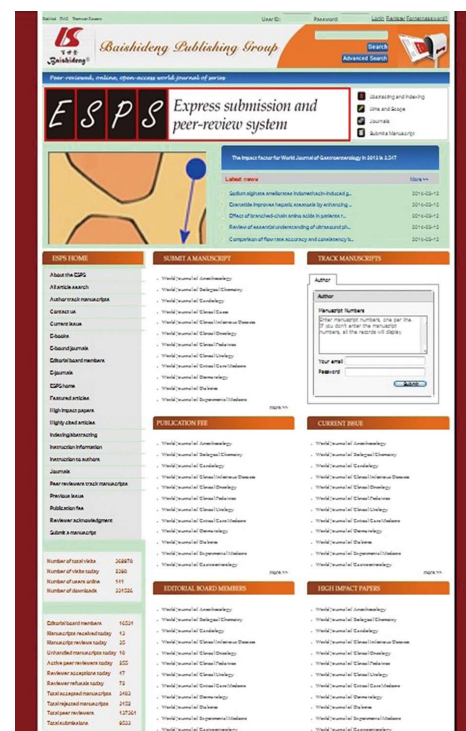
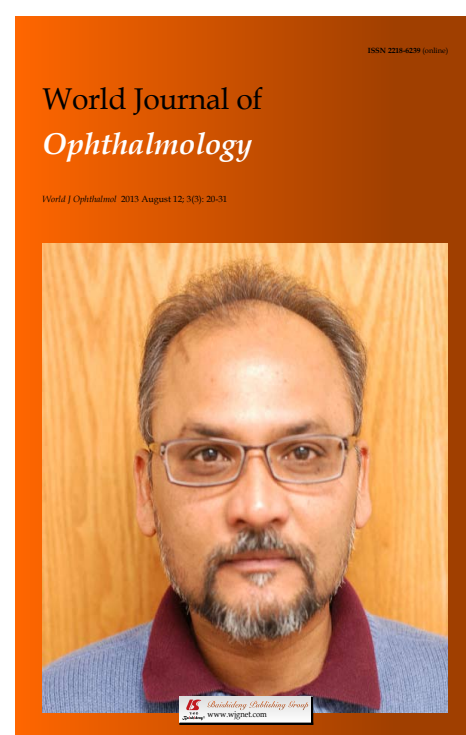


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World J Ophthalmol 2013 February 12; 3(1): 1-15



**ORIGINAL ARTICLE**

1

Paired arcuate and modified circular keratotomy in keratoconus

Quawasmī SA

Contents

World Journal of Ophthalmology
Volume 3 Number 1 February 12, 2013

APPENDIX I-V Instructions to authors

ABOUT COVER Editorial Board Member of *World Journal of Ophthalmology*, Winston W-Y Kao, Professor, Department of Ophthalmology, University of Cincinnati, 3230 Eden Ave, Cincinnati, OH 45267-0838, United States

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Paired arcuate and modified circular keratotomy in keratoconus

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Author contributions: Quawasmi SA solely contributed to this work.

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Abstract

AIM: To reduce astigmatism, increase corneal volume and improve visual acuity.

METHODS: A retrospective, single-surgeon, single-center, clinic-based study of a surgical procedure on twenty-four eyes of fourteen patients diagnosed with stage III or stage IV keratoconus. Paired arcuate keratotomy coupled with modified circular keratotomy was performed at a single center by a single surgeon as an outpatient procedure with local anaesthetic in a minor surgery room. Modified circular keratotomy was performed 7 mm from the pupillary center with depth of incision ranging between 70% and 90% of corneal thickness. Arcuate keratotomy was performed 2.5 mm from the pupillary center with the depth of incision at 90% of corneal thickness. Angular length of the arcs ranged between 60° and 120° depending on the astigmatic power of the cornea.

RESULTS: Astigmatism decreased in 87.5% of the 24 treated eyes, increased in 8.33% and did not change in 4.17%. Corneal volume increased in 91.66% of the 24 eyes and decreased in 8.34%. Visual acuity improved in 100% of the eyes; there was a mean improvement of 59% from preoperative visual acuity, 8.34% of the treated eyes reaching a visual acuity of 1.0 (20/20) with correction. No complications occurred during or

after surgery. No suturing was performed and there was no rupturing at incision sites. There was statistical significance difference between pre.sph against post.sph ($P = 0.001$). Also between pre.cyl against post.cyl ($P = 0.005$), there was no significance difference between pre.axis against post.axis ($P = 0.05$).

CONCLUSION: Paired arcuate keratotomy coupled with modified circular keratotomy should be considered as an intervention before performing keratoplasty.

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Key words: Arcuate keratotomy; Circular keratotomy; Keratoconus; Astigmatism; Keratotomy; Bader procedure; Ectasia

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INTRODUCTION

Keratoconus is a non-inflammatory, progressive, bilateral thinning disease of the cornea^[1,2]. It is characterized by the development of a corresponding protrusion with an apex often located centrally or in an inferior eccentric position^[1,2]. It is also characterized by corneal surface irregularity, astigmatism and ectasia accompanied by myopia and refractive amblyopia^[3]. In the mildest cases, *i.e.*, stages I and II, eyeglasses or contact lenses can be used to correct vision^[1].

As the disorder progresses to stage III or IV, eyeglasses or the various kinds of contact lenses may no longer correct the disorder sufficiently^[1]. If keratoconus is not corrected, keratoplasty may be required^[1]. Intracorneal rings, collagen cross-linking, and many other methods have been used to arrest the progression of keratoconus

before it progresses to later stages^[1]. Two techniques or interventions to address keratoconus are arcuate keratotomy^[1,4-6] and circular keratotomy^[1,7-9].

A new procedure, which I have named the Bader procedure, couples paired arcuate keratotomy^[10] with a modified form of circular keratotomy^[1,7-9] to induce the cornea to correct its topography through its natural healing process^[11,12]. Paired arcuate keratotomy was examined in 1988 as a possible method for the reduction of astigmatism^[10]. Subsequently, the use of an arcuate keratome to make transverse arcuate corneal incisions was examined as a method of correcting astigmatism, and successful use of the instrument in five consecutive eyes with naturally occurring astigmatism was reported^[4,6] used standard arcuate keratotomy in postkeratoplasty eyes, regardless of preoperative astigmatism, and concluded that standard treatment, irrespective of preoperative cylinder, has a linear effect on the reduction of postkeratoplasty astigmatism. Patients with higher degrees of preoperative astigmatism experienced greater reductions in astigmatism following the treatment. Hoffart *et al*^[5] concluded that arcuate keratotomy performed with the Hanna arcitome was effective in reducing postkeratoplasty astigmatism. The device enabled safer, easier arcuate incisions compared with manual incision techniques. However, it was also concluded that predictability and efficacy could be improved by a more accurate nomogram.

Circular keratotomy has been performed using a trephine blade and suturing^[13], some procedures being coupled with the implantation of rings^[7]. In a study of three patients, Leccisotti^[14] concluded that circular keratotomy increased corneal curvature and worsened keratoconus and could therefore not be recommended. However, Krumeich *et al*^[8] reported that circular keratotomy provided significant reduction in astigmatism, improved best spectacle-corrected visual acuity, and stabilized astigmatic changes in most eyes, although some eyes showed limited benefit. Eyes with greater preoperative astigmatism appear to be more likely to benefit from the procedure than those with lower preoperative astigmatism. Circular keratotomy also resulted in reasonable clinical results in the treatment of stage I and II keratoconus^[8].

MATERIALS AND METHODS

All patients in the study came to the clinic after examination by other doctors who had diagnosed them with stage III or stage IV keratoconus. Diagnosis was confirmed by the examiner on their first visit and classified using the Krumeich classification (Table 1). All patients had been informed by other doctors that they required keratoplasty to treat their condition. Preoperative tracking for disease progression was not applicable in this situation because the patient had already progressed to a stage requiring treatment. All operations occurred within 1 wk of their visit to the clinic.

Patient examination and operating techniques

The clinical examination at our center included the E-test,

refractometer, retinoscopy, direct and indirect ophthalmoscopy, sagittal cornea examination, subjective and objective visual acuity tests, ultrasound examination, glare test and Oculus Pentacam topography. Preoperative and postoperative sphere and cylinder measurements were recorded (Table 2), but were not analyzed as dependent variables. The primary outcome variables measured were uncorrected and spectacle-corrected acuity, refractive error with the pupil dilated and undilated, corneal shape, corneal pachymetry, and corneal indices measured by Oculus Pentacam topography (Table 3).

This approach to treatment addresses the irregularity of the cornea and the steepness of the meridian by positioning the circular keratotomy 7 mm from the pupillary center and two arcuate keratotomy incisions 2.5 mm from the pupillary center at 90° to the steepest meridian. Figure 1A represents the angular circumference of the cornea. Figure 1B illustrates one possible calculation and location for the paired arcuate incisions. Figure 1C illustrates the combination of the arcuate keratotomy and modified form of circular keratotomy. Notice that the paired arcuate incisions are of the same angular length.

A Hanna arcitome with micrometric diamond knives was used. The procedure was a modified form of circular keratotomy which used microincision but no trephining. The depth, length, and location of the incisions were predetermined according to topographic readings. Two micrometric diamond knives, each with a width of 1.0 mm and thickness of 0.150 mm, were mounted 180° apart. Local anesthetic was applied and corneal thickness was measured by ultrasonic pachymetry at 1640 m/s. Three measurements were taken in the area where incisions were proposed, and the mean thickness was calculated. The blades were then set to the correct depth. Great care was taken to avoid exposure of the cornea to direct illumination as this affects its thickness during the operation^[15,16].

The diameter of the free cornea zone was marked and the angular length of the cut was set. Dextran solution and antibiotic were applied to moisten the surface of the cornea before, during, and after the incisions. The instrument was then placed on the eye and the blades were inserted in the cornea.

The arcuate incisions were placed at a radial distance of 2.5 mm from the pupillary center on each side of the steepest axis, creating an arcuate incision diameter of 5.0 mm, and were made in one continuous sweep. The arcuate incisions were of a defined angular length extending from 60° to 120° and were determined by the degree of astigmatism. Angular length was calculated using the values of the dioptric power of the cornea, and the difference between K1 and K2 readings obtained in the Pentacam analysis of the cornea. Angular length is directly related to astigmatic corneal power (Table 3).

The seating depth of the blade was adjusted with a calibrated screw mechanism at the top of each knife. The depth of the arcuate incisions ranged between 70% and 90% depending on the thickness of the cornea and corneal power. An area of low corneal power received a deeper incision than an area of high corneal power be-

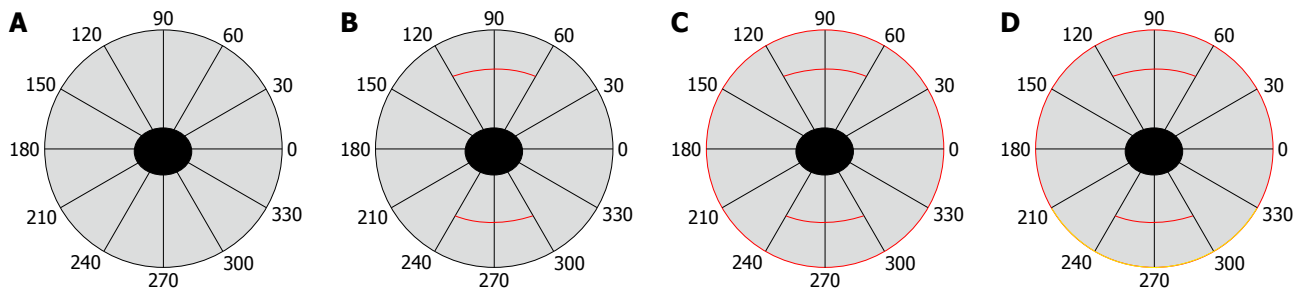


Figure 1 The treatment addresses the irregularity of the cornea and the steepness of the meridian. A: Represents the angular circumference of the cornea; B: Illustrates one possible calculation and location for the paired arcuate incisions; C: Illustrates the combination of the arcuate keratotomy and modified form of circular keratotomy; D: The yellow arc marks the area of low corneal power from 210° to 330° and indicates an area of 90% incision depth, while the incision in the red area would be at a depth of 70%.

cause corneal volume tends to increase more in the area of the deepest incision and less in the area of shallow incision; this allows the cornea to reform or restructure to nearly equalized corneal power. Factors that affect the actual depth of the incision in the cornea are the pachometric readings and location of the corneal thickness. Following the arcuate incisions, the modified form of circular keratotomy was performed.

A full circular incision of 360°, with no corneal suction, was made in one continuous movement at 30°/s. The depth of the circular incision ranged between 70% and 90% depending on the thickness of the cornea and corneal power. For example, if corneal power was low from 20° to 200°, this area would receive an incision of depth 90% and the remaining part would receive an incision of depth 70%. If corneal power was low from 60° to 130° this area would receive an incision of depth 90% and the remaining part an incision of depth 70%. In Figure 1D, the yellow arc marks the area of low corneal power from 210° to 330° and indicates an area of 90% incision depth, while the incision in the red area would be at a depth of 70%. At the conclusion of the procedure, antibiotic drops were applied and the eye(s) were covered with shields with no padding.

Immediate after-care undertaken by the patient included collagen capsules (400 mg) every night before bed coupled with vitamin C (5000 mcg), because vitamin C assists in the pump action of potassium to create pressure equilibrium, reducing haze and facilitating the synthesis of collagen^[17].

G-pilocarpine (2%) drops, which provide the benefit of a parasympathomimetic effect on the epithelial cells, miosis, and maintenance of the anterior chamber pressure so that it is not affected by diurnal variation in intraocular pressure^[3,13], were administered every 3 h during the daytime for the first 6 mo. The refractive power of the eye changes during the first 6 mo of the postoperative period, and the drops were reduced or stopped depending on the improvement in edema. If there was still evidence of edema, the drops were continued for another 6 mo.

Follow-up and postoperative examinations

Follow-up on patients was conducted by phone call to ad-

dress patient concerns only. If during the patient follow-up telephone interviews there were reports of iatrogenic effects, patients would have been asked to see a local physician in their home country and have reports sent to our clinic. No iatrogenic effects were reported. All patients in the study were from other countries in the Middle East region and returned within 11-13 mo for a 1-year post-operative check-up, at which time data were collected. Patients declined to return for follow-up visits during the first year for economic reasons. Insurance in Jordan does not cover many operations in the field of ophthalmology. Patients were, however, informed that they would need to return for a 6-mo and 12-mo follow-up. During post-operative examinations, patient data were collected using the E-test, refractometer, retinoscopy, direct and indirect ophthalmoscopy, sagittal cornea examination, subjective and objective visual acuity tests, ultrasound examination, glare test and Oculus Pentacam tomography and numeric values.

RESULTS

Astigmatism decreased in 87.5% of the 24 treated eyes, increased in 8.33%, and did not change in 4.17%. The percentage decrease in astigmatism ranged between 0% and 92% of the preoperative reading, with a mean decrease of 39% from the original astigmatic reading. The percentage increase in astigmatism ranged from 9% to 20%, with a mean increase of 15% from the original astigmatic reading (Table 3).

Corneal volume increased in 91.66% of treated eyes. The mean increase in corneal volume was 8% of the original corneal volume. Corneal volume decreased in 8.34% of treated eyes. The mean decrease was 8% of the original corneal volume (Table 3).

Visual acuity improved in 100% of treated eyes. There was a mean improvement of 59% from the original visual acuity readings in all treated eyes. Two of the treated eyes (8.34%) improved to a visual acuity of 1.0 (20/20) with assistance (Table 3).

