infarction and

microvascular angina primarily involves microcirculation.[4] Stability of microcirculations plays important role in treatment of diabetic retinopathy. Many steps have been taken to control blindness from diabetes mellitus that ranges from strict glyceamic control, intravitreal administration of anti VEGF to the use of laser and pars plana vitrectomy.

Danshenform Compound {TriCardin) has emerged as a potent research medicine that has additional benefit from targeting the microcirculation in terms of prevention of or reduction in end organ damage.[4]Improved microcirculation results in good oxygen supply resulting in decrease chances of hypoxia related complications in diabetic retinopathy. This compound improves microcirculation at all levels by executing following action,

- Prevention of endothelial cell injury
- Inhibiting leukocyte adhesion
- Inhibiting platelet aggregation
- By acting as an antioxidant

Tall claims of beneficial effects in diabetes of Danshenform Compound resulted in trial of oral capsules in patients of non proliferative diabetic retinopathy that was planned in FFH to see its effects on visual acuity and FFA findings. This is so far the first type of study done.

Subjects and Methods:

This study was an Interventional case series that was carried out in Fauji Foundation Hospital Rawalpindi. Sample size was 30 eyes of the patients who had non-proliferative diabetic retinopathy.

Inclusion Criteria:

- Patients with moderate to severe non-proliferative diabetic retinopathy
- Age of 40 -60 years
- No other ocular pathology or ocular associated systemic pathology
- Either sex

Exclusion criteria:

- Any other Retinal pathology
- Proliferative diabetic retinopathy

Pre-treatment full ocular examination

Patients were examined thoroughly before the start of Danshenform Compound. Best corrected visual acuity, detailed slit lamp examination and fundoscopy including 3 mirror examination was done. Fundus fluorescein angiography before starting treatment was carried out. Capsule Tricardin TDS for 4 weeks & BD for another 4 weeks was prescribed.

Patients were reviewed after 4 weeks & then 8 weeks. Best corrected Visual acuity was assessed on each visit. Detailed fundus examination and FFA was also done at 4 weeks and then at 8 weeks. Findings were noticed & recorded by the same eye person.

Statistical analysis

Wilcoxin signed rank test was applied at 5% level significance. P –values of 0.00 was statistically significant

Results:

The mean age of the study participants was 55 years± 8.15 years, the youngest partipant being 39 years while the oldest was 67 years of age. The descriptive of the three study variables are displayed in Table 2. The variables; baseline visual acuity, the visual acuity at 4 weeks and the visual acuity at 8 weeks were not normally distributed based on Kolmogorov-Smirnov & Shapiro-Wilk tests of normality and even through kurtosis and skewness of histograms. Since the assumptions for paired or dependent sample t test were not fulfilled, therefore Wilcoxin signed rank test (for related samples) was applied at 5% level significance. P –values less than 0.05 were considered statistically significant. When the baseline visual acuity was compared with both the visual acuity at 4 weeks and the visual acuity at 8 weeks were compared, highly statistically significant differences were observed with p –values <0.001 for each. However the visual acuity at 4 weeks and the visual acuity at 8 weeks displayed no

difference at all with exactly same values for every patient and p- value 1.0. (table 3)

Table 1: Categorization of patients according to the Visual Acuity at various visits

Visual Acuity	No of Patients — Before Treatment	No of Patients — After 4 weeks	No of Patients — After 8 weeks
6/6	0	12	12
6/9	9	11	11
6/12	8	2	2
6/18	3	2	2
6/24	3	1	1
6/36	4	2	2
6/60 & <6/60	3	0	0

Table No. 2: Descriptives of the the study variables

Visual Acuity	**Mean**	**± Standard deviations**	**Minimum**	**Maximum**	**25th percentile**	**Median or 50th percentile**	**75th percentile**
Baseline	21.31	±16.16	9	60	9.00	12.00	30.00
4 weeks	10.90	±8.01	6	36	6.00	9.00	9.75
8 weeks	10.90	±8.01	6	36	6.00	9.00	9.75

Table No. 3: Comparison of Visual Acuity at various visits

Comparison of variables	**Mean difference**	**Standard deviations**	**95% Confidence Interval of the Difference**		**Mean ranks**		**z-value**	**p-value**
			Lower	**Upper**	**Positive ranks**	**Negative ranks**		
VA at Baseline & at 4 weeks	10.24	±9.36	6.67	13.80	15.00	0.00	-4.76	<0.001
VA at Baseline & at 8 weeks	10.24	±9.36	6.67	13.80	15.00	0.00	-4.76	<0.001
VA at 4 weeks & at 8 weeks	0	0	0	0	0.00	0.00	0.00	1.0

**Highly statistically significant with p-value ≤ 0.01*

Discussion:

The incidence of diabetes mellitus (DM) is increasing rapidly, thereby grows the risk for macro and microangiopathy such as myocardial infarction, stroke, limb loss and retinopathy.[3]

Diabetic retinopathy (DR) develops in patients with both type 1 and type 2 diabetes and is the major cause of vision loss and blindness in the working population. The severity of vascular injury depends on the individual genetic background and is modified by other epigenetic, metabolic and haemodynamic factors, including hypertension, dyslipidemia and oxidative stress. In diabetes, damage to the retina occurs in the vasculature (endothelial cells and pericytes), neurons and glia, pigment epithelial cells and infiltrating immune competent cells. These activated cells

change the production pattern of a number of mediators such as growth factors, proinflammatory cytokines, vasoactive molecules, coagulation factors and adhesion molecules resulting in increased blood flow, increased capillary permeability, proliferation of extracellular matrix and thickening of basal membranes, altered cell turnover (apoptosis, proliferation, hypertrophy), procoagulant and pro aggregant pattern, and finally in angiogenesis and tissue remodeling[5].

These changes in conjunction with advanced glycation end products, oxidative stress, low grade inflammation, and neovascularization of vasa vasorum can lead to macrovascular complications[6]. The lower capacity of transcapillary passage found in type 2 diabetic subjects is suggested to further aggravate insulin resistance.[7] To treat these changes Danshenform Compound (Tricardin) is one of the options, it is FDA IND approved medicine, with 99.99% purity and accurate composition of ingredients, ensured by patented "multi-fingerprint technology"[8]. It is a multi-functional research medicine, manufactured on 4th Generation Hi-Tech Dripping Pills Technology Plant. Each capsule of TriCardin contains 250mg of Danshenform Compound made up of Salvia Miltiorrhiza 82.80%, Sanqi 16.20% and Borneol 1%. It works by inhibiting endogenous cholesterol synthesis[9] LDL oxidation[(10)] and endothelium-derived vasoconstrictor endothelin-1[9]. Tricardin induces oxidative modification of LDL, leading to the prevention of uptake of LDL by cultured macrophages[9]. It decreases endothelium derived thromboxane A2 and B2.[8]

Danshenform Compound inhibits the activation of nuclear transcription factor NF-kB by blocking its translocation into nuclei by inhibition of intracellular glutathione (GSH) synthesis[8]. There will be additional benefit from targeting the microcirculation in terms of prevention of or reduction in end organ damage.[(4)]Effectively reduces the expression of VCAM-1 and ICAM-1 on vascular endothelium[8]. It inhibits DNA synthesis of noncardiomyocytes and inhibits Stress-activated protein (SAP) kinase activity[10]. It effectively acts on microcirculation by inhibiting endothelium-derived vasoconstrictor endothelin-1, and dissolving microthrombi by facilitating the fibrinolytic system hence reducing the thrombus length and weight[11,12]. This medicine increases the fluidity of blood platelet membranes thereby resisting platelet aggregation and hence the occludence of microvasculature[12]. These beneficial effects of Danshenform Compound (Tricardin) has resulted in popularity of this drug for not only cardiac issues but also for diabetic eye disease.

In our study we gave trial of Tricardin and followed up the patients for 8 weeks and the results were quite promising. Almost all patients showed improvement in visual acuity from the baseline visual acuity with P value 0.00. Out of thirty patients twelve patients become 6/6, eleven patients improved to 6/9 rest of the seven patients also showed improvement in vision. Three patients who had base line vision of 6/60 or less got benefit too in visual outcome. All this visual improvement was seen at fourth week, at eighth week visual status remained same. Serial FFA was done in every patient on each visit and compared with baseline FFA , it showed no changes. Keeping in mind the beneficial effects of Danshenform Compound (Tricardin) on stability of microvasculature we can understand the factors contributing in improvement of vision, but to see the exact effect of Tricardin on thickness of macula OCT is important. We are lacking OCT in our study but satisfactory results have encouraged us to continue this research

project by including OCT as a measuring parameter.

Conclusion:

Although it was a study with small sample size but the visual outcome of almost all the patients with moderate to severe non-proliferative diabetic retinopathy was markedly improved. Although no significant changes in the angiographic findings of 4 and 8 weeks follow up were seen which may require further evaluation of the patients with more advanced investigative modalities like optical coherence tomography to have a more practical evidence.

