

Different Surgical Modalities in Management of Anisometropic Amblyopia in Myopic Children

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Abstract

Purpose: To compare the efficacy and safety of phakic intraocular lens (PIOL) versus intrastromal corneal ring segments (ICRS) implantation for management of amblyopia due to anisometropic high myopia in children.

Methods: Thirty amblyopic children with unsuccessful conventional amblyopia therapy, were randomized into two groups: group A (15 patients) underwent unilateral INTACS corneal rings and group B (15 patients) underwent unilateral PIOL implantation. All patients were evaluated for manifest refraction spherical equivalent (MRSE), best corrected distance visual acuity (CDVA) and endothelial cell count (ECC) at postoperative 1, 3, 6 and 9 months. Children with congenital cataract, anterior chamber depth < 2.8 mm and endothelial cell count < 2600/mm² were excluded from this study.

Results: At postoperative 9 months, the mean MRSE improved significantly in both the groups (-8.60 ± 1.18 D preoperatively vs. -4.12 ± 1.29 D at 9 months in group A [P < 0.001]) and (-12.90 ± 4.07 D preoperatively vs. -0.33 ± 0.70 D at 9 months in group B [P < 0.000]). CDVA improved from 1.08 ± 0.17 log MAR preoperatively to 0.61 ± 0.26 log MAR, in INTACS group (P < 0.001) and from 0.78 ± 0.21 log MAR preoperatively to 0.60 ± 0.24 log MAR, in PIOL group (P > 0.05). While there was no statistically significant decrease in ECC in the INTACS group, PIOL group had significant decrease in ECC at 9 months postoperative.

Conclusion: ICRS may be a viable treatment for clinically significant anisometropic amblyopia, refractory to conventional amblyopia treatment, albeit with limited range of refractive correction. Larger studies are needed to confirm the better safety profile of ICRS compared to PIOLs apparent from the current study.

Keywords: Anisometropia; Amblyopic Children; High Myopia; INTACS; Phakic Intraocular Lens

Abbreviations

PRK: Photorefractive Keratectomy; LASIK: laser *In Situ* Keratomileusis; LASEK: Laser Assisted Sub Epithelial Keratectomy; INTACS: Intrastromal Corneal Ring Segment; PIOL: Phakic Intraocular Lens; MRSE: Manifest Refraction Spherical Equivalent; CDVA: Corrected Distance Visual Acuity; ECC: Endothelial Cell Count

Introduction

Amblyopia refers to the lack of development of vision or a decrease of visual acuity in an eye for which no organic pathology can be detected [1,2]. Anisometropic amblyopia is the most common cause of monocular vision loss in children with an estimated prevalence of 1 - 5% [2-4], Because of the failure of detection or treatment, amblyopia continues to be an important cause of vision loss in adults, with an estimated prevalence of 2.9% [5,6].

The conventional treatment of amblyopia includes correction of refractive error with spectacles or contact lenses, accompanied by occlusion or penalization therapy of the non-amblyopic eye [7]. However, conventional therapy is reported to fail in approximately 10 to

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50% of the amblyopic children who may achieve a final visual acuity of 20/40 or worse [7]. This may be due to a poor compliance to the use of refractive correction measures or due to higher severity of amblyopia, typically associated with high anisometropia or anisostigmatism [8]. In such situations, when conventional therapy fails or yields less than optimal vision, surgical treatment at an earlier age may be a viable alternative to conventional therapy for anisometropic amblyopia in children to prevent persistent residual amblyopia.

The specific refractive procedures that may be applicable for anisometropic amblyopia in children are photorefractive keratectomy (PRK), laser in situ keratomileusis (LASIK), laser assisted sub epithelial keratectomy (LASEK), refractive lens exchange, phakic intraocular lenses (PIOL), and intrastromal corneal rings (ICRS) [7]. However, each of these refractive procedures has its own pros and cons. While the excimer laser procedures such as PRK and LASEK help achieve accurate refractive correction, recovery time may be long with postoperative discomfort [9-12]. In addition, there is a risk of corneal haze, refractive regression, decreased contrast sensitivity and potentially glare [13,14]. With LASIK, there is a risk of flap dislocation, flap-tear, keratectasia and epithelial in-growth [15].

Recently, refractive lens exchange and PIOL are gaining acceptance for treatment of amblyopia [16-18]. However, there is an increased risk of retinal detachment after clear lens extraction, especially in children with axial myopia [7]. There may be loss of accommodation following implantation of monofocal IOL. In addition, the risks of PIOL can be vision threatening, which include cataract development, PIOL dislocation, macular hemorrhage or secondary glaucoma [17,19-22].