DISCUSSION

The Operating procedure is based on the findings of the

Table 1 All patient cornea power pre and post operation

Patient name	Gender	Age (yr)	Eye	Date of operation	Pre operation (corneal power in clockwise 360 degree)										Post operation (corneal power in clockwise 360 degree)										Year					
Aala'a Mare'e	F	29	OD	2007-04-15	33.4	34.5	33.4	37.3	45.1	51.6	54.8	54.5	52.1	48.2	43.5	37.8	51.6	48.8	47.2	48.8	52.3	55.7	58.4	59.9	59.4	58.6	58.1	57.3	2011-12-03	
Khalid Abu Ghalyoon	M	24	OS	2007-11-04	39.7	39.9	43.6	49.3	50.2	51.6	55.5	53.6	52.6	49.9	44.3	42.5	42.1	57.3	59.7	62.2	63.6	64.1	64.8	65.1	64.2	62.4	59.9	57.1	54.3	2011-12-18
Mahmoud Al-Farahaat	M	22	OD	2007-10-21	41.9	38.7	36.2	36.5	39.5	44.7	46.8	49.1	46.6	44.9	41.9	40.7	39.9	38.7	37.1	37.2	40.2	45.0	49.1	48.6	46.9	45.3	43.6	40.7	2008-03-16	
Diana Abu Al-Rub	F	26	OD	2007-02-11	43.3	42.3	42.1	42.3	45.2	48.2	49.1	48.9	45.7	43.9	42.9	43.7	47.0	44.0	41.8	42.1	46.2	52.4	57.0	58.8	57.3	54.1	53.2	52.4	2011-02-27	
Faras Al-Azaam	M	40	OD	2007-11-05	46.7	43.1	43.4	45.3	47.9	50.9	52.5	51.3	47.0	42.9	41.6	41.9	43.4	45.9	48.5	49.7	52.2	56.3	61.9	65.7	65.5	61.6	55.2	49.2	2010-03-09	
Nadeem Bolbol	M	22	OD	2007-06-11	39.1	38.6	37.4	38.0	40.9	43.8	44.8	44.0	40.3	38.7	38.0	38.6	37.8	37.2	37.1	38.4	41.6	45.2	48.0	49.0	46.5	42.6	40.2	38.8	2011-06-08	
Fisal Al-Shaqe'h	M	27	OD	2007-07-11	51.3	50.7	43.3	43.1	47.1	50.8	53.0	54.6	54.4	54.1	54.2	53.8	55.8	55.0	54.4	54.2	55.8	57.5	60.2	61.4	60.8	56.6	58.9	60.0	2010-05-04	
Wa'el Badaweia	M	21	OD	2007-12-11	54.7	47.5	43.0	41.6	45.9	54.3	59.4	60.6	55.2	54.3	52.5	52.0	55.2	53.3	57.9	51.3	52.1	55.7	61.2	64.0	63.7	63.1	61.4	59.9	2010-12-19	
Ahmed Al-Asaaf	M	24	OD	2007-11-21	41.2	40.5	39.2	39.4	43.2	48.5	50.8	52.4	51.0	49.3	46.1	43.0	42.7	41.0	44.0	48.5	53.4	57.7	60.3	62.4	60.9	62.3	59.3	53.0	2009-05-31	
Ra'afat Al-Shaqeer	M	40	OD	2007-07-12	41.0	38.4	35.6	38.0	42.7	49.2	51.2	56.6	56.6	55.1	51.1	45.5	48.8	47.3	47.5	50.2	54.2	60.2	64.5	67.6	67.5	65.7	63.4	59.9	2011-01-17	
Mohammed Al-Muhairi	M	35	OD	2007-04-12	45.4	43.3	39.6	38.0	40.8	43.3	43.8	45.3	45.8	46.3	46.2	46.3	46.0	44.0	42.9	43.5	47.1	52.0	56.1	57.5	55.9	53.1	51.2	48.8	2011-10-15	
Murad Hejazin	M	23	OD	2007-10-12	41.3	40.8	38.6	39.5	44.3	44.4	43.0	46.0	47.0	46.0	44.6	42.6	49.9	47.9	47.1	47.9	50.7	55.4	58.5	58.5	55.7	52.2	51.0	51.3	2010-12-23	
Abdulrahman Mana'a	M	32	OD	2007-11-12	35.1	37.4	33.4	37.8	42.2	49.2	51.9	55.8	55.9	52.0	44.6	39.9	38.5	40.9	51.0	50.5	52.3	51.4	51.3	54.5	58.6	59.3	56.0	51.6	49.8	2009-11-14
Siham Abu Baker	F	36	OD	2007-11-12	38.4	37.4	38.2	41.1	44.2	48.7	50.9	50.0	48.4	46.3	42.9	41.5	41.9	33.6	40.1	44.5	50.3	56.2	60.7	62.9	62.5	59.0	54.8	51.5	2011-03-22	
Shaikha Al-Hajri	F	33	OD	2007-12-12	37.9	37.0	36.9	40.3	43.8	46.6	47.7	47.1	45.3	43.7	42.4	40.2	47.5	45.8	46.7	49.3	52.6	56.8	59.5	59.7	59.4	55.2	53.3	52.3	2010-07-12	
Adel Al-Rashidi	M	26	OD	2007-12-12	40.9	39.8	39.3	40.8	44.6	48.0	49.4	49.2	45.7	43.0	41.7	41.3	45.8	44.8	44.1	44.8	49.8	55.0	58.6	59.8	57.6	53.0	48.2	46.7	2011-03-09	
Sara Al-Amourat	F	28	OD	2007-12-17	54.3	51.0	47.9	47.2	49.2	51.3	53.6	55.4	55.0	53.4	55.4	54.1	62.5	60.1	58.0	57.8	69.6	62.1	64.7	66.1	65.1	64.8	64.1	64.5	2009-10-21	
Mesh'al Al-Khaldi	M	42	OD		40.4	41.4	39.4	44.5	48.0	56.0	57.4	57.8	53.6	48.5	46.9	44.2	43.2	45.0	48.1	45.7	52.6	57.9	58.3	57.1	53.1	51.5	48.1	46.7	2008-04-11	
Hani Abd Al-Ghani	M	31	OS	2007-12-26	42.9	38.5	39.9	42.2	46.8	51.3	53.3	52.1	47.8	43.4	41.2	40.0	40.6	40.4	43.2	45.6	48.3	52.1	52.9	53.1	49.9	46.9	45.2	43.9	2010-07-04	
Rabe'a Al-Qubti	M	33	OD	2008-05-01	38.3	36.6	34.2	35.8	39.7	45.2	47.7	47.5	44.3	42.0	39.9	39.1	47.1	43.2	42.5	44.8	47.7	52.5	55.7	57.0	56.7	55.5	53.3	52.2	2009-07-07	
Hamad Al-Meri	M	31	OD	2008-07-01	32.1	36.5	41.5	48.2	57.5	52.8	54.1	55.0	53.8	48.3	42.9	38.2	57.5	53.5	50.3	54.0	60.7	67.4	71.1	71.3	71.0	69.2	63.3	60.7	2011-01-26	
Noor Abu Halima	F	27	OD	2008-09-01	45.5	43.8	41.0	39.3	41.2	43.8	46.0	47.5	42.7	48.2	47.1	46.0	50.5	47.0	45.1	46.9	50.5	54.0	56.8	59.2	59.7	57.4	56.5	56.4	2010-12-21	
Jamal Al-Remhi	M	31	OD	2008-01-13	43.0	42.0	40.9	46.6	54.8	53.0	53.9	60.3	52.9	53.4	50.8	45.1	49.9	47.8	48.4	50.6	54.6	59.1	57.2	58.3	57.0	55.9	58.2	57.3	2010-07-17	
Abdulrahman Matoot	M	28	OD	2008-01-14	38.3	36.2	35.4	36.5	39.2	41.1	42.8	44.1	43.7	42.4	40.5	38.5	47.5	44.9	43.8	44.1	47.1	51.2	54.1	55.9	55.7	53.2	50.7	50.1	2001-01-11	
Sultan Haij	M	19	OD	2008-02-20	37.3	36.7	35.7	36.1	38.5	41.2	44.4	46.7	44.9	42.6	40.6	39.0	47.2	45.0	42.5	40.7	41.5	46.4	52.7	55.5	56.3	54.5	53.2	52.3	2009-09-04	
Najwaan Ja'afar	F	29	OD	2008-12-03	46.6	41.1	40.1	42.1	47.0	51.0	54.3	56.2	57.4	56.1	54.0	52.3	60.6	59.4	56.3	56.0	58.0	61.6	63.6	64.8	64.4	61.7	58.6	59.0	2009-03-08	
	OS				38.8	40.6	42.2	43.9	47.5	50.4	51.2	48.3	42.1	37.9	37.2	37.3	44.1	47.8	51.5	52.7	54.9	57.2	59.8	60.3	58.8	55.9	50.7	47.1		

Zainab Essa	F	36	OD	2008-03-18	43.7	43.5	38.9	38.5	41.6	45.0	45.9	45.4	45.5	45.2	44.6	44.5	43.4	38.2	40.0	43.9	47.0	46.0	43.8	46.8	46.2	46.8	46.0	2008-04-11
Rabe'a Al-Boom	F	39	OD	2008-03-18	49.7	45.5	43.1	44.5	45.3	45.0	43.8	43.1	43.5	43.4	44.7	44.0	44.2	44.1	46.5	49.3	51.3	53.3	53.0	48.9	46.4	44.7	43.9	2010-10-10
Abdullah Ba'jaah	M	38	OS	2008-03-30	39.0	39.4	39.7	41.6	44.2	46.1	48.0	47.3	44.6	43.5	39.5	39.2	38.8	39.3	41.4	42.5	45.0	49.6	54.2	58.0	58.4	55.6	50.3	2009-06-20
Ahmed Al-Muzai'el	M	27	OD	2008-07-04	38.9	37.0	37.3	41.5	44.7	54.8	52.5	56.2	49.7	46.5	44.7	40.6	37.2	36.5	39.1	46.0	3.8	62.3	66.4	67.8	67.4	63.4	56.9	2009-09-05
Salwa Abdulrahmaan	F	47	OS	2008-07-04	40.6	42.1	46.9	52.1	55.7	57.0	56.0	55.2	52.0	46.1	41.5	40.3	39.3	41.6	45.0	51.9	57.1	61.4	63.4	65.9	68.2	67.1	62.7	2011-12-07
Talal Al-Sharari	M	26	OD	2008-08-04	50.7	47.9	45.4	41.2	45.8	49.6	50.9	50.5	51.2	51.4	51.1	49.0	52.3	53.4	54.3	56.8	58.5	60.4	61.7	61.0	59.3	57.1	54.8	2009-06-05
Fanaar Shahin	M	28	OD	2008-04-30	41.2	37.3	38.0	36.7	42.3	48.3	55.1	53.4	53.4	54.0	50.4	45.7	58.6	57.9	49.0	50.3	62.2	66.2	57.5	57.6	60.0	61.3	49.3	2009-03-16
Abeer Al-Hoosh	F	39	OS	2008-04-05	54.9	64.9	57.0	51.0	47.9	51.5	62.5	53.7	56.6	56.4	62.9	65.3	56.9	53.4	50.8	47.7	44.1	43.3	45.8	50.7	52.5	53.0	55.4	2010-10-24
Faisal Al-Shaqe'h	M	27	OD	2008-05-05	46.7	45.5	42.6	43.4	47.6	52.4	53.8	54.7	54.5	53.2	52.4	49.3	57.0	54.9	52.8	53.4	55.4	58.8	61.9	62.5	61.3	58.8	58.5	2011-05-23
Sumaya Shamaan	F	42	OD	2008-05-15	42.5	41.7	41.6	41.0	42.1	43.1	43.6	45.5	45.5	45.7	45.3	44.2	45.1	44.6	44.9	46.1	47.3	49.2	50.9	51.7	51.8	50.0	49.6	2009-07-10
Emad Al-Ojaili	M	35	OS	2008-05-18	38.9	39.7	41.5	43.5	46.0	47.7	47.6	46.6	44.3	41.5	39.8	38.7	43.2	43.8	44.8	46.6	48.6	48.6	50.6	52.3	53.4	53.0	51.6	2009-07-06
Ahmed Danqela	M	25	OS	2008-05-24	39.3	41.3	42.8	45.8	48.0	47.7	45.0	44.6	44.1	41.8	39.7	38.8	42.8	44.2	47.4	49.8	51.6	43.6	56.2	55.8	56.7	57.3	53.9	2011-04-30
Zahr'a Hasan	F	23	OD	2008-07-06	42.2	41.1	39.8	41.2	45.4	51.1	53.2	52.3	47.6	45.2	42.9	42.3	47.1	46.6	47.4	50.0	54.6	59.1	62.1	62.0	58.2	56.2	53.4	2010-05-15
Ibrahim Al-Natoor	M	24	OS	2008-06-22	43.3	43.6	45.2	46.3	49.0	52.9	53.4	49.6	44.5	40.3	40.1	42.9	49.7	50.8	52.3	53.0	55.5	57.0	60.4	61.2	58.9	54.6	50.3	2011-09-21
Kholod Al-Herbawi	F	34	OD	2008-05-07	43.8	43.5	41.7	42.0	42.5	45.6	48.1	50.6	49.9	48.7	47.4	45.8	51.1	50.5	51.0	52.6	55.9	59.6	62.2	62.3	61.3	59.4	57.4	2010-12-21
Sa'eed Al-Ghamdi	M	28	OD	2008-06-07	42.5	40.4	37.6	38.0	41.5	45.4	47.1	46.5	44.6	43.5	43.0	42.8	44.7	42.7	42.4	45.2	49.3	54.0	57.9	59.4	58.0	55.0	53.0	2010-06-03
Abdullah Al-Fifi	M	30	OD	2008-07-15	40.7	40.7	40.0	40.8	43.8	46.5	48.2	48.8	45.9	43.7	41.2	41.2	40.6	42.8	42.9	43.8	47.3	52.8	57.0	57.8	55.0	50.8	47.4	2009-02-23
Bandar Al-Fifi	M	27	OD	2008-07-15	38.3	36.7	34.9	36.6	39.0	42.7	45.4	47.0	50.4	50.1	45.7	41.1	49.1	47.9	46.9	48.2	49.9	51.7	54.3	55.1	54.7	55.6	55.9	2009-02-23
Sayera Al-Shareh	F	31	OD	2008-07-16	44.7	45.4	47.8	48.4	48.0	45.5	45.9	42.6	41.8	42.6	46.1	46.9	53.8	54.4	53.6	52.2	53.3	55.9	55.9	53.6	49.6	45.8	44.1	2011-07-03
Sa'ed Al-Madi	M	19	OS	2008-07-30	36.4	36.8	42.1	45.8	47.5	54.6	55.8	56.6	50.9	44.7	39.1	36.1	51.0	51.5	52.9	54.6	56.9	59.4	62.6	64.7	65.5	64.2	61.5	2009-01-01
Mohammed Al-Shami	M	23	OS	2008-07-30	44.7	44.9	43.2	42.3	42.7	43.1	43.5	42.8	41.8	40.8	41.9	45.0	44.9	44.5	43.6	42.8	42.8	43.1	43.7	44.1	44.0	43.2	42.1	2009-07-25
Randa Al-Omari	F	36	OS	2008-03-08	38.9	41.0	42.9	44.8	47.5	48.0	48.4	46.9	44.1	41.1	38.8	38.1	41.9	43.1	44.1	46.3	48.3	50.2	51.0	52.3	52.4	51.1	48.3	2009-07-20
Badria Al-Qurani	F	34	OD	2008-12-08	42.1	39.6	38.5	40.8	44.4	48.0	48.0	48.7	46.6	44.5	42.1	40.6	41.1	41.2	45.4	48.2	51.4	56.5	60.3	62.6	60.7	58.9	57.8	2010-04-17
Omar Al-Zubairi	M	25	OD	2008-12-08	41.0	40.4	39.5	39.0	40.4	42.7	44.3	45.1	43.9	42.2	41.3	41.5	41.0	39.5	38.9	39.6	42.0	44.9	47.5	48.9	48.5	47.3	46.5	27-07-2010
Maha Hussein Al-Haaj	F	30	OD	2008-12-08	36.0	36.4	36.2	37.3	40.1	44.9	49.4	50.6	52.5	50.8	46.9	44.6	42.3	39.3	39.5	40.0	42.7	47.7	52.8	56.4	56.3	52.4	49.5	2011-06-07
Fakhra Al-Mashghoni	F	38	OD	2008-08-14	39.9	39.7	39.9	41.8	44.2	45.3	45.8	46.9	46.7	43.7	41.8	40.7	42.1	40.3	39.8	42.5	47.5	52.0	55.3	56.4	54.8	51.1	47.9	2011-01-08
Majdi Al-Atmi	M	24	OD	2008-08-16	38.2	35.6	35.6	37.7	40.9	43.5	44.5	45.3	43.0	40.9	37.5	37.2	45.8	45.7	47.8	52.2	56.7	61.0	63.9	65.0	62.7	57.8	54.5	2009-08-10
Ne'ama Al-Azmi	F	27	OD	2008-08-17	43.1	41.7	40.2	41.2	44.3	47.4	49.7	50.2	48.4	46.5	44.5	43.8	46.2	46.1	45.2	48.6	51.1	55.4	57.4	56.6	59.9	57.1	51.4	2009-08-04
Nuha Al-Buhairi	F	47	OD	2008-08-18	42.2	41.5	41.4	43.3	48.9	53.7	54.6	52.9	50.2	48.4	45.6	44.3	57.1	55.3	54.6	54.5	54.7	62.0	55.9	56.5	56.3	55.7	58.2	2010-07-21
Rabi'a Al-Ajrad	F	49	OS	2008-08-27	47.9	48.6	51.2	47.3	46.9	47.2	46.2	46.5	43.7	45.5	46.5	47.9	60.1	60.4	61.9	64.0	64.5	56.6	66.1	65.5	65.3	63.4	61.2	2009-06-10
Afaf Al-Chamdi	F	26	OD	2008-08-30	38.5	37.4	35.8	36.6	39.9	44.2	46.8	48.1	48.6	46.7	44.3	40.8	48.1	44.1	40.8	40.1	43.2	48.2	52.8	56.2	56.9	55.3	53.9	2009-07-16
Marino Astafinoos	M	24	OD	2008-09-22	41.0	40.6	40.7	39.9	41.2	43.8	45.2	46.2	45.3	44.7	43.3	40.9	54.3	52.4	50.1	49.1	49.6	50.9	52.2	54.2	55.6	55.9	56.2	2011-11-20
	OS				42.2	42.9	44.4	45.6	45.8	44.6	43.8	42.5	41.7	41.2	41.1	41.4	54.7	55.4	54.7	53.2	50.5	49.5	48.7	48.1	48.4	48.7	48.5	