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Data Collection / Assembly: Tehmina Nazir, Fariha Taimur
Drafting: Tehmina Nazir, Fariha Taimur
Review of Literature: Tehmina Nazir, Fariha Taimur
Statistical Analysis: Tehmina Nazir
Critical revision: Badaruddin Athar Naeem

ORIGINAL ARTICLE

Diode Laser Transscleral Cyclophotocoagulation for the Treatment of Secondary Glaucoma

Shaheryar Ahmed Khan[1], Muhammad Hamza[2], Mahnaz Naveed Shah[3]

ABSTRACT:

Objectives: To evaluate the effect of diode laser transscleral cyclophotocoagulation (TSCPC) in eyes with secondary glaucoma in a tertiary care hospital in Karachi, Pakistan.

Subjects and Methods: This is a retrospective chart review of 41 eyes of 36 patients who underwent TSCPC for secondary glaucoma during May 2013 and October 2014. We are assessing the success rate of the treatment (proportion of eyes achieving an IOP reduction of ≤ 22mmHg with or without medication) and reduction in the mean number of glaucoma drugs used.

Results: The mean age at TSCPC is 47± 20 years (12-85). The mean follow-up range is 4 to 6 months. The indications for TSCPC are silicone oil induced glaucoma (19 eyes), advanced glaucoma (9), rubeotic glaucoma (non CRVO) (4), neovascular glaucoma (1), post-PKP glaucoma (1), CRVO (3), post traumatic glaucoma (2), juvenile glaucoma (1) and congenital glaucoma (1). The mean (±SD) pre-TSCPC IOP was 38.4 (9.4) mmHg (range 21–58 mmHg). This is reduced to 16.3(8.5) mmHg (range 4–50) at six weeks after TSCPC. Overall, 35 of 42 (83.3 %) eyes have achieved an IOP of ≤ 22mmHg as a result of TSCPC. The average number of anti-glaucoma drugs used, are decreased from 3 to 1.

Conclusion: Our study supports previous findings that TSCPC is an effective means of controlling IOP in patients with secondary glaucoma. *Al-Shifa Journal of Ophthalmology 2016; 12(4), 183-188. © Al-Shifa Trust Eye Hospital, Rawalpindi.*

Introduction:

Secondary glaucoma refers to the condition in which another disease contributes to increased intraocular pressure resulting in optic nerve damage and vision loss. A number of conditions cause secondary glaucoma e.g. ocular surgeries, uveitis, ocular trauma, advanced cataracts, diabetes, use of corticosteroid drugs and some eye tumors.

Treatment for secondary glaucoma depends on the underlying cause and whether it is open-angle or angle-closure glaucoma. Transscleral cyclophotocoagulation (TSCPC) with diode laser is an established treatment in advanced refractory glaucomas.[1, 2].

The aim of this study is to quantify the success rate of TSCPC in a heterogenous group of patients with secondary glaucoma.

Subjects and Methods:

The clinical records of 41 eyes of 36 patients who have undergone TSCPC for secondary glaucoma from May 2013 to October 2014, at a tertiary care hospital in

1. *North Devon District Hospital, Barnstaple, UK.*
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3. *South City Hospital, Karachi.*

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Karachi, Pakistan have been reviewed. Our institution does not require institutional review board approval for chart review studies. Written informed consent has been obtained from the patients prior to the procedure. Preoperative visual acuity range is from 6/36 to perception of light only; , summarized in table 2. Preoperative therapy consists of topical prednisolone acetate 1% eye drops five times daily one week before surgery. Diode laser TSCPC is performed under local anesthesia using power of 1500 to 2200 mW, duration of two seconds with a maximum of 40 applications over three quadrants, using a 600 micrometer laser delivery probe (G-probe); the probe is placed 1.5 mm posterior to the limbus. The exact 3 and 9 o' clock meridians are spared. Areas of conjunctival or scleral pigmentation/thinning and subconjunctival hemorrhage are avoided. Following TSCPC, all patients are treated with prednisolone 1.0% eye drops four times a day and moxifloxacin eye drops three times daily and atropine 1.0% eye drops twice a day along with oral analgesic. The pretreatment anti glaucoma eye drops are continued. 19 eyes, who have undergone the treatment due to the underlying silicone oil induced glaucoma, did not have the silicone oil removed by the surgeon because of the risk of possible complications, such as retinal detachment and phthisis bulbi. Only 3 eyes out of 41 have undergone pan-retinal photocoagulation as a parallel treatment for the underlying cause; central retinal vein occlusion, however, this did not have a major effect on the outcome of lowering eye pressure in those 3 eyes, as they have developed progressive neovascularization of the angle, which has not regressed with PRP sessions. All patients have been examined at one week after laser treatment initially. They have been followed up for 40 to 150 weeks. The laser procedure is performed by one surgeon who has also determined the number of laser applications. The success of treatment is defined as IOP reduction of ≤22mmHg with or without medications. Re-treatment was performed after six to eight weeks if the IOP was > 22 mm Hg. We have described complete success as attainment of a target IOP without the need for further medication, coupled with preservation of visual function 90%, and qualified success as 86%. We have assessed the success rate of the treatment and also reduction in the mean number of anti glaucoma drugs used post procedure. Gonioscopy findings have also been documented in all patients. The major outcome is intraocular pressure reduction. Additionally, the reduction in the number of anti glaucoma drugs post TSCPC is also assessed. The data variables are entered into SPSS version 18.0 software. Chi-square test is used to analyze data variables where appropriate; p-value < 0.05 is taken as statistically significant.

Results:

The mean age of 36 patients undergoing TSCPC is 47± 20 years (range 12-85 years). The mean follow-up range is 4 to 6 months. Twelve patients (8 males and 4 females) have undergone TSCPC prior glaucoma surgery. The mean (±SD) pre-TSCPC IOP is 38.4 (±9.4) mmHg (range 21–58 mmHg). This reduced to 16.3(±8.5) mmHg (p=0.005) after TSCPC at six weeks. Overall, 35 of 42 (83.3 %) eyes achieved an IOP of ≤ 22mmHg as a result of TSCPC. The average number (±SD) of anti-glaucoma drugs used decreased from 2.5(±0.8) to 1.2 (±1.1).

Visual acuity of 39
out of 41 eyes remained stable and unchanged, but deterioration in vision was recorded in 2 eyes only; in one case, visual acuity deteriorated from perception to light to no perception of light and in other case, from counting fingers to perception of light (Table 3).

Ten eyes required one session of TSCPC. Thirty two eyes required more than one session. The mean number of sessions was

2.1. Qualified success was achieved in 37(86%) and complete success was achieved in 39(90%) patients. The indications for TSCPC are summarized in Table 1. Most number of patients had silicon oil induced glaucoma.

Figure 1: Showing pain control of patients pre and post TSCPC

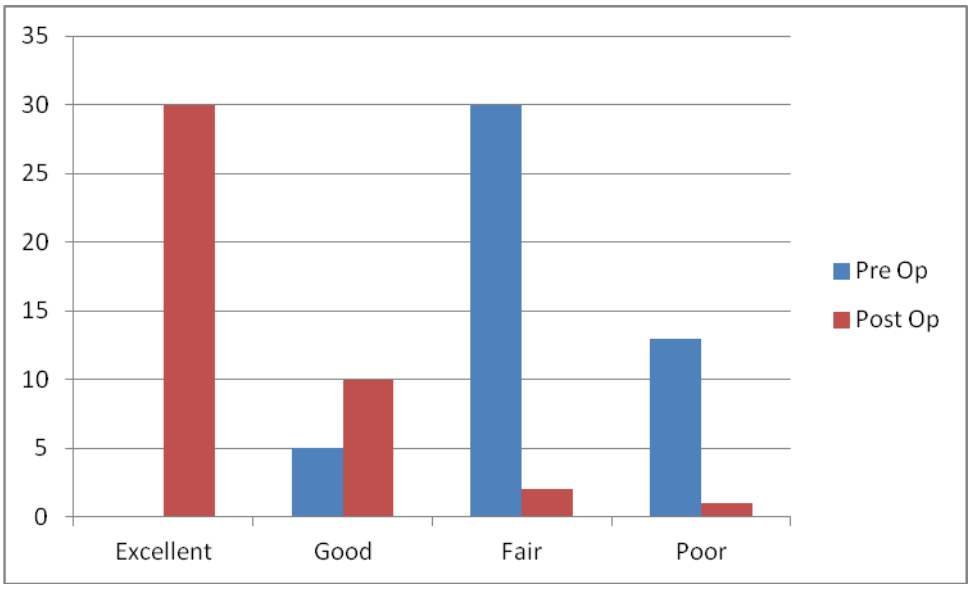

Table 1: Indications for Laser

Indications	No. of eyes
Silicon oil induced glaucoma	19
Advanced glaucoma	9
Rubeotic glaucoma (non CRVO)	4
Neovascular glaucoma	1
Post PKP glaucoma	1
Central retinal vein occlusion	3
Posttraumatic glaucoma	2
Juvenile glaucoma	1
Congenital glaucoma	1