ICRS (INTACS, Addition Technology) implantation is a minimally invasive surgical method developed to restore vision by flattening cornea due to its "arc-shortening" effect. ICRS were first used for the correction of low myopia [23-26]; however, because of the tissue saving character and ability to defer the need for corneal transplantation, they gained popularity in treating keratoconus or iatrogenic keratectasia. There is substantial evidence supporting the safety and efficacy of INTACS for reduction of mild to moderate myopia and the management of ectasia [27-31].

In view of the fact that ICRS can safely and effectively correct myopia, it is logical to use ICRS for the correction of anisometropia in children with amblyopia, especially as the procedure is reversible, that is, the rings can be explanted if needed.

The purpose of the current study is to compare the efficacy and safety of PIOL implantation versus INTACS for correcting high myopic anisometropia in amblyopic children. To our knowledge, this is the first study evaluating the outcomes of ICRS and PIOL implantation in children with amblyopia.

Materials and Methods

This prospective case series comprised of 30 children with refractory amblyopia who were taken up for INTACS or PIOL implantation at Magrabi eye hospital, Kingdom of Saudi Arabia between August 2010 and February 2012. Subjects were randomized into group A and B; group A included 15 subjects who had undergone unilateral INTACS corneal rings and group B included 15 subjects who had undergone unilateral phakic intraocular lens (PIOL) implantation. The age range from 7 to 12 years in INTACS group, and from 4 to 12 years in PIOL group.

The study was approved by ethics committee of Magrabi Aseer hospital. Comprehensive discussion with parents was undertaken pre-operatively and informed consent, including the off-label use of ICRS and PIOL was obtained from all parents.

Inclusion and exclusion criteria

Inclusion criteria were anisometropic amblyopia, with unsuccessful conventional amblyopia therapy (using varying combinations of spectacles, contact lenses, and occlusion therapy). None of the patients were compliant with spectacle wear or contact lens, if applicable. The response to conventional treatment was considered refractory when patients did not show improvement in amblyopia after 2 months of 6 hours per day partial patch occlusion. Exclusion criteria included the presence of congenital cataract, anterior chamber depth less than 2.8 mm and endothelial cell count less than 2600/mm².

Study Parameters

All patients were evaluated for manifest refraction spherical equivalent (MRSE) and best corrected distance visual acuity (CDVA) and endothelial cell count (ECC). Preoperative and postoperative visual acuity was measured using Snellen or Allen vision charts. Additional baseline testing included: anterior/posterior segment examination, anterior chamber depth and white to white and axial biometry measurements, using IOL Master (version 3.00, Zeiss, Germany). Cycloplegic refraction, endothelial cell counts using specular microscopy (TX-10, Canon, Japan). Follow-up examinations were scheduled at 3 days, 1, 3, 6, and 9 months, and then as needed. All patients completed the 9 months follow-up.

Surgical technique

Both procedures were performed under general anesthesia. Benoxinate hydrochloride (0.4%) was used to induce pre-emptive analgesia after loss of consciousness.

PIOL implantation

The surgery was performed through the temporal quadrant. A 3.0-mm tunneled clear cornea incision was created, and the anterior chamber was filled with viscoelastic material (VISCOAT®; Alcon Laboratories, Inc, Fort Worth, Texas). The PIOL (Visian ICL V4c; STAAR Surgical Inc., Monrovia, CA) was loaded into the cartridge, as specified by the manufacturer and injected intraocularly. An iris manipulator was used to place the lens within the posterior chamber. When the intraocular lens was in place, 1.0 ml of miochol (CIBA Vision, Claremont, California) chloride was injected into the anterior chamber. Model V4c with Aquaport, which is designed to restore more natural aqueous flow and eliminate the need for an iridotomy was used in all cases. The viscoelastic material was then removed using the aspiration/irrigation mode of the Ocutome (Storz; Premiere, St. Louis, Missouri). Patients were treated with moxifloxacin 0.5% eye drops (VIGAMOX®, Alcon Laboratories, Inc., Fort Worth, Texas) four times daily, prednisolone acetate 1% (PREDFORTE® Allergan, Inc. Irvine, CA, USA) four times daily, and tropicamide 0.5% (MYDRIACYL®, Alcon Laboratories, Inc., Fort Worth, Texas) once a day for 2 weeks. Predforte eye drops instillations were tapered over a period of 2 additional weeks.