Emad Hamani	M	48	OD	2008-09-21	39.2	37.5	36.9	38.4	43.6	48.9	50.7	51.7	51.5	50.1	47.6	43.2	52.0	49.2	47.9	49.1	52.6	58.2	62.4	64.6	64.9	63.9	61.5	59.0	2009-03-21
Jafar Ahmed Mohsin	M	41	OD	2008-09-23	38.0	38.1	40.3	44.2	50.4	56.5	57.7	54.5	48.1	43.7	41.4	39.1	38.3	40.6	44.6	46.4	48.6	53.2	56.7	56.8	52.1	47.2	43.3	38.4	
Ala'a Al-Tuwaishi	M	22	OD	2008-09-27	41.3	37.6	44.0	41.4	44.7	49.8	51.6	51.5	46.7	45.9	43.4	43.2	48.9	47.8	48.4	51.0	56.7	62.2	64.5	65.5	63.8	61.3	58.6	55.7	2009-07-26
Al-Yazeed Zawawi	M	44	OD	2008-10-26	44.2	42.9	40.9	40.8	44.5	46.4	49.2	50.8	50.2	49.6	48.7	46.4	57.2	54.8	51.3	51.0	53.1	55.6	58.2	60.5	59.0	56.9	57.0	57.5	2009-05-31
Abeer Al-Omari	F	30	OD	2008-10-29	48.1	48.8	49.4	49.2	49.7	50.5	50.8	50.6	49.7	49.1	48.6	48.5	48.9	49.5	49.5	48.9	48.4	47.0	49.6	51.2	51.8	50.8	48.4	46.5	
Ibtisam Al-Omari	F	39	OD	2008-10-29	47.3	46.5	46.9	47.0	47.5	48.5	49.3	49.7	48.1	47.0	47.2	47.4	48.5	48.0	47.4	47.0	47.4	47.8	48.2	49.1	49.0	48.4	48.3	47.9	2009-04-25
Mo'aath Al-Omari	M	22	OD	2008-12-23	41.5	39.2	40.8	45.6	49.8	55.0	56.2	56.1	57.4	53.7	50.4	48.9	44.3	43.3	47.2	45.1	47.6	53.5	55.5	55.8	62.1	56.6	50.9	50.0	2011-03-28
Fahad Al-Zahrani	M	29	OD	2009-05-01	41.0	39.4	38.6	39.6	42.0	46.1	48.6	49.6	48.9	46.9	43.7	41.4	46.4	44.5	42.9	44.8	48.5	53.0	57.0	58.9	57.6	53.8	51.4	50.0	2011-04-09
Tha'er Abu Al-Haija'a	M	28	OD	2009-06-01	50.6	49.8	48.0	46.6	48.2	50.5	50.6	49.3	49.1	50.0	51.5	51.8	49.1	49.2	47.8	47.4	49.3	51.5	51.9	49.8	49.1	50.0	51.5	51.1	2011-03-05
Omar Al-Qa'abi	M	22	OD	2009-10-02	36.6	35.2	36.1	41.1	46.6	51.9	55.2	57.5	59.8	57.0	53.2	48.6	41.1	39.7	41.7	45.7	51.2	55.8	58.2	58.8	57.6	54.7	52.0	49.4	2009-10-19
Naser Al-Qa'abi	M	25	OD	2009-10-02	41.3	39.5	38.8	39.4	41.9	45.0	47.2	49.1	49.8	49.8	48.8	47.6	45.1	42.7	41.6	43.6	46.9	50.4	52.8	53.6	52.9	51.6	51.4	51.0	2009-10-19
Abdullah Al-Zahrani	M	34	OS	2009-02-23	57.6	58.3	59.2	60.8	54.1	68.1	72.4	73.8	72.3	67.3	61.9	59.8	56.5	55.7	55.4	56.1	50.2	66.7	69.4	72.0	71.4	67.3	62.2	58.9	2009-02-22
Fahed Al-Zahrani	M	26	OD	2009-02-22	43.3	40.7	39.6	42.0	44.5	48.6	51.0	51.8	50.7	48.6	46.2	44.5	46.0	43.3	42.2	43.0	46.2	50.7	54.5	56.8	56.7	53.9	51.0	49.1	2010-08-14
Salah Mubarak Sa'eed	M	33	OD	2009-01-03	38.2	36.7	37.9	41.0	45.4	50.4	54.6	57.3	56.2	53.2	50.2	44.3	44.0	42.3	42.3	50.1	61.3	62.5	61.1	60.1	55.8	52.5	50.4	50.4	2010-08-01
Nawaaf Al-Rashidi	M	23	OD	2008-06-01	36.6	35.7	37.2	41.4	45.1	48.5	50.2	51.4	51.1	49.6	45.2	39.3	47.5	46.1	47.1	49.9	54.0	57.5	59.8	61.2	60.3	57.9	56.3	54.8	27-02-2011
Budour Al-Omraan	F	33	OS	2009-03-03	36.6	37.2	42.0	46.3	48.9	49.2	49.3	48.2	45.7	42.2	38.4	35.4	37.9	40.0	44.7	49.5	52.5	54.6	55.9	56.3	56.3	54.9	52.1	46.7	
Dina Sharayha	F	28	OS	2009-05-04	36.3	37.6	41.6	46.6	51.3	54.8	57.4	59.1	58.0	54.0	49.0	44.1	46.3	49.3	52.0	53.7	55.3	57.0	58.9	60.8	59.4	64.4	50.0	46.5	2010-03-21
Rasha Abu Al-Khair	F	24	OD	2009-04-13	44.2	43.0	40.9	40.5	41.2	43.7	46.2	46.9	46.1	45.1	44.2	44.5	47.0	45.3	43.7	42.7	44.3	47.4	50.3	52.1	52.4	51.1	49.6	48.5	2010-01-23
Abdulaziz Al-Munath	M	29	OD	2009-04-20	40.5	39.4	39.3	41.1	43.8	47.5	49.9	50.4	48.9	46.7	44.9	43.5	43.8	42.6	43.2	44.1	47.0	51.4	53.8	53.4	51.8	49.9	48.2	47.2	2010-07-08
Munira Bo Qaba'a	F	35	OD	2009-04-21	42.1	40.5	40.3	41.7	44.2	48.7	53.1	55.9	57.3	56.5	54.2	51.5	46.0	43.8	43.8	45.0	48.0	51.5	55.9	59.8	60.0	58.2	57.0	54.6	2009-10-11
Joman Nuaimaat	F	27	OD	29-04-2009	41.4	39.5	39.8	42.4	46.3	50.3	52.8	53.6	52.0	50.0	49.0	47.6	42.9	40.6	40.4	43.3	47.5	51.9	54.7	55.3	53.9	51.6	50.2	48.8	2011-07-30
Rana Sabri Al-Lami	F	33	OD	2009-10-05	39.6	38.2	39.2	42.4	45.9	49.1	52.4	53.6	52.0	50.0	47.7	45.3	42.3	41.3	40.9	44.2	48.8	52.5	55.4	56.0	54.5	52.9	51.0	48.5	2010-04-03
Amaar Al-Akhras	M	31	OD	2009-05-16	36.9	36.3	37.1	40.3	43.7	47.1	49.9	51.2	50.5	48.0	44.8	41.5	38.7	37.5	37.8	40.7	44.4	47.7	50.3	51.5	50.9	48.1	45.2	42.6	2011-03-03
Fatima Al-Saat	F	33	OD	2009-05-18	42.9	42	41.7	43.4	45.9	48.6	50.6	50.6	48.6	46.3	44.5	43.5	43.0	42.5	42.8	44.0	45.4	48.5	48.8	44.0	44.5	43.3	42.8	43.1	2011-10-07
Rasha Al-Haj Al-Amin	F	28	OD	2009-05-19	48.1	48.6	51.4	56.4	60.9	66.5	67.8	75.2	73.0	65.0	61.8	55.7	51.7	51.7	53.2	59.3	63.6	67.6	71.8	75.0	74.9	66.8	61.9	58.1	2011-12-03
Obaid Al-Qatabi	M	32	OD	2009-03-06	41.0	40.3	40.7	43.5	45.7	48.4	51.2	52.2	49.3	46.5	44.8	43.2	39.6	38.6	33.0	42.2	46.2	51.1	54.6	56.2	54.4	49.5	46.6	44.4	2009-12-28
Asaaf Al-Awaji	M	30	OD	2009-06-06	43.2	42.9	42.0	41.0	43.9	41.1	41.7	42.0	41.8	41.8	41.6	42.0	42.6	42.0	41.2	41.1	40.8	41.3	41.9	42.3	42.0	41.8	41.8	41.9	2010-12-12
Natel Al-Salamin	M	25	OD	2009-04-07	58.8	57.6	56.1	56.8	57.6	60.4	63.1	63.6	62.7	60.5	58.8	58.2	52.8	52.7	55.0	58.6	65.2	73.7	80.2	82.1	77.7	70.5	63.3	57.1	2010-07-10
Mohammed Amin Yaghi	M	21	OD	2009-07-07	59.5	57.9	56.4	56.9	60.0	62.9	65.2	64.0	62.4	59.2	59.1	59.0	58.1	56.4	55.7	56.6	60.7	64.7	66.9	66.7	64.8	61.3	60.8	59.4	2020-01-08
	OS				53.1	55.2	58.4	57.9	59.0	60.3	62.0	64.3	63.9	60.7	56.4	52.2	54.4	55.6	55.7	55.5	55.7	57.6	60.2	54.0	66.5	65.4	62.8	57.4	