Table 2: Pre-op Visual Acuity

Visual Acuity	Number of eyes
NPL	-
PL	1
CF	19
HM	11
6/60	7
6/36	3

Table 3: Post-op Visual acuity

Visual Acuity	Number of eyes
NPL	1
PL	1
CF	18
HM	11
6/60	7
6/36	3

Discussion:

Transscleral Diode laser cycloablation is a recognized therapeutic approach to refractory glaucoma that involves photocoagulation of the pars plicata of the ciliary body with reduction of aqueous secretion resulting in intraocular pressure (IOP) reduction.[1] Of the 41 eyes treated with TSCPC, 19 have uncontrolled glaucoma following intravitreal silicon oil injection for complicated retinal detachment. All patients have achieved an intraocular pressure below 20 mmHg after treatment. Similar results have been depicted in a comparable study done by Soo Kyung Han, where the efficacy of this treatment in the eye retaining silicone oil has been reported. They found that with cyclodiode transscleral photocoagulation treatment, a qualified success of lowering IOP, was achieved in 81.8% eyes and a complete success in 54.5% with relief of ocular pain and corneal edema.[3]

The overall success rate of 83.3% in our study is better than most other studies on the use of TSCPC in patients with heterogeneous glaucoma, however, a two centre study on diode laser effect on refractory glaucoma done by J.P Diamond, has results similar to but slightly better than our study. They reported that, following cyclodiode laser, 89% of patients achieved an IOP of less than 22mm of Hg in their study.[4] The number of re-treatments in our study (78%) is similar to the study done by Scholte et al.[5] The use of high power settings have resulted in sustained IOP control in a study done by nouredin. It also reports a low incidence of complications, lesser need for re treatments and reduction in the use of anti glaucoma medication.[6] Since our

patients were primarily of Asian origin, similar results were obtained using titrated energy protocols in a power range of 1500-2200. This has been supported by a study by kaushak S, done on Asian Indian eyes.[7]

The results of our study indicate that TSCPC can be a procedure with a low risk for complications in secondary glaucomas. There were no cases of phthisis bulbi, one case of ocular hypotony and one case of scleral burn. In addition, increased perilimbal conjunctival pigmentation was seen. No corneal complications were seen in our study, however, a case of corneal edema following diode laser cyclophotocoagulation in an eye with secondary glaucoma has been reported by Harsh Kumar, Shaifali Gupta and Ashu Agarwal[8]. TSCPC in primary glaucoma or as a primary intervention seems to be associated with less IOP decrease and less reduction of medication although, also, with fewer re-treatments [9,10].

The published literature suggests that this type of treatment is usually reserved for eyes with end stage disease and poor visual potential. A study has reported stable or improved visual acuity in patients after TSCPC and deterioration of visual acuity in 38% of their patients[11.] Our results suggest that no significant changes have taken place in visual acuity in most patients. Visual acuity has remained stable in 39 eyes and deteriorated in only 2 eyes in the study (Table 3). Our study has the following limitations. It is a retrospective one, with relatively small number of patients. The patients belong to a heterogeneous group and are not standardized.

Conclusion:

Diode laser cyclophotocoagulation is a simple, effective and safe means of controlling IOP in the treatment of secondary glaucoma. It is a useful tool as an adjunctive or primary treatment. We recommend early use of TSCPC especially in high risk surgical patients or patients with drug toxicity. In addition, it could be considered in patients with good visual acuity. It may become the procedure of choice in treating secondary glaucoma because the risk of complications is probably lower than with other procedures. Further studies with adequate sample size are required to analyse the long term effects of TSCPC.

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ORIGINAL ARTICLE

Comparative Results of with and without Intraoperative Mitomycin C application in Dacryocystorhinostomy

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ABSTRACT

Objective: To evaluate the results of intraoperative mitomycin C application in dacryocystorhinostomy (DCR) surgery compared with results of the conventional procedure.

Subjects and Methods: This study was conducted at Khyber Teaching Hospital, Peshawar, KPK from 5th Jan 2014 to 31st May 2015. In this prospective randomized controlled study, a total of 66 patients diagnosed with acquired nasolacrimal duct obstruction were randomly divided into a conventional DCR group and mitomycin C group in which mitomycin C was used during DCR surgery. The surgical procedures in both groups were exactly the same, except that in the patients in the mitomycin C group, a piece of cotton soaked with 0.2 mg/ml mitomycin C was applied to the osteotomy site for 3 minutes. The results of the DCR surgeries were evaluated by objective findings such as irrigation and the height of tear meniscus and subjective symptoms by asking patients the condition of tearing improvement.

Results: Among the 33 patients in the mitomycin C group, 94% of patients remained totally symptom free after 6 months of follow up; while in the conventional group, 69.6% of patients were reported to be symptom free and 18% of patients to have an improvement in their symptoms. There was a significant difference between these two groups. As far as objective findings were concerned, there were 30 patients in the mitomycin C group classified as having a normal and one eye with moderate tear meniscus level, compared with 24 and 5 patients, respectively, in the conventional group and a significant difference between these two groups. The non-patency rate in the mitomycin C group is 6% compared with 15.15% in the conventional group.

Conclusion: Intraoperative mitomycin C application is effective in increasing the success rate of DCR surgery in standard nasolacrimal duct obstruction, and no significant complications resulted from its use. *Al-Shifa Journal of Ophthalmology 2016; 12(4), 189-194.*

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Introduction

Dacryocystorhinostomy (DCR) is widely accepted as the procedure of choice for surgical correction of lacrimal drainage system obstruction distal to common canaliculus in adults[1]. Obstruction in the lacrimal passage, is, usually the forerunner of infections/inflam-mations in this region, Continuous epiphora with or without infection is not only a constant hazard for the eye, but a spiteful social malady also. The correct treatment, obviously lies in removing or by-passing the site of obstruction. Prior to Toti[2], who envisaged, communicating the lacrimal sac

with nose, the best we could do for these patients, was to extirpate the infected sac; which no doubt removed the infection but left the patient condemned for the rest of the life with constant epiphora. The success rate of DCR has been reported to be from 63% to 99%[3]. Factors influencing the outcome of lacrimal drainage system surgery include the surgical approach (i.e. intranasal DCR, vs. external DCR), the presence of preoperative acute dacryocystitis or postoperative soft tissue infection, a history of trauma to the lacrimal drainage apparatus, and the use of silicon tubes.

DCR failure has been attributed to membranous occlusion of the rhinostomy site, common canalicular obstruction, and an inappropriate size or location of bony ostium[4].Membranous failure, caused by soft tissue fibrosis at the rhinostomy site, is considered by many authors as the most common cause of primary DCR failure [5]. Thus, if we can inhibit fibrous tissue growth and scarring by applying antiproliferative agents like mitomycin C over the anastomosed flaps and osteostomy site, the failure rate may be decreased.

Mitomycin- C is derived from streptomyces caespitosus, is an alkylating agent with anticancer property. It reduces fibroblast collagen synthesis by inhibiting DNA dependant RNA synthesis and can suppress cellular proliferation in any period of the cell cycle. In order to prevent excessive scar formation mitomycin-C has been used as a surgical adjuvant in glaucoma filtration surgery and pterygium excision[6,7]. More recently its use has been described in primary lacrimal drainage surgery [8]. The beneficial effect of MMC as a surgical adjuvant is thought to be related to its potent inhibition of fibroblast proliferation [5]. Intraoperative use of Mitomycin C in DCR may possibly improve the success rates over the traditional dacryocystorhinostomy procedure.

Subjects and Methods:

During Jan 2014 to May 2015, 66 patients with a diagnosis of primary acquired nasolacrimal duct obstruction were randomly assigned into mitomycin C group(Group A) and conventional DCR group(Group B). All the procedures were performed by two surgeons. The mean age of the conventional group was 57.4 (SD 10.2) years, and that of the mitomycin C group was 57.9(SD 7.4) years. All the patients had been followed up for 6 months for the evaluation of objective findings as well as subjective symptoms.