INTACS implantation

The geometric center of the cornea was identified using the 11 mm zone marker, and the center was marked using a Sinsky hook. Radial incision was made on the steepest meridian. Intrastromal tunnel was created with femtosecond laser (Intralase Corporation, Irvine, CA) at 70% depth of the cornea. The pulse duration was 150 femtoseconds, with the inner to outer diameter of the INTACS tunnel set from 6.7 to 8.2 mm. Spot size was 1 mm, and the energy was 6 mJ. Two symmetric INTACS segments were implanted inferiorly and superiorly based on patients' preoperative spherical equivalent. Postoperatively, moxifloxacin 0.5% (VIGAMOX®, Alcon Laboratories Inc., Fort Worth, TX, USA) and prednisolone acetate 1% (PRED FORTE®, Allergan, Inc., Irvine, CA, USA) QID for 2 weeks were prescribed.

Postoperative patching

The importance and need of postoperative patching of the good eye was explained to the parents. Patching the good eye was recommended for 6 hours per day postoperatively until the visual acuity improved near to the level of non-amblyopic eye.

Statistical Analysis

Statistical analysis was performed using SPSS software (IBM Corp, Somers, NY). Repeated-measures ANOVA with Bonferroni corrected post hoc testing and descriptive statistics were used to analyze the change from baseline (pre-procedure levels) to 1, 3, 6 and 9 months values as well as other successive time intervals i.e., 1 to 3 months, 3 to 6 months and 6 to 9 months. Between the groups comparison were done using independent t-test. A statistically significant difference was based on the level $\alpha = 0.05$.

Results

This prospective case series comprised of 30 children with refractory amblyopia with mean age of the subjects in INTACS group was 9.47 ± 1.73 years (range 7 - 12 years), and in the PIOL group was 8.73 ± 2.55 years (range 4 - 12 years).

The mean preoperative MRSE in group A was -8.60 ± 1.18 D and in group B was -12.90 ± 4.07 D. At postoperative 9 months, MRSE improved significantly to -4.12 ± 1.29 D in group A ($P < 0.001$) and to -0.33 ± 0.70 D in group B ($P < 0.001$). At postoperative 1, 3, 6 and 9 months, MRSE improved significantly in both groups compared to baseline (Figure 1a and 2a).

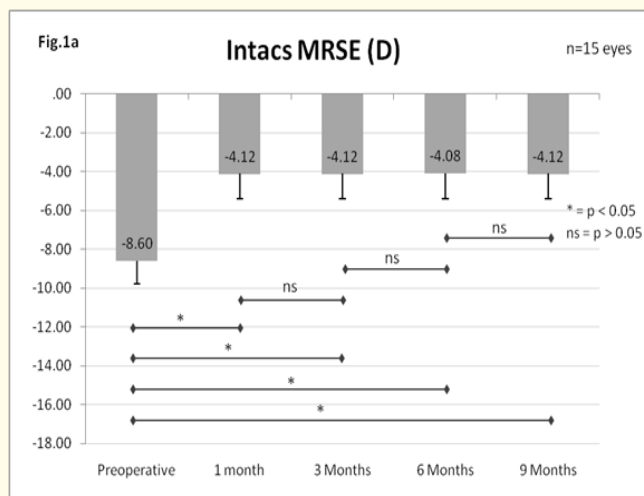


Figure 1a: INTACS MRSE preoperative and at 1,3,6,9 months postoperative.

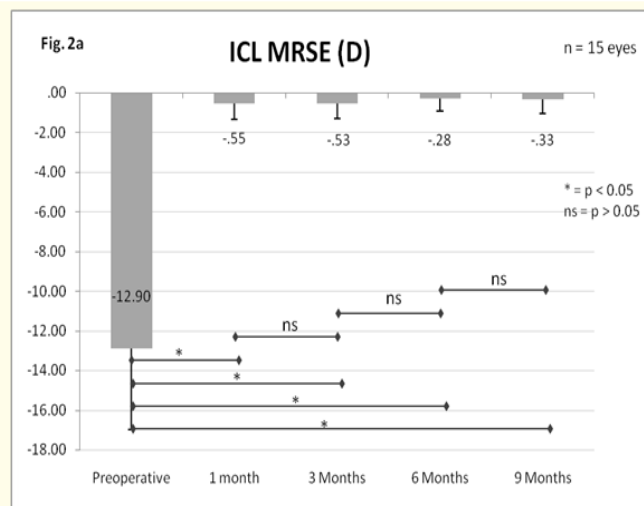


Figure 2a: ICL MRSE preoperative and at 1,3,6,9 months postoperative.