Mohammed Al-Nuaimaat	M	20	OS	2009-11-07	40.0	43.0	45.5	46.0	48.9	50.9	51.9	52.8	52.0	49.4	45.7	42.1	42.2	45.1	47.6	48.4	50.3	52.6	54.6	56.0	54.9	51.8	47.6	44.0	2010-07-06
Aa'esha Al-Huwaiti	F	24	OD	2009-11-07	39.7	38.6	38.2	38.1	38.1	40.4	42.9	45.8	48.2	49.7	49.1	46.6	42.0	39.2	37.8	37.6	39.5	41.0	43.7	46.2	48.3	49.6	50.2	49.1	2011-06-22
			OS		56.6	58.4	55.3	50.6	45.6	43.0	42.5	42.2	44.3	45.9	46.4	48.9	59.3	60.7	59.5	56.8	52.7	49.6	48.1	45.9	46.9	48.6	47.8	50.2	
Khalid Al-Hwaaiti	M	16	OD	2009-12-07	38.6	39.1	39.1	40.9	44.7	49.4	52.8	53.8	52.8	49.7	46.7	44.7	40.2	42.1	43.3	46.2	50.9	54.0	57.1	57.0	54.6	51.5	47.6	45.6	2010-03-10
Mane'a Al-Onaizi	M	23	OD	2009-12-07	43.5	42.1	41.7	42.6	46.0	50.9	52.5	51.8	50.3	49.4	47.4	47.2	43.3	42.6	42.2	43.5	48.3	53.7	52.2	48.4	54.8	54.8	51.7	50.2	2011-12-11
	OS			47.2	49.5	50.7	49.8	50.6	52.8	54.5	54.7	54.6	52.9	49.9	47.9	50.6	51.7	52.9	53.3	52.6	48.1	39.9	37.8	41.0	43.1	47.7	48.8		
Mohammed Shooman	M	40	OD	2009-07-13	44.9	42.6	40.9	41.8	44.2	48.1	52.0	54.1	56.2	57.1	54.8	51.7	44.9	42.1	41.7	43.0	47.8	51.8	55.2	58.3	60.7	61.1	57.7	54.4	2010-03-22
	OS			42.4	45.6	50.2	54.7	58.4	60.9	59.8	56.8	52.3	47.0	42.8	40.9	42.0	45.9	50.3	60.2	61.4	61.0	58.6	53.9	50.2	46.4	43.7			
Abdullah Al-Rashidi	M	22	OD	2009-07-14	41.6	41.0	40.4	40.7	43.6	46.2	48.8	50.2	50.1	49.9	49.4	48.8	50.3	46.6	44.3	46.8	50.0	56.0	59.8	60.3	60.7	58.4	56.5	55.9	2010-02-11
	OS			43.2	46.3	48.8	49.6	50.6	52.0	53.8	55.2	53.9	51.6	47.4	42.6	45.3	49.2	52.7	53.5	54.8	56.6	58.9	60.6	60.0	56.7	51.1	46.4		
Thafer Al-Rashidi	M	22	OD	2009-07-15	54.7	55.1	54.6	55.7	57.7	59.6	59.9	59.4	57.6	55.5	63.9	53.2	56.2	55.7	54.2	56.6	57.9	58.4	60.6	61.5	61.1	59.2	55.8	54.9	2011-05-11
	OS			45.5	46.8	47.3	46.4	45.3	44.6	45.0	45.9	45.5	45.1	45.0	44.4	53.3	52.2	50.9	50.1	50.1	51.6	54.6	57.3	57.7	58.3	56.0	53.9		
Aala'a Omer Al-Marimi	F	17	OD	2010-10-01	41.6	39.6	38.7	40.3	43.5	47.5	51.1	53.4	53.3	51.4	48.2	46.9	44.4	42.6	41.4	41.5	43.4	47.7	50.8	52.7	53.2	52.4	50.2	48.8	2010-07-17
	OS			39.8	40.8	44.0	45.4	46.8	48.1	48.9	49.5	48.5	46.0	43.3	40.3	41.7	44.9	47.6	50.3	52.1	53.9	54.6	54.1	53.6	51.1	47.6	43.7		
Abdullah Al-Onaizi	M	43	OD	2009-07-21	49.3	50.8	53.5	54.8	56.3	58.0	59.5	59.2	58.8	55.5	51.2	48.5	52.7	54.5	56.5	53.8	54.2	54.2	54.2	54.2	51.0	49.2	48.1		
	OS			42.8	43.1	44.1	45.4	47.1	48.4	49.3	49.7	49.7	48.9	47.4	45.8	43.0	43.4	44.1	45.4	47.1	48.5	49.4	49.8	49.6	48.5	47.2	45.7		
Sa'eed Al-Aameri	M	31	OD	2009-07-26	39.7	38.3	38.6	40.4	43.2	45.7	47.7	48.5	48.2	46.5	44.7	43.1	39.1	38.2	38.8	42.3	47.5	52.6	55.7	56.7	56.5	55.3	54.1	51.9	2010-02-03
	OS			39.8	40.8	44.0	45.4	46.8	48.1	48.9	49.5	48.5	46.0	43.3	40.3	41.7	44.9	47.6	50.3	52.1	53.9	54.6	54.1	53.6	51.1	47.6	43.7		
Nihal Al-Otaibi	F	24	OD	2009-07-29	40.9	40.4	40.3	41.5	44.5	47.3	50.0	51.8	51.3	49.3	46.9	44.6	41.2	41.1	42.0	43.5	46.3	49.4	51.4	52.5	52.5	50.4	47.8	45.3	2010-04-17
	OS			44.5	47.9	52.6	56.1	57.8	55.5	55.1	48.5	40.7	44.0	44.0	44.4	44.7	46.1	45.5	44.9	45.6	46.8	47.6	47.5	46.5	45.4	44.2	44.1	44.6	2010-04-17
Monira Al-Otaibi	F	36	OD	2009-07-29	45.1	44.8	44.4	44.4	45.1	45.9	46.2	46.1	45.6	44.9	44.4	44.4	44.7	46.1	45.5	44.9	45.6	46.8	47.6	47.5	46.5	45.4	44.2	44.1	44.6
	OS			44.9	45.6	45.4	44.6	44.3	45.1	45.9	46.4	46.6	45.9	44.8	43.9	46.6	46.3	45.7	45.0	44.4	44.9	45.5	46.4	46.9	46.6	45.7	45.2		
Mohammed Haimoor	M	22	OD	2009-07-28	44.0	42.6	42.8	43.9	45.2	48.2	51.5	54.8	56.6	55.9	53.4	50.5	45.6	43.6	43.3	44.2	46.7	49.7	53.1	55.6	56.8	56.3	54.4	52.3	2009-07-28
	OS			42.6	43.6	45.4	48.1	51.5	54.7	57.6	58.1	55.6	51.7	47.8	44.7	42.5	43.5	45.7	48.5	52.2	55.7	58.1	58.7	57.0	52.9	48.6	45.4		
Latifa Al-Shemmeri	F	22	OD	2009-02-08	47.6	43.7	39.6	37.9	39.5	43.0	46.3	48.8	49.9	49.8	50.4	51.5	49.0	46.1	44.3	45.2	48.0	50.9	53.1	54.5	53.3	52.3	52.1	52.1	2011-07-14
	OS			41.0	42.1	42.7	43.1	44.8	47.0	49.0	49.2	49.6	45.1	41.4	39.0	45.0	46.2	48.1	48.2	48.9	48.9	50.9	52.9	54.7	53.4	50.0	45.7	43.3	
Mohammed Al-Falasi	M	34	OD	2009-03-08	41.8	41.9	41.7	41.1	41.0	41.1	41.4	41.8	42.0	41.8	41.5	41.7	42.0	42.1	41.0	40.9	41.2	41.7	41.8	41.9	41.7	41.5	41.6	2011-11-01	
	OS			42.7	42.7	41.5	40.6	40.5	42.0	43.2	39.7	36.5	37.1	39.1	38.7	43.3	42.7	43.1	44.0	42.6	42.0	44.5	44.7	41.2	39.3	38.8	39.9		
Nader Al-Balawi	M	22	OD	2009-08-19	58.6	56.8	55.2	53.6	54.9	57.6	60.3	61.6	61.4	59.8	58.5	57.8	64.8	61.2	60.8	58.9	59.3	62.1	57.4	49.5	38.7	63.2	65.9	64.4	2011-09-29
	OS			54.2	51.3	46.5	44.9	46.3	46.9	46.0	47.5	49.5	54.2	58.2	61.6	53.3	57.3	54.5	49.7	49.8	50.2	47.6	45.0	45.0	52.9	56.5	60.5		
Abdulrahman Al-Nawafia	M	24	OD	2009-08-19	39.9	37.4	39.6	41.3	43.8	48.2	52.6	55.6	57.4	58.1	56.4	51.4	37.9	37.4	38.5	43.3	48.4	52.3	54.9	57.3	60.9	61.6	56.9	52.2	2010-10-05
	OS			74.7	75.6	60.2	61.9	61.9	63.3	63.0	65.2	62.1	59.4	60.2	56.2	62.6	58.3	71.3	65.8	58.9	58.3	55.9	60.0	60.6	60.8	60.1	59.2		
Naif Sa'eed Al-Hajni	M	28	OD	2009-01-09	39.9	38.6	39.1	41.3	44.4	48.7	52.6	54.6	53.7	51.2	48.9	46.2	39.4	37.3	38.3	41.7	46.2	52.4	56.3	58.7	58.5	54.1	50.8	47.4	2011-03-23
	OS			43.8	42.3	41.7	42.0	42.3	40.6	43.6	49.5	52.0	53.2	53.1	51.1	58.9	56.3	52.6	48.5	45.1	40.4	40.9	47.3	52.0	55.3	55.5	56.3		
Emad Taha Al-Oshi	M	17	OD	2009-09-15	34.2	34.4	35.6	39.5	45.4	50.7	55.2	56.4	53.7	49.6	45.1	41.0	39.7	39.5	41.3	44.7	50.0	54.7	56.6	57.6	55.5	50.9	46.8	43.7	2010-05-12
	OS			38.9	43.1	47.6	52.3	56.5	60.0	63.7	64.0	60.4	60.4	53.3	44.0	43.3	44.4	45.6	48.9	53.3	57.3	62.3	62.7	60.3	56.1	51.1	47.5		
Sa'eed Bin Ayaad	M	42	OD	2009-09-29	44.8	55.0	54.4	57.2	58.1	50.9	41.7	43.5	45.2	44.7	47.0	45.7	58.5	61.3	61.1	57.1	57.6	59.1	56.3	51.1	46.8	42.9	44.9	48.8	2011-03-31
	OS			57.2	53.9	52.4	48.5	42.5	39.4	42.7	48.0	46.7	48.0	48.6	45.8	60.0	59.2	56.4	52.8	46.7	45.1	51.2	58.9	60.0	55.9	55.0	52.8		
Alyaa'a Al-Zahrani	F	24	OD	2009-06-10	37.8	40.9	49.3	40.0	57.2	69.4	51.8	60.4	64.8	57.1	47.8	50.0	49.4	45.8	42.7	43.2	46.7	51.6	55.3	57.8	59.1	58.1	56.4	55.5	2010-04-06
	OS			41.9	46.3	52.1	62.1	59.3	50.8	48.3	53.4	54.3	47.4	39.4	35.6	39.5	43.2	47.9	51.7	54.6	57.2	59.2	59.8	57.5	53.5	48.0	43.7		
Joma'a Al-Shamsi	M	34	OD	2009-10-20	39.7	38.3	37.5	35.7	34.8	34.3	35.6	37.3	39.3	41.0	42.0	41.9	41.5	39.1	37.0	36.1	33.9	33.8	34.8	36.4	38.5	40.1	41.1	41.2	2010-07-13
	OS			37.5	37.5	40.5	41.7	41.8	40.7	39.0	36.5	34.4	34.3	34.1	35.6	38.9	40.5	40.6	41.2	41.7	41.0	39.0	36.2	34.7	33.5	32.6	33.5		
Madeeha Taimani	F	28	OS	2009-10-24	45.6	49.3	54.4	56.8	58.6	61.1	62.9	64.0	61.8	55.1	48.0	43.8	45.9	49.2	52.5	55.5	57.4	59.8	62.2	62.8	61.0	57.2	50.7	46.2	2010-07-25
Mohammed S Al-Ghamdi	M	36	OS	2009-01-12	50.6	54.2	55.5	56.3	56.9	57.3	57.5	57.2	55.5	52.8	49.7	47.0	51.1	53.7	55.6	55.6	56.0	56.6	57.3	57.8	56.2	53.5	50.9	47.9	2011-06-26
Ayman Al-Nator	M	27	OD	2009-09-12	38.1	37.4	38.2	40.4	42.9	46.5	49.1	49.3	47.6	45.0	44.3	42.4	43.2	43.7	45.9	50.3	55.4	60.7	63.6	64.7	61.4	58.0	54.0	50.3	2011-10-04
	OS			37.3	39.1	40.7	42.8	45.1	47.1	48.7	49.3	48.2	45.1	41.5	38.4	39.8	43.4	45.8	40.2	51.3	55.7	59.3	61.2	59.5	53.8	47.6	41.8		
Misfer Al-Qurani	M	28	OD	2009-12-13	30.9	40.3	42.2	45.1	48.0	43.7	50.9	51.0	50.2	48.1	45.5	43.2	43.0	42.5	42.2	43.1	45.6	48.0	49.3	50.0	49.6	49.0	47.8	46.4	2011-04-12

Abd Al-Mu'ati Al-Rabi'ae	M	24	OD	2009-12-14	40.0	40.7	40.4	40.6	41.4	42.2	43.2	43.9	44.6	44.1	43.2	42.3	41.2	40.9	40.7	41.6	42.8	43.9	45.3	45.9	45.5	44.5	43.7	43.0	2010-06-27
Mohammed Saleh Hamad	M	33	OD	2010-09-01	54.9	53.9	53.3	56.9	61.0	67.5	71.0	71.3	68.8	65.4	61.5	59.1	57.6	56.0	57.3	62.2	66.7	69.9	71.0	70.6	68.2	65.3	63.8	61.6	2011-12-31
Yousri Hodod	F	19	OD	2010-10-01	51.9	49.1	46.3	46.5	48.1	52.7	57.1	59.2	58.6	57.0	55.1	54.9	59.4	56.7	55.6	55.9	58.6	63.1	65.7	65.3	63.4	60.6	58.0	57.9	2010-07-17
Mohammed Al-Khalidi	M	26	OD	2010-01-27	38.4	36.1	35.7	39.4	42.7	46.9	51.9	55.2	56.2	54.9	51.3	47.6	39.8	38.2	39.5	41.7	44.0	48.8	52.8	55.9	57.6	56.3	53.2	49.2	2011-04-26
Tahani Al-Shemmeri	F	21	OD	2010-02-24	44.1	41.5	42.1	44.7	49.6	54.6	57.3	58.6	56.8	53.7	51.6	50.0	46.0	44.0	43.5	45.5	49.7	54.6	57.5	58.3	56.9	53.8	51.7	50.2	2011-06-25
Bilal Al-Shayeb	M	19	OD	2010-09-02	54.7	53.5	59.3	55.1	52.4	55.5	56.0	56.0	53.4	50.1	54.3	60.8	59.5	57.9	58.7	56.5	56.4	58.1	58.2	57.3	55.5	55.5	55.1	57.0	2010-10-17
Muna Al-Raqeeb	F	45	OD	2010-03-13	39.2	39.9	41.9	44.1	46.0	48.0	49.7	48.9	46.5	44.4	43.1	41.7	39.9	40.5	42.4	44.7	46.5	47.9	49.2	48.4	46.0	44.2	43.0	41.9	2011-09-17
Salem Al-Shahrani	M	34	OD	2010-04-13	39.8	39.1	39.5	40.5	42.0	43.6	45.1	44.8	43.4	42.2	41.0	40.9	41.0	40.0	40.4	42.4	44.5	47.6	50.1	50.2	48.6	46.8	45.4	44.4	2011-07-25
Salama Al-Huwaiti	M	32	OD	2010-05-07	41.1	40.9	41.6	42.1	43.3	43.0	40.8	39.5	41.9	44.5	44.3	44.0	39.9	40.6	41.9	43.5	44.9	44.2	43.3	43.6	45.0	45.8	45.1	43.8	2011-10-09
Muhana Al-Subai'ee	M	26	OS	2010-10-07	40.4	46.7	51.0	69.3	55.5	59.5	63.5	64.6	60.1	52.1	43.6	35.6	44.5	48.9	51.0	51.3	52.6	56.2	60.1	60.9	58.9	53.6	46.5	40.5	2011-04-04
Khalid Bandar Duwaish	M	37	OD	2010-07-13	46.3	44.6	43.0	42.9	44.0	46.1	48.5	50.5	50.9	50.4	50.4	49.9	44.6	43.5	43.5	45.4	47.9	50.9	53.9	54.6	52.8	50.8	49.5	48.7	2011-02-07
Ghada Al-Tumi	F	14	OD	2010-07-19	43.4	42.3	41.4	40.9	40.3	41.9	42.2	42.2	42.0	41.7	41.8	41.9	42.8	42.2	42.4	41.9	41.1	42.1	42.8	42.8	42.9	42.1	42.2	42.3	2011-01-27
Abd Al-Sataar Al-Tumi	M	17	OD	2010-07-19	44.4	43.7	42.0	41.6	41.7	42.8	41.3	40.7	42.6	43.2	41.8	41.9	44.3	43.5	42.0	41.6	41.9	42.4	42.2	42.1	42.7	41.9	41.0	41.4	2011-01-26
Aa'eshah al-Hatmi	F	29	OD	2010-01-08	37.5	34.5	36.1	39.7	47.1	56.0	61.6	65.1	66.4	62.0	54.5	48.1	39.2	39.8	43.2	47.6	53.1	58.5	62.8	65.7	64.3	60.1	63.1	47.3	2011-02-15
Basem Handila	M	26	OD	2010-09-20	40.4	40.6	41.8	44.9	48.2	52.7	54.4	58.2	63.9	61.6	54.4	49.9	40.2	41.1	44.1	48.6	52.7	56.0	58.9	60.4	61.2	57.9	63.8	49.7	2011-12-24
Ahmed Meqbaas Al-Zahrani	M	26	OS	2010-11-21	40.8	41.7	42.6	43.6	45.7	48.9	52.4	54.4	53.8	50.3	44.8	41.6	41.8	42.6	43.9	43.8	44.7	48.0	52.0	55.6	55.1	51.6	45.8	52.6	2011-05-25
Faisal Meqbaas Al-Zahrani	M	20	OD	2010-11-21	42.5	41.7	40.0	38.9	39.8	42.2	44.5	46.4	47.1	46.4	44.8	43.5	41.9	41.4	40.4	39.6	40.9	43.8	45.0	46.0	47.3	46.5	44.2	42.9	2011-05-25
			OS		40.8	40.7	41.0	41.3	43.1	45.2	46.9	47.6	46.3	44.1	41.4	39.9	41.1	41.6	41.5	41.7	43.7	46.3	48.5	49.7	48.4	45.5	42.4	40.2	

F: Female; M: Male.

PERK Study Group^[12], which states that the cornea is capable of regenerating cells for an indefinite period because of its ectodermal origin^[18,19]. The natural healing process of the cornea should therefore be able to improve the keratoconic state by addressing any irregularity or steepness of the cornea and myopia.

Immediately after this procedure the cone of the cornea relaxes and visual acuity improves. We have found that the greater the surface tension we can keep on the cornea during the procedure, the easier the procedure is to perform. During the healing process, the patient experiences foggy vision, which develops because of the laying down of keratocytes and edema of the cells^[20].

Absence of edema becomes obvious when the whitish coloration begins to disappear at the areas of incision, visual acuity improves, and the patient reports fewer shadows in vision. Funderburgh's group postulated that multipotent cells are present in the corneal stroma^[11,21], the cornea responds to acute wounds by activating nearby keratocytes, which assume a fibroblastic phenotype and secrete a non-transparent extracellular matrix, and since this regeneration occurs with no disruption of corneal function, it seems likely that the replacement cells arise from progenitor cells. The disappearance of the whitish color also may indicate that CTGF7 (a connective tissue growth factor) is present, creating the transparency necessary for vision^[22].