The standard surgical techniques of an external DCR were used in all patients of both groups. Local infiltrative anesthesia, consisting of 2% lignocaine (lidocaine) and 1:100 000 adrenaline (epinephrine), was administered in the region of the medial canthus and lower lid. The nasal mucosa was anaesthetized and vasconstricted with pledgets saturated with a mixture of 4% Xylocaine and 1:100 000 adrenaline. A skin incision was performed and blunt dissection to the periosteum overlying the anterior lacrimal crest was undertaken. The periosteum was then incised and elevated off the lacrimal sac fossa. The osteotomy was created over the lacrimal fossa with a bone punch. The lacrimal sac was opened in a longitudinal fashion to form anterior and posterior flaps. The nasal mucosa was cut in a similar fashion to the lacrimal sac. Then, the posterior nasal and posterior lacrimal flaps were removed. In the mitomycin C group, a piece of cotton saturated with 0.2 mg/ml mitomycin C was placed over the osteotomy site and was then removed transnasally after an application time of 3 minutes. The anterior nasal and lacrimal sac flaps were closed with additional 5-0 Vicryl sutures, as were the periosteum and orbicularis muscle in separate layers. The skin incision was sutured with a running 6-

0 nylon suture. In the conventional group, the same procedures were performed except for the absence of the mitomycin C application.

To evaluate the long-term results of both groups, we documented the subjective symptoms and classified them as symptom free (no tearing) ,improvement and no improvement in tearing by asking patients about the tearing condition at 6 months follow-up after operation. In addition, two objective findings such as the height of tear meniscus with fluorescein dye and patency of irrigation were documented. We measured the height of tear meniscus with fluorescein paper applied in unanesthetized lower fornix under cobalt blue light at slit lamp for each patient, and graded it as high tear meniscus (≥0.2 mm), moderate tear meniscus (0.1 mm <<0.2 mm) and normal tear meniscus (≤0.1 mm).All of patients with high tear meniscus and subjective finding (tearing) underwent probe and irrigation at 6-month follow-up after operation.

Results:

There were 66 DCR surgeries in this study; 33 patients were in the mitomycin C group (Group A) and the remaining 33 patients were in the conventional group(Group B). There was no significant difference in age between the two groups (p >0.1). All patients except two in the Group B remained symptom free (31 eyes) after 6 months' follow up. The satisfaction rate in the Group A was 94% (31/33). While in Group B there were four patients with excessive tearing after DCR surgery, 23 remained symptom free (no tearing), and six patients improved. There was a significant difference between the two groups (p <0.05).

As far as the objective findings were concerned, there were two patients in the Group A classified as having a high tear meniscus. One patient was classified as having moderate and 31 as having normal tear meniscus levels. In the Group B, four patients were classified as having a high tear meniscus, 5 as a moderate tear meniscus, and 24 patients as a normal tear meniscus. The objective findings of tear meniscus height showed a significant difference between the two groups(p <0.05).

In Group A, all patients except two showed patency of the lacrimal drainage system; while in Group B, five patients revealed non-patency of the drainage system. Transnasal findings in these seven eyes (two in Group A and five in the Group B) showed either total septo-osteotomy adhesion or complete obstruction of the osteotomy area, revealing that fibrous tissue growth, scarring, or granulation tissue formation had been noted at the osteotomy area. The patency rate of the lacrimal drainage system in Group A was 94%, and that in the Group B was 84.8%.

During the follow up period, no complications such as abnormal nasal bleeding, mucosal necrosis, or infection were noted in any patients.

Discussion:

Lacrimal surgery, described as the step child of ophthalmology, deserves to be more affectio-nately treated and its care should not be entrus-ted to outsiders like rhinologist or orthopaedician for fear of maltreatment or pampering. Toti[2], was the first to devise the communi-cating operation and later Dupuy-Dutemps and Bourget[9], modified the technique. In spite of various modifications suggested from time to time, the basic idea remains the same.

DCR is a widely accepted technique for correction of nasolacrimal obstruction. [1]. A review of the literature reveals an average failure rate of 9.4%[3,10]. Failure is generally defined as having symptoms of excessive tearing with the inability to

irrigate. McPherson and Egelston noted that three out of seven patients in their study who underwent a second operation were found to have dense scar tissue present at the osteotomy site[11]. Allen and Berlin in 1989 reported 20 failed DCRs with the postoperative obstruction distal to common canaliculus. In their study, there were 13 cases with cicatrical closure of the rhinostomy with granulation tissue and three cases with scarring of the osteotomy to the turbinate or septum[4]. McLachlan *et al*, on the other hand, proposed the higher incidence of common canalicular obstructions as a cause of DCR failures[12].

From the literature described above, we see that fibrous tissue growth, scarring, and granulation tissue formation during the healing process will decrease or compromise the created surface area of the osteotomy site, leading to surgical failure. The same healing process will also promote adhesion of the osteotomy to the turbinate and septum, or induce obstruction of the common canaliculus. Linberg *et al* showed that an appropriately large osteotomy made during surgery can narrow down to a final size of approximately 2 mm due to tissue growth and scarring[13]. Thus, if we can reduce fibrous proliferation at the osteotomy site and at the anastomosed flaps, the success rate of DCRs may become much higher.

Antimetabolites which can inhibit DNA or RNA replication, cell division , protein synthesis, and fibroblast proliferation have been used as adjunctive therapy to prevent excessive scar formation in DCR surgery, glaucoma surgery, and pterygium removal. MMC is the most popular antifibrotic agent used intraoperatively. It is highly toxic when used systemically in antitumor therapy. Intraoperative application of MMC in lacrimal surgery is a new indication. When used as a 0.5mg/ml concentration for 2.5 minutes, intraoperative application of MMC favorably affected the wound healing process [14] .

Fibroblasts have other actions besides proliferation during wound healing, including migration collagen production, and contraction. MMC causes cell death by toxicity and induced apoptosis and also may influence these steps when it is used in DCR. The interaction of epithelial and vascular endothelial cells with fibroblasts also may influence the scar formation [14].

Ugurbas *et al* studied the histopathological effects of mitomycin C on transnasal DCR by using 0.5 mg/ml mitomycin C and soaking for 2.5 minutes over the osteotomy site. The light and electron microscopy showed attenuated epithelium as well as looser and hypocellular subepithelial connective tissue on mitomycin C soaking specimens. They concluded that mitomycin C soaking can result in a decrease in density and cellularity of mucosa, and hence, enhance the success of DCR surgery[15]. Yeatts and Neves reported eight cases of repeat DCR using mitomycin C soaking with successful results[16]. They recommended that the adjunctive use of mitomycin C may increase the success rate of repeat DCR.

Kao et al [17] studied the effect of MMC on the maintenance of size of osteotomy site after external DCR. They showed that the mean surface area of osteotomy site in MMC group was 27.10 + 5.78 mm 2 at the end of 6th post operative month was statistically significant compared to 10.63 + 3.37mm 2 of the control group. They stated that intra-operative MMC is effective in maintaining larger osteotomy site and the surface area in their study was measured using computer aided digitiser.

In our study, there were 31 patients totally free from epiphora in the mitomycin C group after 6 months' follow up. Only two out of 33 patients (6%) failed to response

to DCR surgery. While in the conventional group four out of 33 patients (12.12%) were reported to be unsatisfactory with the results of DCR surgery; 23 patients were free from epiphora and six patients reported to be improved in this group. There was a significant difference between the two groups according to the subjective symptoms reported by patients. The height of the tear meniscus was also measured and compared between the mitomycin and conventional groups. Thirty patients in the mitomycin C group were classified to have a normal tear meniscus and one eye to have a moderate tear meniscus compared with 24 patients in the conventional group to have a normal and five patients to have a moderate tear meniscus. Also, there were four patients in the conventional group classified to have a high tear meniscus compared with two eyes in the mitomycin C group. This was also significant.

As for the patency of the lacrimal drainage system and transnasal findings, we found that two eyes in the mitomycin C group showed non-patency of the lacrimal drainage system when irrigated, and an obstruction over the osteotomy area. In the conventional group, there were five eyes reported to be non-patent with obstruction over the osteotomy site diagnosed by irrigation as well as transnasal examination. The patency rate of the lacrimal drainage system after DCR surgery was 94% in the Mitomycin C group compared with 84.8% in the conventional group.

From the results described above, it seems reasonable to conclude that intraoperative Mitomycin C application can improve the satisfaction rate and the success rate of DCR surgery. Many complications due to a Mitomycin C application have been reported in both pterygium and glaucoma filtration operations. Severe secondary glaucoma, corneal perforation, corectopia, secondary cataract, and scleral calcification are documented as complications in using topical Mitomycin C as a medical adjunct to pterygium surgery[18]. Hypotony related maculopathy, infection, and endophthalmitis have been found in patients undergoing glaucoma filtration surger y after exposure to Mitomycin C[11,19]. Fortunately, in our study, there were no complications such as abnormal nasal bleeding, mucosal necrosis, or infection noted with Mitomycin C soaking. In summary, although a high success rate of external DCR surgery has been reported, 10% of cases still fail. In our experience, DCR with intraoperative Mitomycin C soaking over the osteotomy and anastomosed flaps can minimize the adhesions around the septoosteotomy area as well as the opening of the common canaliculus. In this way, Mitomycin C soaking during DCR surgery is a useful modified procedure to improve the success rate of external DCR.