In INTACS group, CDVA improved from 1.08 ± 0.17 log MAR preoperatively to 0.61 ± 0.26 log MAR at postoperative 9 months ($P < 0.001$). Eyes in PIOL group also showed an improvement in CDVA from 0.78 ± 0.21 log MAR preoperatively to 0.60 ± 0.24 log MAR at post-

operative 9 months; however, the change was not statistically significant ($P = 0.207$). Comparison of postoperative CDVA between the 2 groups was not statistically significant at any time point (1, 3, 6 and 9 months) (Figure 1b, 2b).

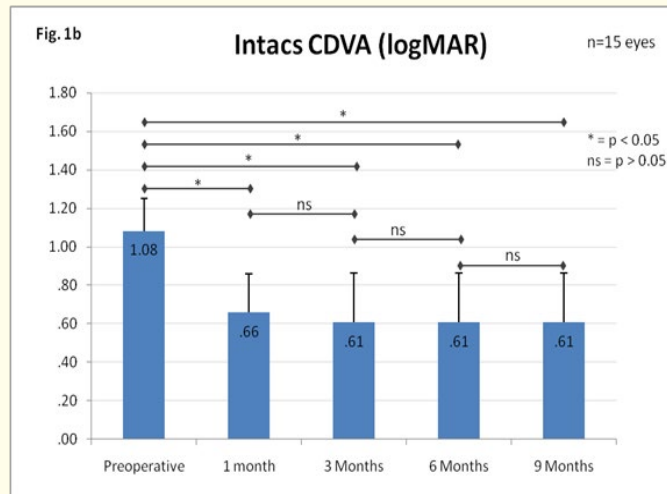


Figure 1b: INTACS CDVA (LogMAR) preoperative and at 1,3,6,9 months postoperative.

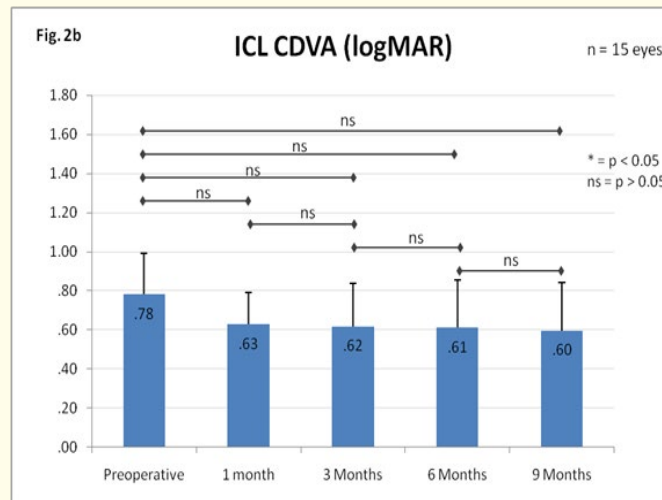


Figure 2b: ICL CDVA (LogMAR) preoperative and at 1, 3, 6, 9 months postoperative.

Analysis of change in ECC revealed that there was no statistically significant change in ECC in the INTACS group at any time point post-operatively. While there was no statistically significant change in ECC in the PIOL group at 1, 3 and 6 months with statistically significant decrease in ECC at 9 months follow-up (compared to preoperative values) (Figure 1c and 2c).

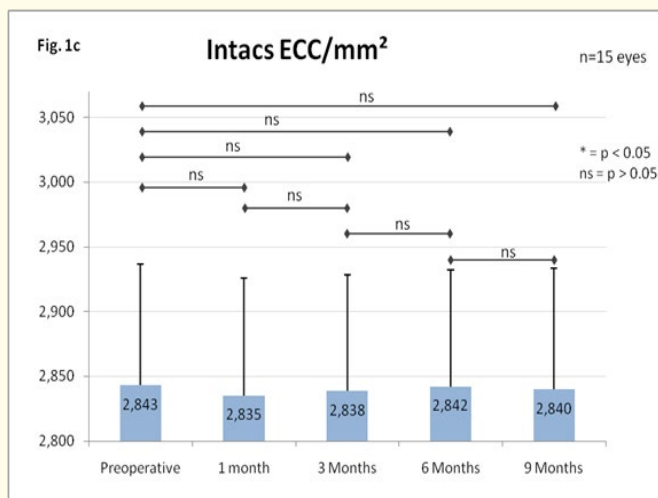


Figure 1c: INTACS ECC preoperative and at 1,3,6,9 months postoperative.