There also tends to be an increase in corneal dioptric power and the thickness of the cornea in different areas, which causes increased myopia. These changes have been noted in all incisional areas around the circumference of the cornea except the upper nasal portion. A habit that is formed during the progression of keratoconus is squinting

Table 2 Cornea back pre and post operation

Patient name	Gender	Age (yr)	Eye	Cornea back										Year
				Pre operation					Post operation					
				K1 (D)	K2 (D)	Km (D)	Astig (D)	Rmin (mm)	K1 (D)	K2 (D)	Km (D)	Astig (D)	Rmin (mm)	
Faisal Alzahani	M	21	OD	-6.7	-7.9	-7.2	1.2	4.51	-6.7	-7.9	-7.3	1.2	4.25	2010-11-21
Faisal Alzahani	M	21	OS	-6.5	-7.8	-7.1	1.2	4.44	-6.5	-7.8	-7.1	1.3	4.47	
Ahmad A/zahrani	M	23	OD	-5.4	-7.0	-6.1	1.5	5.27	-5.4	-6.8	-6.0	1.4	5.31	2010-11-21
Basem Hendeleh	M	22	OD	-11.0	-9.1	-10.0	1.8	2.64	-10.4	-11.0	-10.7	0.6	2.31	2010-09-20
Basem Hendeleh	M	22	OS	-6.5	-7.1	-6.8	0.6	5.42	-6.6	-7.0	-6.8	0.5	5.36	
Aysha Alhetmi	F	20	OD	-8.3	-9.0	-8.6	0.7	3.16	-8.2	-9.7	-8.9	1.5	3.21	2010-01-08
Aysha Alhetmi	F	20	OS	-9.9	-6.6	-7.9	3.3	3.15	-8.8	-9.5	-9.1	0.7	3.22	
Abdalsattar Tomi	M	17	OD	-5.9	-6.6	-6.2	0.7	5.76	-6.0	-6.6	-6.3	0.6	5.74	2010-07-19
Abdalsattar Tomi	M	17	OS	-6.0	-6.6	-6.3	0.6	5.89	-6.1	-6.5	-6.3	0.4	5.77	
Gada Omran	F	14	OD	-6.0	-6.6	-6.3	0.6	5.86	-5.9	-6.6	-6.2	0.7	5.91	2010-07-19
Khaled Dwesh	M	37	OD	-7.3	-7.3	-7.3	0.0	4.90	-7.5	-7.4	-7.4	0.1	5.06	2010-07-13
Khaled Dwesh	M	37	OS	-7.7	-6.9	-7.3	0.8	4.91	-7.6	-6.9	-7.2	0.7	4.91	
Mhana Sbea	M	26	OS	-8.1	-11.1	-8.4	3.0	2.70	-7.6	-10.6	-8.8	3.0	3.01	2010-10-07
Salameh Alhweti	M	32	OD	-6.4	-5.7	-6.0	0.7	6.19	-6.5	-5.6	-6.0	0.9	6.07	2010-05-07
Salameh Alhweti	M	32	OS	-6.9	-5.4	-6.1	1.5	5.54	-7.5	-6.3	-6.9	1.1	4.95	
Mona Alhlali	F	45	OD	-6.5	-5.4	-5.9	1.1	5.28	-6.5	-5.2	-5.8	1.3	5.21	2010-03-13
Thani Alshemari	M	21	OD	-8.1	-9.3	-8.7	1.2	3.48	-8.3	0.5	-8.9	1.3	3.62	2010-02-24
Thani Alshemari	M	21	OS	-9.8	-10.5	-10.1	0.8	3.14	-9.8	-10.7	-10.2	0.9	3.27	
KawtharAgzoroq	F	26	OD	-10.8	-12.7	-11.7	1.9	2.00	-10.7	-12.3	-11.4	1.6	2.62	2010-01-30
Mohammad Al Kaldey	M	26	OD	-6.5	-7.9	-7.1	1.5	4.00	-7.6	-8.1	-7.9	0.5	3.57	2010-01-27
Yousra Hadood	F	19	OD	-9.4	-10.6	-8.9	1.2	3.55	-8.3	-10.1	-9.1	1.8	3.58	2010-10-01
Yousra Hadood	F	19	OS	-9.5	-10.7	-10.1	1.3	3.29	-8.4	-10.3	-9.3	1.8	3.41	
Mohammad Hamad	M	33	OD	-11.2	-12.7	-11.9	1.5	2.59	-12.2	-11.2	-11.6	1.0	2.63	2010-09-01
Mohammad Hamad	M	33	OS	-8.7	-7.9	-8.3	0.8	3.98	-9.4	-9.7	-9.6	0.3	3.49	
Abdalmo'ti Alrabieei	M	30	OD	-6.5	-6.9	-6.7	0.4	5.30	-6.3	-7.1	-6.7	0.8	5.09	2009-12-14
Abdalmo'ti Alrabieei	M	30	OS	-7.0	-7.7	-7.3	0.7	4.67	-7.2	-8.1	-7.6	0.9	4.19	
Mesfer Alqarni	M	27	OD	-7.2	-7.8	-7.5	0.6	4.37	-7.4	-7.7	-7.5	0.4	4.18	2009-12-13
Mesfer Alqarni	M	27	OS	-7.1	-7.4	-7.3	0.3	4.66	-7.2	-7.4	-7.3	0.1	4.34	
Ayman Alnatoor	M	27	OD	-6.3	-6.6	-6.5	0.3	5.27	-6.9	-7.8	-7.3	0.9	4.55	2009-09-12
Ayman Alnatoor	M	27	OS	-6.3	-6.5	-6.4	0.2	5.15	-6.7	-7.2	-7.0	0.5	4.58	
Mohamad Alghamdi	M	36	OS	-9.6	-11.3	-10.4	1.6	2.83	-10.6	-11.3	-10.9	0.8	2.88	2009-01-12
Madeha Altemani	F	27	OS	-10.8	-12.0	-11.4	1.2	2.59	-10.5	-11.4	-11.0	0.9	2.85	2009-10-24
Jom'a Shamesi	M	34	OD	-6.0	-5.7	-5.8	0.3	6.51	-5.7	-5.9	-5.8	0.2	6.47	2009-10-20
Jom'a Shamesi	M	34	OS	-5.6	-6.0	-5.8	0.4	6.41	-5.6	-5.7	-5.6	0.1	6.25	
Alia Al Zahrani	F	24	OD	-8.5	-9.5	-8.9	1.1	2.96	-9.4	-10.6	-10.0	1.2	2.94	2009-06-10
Alia Al Zahrani	F	24	OS	-7.6	-8.9	-8.2	1.3	3.23	-8.9	-9.0	-9.0	0.2	3.05	
Saeed Ben Ayyad	M	43	OD	-5.8	-7.5	-6.5	1.7	4.35	-5.7	-8.6	-6.8	2.9	4.26	2009-09-29
Saeed Ben Ayyad	M	43	OS	-5.2	-8.1	-6.3	2.9	4.13	-5.4	-8.2	-6.5	2.9	4.70	
Emad Asha	M	26	OD	-6.8	-7.2	-7.0	0.3	3.96	-7.4	-8.6	-7.9	1.2	3.72	2009-09-15
Emad Asha	M	26	OS	-9.5	-10.4	-9.9	0.9	2.88	-8.7	-9.7	-9.2	0.9	3.17	
Mahmood I'lian	M	32	OD	-7.8	-8.2	-8.0	0.4	4.21	-8.4	-9.1	-8.7	0.7	3.58	2009-05-09
Naief Aljohani	M	28	OD	-7.6	-6.4	-6.9	1.2	4.69	-7.9	-6.9	-7.3	1.0	4.27	2009-01-09
Naief Aljohani	M	28	OS	-6.8	-7.2	-7.0	0.5	5.41	-7.6	-7.0	-7.3	0.6	5.05	
Nader Alblwi	M	20	OD	-9.5	-10.9	-10.1	1.5	3.13	-10.4	-11.2	-10.8	0.7	3.00	2009-08-19
Nader Alblwi	M	20	OS	-6.1	-7.4	-6.7	1.3	4.89	-6.2	-8.5	-7.2	2.4	4.03	
Abdelrhman Alnwafla	M	24	OD	-8.0	-7.9	-8.0	0.1	3.39	-8.0	-8.4	-8.2	0.4	2.96	2009-08-19
Abdelrhman Alnwafla	M	24	OS	-10.2	-10.5	-10.4	0.3	3.25	-10.6	-9.5	-10.0	1.1	3.13	
Mohamad Alflassy	M	34	OS	-4.7	-6.5	-5.5	1.7	5.96	-5.8	-6.5	-6.2	0.7	5.50	2009-03-08
Latifa Alshamari	F	22	OD	-7.2	-9.2	-8.1	2.0	3.71	-8.4	-9.6	-8.9	1.3	3.59	2009-02-08
Latifa Alshamari	F	22	OS	-6.4	-8.2	-7.2	1.8	4.17	-7.6	-8.7	-8.1	1.1	3.94	
Mohamad Haimour	M	22	OD	-8.0	-8.3	-8.1	0.3	3.80	-8.5	-9.6	-9.0	1.0	3.30	2009-01-08
Mohamad Haimour	M	22	OS	-7.9	-8.3	-8.1	0.4	3.78	-8.1	-8.5	-8.3	0.3	3.79	
Monira Etebi	F	36	OD	-6.1	-6.6	-6.4	0.5	5.84	-6.2	-6.5	-6.3	0.3	5.91	2009-07-29
Monira Etebi	F	36	OS	-6.1	-6.7	-6.4	0.6	5.85	-6.1	-6.5	-6.3	0.3	5.98	
Nehal Etebi	F	25	OD	-7.4	-8.1	-7.7	0.6	4.48	-7.3	-8.6	-7.9	1.3	3.66	2009-07-29
Nehal Etebi	F	25	OS	-10.8	-13.1	-11.8	2.4	2.22	-11.6	-12.7	-12.1	1.1	2.46	
Sa'eed A/a'amri	M	31	OD	-7.0	-6.3	-6.6	0.6	4.88	-7.3	-9.0	-8.0	1.7	3.73	2009-07-26
Sa'eed A/a'amri	M	31	OS	-7.5	-6.4	-6.9	1.1	4.69	-8.4	-7.4	-7.9	1.0	4.03	
Nooralhoda Almrzawy	F	31	OD	-6.2	-6.5	-6.3	0.3	5.78	-6.2	-7.1	-6.6	0.9	5.11	2009-07-25
Nooralhoda Almrzawy	F	31	OS	-6.3	-7.0	-6.6	0.6	5.19	-6.6	-7.6	-7.1	1.0	4.64	
Abdolah Aleenazy	M	40	OD	-8.2	-7.4	-7.8	0.8	4.52	-8.1	-9.0	-8.5	0.9	3.86	2009-07-21
Abdolah Aleenazy	M	40	OS	7.3	-6.7	-7.0	0.6	5.04	-7.1	-6.6	-6.8	0.5	5.08	
Alaa Almaremi	F	17	OD	-7.6	-9.3	-8.4	1.6	3.65	-7.7	-9.2	-8.4	1.5	3.77	2009-07-21
Alaa Almaremi	F	17	OS	-10.4	-11.7	-11.0	1.3	2.63	-9.8	-10.5	-10.2	0.7	2.73	