Recently, new reports have shown that endonasal laser assisted DCR can be an alternative to conventional external DCR [20-22]; maybe it will be helpful to apply Mitomycin C over a laser created osteotomy site to increase the success rate of laser assisted DCR and revised DCR surgery.

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ORIGINAL ARTICLE

Assessment of Patterns of Refractive Errors: A Hospital Based Study

Maria Manzoor[1], Hanif Malik[1], Hina Sharif[2]

ABSTRACT

Objectives: The objectives of this study were to find the occurrence of different types of refractive errors and to determine association of the outcome with independent variables (age, gender, residence etc.).

Subjects and Methods: It was cross-sectional study in Al-Shifa Trust Eye Hospital Rawalpindi and a sample of 1500 children aged 1 to 15 years was collected by convenience sampling. Structured questionnaire was used form to collect data. Descriptive and inferential statistics were used to analyze results. Chi square was used ($p<0.05$ as significant) with odds ratio where necessary.

Results; Results showed the Percentage of Astigmatism as (41.4%), hyperopia (36.5%) and myopia (22.1%). Types of refractive errors were found to be statistically different for different age and residence of respondents ($p<0.001$).

Conclusion: Astigmatism was the most common refractive error found in children aged 1 to 15 years. There is need of regular screening for refractive errors for school going children especially of rural areas. Community health workers or primary healthcare centers can be utilized for this purpose. *Al-Shifa Journal of Ophthalmology 2016; 12(4), 195-201.*

Introduction

A global initiative that aims to eliminate avoidable blindness by the year 2020 termed as "Vision 2020". It was introduced on 18 February 1999 by the World Health Organization together with the more than 20 international non-governmental organizations involved in prevention and management of blindness that comprise the International Agency for the Prevention of Blindness (IAPB). VISION 2020 is a partnership that provides guidance, technical and resource support to countries that have formally adopted its agenda[1].

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According to UNICEF prevalence of visual impairment among children of different region is related to social economical and culture factors .Childhood blindness is an important cause contributing to the burden of blindness. Genetic mutation, birth defects, premature birth nutritional deficiencies, infections, injuries are some of the important determinants of childhood blindness. Cataract, Glaucoma, Retinopathy of prematurity and uveitis are treatable causes and corneal scarring and refractive error are preventable causes of childhood blindness[2].

Childhood visual impairment due to refractive error is one of the most common

problem among school age children and second leading cause of treatable blindness[3].According to world health organization 285million people were visually impaired out of which 39 million were blind and 246 million had low vision[4].

An optical state of eye in which incident parallel rays of light fail to focus on the retina is refractive error . The symptoms of refractive error are blur vision, difficulty in reading and crossing of eye in children (esotropia) [5,] it reduces employment opportunities, social isolation and reduces independence and mobility and has substantial effects on individual but also the community. It affects the large number of population worldwide, irrespective of age, sex and ethnic group. Refractive error remained uncorrected due to lack of awareness and recognition of problem at personal and family level. At the community level the affordability of services for testing refractive error is a barrier[6].

The age of 1 to 15 year is developing stage of children and in this age if refractive error is not corrected it affects the quality of life Hyperopia which is one of the type of refractive error if is not corrected in young children it causes amblyopia (lazy eye).Lazy eye doesn't see clearly because brain ignores the image when it receives signals. Fortunately amblyopia is treatable in young children with patching. Myopia which is another type of refractive error, also affects the quality of life such as education of children because they can't read clearly from distance. Headache during reading, holding books very close to eye, pain in eyes and watering are some of the manifestations among children with uncorrected refractive error.

The prevalence of refractive errors varies according to age, gender, race and geographic location. A study conducted in south estern iran documented hyperopia as a major proportion of refractive error (58%) followed by myopia 6.3% and astigmatism 3.4%while remaining were emmetropic[7].

The studies done at Lahore, Rawalpindi medical college, Saudi Arabia and Karachi revealed that prevalence of refractive error is higher among female than male[8, 9, 10, 11]. Another study conducted in the Bayelsa state of Nigeria concluded that the refractive status of subjects was independent of gender (p=0.550). However it was dependent upon age of subjects (p=0.000)[12] .While another study reported highest prevalence of myopia ,the difference is basically due to different demographic features of respondents and difference in operational definition of refractive error[8].

The objectives of this study were to find the frequency of different types of refractive and to determine association of the outcome with independent variables (age, gender, residence etc)

Subjects and Methods:

This was crossectional, hospital based study that was carried out from 1 August to 30 January, 2015 with all patients available in paediatric department. Age of respondents was between 1 to 15 years of age.

The Study was carried out in peadritic department of Al-Shifa trust Eye Hospital Rawalpindi. These patients came from different area of Pakistan, mostly from Punjab, Khyber Pakhtunkhwa and Kashmir. Study was completed in 6 months from 1st August 2015 to 30th January, 2016.

All children age less than 15 year with decreased vision were included in this study. A sample size of 1500 children was selected by convenient sampling and all patients were evaluated under the supervision of a senior optometrist. Data

of patients was collected on a proforma designed with the assistance of senior optometrist.

Operational definitions:

Refractive error**:** is very common eye disorder that occurs when an eye cannot focus image from outside world on the retina[5].

Child: is anyone who is under the age of 15 year[2].

Ametropia: parallel rays of light coming from infinity are focused either in front or behind the retina in one or both the meridian[5,13].

Myopia is an optical condition of the non-accommodating eye in which parallel rays of light entering the eye are brought to a focus anterior to the retina[14].

Hypermetropia or Farsightedness parallel rays of light are brought to a focus at a point beyond the retina, so that divergent or parallel rays cause diffusion circles and a blurred image[15]. Astigmatism is a refractive error that is not equal in all the meridians, thus the image is not focused as a single point[16].

Clinical procedure:

For this study, visual impairment was defined as visual acuity worse than 6/9 in either eye. According to the age of patients, different visual acuity charts were used to record visual acuity, such as Lea grating, Cardiff acuity card, Lea numbers, Lea symbols and Snellens chart. Routine ocular examination was done by ophthalmoscope. Visual acuity was also measured with glasses in children who were already using them, and if any change in glasses was observed with refraction, then the change in prescription was noted. Pin hole visual acuity was taken to differentiate refractive error from organic pathology. After measuring visual acuity, Auto refraction, cycloplegic refraction and subjective refraction was performed according to age of patient. Conformation of auto refraction was done by subjective refraction. Cycloplegic refraction was performed by instillation of 0.5% Cyclopentolate to relax the accommodation. Post midriatic refraction was performed in those children who were high myopic. Children having any ocular pathology other than refractive errors were excluded from this study. Glasses were prescribed to all children having visual acuity less than 6/9.

A structurred questionnaire was used with visual acuity measuring chart:lea grattings,cardiff cards, lea numbers,lea symbols,snellen chart. Retinoscopey, subjective refraction and ophthalmoscopy.

The data were dual entered in SPSS 17 and MS Excel 2010. The data were summarized by using descriptive statistics depending upon the nature of data. Categorical data were represented by frequency, percentage and cross tabulation. To find the association chi square test was done and p value less than 0.05 were taken as significant.

The ethical guidelines of Al-Shifa Trust Eye Hospital were taken into consideration. The anonimity, autonomy and privacy of participants was considered. Respondents were explained about research work verbally and through written consent form.

Results:

A total of 1500 children examined in the peadritic department of hospital were included. The outcome of the study (Frequency of refractive error and its types) was categorical data. Independent variables were also categorical; both nominal and ordinal (Table-I). The demographic variable of age was divided into three groups, infants (1-2 years) constituted 11.9%, pre-school children (3-5 years) constituted 20.6% and school going age constituted 67.5% of the total sample. Among 1500 children, 937 (62.4%) were male and remaining were female. When respondents were split into

type of residence, major portion was from urban areas (Figure I).

Descriptive statistics revealed that astigmatism among patients was major type of refractive error (41%) followed by Hypermetropia 36.5% and myopia 22.1%. Compound hyperopic astigmatism (12.7%), was more than other type of astigmatism such as simple astigmatism (9.9%), compound myopic (9.7%) and mixed astigmatism (9.1%).

The results of this study showed mild visual impairment among 889 (59.3%) participants, moderate visual impairment in 367(29.3%) participants while 244(16.3) had severe visual acuity loss.

Inferential Statistics:

Association of gender, age and residence with type of refractive error:

The study showed that gender had no association with type of refractive error (Table 1I). Chi-square revealed that male (62.4%) and female (37.6%) has no significant difference for having different type of refractive error (P=0.427).

Chi square test was used to find the association between different groups for age of patient and type of refractive error Table II. This association was statistically significant (chi-square p<0.001). So it can be concluded that proportion for different types of refractive error differ with various age groups.