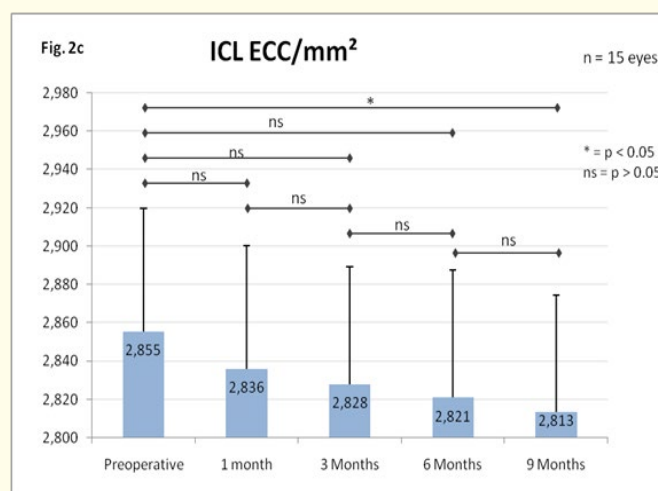


Figure 2c: ICL ECC preoperative and at 1,3,6,9 months postoperative.

While no complications were observed in the INTACS group; two cases of cataract, one case of glaucoma and one case of uveitis were noticed in PIOL group.

Discussion

Amblyopia is the most common cause of monocular vision loss in children and its treatment should be initiated at an early age to prevent permanent vision loss persisting into adulthood. It has been documented that the treatment of amblyopia in early childhood results in a substantial lifetime gain in quality-of-life years [32].

The most preferred treatment modalities for anisometropic amblyopia are correction of refractive error with spectacles or contact lenses along with occlusion therapy. Atropine penalization may be tried in children who are not compliant with patching. In difficult cases of anisometropic amblyopia, where conventional therapy has failed, surgical intervention has been reported to be successful. These in-

clude PRK, LASIK, LASEK, clear lens extraction, PIOL and ICRS. While all the procedures have their pros and cons, due to reversibility and better safety profile phakic IOL (anterior or posterior chamber) implantation has gained good acceptability in treating amblyopia [33].

There is substantial evidence demonstrating the efficacy and safety of ICRS to correct myopia and manage keratoconus [28]. It has led to suggestions that ICRS implantation may be a viable surgical treatment in the amblyopic children especially because of the tissue-saving character of this technique [7]. Additionally, the procedure is reversible and there is little risk of corneal or intraocular complications typically associated with excimer laser procedures or PIOLs. The aim of this study was to compare the outcomes and complications of INTACS and PIOL in patients with amblyopia.

The present study found a statistically significant improvement in MRSE in both groups at postoperative 1, 3, 6 and 9 months, compared to baseline suggesting effective refractive correction in both the groups. While the improvement in MRSE translated into statistically significant improvement in CDVA in the INTACS groups, it did not yield a statistically significant improvement in the PIOL group. Although our study did not find a statistically significant improvement in the visual acuity after PIOL implantation, there is previous literature supporting the efficacy and safety of PIOL in the treatment of amblyopia in highly myopic amblyopic children. The difference in findings of our study was due to the cataract development in two eyes, and due to non-improvement of amblyopia in one eye. As such, phakic IOLs have been reported to cause glaucoma, corneal endothelial cell loss, chronic inflammation and cataract development. While as low as 1.3% of eyes have been reported to develop cataract after ICL implantation in adults [34]; theoretically, pediatric patients have a higher risk of cataract and glaucoma after PIOL implantation because of smaller anterior chamber and higher propensity for eye rubbing [13].

Postoperative ECC in INTACS group did not change significantly at any time point. Our results are in agreement with previously documented results [24-35]. Similarly in ICL group, ECC did not change significantly at postoperative 1, 3 and 6 months compared to preoperative counts. However, 9 month's ECC was statistically significantly less than the preoperative counts, representing a loss of 1.47% (from preoperative ECC of 2855 cell/mm² to 2813 cells/mm² at 9 months) (Figure 2c). As such, the endothelial cell loss following PIOL implantation in our study is less than those previously documented. Jimenez-Alfaro, *et al.* reported 4.83% and 5.17% endothelial cell loss after 6 and 12 months of posterior chamber phakic intraocular lens (PCPIOL) implantation respectively in patients with high myopia, 36 compared to 1.47% at 9 months in our study. While it may not be directly comparable, the long term endothelial cell loss after 3 to 5 years of PCPIOL implantation range from 2% to 12.8% [17,34-37].

From the results of this study, it is reasonable to conclude that in amblyopic children, non-compliant to spectacle/contact lens wear, both PIOL and ICRS are viable surgical treatments. However, ICRS was found to be safer with fewer complications. In addition, there is potential for reversing the procedure. Future studies with larger data set and longer follow-up are recommended to evaluate the long-term benefits of ICRS implantation in amblyopic children.

Conflict of Interest

None of the authors has conflict of interest in any material used in the study.

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