Quawasmi SA. Bader Procedure

Dafear Alrashede	M	22	OD	-7.3	-8.1	-7.7	0.7	3.59	-7.6	-8.4	-8.0	0.8	3.72	2009-07-15
Dafear Alrashede	M	22	OS	-6.6	-6.6	-6.6	0.0	5.17	-7.5	-7.1	-7.3	0.4	4.75	
Abdallah alrasgede	M	22	OD	-6.8	-8.4	-7.5	1.6	4.04	-8.5	-9.6	-9.0	1.0	3.62	2009-07-14
Abdallah alrasgede	M	22	OS	-7.5	-9.5	-8.4	2.0	3.53	-8.9	-10.0	-9.4	1.0	3.28	
Mohammad Shoman	M	40	OD	-8.9	-9.2	-9.1	0.2	3.19	-9.8	-10.2	-10.0	0.4	2.68	2009-07-13
Mohammad Shoman	M	40	OS	-8.6	-8.9	-8.8	0.3	3.09	-8.2	-10.4	-9.2	2.2	2.70	
Manea Alanezi	M	23	OD	-7.3	-8.9	-8.1	1.6	3.82	-8.4	-9.4	-8.9	1.1	3.35	2009-12-07
Manea Alanezi	M	23	OS	-7.5	-8.4	-7.9	0.9	4.50	-6.6	-8.0	-7.2	1.4	4.32	
Khaled Alhwati	M	16	OD	-7.4	-8.6	-8.0	1.2	3.77	-8.1	-8.8	-8.5	0.7	3.90	2009-12-07
Khaled Alhwati	M	16	OS	-6.0	-6.4	-6.2	0.5	5.96	-5.9	-6.4	-6.2	0.5	5.79	
Aysheh Alhweti	F	24	OD	-6.8	-7.4	-7.1	0.7	4.59	-6.6	-7.7	-7.1	1.0	4.56	2009-11-07
Aysheh Alhweti	F	24	OS	-6.2	-7.4	-6.7	1.2	4.29	-6.6	-7.4	-6.9	0.8	4.53	
Mohamad Alna'emat	M	21	OD	-6.9	-8.7	-7.7	1.8	3.85	-6.9	-8.7	-7.7	1.8	3.90	2009-11-07
Mohamad Alna'emat	M	21	OS	-8.2	-9.8	-8.9	1.6	3.05	-8.5	-10.0	-9.2	1.5	3.28	
Mohamad Yagi	M	21	OD	-8.6	-10.3	-9.4	1.7	3.32	-9.5	-9.4	-9.4	0.1	3.06	2009-07-07
Mohamad Yagi	M	21	OS	-9.4	-10.1	-9.8	0.7	3.59	-9.7	-9.1	-9.4	0.7	3.47	
Naeal Alslamean	M	25	OD	-8.7	-8.2	-8.4	0.5	3.84	-11.4	-8.4	-9.7	3.0	2.82	2009-04-07
Naeal Alslamean	M	25	OS	-7.5	-10.1	-8.6	2.6	3.44	-5.7	-8.5	-6.8	2.7	3.64	
Assaf Alawgi	M	31	OD	-5.9	-6.0	-5.9	0.2	6.15	-5.9	-6.2	-6.0	0.3	6.16	2009-06-06
Assaf Alawgi	M	31	OS	-5.8	-6.1	-6.0	0.3	6.32	-5.9	-6.0	-5.9	0.1	6.35	
Ibead Alketby	M	32	OD	-6.9	-8.3	-7.5	1.4	4.18	-7.1	-8.7	-7.8	1.6	3.78	2009-03-06
Ibead Alketby	M	32	OS	-6.9	-6.3	-6.6	0.6	4.70	-6.4	-6.6	-6.5	0.3	4.83	
Khaled Salman	M	42	OD	-6.2	-6.3	-6.2	0.1	5.28	-6.6	-6.4	-6.5	0.2	5.19	2009-05-27
Khaled Salman	M	42	OS	-6.6	-6.2	-6.4	0.4	5.22	-7.0	-6.2	-6.6	0.8	5.11	
Imad Alakhras	M	31	OD	-6.3	-7.0	-6.6	0.7	4.80	-6.0	-6.9	-6.4	0.9	4.43	2009-05-16
Imad Alakhras	M	31	OS	-6.3	-5.9	-6.1	0.4	5.28	-6.3	-5.9	-6.1	0.4	5.21	
Rana Allamy	F	33	OD	-7.5	-6.6	-7.0	0.9	4.57	-7.0	-8.4	-7.6	1.3	3.83	2009-10-05
Rana Allamy	F	33	OS	-6.4	-7.9	-7.1	1.5	4.07	-7.2	-8.2	-7.7	1.0	3.94	
Gomana Alenemat	F	27	OD	-7.2	-8.3	-7.7	1.1	4.46	-7.3	-8.4	-7.8	1.1	4.28	2009-04-29
Gomana Alenemat	F	27	OS	-7.6	-8.2	-7.9	0.7	4.30	-7.8	-8.1	-8.0	0.3	4.38	
Monyrah Almgby	F	35	OD	-8.4	-7.6	-8.0	0.7	4.15	-9.0	-8.4	-8.7	0.5	3.87	2009-04-21
Monyrah Almgby	F	35	OS	-5.1	-14.1	-7.4	9.1	-18.16	-9.7	-10.7	-10.2	1.0	3.06	
Abdalzzyz Almnye	M	29	OD	-7.7	-6.8	-7.2	1.0	4.71	-7.5	-8.4	-8.0	0.9	4.15	2009-04-20
Abdalzzyz Almnye	M	29	OS	-6.9	-6.1	-6.4	0.8	5.26	-7.4	-7.0	-7.2	0.4	5.06	
Rasha Abo Alkheer	F	24	OD	-6.7	-8.0	-7.3	1.3	4.01	-7.1	-8.3	-7.7	1.2	3.74	2009-04-13
Rasha Abo Alkheer	F	24	OS	-7.3	-7.7	-7.5	0.3	3.75	-7.8	-8.5	-8.2	0.7	3.67	
Dena Sharaiha	F	28	OD	-6.3	-5.5	-5.9	0.8	5.10	-6.4	-5.5	-5.9	0.9	5.17	2009-05-04
Dena Sharaiha	F	28	OS	-7.4	-6.8	-7.1	0.6	4.54	-7.9	-8.8	-8.3	1.0	4.16	
Bdoor Alo'mran	F	33	OD	-6.0	-6.5	-6.2	0.5	5.60	-5.9	-6.6	-6.2	0.7	5.49	2009-03-22
Bdoor Alo'mran	F	33	OS	-6.9	-5.5	-6.1	1.3	5.43	-6.9	-8.0	-7.4	1.1	4.43	
Nawaf Alrashedi	M	23	OD	-9.0	-10.8	-9.8	1.8	2.52	-9.5	-10.4	-10.0	0.9	2.81	2008-06-01
Nawaf Alrashedi	M	23	OS	-7.2	-8.1	-7.6	0.9	4.05	-8.7	-7.6	-8.1	1.1	3.58	2009-03-03
Salah Said	M	33	OD	-6.3	-8.1	-7.1	1.7	4.30	-7.9	-9.5	-8.6	1.6	3.62	2009-01-03
Salah Said	M	33	OS	-11.2	-9.0	-9.9	2.2	2.93	-11.0	-10.2	-10.6	0.8	2.87	
Fhad Alzahrany	M	26	OD	-6.7	-8.2	-7.4	1.5	4.24	-7.9	-8.7	-8.3	0.8	4.08	2009-02-22
Fhad Alzahrany	M	26	OS	-7.3	-9.1	-8.1	1.8	3.71	-8.6	-10.0	-9.3	1.4	3.61	
Msfer Alzahrani	M	34	OS	-12.5	-13.1	-12.8	0.6	2.28	-13.5	-12.4	-12.9	1.1	2.05	2009-02-22
Naser Alka'bi	M	25	OD	-7.5	-8.3	-7.9	0.9	4.11	-7.7	-9.3	-8.5	1.6	3.71	2009-10-02
Omer Alkaby	M	22	OD	-8.5	-8.9	-8.7	0.4	3.08	-8.3	-9.2	-8.7	0.9	3.36	2009-10-02
Thaer Aboelhega	M	28	OD	-9.5	-10.6	-10.0	1.1	2.48	-9.6	-10.4	-10.0	0.8	2.77	2009-06-01
Thaer Aboelhega	M	28	OS	-9.8	-10.5	-10.1	0.7	3.09	-9.4	-10.4	-9.9	0.9	3.14	
Fahed Alzahrani	M	29	OD	-8.1	-8.4	-8.2	0.3	3.66	-8.2	-9.1	-8.6	0.9	3.97	2009-05-01
Fahed Alzahrani	M	29	OS	-7.4	-8.0	-7.7	0.6	3.80	-10.0	-8.6	-9.2	1.4	3.63	
Moa'd Alomari	M	29	OD	-7.6	-8.6	-8.1	1.0	3.67	-7.3	-8.8	-8.0	1.5	3.85	2008-12-23
Ebtesam Alomari	F	39	OD	-6.6	-7.1	-6.8	0.5	5.46	-6.7	-7.2	-6.9	0.4	5.43	2008-10-29
Ebtesam Alomari	F	39	OS	-6.8	-7.4	-7.1	0.5	5.36	-6.9	-7.2	-7.0	0.3	5.38	
Abeer Alomari	F	30	OD	-6.8	-7.4	-7.1	0.5	5.26	-6.8	-7.3	-7.0	0.4	5.28	2008-10-29
Abeer Alomari	F	30	OS	-7.0	-7.1	-7.1	0.1	5.27	-7.0	-7.3	-7.2	0.2	5.34	
Alyazeed Zwawi	M	44	OD	-7.8	-9.4	-8.5	1.6	3.81	-9.2	-9.1	-9.2	0.1	3.93	2008-10-26
Alyazeed Zwawi	M	44	OS	-6.5	-7.5	-7.0	1.0	4.93	-8.1	-7.2	-7.6	0.9	4.40	
Neaamah Barakat	F	27	OD	-6.9	-8.5	-7.6	1.6	3.90	-8.4	-8.7	-8.5	0.3	3.69	2008-07-10
Alaa Altwaisi	M	22	OD	-6.7	-8.4	-7.4	1.6	3.96	-9.5	-9.6	-9.6	0.1	3.26	2008-09-27
Ja'far Mehzen	M	41	OD	-6.1	-6.0	-6.1	0.1	4.50	-7.0	-6.8	-6.9	0.2	4.47	2008-09-23
Ja'far Mehzen	M	41	OS	-6.0	-5.0	-5.5	0.9	5.62	-6.0	-5.3	-5.7	0.7	5.56	
Mareno Emad	M	24	OD	-8.6	-10.3	-9.4	1.6	2.76	-10.0	-10.4	-10.2	0.4	3.25	2008-09-22
Mareno Emad	M	24	OS	-7.2	-7.8	-7.5	0.7	4.27	-7.9	-8.9	-8.4	1.0	4.17	
Emad Salem	M	48	OD	-10.0	-10.0	-10.0	0.0	3.21	-10.8	-11.9	-11.3	1.1	2.70	2008-09-21
Emad Salem	M	48	OS	-10.4	-10.6	-10.5	0.2	2.95	-9.8	-10.9	-10.3	1.0	2.93	
Afaf Algamdy	F	27	OD	-6.9	-8.8	-7.7	1.9	3.78	-7.4	-9.5	-8.3	2.1	3.65	2008-08-30
Afaf Algamdy	F	27	OS	-7.1	-8.5	-7.7	1.4	3.59	-10.2	-9.0	-9.5	1.2	3.20	
Rabeeaa Alajrad	F	49	OS	-14.7	-15.3	-15.0	0.6	1.76	-15.7	-16.1	-15.9	0.4	1.60	2008-08-27

Nuha Albehairi	F	47	OD	-7.9	-9.1	-8.4	1.3	3.78	-8.8	-10.2	-9.5	1.4	3.51	2008-08-18
Nuha Albehairi	F	47	OS	-11.0	-8.3	-9.5	2.7	2.58	-9.3	-10.2	-9.7	0.9	2.72	
Majdi Alotmi	M	24	OD	-6.1	-7.2	-6.6	1.1	4.22	-8.4	-9.4	-8.9	0.9	3.48	2008-08-16
Majdi Alotmi	M	24	OS	-6.8	-0.1	-0.2	6.7	6.85	-9.9	-12.4	-11.0	2.5	2.63	
Fakhra Almsghooni	F	38	OD	-6.5	-8.0	-7.2	1.4	3.84	-6.7	-8.5	-7.5	1.8	3.75	2008-08-14
Fakhra Almsghooni	F	38	OS	-6.8	-6.1	-6.4	0.7	4.84	-7.4	-6.8	-7.1	0.7	4.59	
Maha Alhaj	F	30	OD	-6.1	-7.8	-6.8	1.8	4.37	-7.0	-8.8	-7.8	1.7	3.74	2008-12-08
Maha Alhaj	F	30	OS	-10.8	-12.7	-11.7	1.9	2.29	-10.6	-11.4	-11.0	0.7	3.02	
Amr Zobairi	M	25	OD	-5.9	-6.6	-6.2	0.7	5.45	-6.2	-7.1	-6.6	0.9	5.04	2008-12-08
Amr Zobairi	M	25	OS	-7.4	-6.4	-6.8	1.0	4.56	-8.1	-7.6	-7.8	0.4	4.30	2008-08-17
Badreyeh Qarni	F	35	OD	-7.3	-8.0	-7.7	0.7	4.15	-8.7	-10.1	-9.4	1.4	3.33	2008-12-08
Badreyeh Qarni	F	35	OS	-6.9	-7.7	-7.3	0.8	4.37	-8.7	-10.1	-9.4	1.4	3.33	
Randa Alomari	F	36	OD	-6.6	-7.1	-6.8	0.4	4.79	-6.6	-7.0	-6.8	0.4	4.95	2008-03-08
Randa Alomari	F	36	OS	-7.6	-6.0	-6.7	1.6	4.45	-7.0	-7.4	-7.2	0.4	4.50	
Mohammad Alshamsi	M	23	OS	-6.0	-6.7	-6.4	0.6	5.81	-6.0	-6.8	-6.4	0.8	5.56	2008-07-30
Saaed Madi	M	22	OS	-12.3	-7.8	-9.6	4.5	-3.89	-10.8	-12.1	-11.4	1.3	2.71	2008-07-30
Sayrah Al Sheryeh	F	31	OD	-6.6	-7.8	-7.2	1.2	1.20	-6.5	-7.7	-7.1	1.2	4.56	2008-07-16
Bandar Alfefi	M	27	OD	-7.7	-9.2	-8.4	1.6	3.28	-8.8	-10.4	-9.5	1.6	3.13	2008-07-15
Bandar Alfefi	M	27	OS	-10.1	-11.8	-10.9	1.6	2.95	-8.3	-10.4	-9.3	2.1	3.32	
Abdallah Alfefi	M	30	OD	-6.8	-8.0	-7.4	1.3	4.21	-7.3	-8.1	-7.6	0.8	3.90	2008-07-15
Abdallah Alfefi	M	30	OS	-6.8	-7.8	-7.2	1.0	4.52	-7.0	-8.3	-7.6	1.4	4.19	
Saeed Alghamedi	M	28	OD	-6.9	-7.7	-7.3	0.8	4.42	-8.0	-8.6	-8.3	0.5	4.09	2008-06-07
Saeed Alghamedi	M	28	OS	-7.6	-7.9	-7.8	0.3	4.22	-8.5	-8.8	-8.7	0.4	3.45	
Kholoud Alhrbawy	F	34	OD	-9.2	-10.3	-9.7	1.1	3.39	-10.1	-11.2	-10.6	1.0	2.89	2008-05-07
Kholoud Alhrbawy	F	34	OS	-8.4	-9.7	-9.0	1.3	3.57	-10.5	-11.3	-10.9	0.8	2.96	
Ibraheem Alnatoor	M	24	OS	-9.8	-10.4	-10.1	0.6	3.15	-9.9	-10.8	-10.4	0.9	3.06	2008-06-22
Zahraa Hassan	F	23	OD	-7.2	-7.8	-7.5	0.6	4.06	-8.1	-9.2	-8.6	1.0	3.96	2008-07-06
Zahraa Hassan	F	23	OS	-9.8	-11.3	-10.5	1.5	2.88	-9.6	-11.3	-10.4	1.6	3.00	
Ahmad Donqola	M	25	OD	-6.6	-7.4	-7.0	0.8	4.84	-6.9	-8.0	-7.4	1.0	4.30	2010-01-03
Ahmad Donqola	M	25	OS	-8.0	-9.7	-8.7	1.7	3.08	-8.8	-10.2	-9.5	1.4	2.89	2008-05-24
Emad Alejely	M	35	OS	-7.9	-8.8	-8.3	0.9	3.38	-7.6	-9.1	-8.3	1.5	3.39	2008-05-18
Sumaia Ahaman	F	46	OD	-7.0	-6.7	-6.8	0.3	5.27	-7.4	-6.8	-7.1	0.6	5.07	2008-05-15
Sumaia Ahaman	F	46	OS	-8.2	-7.8	-8.0	0.4	4.05	-7.6	-8.0	-7.8	0.4	4.65	
Faisal Alshogeh	M	27	OD	-10.0	-10.6	-10.3	0.6	2.96	-10.2	-10.7	-10.5	0.5	2.89	2008-05-05
Abeer Alhoush	F	39	OS	-6.2	-2.5	-3.5	3.7	4.78	-6.1	-7.4	-6.7	1.4	3.86	2008-04-05
Fanar Shaheen	M	28	OD	-10.7	-13.5	-11.9	2.8	2.31	-10.0	-11.6	-10.7	1.6	2.72	2008-04-30
Hassan Hussien	M	26	OS	-7.8	-8.8	-8.3	1.0	3.35	-8.6	-9.6	-9.1	0.9	3.29	2008-04-14
Talal Alsharari	M	28	OD	-7.6	-9.8	-8.6	2.1	3.65	-9.1	9.8	-9.4	0.7	3.72	2008-08-04
Salwa Abdalrahman	F	48	OS	-6.2	-8.5	-7.2	2.3	3.89	-6.6	-9.0	-7.6	2.3	3.58	2008-07-04
Ahmad Mza'l	M	27	OD	-8.9	-11.4	-10.0	2.5	2.56	-9.0	-10.6	-9.8	1.6	2.40	2008-07-04
Ahmad Mza'l	M	27	OS	-12.1	-14.1	-13.0	2.0	2.10	-9.7	-10.7	-10.2	0.9	2.45	
Abdallah Baagaga	M	38	OS	-6.5	-7.3	-6.9	0.8	4.57	-6.9	-7.7	-7.2	-0.8	4.17	2008-03-20
Rabeaa Albom	F	39	OD	-6.6	-7.5	-7.0	0.9	4.98	-6.4	-7.1	-6.8	0.7	5.07	2008-03-18
Zainab Eisa	F	36	OD	-10.0	-10.5	-10.3	0.5	3.00	-11.4	-11.5	-11.4	0.1	2.43	2008-03-18
Zainab Eisa	F	36	OS	-6.2	-6.8	-6.5	0.6	5.77	-6.3	-6.8	-6.5	0.5	5.64	
Najwan Jaffar	F	29	OD	-11.2	-11.4	-11.3	0.2	2.87	-9.9	-11.2	-10.5	1.3	3.33	2008-12-03
Najwan Jaffar	F	29	OS	-7.8	-7.9	-7.9	0.1	3.85	-8.9	-9.9	-9.4	1.0	3.42	
Soltan Alhag	M	18	OD	-6.3	-8.1	-7.1	1.8	4.41	-7.9	-9.2	-8.5	1.3	3.97	2008-02-20
Soltan Alhag	M	18	OS	-8.5	-9.5	-9.0	1.1	3.74	-9.1	-10.0	-9.5	0.9	3.50	
Abd Alrahman Sa'eed	M	28	OD	-5.9	-7.5	-6.6	1.5	3.97	-7.5	-9.0	-8.2	1.4	3.82	2008-01-14
Abd Alrahman Sa'eed	M	28	OS	-11.2	-10.6	-10.9	0.6	2.87	-10.9	-10.2	-10.5	0.7	3.17	
Gamal Alramahi	M	30	OD	-7.4	-9.0	-8.1	1.6	3.92	-8.8	-9.5	-9.2	0.6	3.91	2008-01-13
Nour Abuhalemeleh	F	25	OD	-6.9	-9.1	-7.8	2.3	3.72	-8.7	-10.0	-9.3	1.4	3.30	2008-09-01
Nour Abuhalemeleh	F	25	OS	-6.5	-8.0	-7.2	1.5	4.31	-7.4	-8.6	-8.0	1.1	4.01	
Hammad Almri	M	31	OD	-14.7	-10.1	-12.0	4.6	1.76	-13.8	-15.7	-14.7	2.0	1.74	2008-07-01
Rabee' Alqobty	M	33	OD	-6.9	-8.2	-7.5	1.4	4.00	-8.5	-9.8	-9.1	1.4	3.40	2008-05-01
Rabee' Alqobty	M	33	OS	-9.2	-9.8	-9.5	0.6	3.39	-9.8	-10.3	-10.1	0.5	3.43	
Hani Abd Algani	M	31	OS	-8.6	-9.3	-9.0	0.7	3.47	-9.6	-10.7	-10.1	1.1	3.12	2007-12-20
Mash3al Alkhalidi	M	42	OD	-14.2	-15.2	-14.7	0.9	1.75	-14.1	-13.7	-13.9	0.4	2.09	2007-12-18
Mash3al Alkhalidi	M	42	OS	-7.9	-6.6	-7.2	1.3	4.09	-7.8	-8.0	-7.9	0.3	3.29	
Sarah Alo'morat	F	28	OD	-12.1	-13.3	-12.7	1.1	2.34	-12.0	-13.3	-12.6	1.2	2.40	2007-12-17
Sarah Alo'morat	F	28	OS	-12.6	-11.9	-12.2	0.7	2.65	-11.1	-12.7	-11.8	1.6	2.66	
Adel Alrashedi	M	26	OD	-6.4	-8.8	-7.4	2.5	3.99	-8.0	-9.1	-8.5	1.1	3.80	2007-12-12
Adel Alrashedi	M	26	OS	-6.0	-7.1	-6.5	1.0	5.16	-6.1	-7.1	-6.6	1.0	5.26	
Shekha Al Hajeri	F	33	OD	-8.5	-9.3	-8.9	0.8	3.04	-9.8	-10.8	-10.3	1.0	2.94	2007-12-12
Shekha Al Hajeri	F	33	OS	-6.2	-7.3	-6.7	1.0	5.10	-8.1	-7.0	-7.5	1.1	4.39	
Siham Abu Baker	F	36	OD	-7.8	-9.4	-8.5	1.6	3.32	-8.4	-9.1	-8.7	0.7	3.51	2007-11-12
Abdalrhmaq'n Kana'ah	M	32	OD	-11.9	-14.8	-13.2	3.0	1.80	-12.7	-14.3	-13.5	1.6	2.03	2007-11-12
Abdalrhmaq'n Kana'ah	M	32	OS	-7.7	-8.7	-8.1	1.0	3.13	-7.9	-9.2	-8.5	1.4	3.01	
Murad Hjazeen	M	23	OD	-7.4	-8.6	-7.9	1.3	4.20	-8.0	-9.1	-8.5	1.1	4.11	2007-10-12
Murad Hjazeen	M	23	OS	-7.1	-8.1	-7.6	1.0	4.45	-8.2	-8.7	-8.4	0.6	4.34	