Chi square test was used to find the association between residence of patient and type of refractive error (Table II). Both were associated and this association was statistically significant, (p=0.000).

Association of myopia with gender and age:

There was no association between myopia and gender of patient (p=0.915) when assessed with chi square test (Table III). Therefore, male or female both had equal chance of getting myopia. The odds ratio was equal to one which also supported non-significant relation between both variables (O.R = 1, 95% C.I= 0.557-1.01). In order to assess association of age on myopia, chi square test was used and the results of the test showed that there was statistically significant association between age and myopia with x^2 (2) = 16.7, p=0.000.Table III.

Association of hyperopia with gender and age:

Chi square test was used to assess the association between hyperopia and gender of patient no association was found with p=0.103. Therefore, there is equal chance of getting hyperopia by both male and female. The odds ratio when calculated also showed no significant relation between both (O.R =1, 95% C.I= 0.93-1.51).Table IV

Hypermetropia when assessed with categorical variable of age by using chi square, results showed that both are associated (Table VI) and it was a significant association (chi-square, p<0.001).Table IV

Table I: Variables used in study

S.No.	Name of Variable	Type of Variable
1.	Presence of Myopia	Categorical (Binary/Ordinal)
2.	Presence of hyperopia	Categorical (Binary)
3.	Presence of astigmatism	Categorical (Binary)
4.	Age	Categorical (Ordinal)
5.	Gender	Categorical (Nominal)
6.	Residence (rural and urban)	Categorical (Nominal)

Table II: Types of Refractive Errors

Variable	Type of Refractive Error			X^2 (d.f)	p-value
Gender	Hyperopia	Astigmatism	Myopia		
• Male	334	387	217	1.702(2)	0.427
• Female	213	236	115		
Age (years)	Hyperopia	Astigmatism	Myopia		
• <3	91	52	55		
• 3-5	135	136	38	47.981(4)	0.000
• >5	321	433	259		
Residence	Hyperopia	Astigmatism	Myopia		
• Urban	363	467	257	16.610(2)	0.000
• Rural	184	154	75		

Table III: Association of myopia with gender and age:

Variable	Myopia	X^2 (d.f)	p-value
Gender			
• Male	173	0.011(1)	0.915
• Female	103		
Age (Years)			
• <3	147		
• 3-5	276	16.693(2)	0.000
• >5	801		

Table IV: Association of hyperopia with gender and age:

Variable	Hyperopia	X^2 (d.f)	p-value
Gender			
• Male	276	2.663(1)	0.103
• Female	189		
Age (Years)			
• <3	86		
• 3-5	114	41.059(2)	0.000
• >5	265		

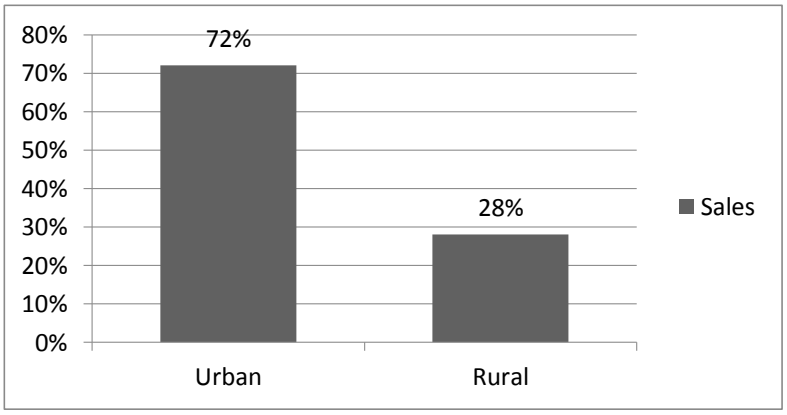

Figure 1 Residence of respondents

Discussion:

Refractive error is one of most easily avoidable and treatable disease but still it is important burden on medical staff of hospital. In this study 1500 children were evaluated. It was found that male comprised(62.4%) of sample while female were 37.6% .Most of the studies conducted in Pakistan related to eye disease had higher proportion for male patients. Like study in eye unit Lady Reading Hospital Peshawar Shah also found that 56% patient were male while 44% were female. Another study conducted in Rawalpindi medical college showed that female (65.55%) were higher than male (34.45%) [9]. This study showed that there is no association of type of refractive error with gender (p=0.427), this was different from multicounty survey of refractive error in children in Saudi Arabia (p<0.012)[10] and a study in Rawalpindi medical college[9] (p<0.01) and Karachi (p=0.001) where refractive error were significantly higher in females than males.

The sample of this study included children from 1 to 5 years old. However most of the other studies were school based which did not include children from 1 to 5 years like study in mayo hospital Lahore only school going children were selected[8].

In this study frequency of hyperopia decreased with age and was significantly associated with age group (p<0.001). Frequency of myopia increased with age: in infants (19.7%), preschool (12.3%) and in school going (25.6%) with p<0.001. These findings were similar to study conducted in Iran which revealed that with increasing age the prevalence of myopia increased, with (P<0.001) and hyperopia decreased, with (P=0.007)[17].

The study revealed that compound hyperopic astigmatism (12.7%), is more than other type of astigmatism such as simple astigmatism (9.9%), compound myopic (9.7%) and mixed astigmatism (9.1%). Percentage of anisometropia (9.1% is lower, similar to the study conducted in Australia[18].

The study was done in hospital with good medical team and apparatus. As this was hospital based study so only the children who visited hospital were included and others were missed this may be the limitation of study. Another limitation can be the use of convenience sampling to collect data.

Conclusion:

Astigmatism was the most common refractive error found in this study. Children, significantly suffering from refractive errors and need to be diagnosed for refractive errors especially in rural areas and should be given refractive correction.

Recommendations:

1. Vision testing programs for children age 1 to 15 should be maintained properly in schools and maintenance of eye health programs in both urban and rural settings.
2. Community health workers could be trained on vision testing. Each community health worker would be supplied a kit (measuring tape, torch, marker and occlude).
3. There should be refractionists at primary healthcare level who will do the refraction and will reduce the burden on the hospitals.
4. Awareness regarding prevention of refractive error through better nutrition and screening should be done through mass media.

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ORIGINAL ARTICLE

Comparison between Immersion and Contact Biometry for Axial Length Measurement before Cataract Surgery

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ABSTRACT

Objective: To determine the accuracy of immersion method in measuring the axial length of the eye by comparing it with the contact method.

Study Design: Cross sectional study.

Subjects and Methods: This study was done in The Department of Ophthalmology, Pakistan Institute of Medical Sciences, Islamabad for six months from 11-12-2012 to 10-06-2013 on 180 patients. The patients with age related cataract were included. The ultrasound biometry was performed in all patients with the same apparatus, first by the contact technique and then after an interval of 10 minutes by the immersion technique. Mean of the axial lengths of all the patients measured by the immersion technique was compared with the mean axial length obtained by the contact method.

Results: A total number of one hundred and eighty patients were included in the study. There were 93 males and 87 females. The mean axial length by contact was found to be 23.36±0.9 mm and by immersion method was 23.33±0.9 mm. The difference between the two means was 0.03mm. The two methods of axial length measurement were found to be significantly correlated. (Pearson's correlation 0.995, $p < 0.001$)

Conclusion: There is no significant difference in the findings of contact and immersion techniques, with no clinically significant difference in the mean axial length measurements.
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Introduction:

Biometrical measurement is an everyday routine in ophthalmological practice. One major reason for the measurement is in planning the surgical removal of cataracts.

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The expectations of patients for precise postoperative refractive results after cataract surgery have increased tremendously. In order to meet these, accurate intraocular lens power calculation should be carried out. This requires accurate biometry and appropriate intraocular lens power formula selection with optimized lens constants. Of these factors, accurate preoperative measurement of axial length (AL) is considered to be a key determinant in calculating the IOL power to be implanted[1].

Axial length measurement by ultrasound (A-scan) can be performed by the contact method, where the probe is in direct contact with the cornea. This is a simple

and convenient way to determine the axial length. However, errors in measurement can result from the probe indenting the cornea and shallow the anterior chamber. The IOL power calculations using these measurements will lead to an overestimation of the IOL power. In shorter eyes, this effect is amplified[2,3]. A mean shortening of 0.25mm can translate into an error in IOL power by approximately 1D[4].

The other method is the immersion method which requires placing a saline filled scleral shell between the probe and the eye. Since the probe does not exert direct pressure on the cornea, compression of the anterior chamber is avoided[5]. The eye axial length gained by means of the immersion technique may be longer than that obtained by the contact technique. This means immersion method can help to decrease errors in calculating the dioptric power of IOL and produce visual outcome to the expectations of the patient and the surgeon postoperatively.

Kronbauer et al showed that the mean axial length using the contact technique was 23.28 mm compared to the mean of 23.38 mm gained by immersion technique. The standard deviation of the measurements using both techniques was less than 0.1mm. A statistically significant difference was proved between the contact and immersion techniques[6].

Abbas et al found the mean axial length by immersion method to be 22.92±1.2mm and that with the contact technique using the same probe to be 22.75±0.92. The difference of 0.17 mm was not statistically significant[7]. Also, no significant difference in the repeated findings of contact and immersion techniques was seen when controlling the confounding factors and performed by experienced operators. Different studies thus give different results regarding the accuracy of the immersion method.

The current study objective involves determining the accuracy of immersion method of A-scan in measuring the axial length of the eye by comparing it with the contact method of A-scan in patients undergoing cataract surgery.

Subjects and Methods:

This study was conducted in Department of Ophthalmology, Pakistan Institute of Medical Sciences Islamabad from 11-12-2012 to 10-06-2013. Using the WHO calculator for sample size calculation, the sample size of 180 patients was obtained. Non-probability consecutive sampling was performed, with inclusion criteria of patients presenting with age related cataract between the ages of 40 to 90 years of both genders. Patients with known corneal abnormalities like corneal opacities and ectasias and corneal surgeries such as penetrating keratoplasty or refractive procedures were excluded from the study.

The axial length measurement was carried out By Optikon Bioline A-scan machine. It measures the length of the anterior chamber (AC), the thickness of the lens (LNS) and the axial length (AXL). The average of the measurements stored (up to 5) is indicated in larger figures. Under the average axial length the number of averaged measurements (AVG) is indicated. The accuracy of the measurements is deduced from the standard deviation. The standard deviation of a series of accurate measurements must not exceed +/-0.3 mm.

A Performa was used to collect pertinent information from all patients. The ultrasound biometry was performed in 180 patients with the Optikon Bioline A scan, first by the contact technique and then after an interval of 10 minutes by the immersion technique using an immersion scleral shell designed in the form of a Prager shell. Mean of the axial lengths of all the patients measured by the immersion technique was compared with the mean

axial length obtained by the contact method. All the collected information was entered into SPSS version 12 and analyzed.

Results:

A total number of one hundred and eighty patients were examined. The baseline characteristics of these patients were as follows:

The mean age of all the patients was 62.59±9.7years. There were 93 males (51.66%) and 87 females (48.33%). (Table 1). In 103 (57.22%) patients axial length measurement of right eye was performed while 77 (42.77%) patients had the biometry done of the left eye.

The mean axial length by contact was found to be slightly longer (23.36±0.9) than the mean axial length by immersion method of A-scan (23.33±0.9) (Table 2). The difference between the two means is not statistically significant. The two methods of axial length measurement were found to be significantly correlated. The Pearson's correlation value was found to be 0.995 and the significance level was <0.001.

Table 1: Distribution of cases by gender (n=180)

Gender	Number	Percentage
Male	93	51.66
Female	87	48.33

Table 2. Mean and standard deviation of contact and immersion method

Method	Mean	SD	Significance
Contact	23.36 mm	0.9	Pearson's correlation 0.995 (p<0.001)
Immersion	23.33 mm	0.9	

Discussion:

Cataract is the main cause of reversible blindness worldwide and cataract blindness is thought to be increasing by 1-2 million per year[8]. Modern cataract surgery has evolved from a simple operation involving Graefe knife and no lens replacement to a refractive surgical procedure capable of improving both uncorrected and best corrected visual acuity. With the introduction of the intraocular lens and consequent improvement in prediction of IOL power, the spherical component of patient's refractive error has become reasonably predictable. This has led to greater expectations by the surgeon and patient for rapid and stable visual rehabilitation following cataract surgery[9].

Cataract extraction with implantation of intraocular lens is one of the most frequently and successfully performed ophthalmic procedures. Visual impairment is by far the most common indication for cataract surgery. Patients stress for perfect refractive outcome with early visual rehabilitation. Although good surgical techniques with low complication rates are important, biometry is often the most critical factor in obtaining the expected refractive results[10]. The most critical step in biometry is precise measurement of axial length, defined as the distance between the anterior corneal surface and the sensory retina.

Studies based on ultrasound showed that 54% of the errors in predicted refraction after IOL implantation are attributed to

errors in AL measurement. A 1-mm error in AL measurement results in a refractive error of approximately 2.35 D in an average eye[11].

Although contact method is most commonly used, it is cumbersome to the patient due to direct contact of probe with cornea also increasing the risk of corneal erosion. If the probe is pressed against the cornea, an abnormally short axial length is recorded resulting in inaccurate calculation of intraocular lens power and refractive outcome is not as expected. Immersion technique eliminates corneal depression[12].

In our study, mean axial length by immersion technique was 23.33±0.9 as compared with the study of Kronbauer et al the mean axial length was found to be 23.19±0.4 using the same probe. In our study contact mean axial length was 23.36±0.9 compared with the study mean of 22.93±0.9 with the contact technique.

Hennessy et al compared the repeatability and agreement of contact and immersion ultrasound biometry of axial length. Axial length measurement was longer with the contact method than with immersion by 0.03 mm. The repeatability of the two techniques was similar[13].

Watson and Armstrong evaluated those measurements of eye axial length obtained by the immersion technique averaged 0.1 mm longer than those obtained by the contact technique. Both techniques give consistent results, but the difference between axial lengths measured by the two techniques has implications for choice of intra-ocular lens power.

A carefuly performed contact A-scan by an experienced technician eliminates the need of immersion biomety. Important considerations while doing contact biometry are ensuring that the machine is calibrated and set for the correct velocity setting (e.g. cataract, aphakia, pseudophakia), the echoe spikes from cornea, anterior lens, posterior lens, and retina should be present and of good amplitude, the gain should be set at the lowest level at which a good reading is obtained , only slightly touching the cornea and not pushing it hard and an average of the 5-10 most consistent results and having the lowest standard deviation (ideally < 0.06 mm)[14].

While doing ultrasound biometry, special note should be taken of eyes that are very short (less than 22 mm) or very long (more than 25 mm). Axial length errors are more significant in short eyes and a posterior staphyloma may be present in a long eye[15].

The other most common error is misalignment, either by not obtaining perpendicularity to the macular surface or by not directing the sound beam through the visual axis. Perpendicularity to the macular surface is achieved when the retinal spike and scleral spike are of high amplitude, and the retinal spike arises steeply from baseline. No sloping of the retinal spike should be present and no jags, humps, or steps should be present on the ascending edge of that spike[16].

If either the posterior or anterior lens spike are not of high amplitude, the sound beam could be misaligned at an angle through the lens and, therefore, not through the visual axis. The posterior lens spike may be slightly shorter than the anterior lens spike because the convex curvature of the posterior lens is steeper than the convex curvature of the anterior lens surface, allowing for reflection of the echoes away from the probe tip.

Conclusion:

There is no significant difference in the repeated findings of contact and immersion techniques when controlling the confounding factors and performed by experienced ophthalmologists. The precision of contact ultrasound biometry was comparable to that of immersion, with no clinically significant difference in mean axial length measurements.

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ORIGINAL ARTICLE

Horizontal Corneal Diameter Measurements Using Visante OCT, IOLMASTER, ATLAS Topography and Surgical Calipers for Optimal Sizing of Phakic Intraocular Lenses

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ABSTRACT

Purpose: To assess the conformity among various modalities used to approximate the posterior chamber horizontal diameter for optimal sizing of phakic intraocular lenses (pIOL).

Methods: Three different devices that estimate the white to white (WTW) diameters of the eye were used to obtain the measurements in 102 eyes of 51 normal patients aged 22-47; *IOLMaster*, *Atlas* Corneal Topographer (all devices by *Carl Zeiss Meditec, Inc*.) and a surgical caliper. Angle to angle (ATA) and sulcus to sulcus (STS) was measured using *Visante* OCT.

Results: The mean WTW was 12.09 ± 0.43, 12.44 ± 0.51 and 12.18 ± 0.42 mm with *IOLMaster*, *Atlas* topography and calipers respectively. Mean ATA and STS with Visante OCT were 11.85 ± 0.49 and 12.44 ± 0.48 mm respectively All combination differences were significant among the four devices used to estimate the horizontal diameter of the sulcus. Repeated measure ANOVA was done by Greenhouse-Geisser test. Pair wise comparison was done and all the combination differences among the devices were statistically significant ($p < 0.0001$).

Conclusion: The various available imaging modalities used to get the approximate horizontal diameter of the posterior chamber for a best fit phakic intraocular lens cannot be used interchangeably. *Al-Shifa Journal of Ophthalmology 2016; 12(4): 207-212. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

Introduction

Measurement of corneal diameter from limbus to limbus (white-to-white distance, WTW) is used in cataract, refractive surgery and diagnosing a variety of corneal diseases. WTW distance is essential when approximating anterior chamber depth (ACD) and ciliary sulcus size for an anterior chamber or sulcus-implanted phakic IOL. Precise determination of WTW distance is of paramount importance with the recent increased use of phakic IOLs (pIOL).