Ali Alna'emi	M	26	OD	-6.7	-7.9	-7.3	1.1	4.18	-7.6	-8.4	-8.0	0.9	3.76	2007-09-12
Ali Alna'emi	M	26	OS	-6.3	-7.0	-6.6	0.7	4.70	-7.4	-6.8	-7.1	0.7	4.57	
Raafat Shqear	M	40	OD	-9.1	-10.8	-9.9	1.6	2.98	-10.0	-10.9	-10.4	1.0	2.90	2007-07-12
Raafat Shqear	M	40	OS	-9.0	-10.0	-9.4	1.0	3.37	-10.0	-10.9	-10.4	1.0	2.90	
Mohamad Almheri	M	34	OD	-6.1	-8.1	-7.0	2.0	4.33	-7.5	-9.3	-8.3	1.7	3.82	2007-04-12
Mohamad Almheri	M	35	OS	-6.1	-6.9	-6.5	0.8	5.15	-6.0	-6.9	-6.4	0.9	5.28	
Adel Al Yousef	M	28	OD	-6.6	-7.3	-6.9	0.7	4.22	-6.4	-8.0	-7.1	1.6	4.18	2007-03-12
Adel Al Yousef	M	28	OS	-10.3	-10.8	-10.5	0.6	2.97	-10.3	-10.3	-10.3	0.0	2.94	
Ahmad Alasaf	M	24	OD	-9.2	-10.0	-9.6	0.8	3.09	-9.4	-9.6	-9.5	0.3	3.03	2007-11-21
Ahmad Alasaf	M	24	OS	-7.9	-6.6	-7.2	1.3	4.02	-8.7	-8.8	-8.8	0.1	3.34	
Wael Badawea	M	21	OD	-7.1	-9.3	-8.0	2.2	3.52	-9.6	-3.7	-5.4	5.9	3.17	2007-12-11
Wael Badawea	M	21	OS	-8.3	-9.9	-9.0	1.6	3.43	-7.7	-9.0	-9.3	1.4	3.04	
Faisal Shkeh	M	27	OD	-9.5	-10.3	-9.9	0.8	2.74	-9.6	-10.7	-10.1	1.1	2.99	2007-07-11
Nedam Bolbol	M	22	OS	-8.9	-10.4	-9.6	1.5	3.01	-9.9	-9.0	-9.4	0.8	2.95	2007-06-11
Firas Alazzam	M	40	OD	-7.6	-8.1	-7.8	0.5	4.30	-8.6	-9.6	-9.1	1.0	3.63	2007-05-11
Firas Alazzam	M	40	OS	-8.6	-9.4	-9.0	0.8	3.43	-8.8	-10.1	-9.4	1.3	3.59	
Diana Abu Alroub	F	26	OD	-7.0	-8.2	-7.5	1.2	4.11	-7.6	-9.3	-8.3	1.7	3.67	2007-02-11
Diana Abu Alroub	F	26	OS	-8.5	-9.6	-9.0	1.1	3.30	-9.2	-10.0	-9.6	0.7	3.00	
Mahmoud Al Eishat	M	22	OD	-6.6	-8.4	-7.4	1.8	4.09	-6.9	-8.5	-7.6	1.7	3.90	2007-10-31
Yosef Alaham	M	28	OD	-6.5	-7.4	-6.9	0.9	4.89	-6.5	-7.7	-7.1	1.2	4.72	2007-09-10
Mai Awadallah	F	26	OD	-7.2	-7.9	-7.5	0.8	3.70	-8.2	-9.2	-8.7	1.0	3.68	2007-09-16
Mai Awadallah	F	26	OS	-8.4	-9.0	-8.7	0.5	3.50	-8.6	-9.0	-8.8	0.4	3.78	
Ahmad Hamam	M	21	OD	-5.4	-6.5	-5.9	1.0	6.06	-5.4	-6.6	-6.0	1.1	5.93	2007-06-16
Ahmad Hamam	M	21	OS	-5.6	-6.3	-5.9	0.7	6.16	-5.6	-6.4	-6.0	0.8	6.04	
Ala'a Maree	F	29	OD	-8.3	-9.4	-8.8	1.0	3.21	-9.3	-10.4	-9.9	1.1	3.25	2007-04-15
Ala'a Maree	F	29	OS	-11.1	-11.5	-11.3	0.4	2.88	-11.3	-11.6	-11.5	0.4	2.88	
Khaled Abu Galuon	M	24	OS	-6.0	-6.6	-6.3	0.6	5.11	-6.1	-7.1	-6.6	1.0	5.06	2007-11-04
Kher Aldeen Al Salaq	M	43	OS	-14.6	-16.0	-15.3	1.3	1.61	-18.6	-17.0	-17.8	1.6	1.36	2006-11-20
Marwa Al Rawashdeh	F	26	OD	-8.3	-8.7	-8.5	0.4	3.69	-8.4	-8.8	-8.6	0.4	3.71	2006-12-08
Marwa Al Rawashdeh	F	26	OS	-9.4	-10.3	-9.8	0.9	3.47	-9.6	-10.5	-10.0	0.9	3.45	
Mohammad Al Kazali	M	27	OD	-7.1	-7.9	-7.5	0.8	4.57	-7.7	-7.2	-7.4	0.6	4.60	2006-06-29
Mohammad Al Kazali	M	27	OS	-6.9	-8.2	-7.5	1.3	4.32	-6.9	-8.1	-7.4	1.2	4.57	
Nazek Alazam	F	25	OD	-7.3	-8.6	-7.9	1.2	3.60	-7.5	-8.4	-8.0	0.9	4.21	2006-06-28
Nazek Alazam	F	25	OS	-6.9	-8.5	-7.6	1.6	3.88	-7.0	-8.7	-7.8	1.8	3.90	
Mansour Dyabat	M	33	OD	-7.3	-9.0	-8.1	1.7	4.08	-7.6	-8.9	-8.2	1.4	4.08	2005-10-22
Mansour Dyabat	M	33	OS	-7.4	-8.7	-8.0	1.3	4.12	-7.4	-8.7	-8.0	1.3	4.13	
Hamed Alabadi	M	22	OD	-8.2	-9.6	-8.8	1.4	3.78	-8.1	-9.5	-8.8	1.3	3.84	2005-08-17
Hamed Alabadi	M	22	OS	-7.6	-9.5	-8.5	1.9	3.71	-7.6	-9.4	-8.4	1.8	3.67	
Senan Balha	M	30	OD	-8.2	-8.7	-8.4	0.5	3.85	-9.6	-10.4	-10.0	0.8	3.51	2004-08-24
Senan Balha	M	30	OS	-9.4	-9.7	-9.5	0.3	2.99	-11.7	-11.8	-11.8	0.2	2.54	
Average				-7.7	-8.5	-10.5	1.2	3.91	-8.2	-8.8	-8.6	1.0	3.87	
SD				2.0	2.1	38.2	1.0	1.83	1.8	2.3	1.8	0.6	0.97	

F: Female; M: Male.

Table 3 Relationship between astigmatic dioptric power and angular length of arcuate incision

Astigmatic dioptric power	Angular length
1D-3D	60
3D-5D	80
5D-7D	100
> 7D	120

to gain better vision. The squeezing that occurs during squinting can cause changes in the regular arrangement of the collagen stroma^[23]. As a result of the procedure there is also an increase in astigmatic power until edema starts to subside.

No suturing is used in our procedure because suturing is known to have a harmful iatrogenic effect^[14]. Ectasia is a known complication after corneal surgery^[16], but has not been seen in any patient receiving this procedure, in which no foreign body is implanted in the cornea. During the healing process, the elliptical, irregular shape of the

head of the cornea tends to become round and regain its regularity. Corneal dioptric power and the thickness of the cornea change as a result of this procedure. In this method of treatment, there is an increase in the thickness and width of the incision site and a change in the nomogram of the cornea and its indices, with its vertical and horizontal meridian releasing steepness tension, resulting in improved visual acuity. Visual acuity improves over time and the improvement depends on the speed at which the incision gap heals.

It is important to note that, during preoperative and postoperative examinations, an inaccurate refractometer reading and an inaccurate astigmatic Pentacam reading are possible as a result of human error. Inaccurate postoperative readings may be obtained because of edema of the eye, which, in my opinion, scatters the light. The refractive error of each eye must therefore be corrected by the examining physician using the duochrome test and the fan test, starting with astigmatic correction and then sphere correction to eliminate human error. Objective

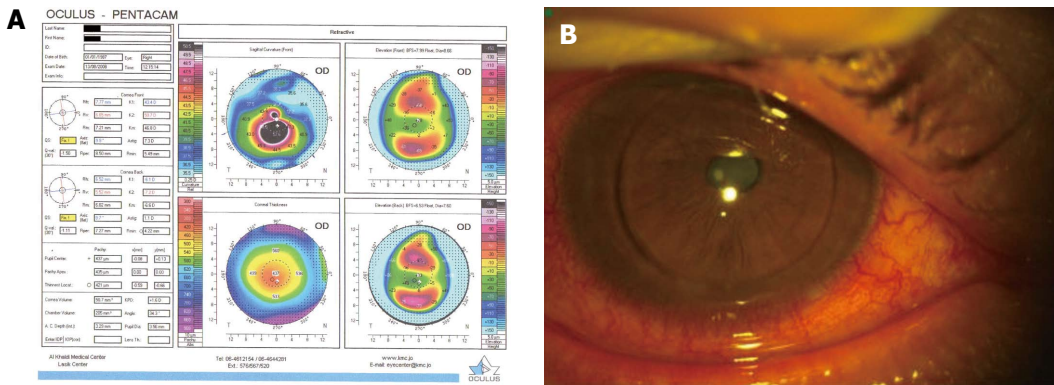


Figure 2 Pre-op Oculus Pentacam tomography. A: Pre-op Oculus Pentacam tomography for the patient's right eye; B: The patient's eye on the day of the surgery immediately after the operation.

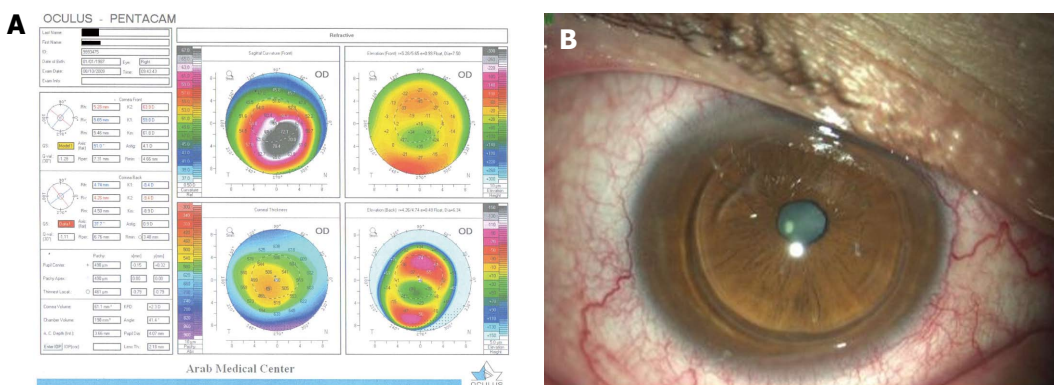


Figure 3 Post-op Pentacam tomography 13 mo after surgery. A: Post-op Pentacam tomography of the same patient's eye almost 13 mo after surgery; B: The same patient's eye 13 mo after surgery.

and subjective tests are essential at this point to obtain accurate readings. As the cornea thickens, its dioptric power changes - the normal range of dioptric power in human eyes is from 43 to 45 diopters^[24]. This dioptric power facilitates proper interpretation of visual stimuli by the visual cortex. In the present study and our research on keratoconus, we found that there is low corneal dioptric power in some areas of the cornea and high dioptric power in other areas of the cornea, as observed by Pentacam Oculus Pentacam tomography. After corneal dioptric power begins to increase, the visual cortex is able to better interpret images received by the eye.

It is our belief that the incisions, due to their unity, sharpness, and regularity, create the basis for the creation of a "tectonic plate" for the production of new stromal cells. Production of these cells continues for an indefinite period, and we have found that cell production is still occurring at the last follow-up but does not continue in all areas of incision. The body will stop the production of new cells once it reaches its genetic capacity, just like a wound or injury to the skin. We believe that, through circular and arcuate keratotomy, we are inducing cell growth in a ring-like pattern. Our findings can be more clearly seen by examining the case of one particular patient.

This patient's readings reflect an approximation of

the mean changes that occurred in the present study. The predetermined surgical plan for this patient was to make paired arcuate keratotomy incisions 2.5 mm from the pupillary axis. The steepest axis was at 10°, the angular length of the arcuate incisions was calculated to be 100°, and the depth for the arcuate incisions was calculated to be 4.4 mm. A circular incision was made 7 mm from the pupillary center and the depth was 5.5 mm (90% of corneal thickness) from 210° to 330° and 4.9 mm in the remaining part (70% of corneal thickness).

Figure 2A shows the preoperative Oculus Pentacam tomography for the patient's right eye and Figure 3A is the postoperative Oculus Pentacam tomography of the same patient's eye almost 13 mo after surgery. Notice the corneal dioptric power and thickness of the cornea from 210° to 330°. The preoperative axis of the eye was at 9.9°. One year after surgery the axis had shifted to 51°. Additionally, the astigmatic power of the cornea front had changed from 7.3 D preoperatively to a postoperative reading of 4.1 D. The astigmatic power of the rear of the cornea was 1.1 D preoperatively and 0.9 D postoperatively.