Methods used to measure WTW distance include manual calipers, millimeter scales on slit lamps, Orbscan, Pentacam, Galilei, IOLMaster and anterior segment optical coherence tomography (AS-OCT). Sulcus to sulcus measurements can be obtained with an ultrasound biomicroscopy (UBM) or AS-OCT. The results obtained vary considerably with the modality used.

Measurements of posterior chamber dimensions are important for appropriate

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sizing of pIOL. An oversized lens can cause excessive vaulting, angle closure glaucoma and pigment dispersion where as an undersized lens is unstable and predisposes the eye to cataract formation. Calculation of pIOL takes into account the WTW distance and ACD in addition to the refractive error for optimal sizing in the ciliary sulcus. The present study assesses the agreement among different techniques used to estimate the size of ciliary sulcus and whether they can be used interchangeably.

Subjects and Methods:

This cross sectional study was conducted at Dhahran Eye Specialist Hospital (DESH) Kingdom of Saudi Arabia in October 2013 on 102 eyes of 51 patients. All subjects had no history of any ocular disease or previous ocular surgery. All patients were examined by a single examiner. The WTW diameters of all eyes were measured using; a measuring caliper, IOLMaster and Atlas topographer. Angle to angle (ATA) and sulcus to sulcus (STS) was measured using Visante OCT. All measurements were taken in a single visit.
Castroviejo surgical measuring calipers were used which had a scale in 1.0 mm steps ranging from 0 - 20.0 mm. The measurements were taken under topical anesthesia. The WTW distance was measured by placing the tips of the caliper on the nasal and temporal limbus and reading off the caliper scale. Using IOLMaster the WTW was measured by a digital gray-scale photograph of the AS of the eye. The limbus was detected automatically (the border between white sclera and darker iris image) and the device calculated the corneal diameters. The ATLAS corneal topographer system automatically measured the WTW by measuring the horizontal distance between the outer rings (limbus-to-limbus).

The Visante AS-OCT has several scanning protocols; of which the enhanced anterior segment single scan and the high resolution raw scan are useful for angle assessment. Visante OCT calculated the distance between the vertexes of two iridocorneal angles to give the ATA. The contrast settings of the image were increased to maximum to help visualize the edges of the ciliary sulci at the horizontal meridian and STS was measured.

Descriptive analyses were performed to determine mean and standard deviation. Normal range was reported as mean ± standard deviations from the mean. Frequencies of each WTW measurement value were counted and plotted in a histogram. Measurements obtained from the different methods were compared using an analysis of variance (ANOVA) with repeated-measures. Pearson's coefficient of determination (R2) was used to assess for significance of correlation. A p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences software version 19 (SPSS Inc, Chicago, Illinois).

Results:

Hundred and two eyes of 51 normal patients (14 women, 37 men) were included in the study. Mean age of the patients was 30.78 ± 6.17 years (range: 22-47 years). The mean WTW was 12.09 ± 0.43, 12.44 ± 0.51 and 12.18 ± 0.42 mm with IOLMaster, Atlas topography and calipers respectively. Standard errors (SE) of mean were 0.042, 0.051 and 0.042 mm for IOLMaster, Atlas topography and calipers respectively. Mean ATA and STS with Visante were 11.85 ± 0.49 and 12.44 ± 0.48 mm respectively with standard errors (SE) of mean of 0.048 and 0.047 mm respectively. (Table 1)

All measurements from the each device followed a normal distribution. Repeated measure ANOVA was done by Greenhouse-Geisser test: F=71.503, *dF*

(2.556, 258.118), P < 0.0001; 41.5% (partial eta^2) of variation among the measurements is due to differences between devices. Pair wise comparison was done; there was no statistically significant difference between Atlas and Visante STS. All other combination differences were significant (p < 0.0001). (Table 2)

Table 1 :Descriptive table for all devices showing mean, SD, precision and 95% CI of each device of 102 eyes.

Device	Mean (mm)	SD (mm)	SEM (precision)	95% Confidence Interval	
				Lower Bound	Upper Bound
IOLmaster	12.091	.42723	.042	12.008	12.175
Atlas	12.438	.51320	.051	12.337	12.539
Visante ATA	11.854	.48590	.048	11.759	11.950
Caliper	12.181	.42092	.042	12.099	12.264
Visante STS	12.444	.47800	.047	12.350	12.538

Table 2: Pair wise comparisons measurement of each device

Device	Device	Mean Difference	P value[b]	95% Confidence Interval for Difference[b]	
				Lower Bound	Upper Bound
IOLmaster	Atlas	-.347*	.000	-.436	-.257
	Visante ATA	.237*	.000	.148	.326
	Caliper	-.090	.007	-.155	-.025
	Visante STS	-.353*	.000	-.439	-.266
Atlas	IOLmaster	.347*	.000	.257	.436
	Visante ATA	.584*	.000	.486	.682
	Caliper	.257*	.000	.171	.343
	Visante STS	-.006	.905	-.101	.090
Visante ATA	IOLmaster	-.237*	.000	-.326	-.148
	Atlas	-.584*	.000	-.682	-.486
	Caliper	-.327*	.000	-.412	-.242
	Visante STS	-.590*	.000	-.607	-.572
Caliper	IOLmaster	.090	.007	.025	.155
	Atlas	-.257*	.000	-.343	-.171
	Visante ATA	.327*	.000	.242	.412
	Visante STS	-.263*	.000	-.346	-.179
Visante STS	IOLmaster	.353*	.000	.266	.439
	Atlas	.006	.905	-.090	.101
	Visante ATA	.590*	.000	.572	.607
	Caliper	.263*	.000	.179	.346

Discussion:

Posterior chamber pIOL namely STAAR surgical implantable collamer Lens (ICL) is widely used to correct high myopia with or without astigmatism[1, 5, 7, 9, 18]. It is vital to measure the sulcus diameter accurately for proper sizing of a pIOL[3-9]. Many complications arise due to inadequate sizing of a PC pIOL such as cataract, glaucoma and endothelial damage[16, 17]. The formula used to calculate the size of a PC pIOL (STAAR surgical ICL) requires measurement of diameter of the sulcus. This measurement can be estimated with several devices i.e. IOL master, Orbscan, Atlas topographer, Visante OCT and a surgical caliper. A 35 MHz UBM can be used to directly measure the sulcus diameter however it is not widely available in clinical practices[14,15].

Many studies have been conducted to find correlation between WTW measurements obtained with one or another device. *Fea et al* found a weak correlation between ciliary sulcus diameter measured with high resolution magnetic resonance imaging (MRI) and WTW distance measured with scanning-slit corneal topography (Orbscan II) [13]. *Werner et al* found no correlation between WTW distance measured with a caliper and the sulcus diameter measured after sectioning the eye in post mortem eyes[12]. *Pop et al* describe a weak correlation between the horizontal corneal diameter measured with a surgical caliper and that obtained with a 50 MHz UBM[10]. In a study by *Pin˜ero,* the WTW distance measured with a topographer was greater than the ATA distance measured by Visante OCT [2]. *Baikoff* found that these values obtained with IOLMaster and anterior chamber OCT to be equivalent[11].
In our study we tried to compare various measurements to estimate the sulcus diameter obtained with four different devices. We also tried to measure the sulcus diameter with Visante OCT by directly measuring the distance between the two sulci. The contrast setting of the anterior segment image was increased to the maximum to help view the angle of the sulcus.

The purpose of our study was to study the agreement on estimated sulcus diameter readings among four different modalities and whether these measurements can be used interchangeably. We found that all the measurements obtained with the mentioned devices cannot be used interchangeably. The means of all the measurements obtained were significantly different among one another except for the WTW obtained with Atlas topographer and STS measurement with Visante OCT. This means the surgeon cannot pick just any measurement of posterior chamber diameter estimated by a machine. Since all measurements differ among themselves, it seems more appropriate to stick to the manufacturers recommended way of sulcus measurement.

The sulcus can be measured directly with a 35 MHz UBM, however we have tried to obtain this information with Visante OCT machine. Further studies need to be done to compare the sulcus to sulcus measurement taken with Visante OCT and a UBM to ascertain the reliability of Visante OCT measurements. If the OCT findings are reliable, they can be used interchangeably with Atlas WTW measurements as there is no statistically significant difference between the WTW and STS measurements of Atlas and Visante OCT.
In conclusion the posterior chamber diameter needs to be accurately measured to prevent complications due to inappropriate sizing of the p IOL. If direct measurement of the sulcus diameter is not possible it is wise to use the recommended way of measuring the sulcus by the pIOL providing company.

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Authors Index

Subject Index