The corneal volume preoperatively was 50.7 mm³ and after 1 year it was 61.1 mm³. These readings indicate that the cornea's Oculus Pentacam tomography was changing. Figure 2B shows the patient's eye on the day of the

surgery immediately after the operation, and Figure 3B shows the same patient's eye 13 mo after surgery. Clinically, the thickness of the wound appeared to have increased in all areas, with edema and fogginess at the sites of the arcuate and circular incisions. Notice that there was a notch in the left arcuate incision at approximately 160° because of movement by the patient during the procedure. Also notice that the nasal portion was not as thick and some areas had less edema than others.

In conclusions, the results of this study indicate that the Bader procedure is effective and promising in the treatment of stage III and stage IV keratoconus. It is necessary to understand that treatment with the Bader procedure involves a long-term relationship between the doctor and patient because the healing of the cornea occurs as a natural process of the body. There will be many in the scientific community who feel that incision in the cornea increases the potential for rupture. However, there has been no postoperative rupture in any patient who has undergone this procedure. Since arcuate keratotomy is performed after keratoplasty to reduce astigmatism, it makes sense, on the basis of our findings, to consider arcuate keratotomy coupled with modified circular keratotomy as an additional treatment procedure before performing keratoplasty as a final option for correction.

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COMMENTS

Background

To reduce astigmatism, increase corneal volume, and improve visual acuity. In other words, the authors commit actual changes in the ovality of the cornea, by this, the authors reduce the astigmatism, with the formation of new cells, the authors increase the corneal volume in the areas where there is thinning and irregular, when the above achieved the corneal dioptric power changed which enhance a good image to the brain to interpret proper image and registered in the brain.

Research frontiers

Keratoconus is a disease contain the following disorders: (1) Irregularity of the corneal surface from the front and the back; (2) Oval shape of the cornea I mean astigmatism; (3) High myopia due to the invagination of the cornea with forward displacement; and (4) Functional Amlyopia. With Bader Procedure it tends to correct almost the mentioned above.

Innovations and breakthroughs

The Bader Producer is a new way, utilizing the natural process of the cornea to correct it self according to the genetic order of the body in repairing it self without changing or replacing a donor which works as foreign body with the possibility of side effect.

Applications

The authors compare Pre-Op values with Post-Op values, which give the ideas about the improvement occur as a result of the implication done, carrying out another implication could be noticed from the difference of the values.

Peer review

This is a nice and well present case series of patients with keratoconus who underwent paired arcuate and circular keratotomies. The manuscript presents interesting results.

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- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature

of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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- 4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

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- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

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- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

- 7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

- 8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

- 9 Outreach: Bringing HIV-positive individuals into care. *HRS-A Careaction* 2002; 1-6 [PMID: 12154804]

Books

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- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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- 15 Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/eid/index.htm>

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- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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**EDITORIAL**

- 16 Topical biological agents targeting cytokines for the treatment of dry eye disease
Yoon KC

Contents

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APPENDIX I-V Instructions to authors

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Topical biological agents targeting cytokines for the treatment of dry eye disease

Kyung Chul Yoon

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Abstract

Because inflammation plays a key role in the pathogenesis of dry eye disease and Sjögren's syndrome, topical anti-inflammatory agents such as corticosteroids and cyclosporine A have been used to treat inflammation of the ocular surface and lacrimal gland. Systemic biological agents that target specific immune molecules or cells such as tumor necrosis factor (TNF)- α , interferon- α , interleukin (IL)-1, IL-6, or B cells have been used in an attempt to treat Sjögren's syndrome. However, the efficacy of systemic biological agents, other than B-cell targeting agents, has not yet been confirmed in Sjögren's syndrome. Several studies have recently evaluated the efficacy of topical administration of biological agents targeting cytokines in the treatment of dry eye disease. Topical blockade of IL-1 by using IL-1 receptor antagonist could ameliorate clinical signs and inflammation of experimental dry eye. Using a mouse model of desiccating stress-induced dry eye, we have demonstrated that topical application of a TNF- α blocking agent, infliximab, could improve tear production and ocular surface irregularity, decrease inflammatory cytokines and Th-1 CD4+ cells on the ocular surface, and increase goblet

cell density in the conjunctiva. Although controversy still remains, the use of topical biological agents targeting inflammatory cytokines may be a promising therapy for human dry eye disease.

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Key words: Dry eye disease; Sjögren's syndrome; Biological agent; Tumor necrosis factor- α ; Interleukin-1; B cell; Cytokine

Core tip: Although the debate remains about the efficacy of systemic biological agents on Sjögren's syndrome, topical biological agents targeting inflammatory cytokines can be applicable for the treatment of dry eye disease.

Yoon KC. Topical biological agents targeting cytokines for the treatment of dry eye disease. *World J Ophthalmol* 2013; 3(2): 16-19 Available from: URL: <http://www.wjgnet.com/2218-6239/full/v3/i2/16.htm> DOI: <http://dx.doi.org/10.5318/wjo.v3.i2.16>

INTRODUCTION

It is well known that tear film hyperosmolarity activates inflammation of the ocular surface, resulting in dry eye disease. Increased expression of inflammatory cytokines, chemokines, matrix metalloproteinases, apoptotic markers, CD4+ Th-1 cells, and Th-17 cells on the ocular surface and in the lacrimal gland have been demonstrated in clinical and experimental dry eye studies^[1-15]. Current treatments for dry eye include artificial tears, topical anti-inflammatory agents including corticosteroids and cyclosporine A, punctal plugs, and contact lenses^[16-21]. As biological products, variants of serum and plasma, such as autologous serum, umbilical cord serum, and platelet-rich plasma, can also be used topically in severe dry eye^[22-25]. Despite these treatments, patients with severe dry eye or

Sjögren's syndrome still complain of discomfort and have signs of persistent inflammation on the ocular surface.

SYSTEMIC BIOLOGICAL AGENTS

Systemic biological agents that target specific immune molecules or cells have been used in an attempt to treat autoimmune diseases such as Sjögren's syndrome. These targets include tumor necrosis factor (TNF)- α , interferon (IFN)- α , interleukin (IL)-1, IL-6, and B cells^[26-29].

Although anti-TNF- α agents were found to be successful in modulating other autoimmune diseases, such as rheumatoid arthritis, controversy exists regarding the efficacy of systemic TNF- α blocking agents in Sjögren's syndrome. In a study using a rabbit model of dacryoadenitis, the transfer of a TNF- α inhibitor gene suppressed the appearance of Sjögren's syndrome-like features including reduced tear production and lacrimal gland immunopathology^[30]. However, TNF- α inhibitors had no therapeutic effect in an autoimmune murine model of Sjögren's syndrome^[31]. In clinical studies, application of a anti-TNF- α agent, infliximab, caused a rapid and sustained improvement in symptoms and signs without any major adverse reaction, whereas it did not show a therapeutic response in patients with primary Sjögren's syndrome compared with controls^[32,33]. In addition, oral or subcutaneous administration of etanercept was ineffective in Sjögren's syndrome patients^[34,35].

Oral administration of low dose IFN- α showed inconsistent efficacy in various studies but failed to achieve the primary endpoint in a randomized controlled trial^[27,36-38]. The efficacy of IL-1 and IL-6 and other cytokines in Sjögren's syndrome is still under investigation^[28,29].

In contrast, systemic B-cell targeted therapy has shown clinically promising results in patients with Sjögren's syndrome. Several controlled trials demonstrated considerable improvements in sicca features, salivary flow, ocular surface staining by lissamine green, fatigue, extraglandular manifestations, and quality of life scores after treatment with the B-cell-depleting anti-CD20 antibody, rituximab^[39,40]. Although the marked inflammatory infiltrate in the affected glands includes a high percentage of T cell, there is abundant evidence that B cell hyperactivity is a main pathogenic factor in Sjögren's syndrome^[41]. Administration of the anti-CD22 antibody, epratuzumab, also showed marked improvements in fatigue and subjective outcomes in patients with Sjögren's syndrome^[42]. The B-cell-activating factor (BAFF), which stimulates the production of antibodies by B cells, may be another target for therapy.

TOPICAL BIOLOGICAL AGENTS

Among many targets including cytokines, cytokine signaling pathways, and cell adhesion or leukocyte trafficking, cytokines are the most commonly used therapeutic target for Sjögren's syndrome and inflammatory dry eye. Compared with systemic biological agents for Sjögren's syndrome, only a few studies have evaluated the efficacy

of topical administration of biological agents that block pro-inflammatory cytokines in the treatment of dry eyes. Okanobo *et al*^[43] demonstrated the therapeutic efficacy of topical blockade of IL-1 in the treatment of experimental dry eye disease. According to their study, application of topical formulations containing 5%IL-1 receptor antagonist (IL-1Ra) was effective in reducing clinical signs and inflammation of dry eye, as evidenced by a decrease in corneal fluorescein staining, the number of central corneal CD11b+ cells, corneal lymphatic growth, and corneal IL-1 β expression^[43]. The effects by topical IL-1Ra were comparable with those by topical methylprednisolone.

We previously investigated the effects of topical infliximab on the tear film and ocular surface of desiccating stress-induced murine dry eye^[44]. Our results showed that mice treated with 0.01% or 0.1% infliximab eye drops had a significant improvement in tear production and corneal surface irregularity. Treated mice also had lower levels of inflammatory cytokines (IL-1 β , IL-6, IL-17, IFN- γ , and TNF- α) and Th-1 CD4+ cells and higher goblet cell density in the conjunctiva compared with controls. The reason why the topical anti-TNF- α agent was effective in ocular surface inflammation in contrast to systemic agents could be explained by the dual effect of anti-TNF- α which can enhance T cell receptor-mediated Th1 and Th17 cell activation in peripheral blood and prevent the migration of pathogenic T cells to inflamed tissues, thereby inhibiting inflammation in target tissues^[45]. The topical administration of TNF- α blocking agents may be effective in treating dry eye by affecting the inflamed ocular surface directly^[44].

Recently, we have reported the therapeutic effect of topical adiponectin, a protein secreted by the adipose tissue, in a mouse model of experimental dry eye^[46]. Adiponectin is known to have anti-inflammatory effects as well as anti-diabetic, anti-atherogenic, and anti-angiogenic properties^[47-50]. The globular region of adiponectin is structurally similar to TNF- α . Adiponectin can inhibit TNF- α and TNF- α -mediated activation of nuclear factor- κ B^[51,52]. It can activate adenosine monophosphate-activated protein kinase and protect salivary gland epithelial cells from spontaneous and IFN- γ -induced apoptosis in autoimmune inflammation^[53]. CD4+ T-cell-produced IFN- γ plays a pivotal role in Sjögren's syndrome-like conjunctival epithelial apoptosis *via* activation of the extrinsic apoptotic pathway^[54]. Our study suggest that topical application of 0.001% or 0.01% globular adiponectin could improve tear production and corneal surface irregularity, decrease levels of inflammatory cytokines (IL-1 β , IL-6, TNF- α , IFN- γ , and CXCL9) and Th-1 CD4+ cells in the conjunctiva and lacrimal gland, and could increase conjunctival goblet cell density.

Our experiments show that topical application of a TNF- α blocking agent can improve the tear film and ocular surface parameters by inhibiting inflammatory cytokines, chemokines, and T cells in the conjunctiva and lacrimal glands, and could therefore be useful in the treatment of dry eye disease. Other candidate cytokines

like IL-12, IL-17, and IL-23 may provide promising targets for Sjögren's syndrome. In addition, considering the favorable results of systemic B-cell targeted therapy observed in patients with Sjögren's syndrome, topical B-cell targeting agents such as BAFF could potentially be used as a treatment for autoimmune and inflammatory dry eye.

CONCLUSION

Although some debate still remains about the effect of systemic biological agents on Sjögren's syndrome, topical biological agents that target various inflammatory cytokines can be applicable for the treatment of human dry eye disease. Clinical studies on the safety and efficacy of topical biological agents targeting cytokines in patients with dry eye disease will be needed in the near future.

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**THERAPEUTICS**

20

Keratoconus therapeutics advances

ADVANCES*Jaimes M, Ramirez-Miranda A, Graue-Hernández EO, Navas A*

Contents

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Keratoconus therapeutics advances

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intraocular lens implant, phakic intraocular lenses and the combination of these alternatives. Some authors have been using excimer laser in patients with keratoconus but the safety of the procedure is controversial. Currently, the techniques for the management of keratoconus can be classified in 3 types: corneal strengthening techniques, optical optimization techniques and combined techniques.

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Key words: Keratoconus; Treatment; Management; Corneal ectasia; Therapeutics

Core tip: There are several treatment options for the current management of keratoconus patients. These alternatives are increasing and better outcomes could be obtained. The purpose of this review is to summarize the therapeutics advances in keratoconus.

Abstract

Keratoconus is a progressive, usually bilateral disease of the cornea that significantly diminishes visual acuity, secondary to a progressive corneal deformity which is characterized by corneal thinning, variable degrees of irregular astigmatism and specific abnormal topographic patterns. Normally it initiates during puberty and is progressive until the third or fourth decade of life, when normally the progression rate is diminished or waned. There are multiple scales to clinically classify keratoconus. One of the most commonly used is Amsler-Krumeich and recently with the development of morphometric and aberrometric techniques, additional scales have been created that allow keratoconus to be classified according to its severity. Despite certain etiology of keratoconus remains unknown, current treatment options are available in patients with ectatic corneas and they vary depending on the severity of the disease and they include spectacles, contact lenses, intrastromal rings, keratoplasty both penetrant or lamellar, cross-linking, refractive lens exchange with

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INTRODUCTION

Keratoconus is a corneal ectasia that significantly diminishes visual acuity, secondary to a progressive corneal deformity which is characterized by corneal thinning, variable degrees of irregular astigmatism and specific abnormal patterns (Figure 1) of corneal elevation^[1].

It has an approximate incidence, which varies between 50 to 230 cases in 100000 inhabitants in general population (1:2000). The estimated prevalence is of 54.5:100000 inhabitants. Normally it initiates during puberty and is progressive until the third or fourth decade of life, when normally the progression rate is diminished or waned^[2].

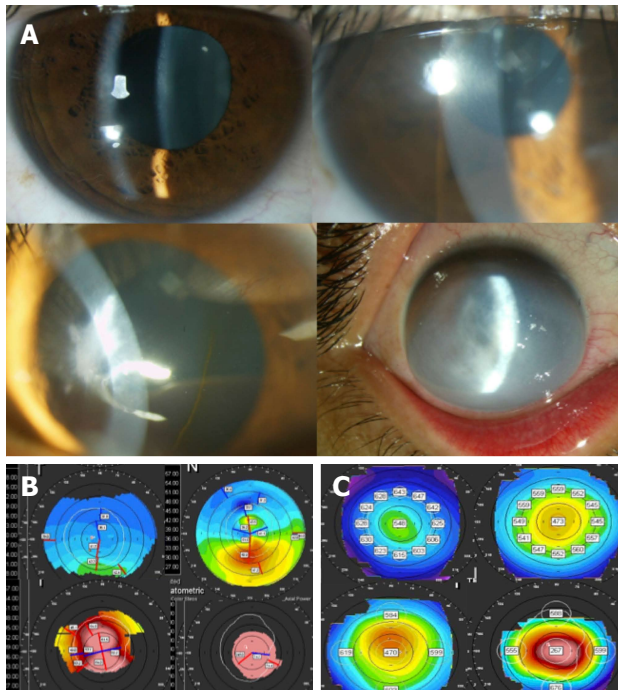


Figure 1 Keratoconus clinical and topographic variation examples. A: Several clinical presentations and severity of keratoconus cases; B: Different keratometric stages of keratoconus; C: Pachymetric maps showing different grades of KC cases.

There are multiple scales to clinically classify keratoconus. One of the most commonly used is Amsler-Krumeich^[3] (Table 1) and recently with the development of morphometric and aberrometric techniques, additional scales have been created that allow keratoconus to be classified according to its severity^[4] (Table 2).

Currently, the techniques for the management of keratoconus can be classified in 3 types: corneal strengthening techniques, optical optimization techniques and combined techniques^[5].

Among the strengthening techniques are: corneal collagen cross-linking and placement of intrastromal rings segments (which also have a refractive effect). The optical optimization techniques include the use of spectacles, rigid, soft or optimized contact lenses; excimer laser, lamellar or penetrating keratoplasty (which also have a strengthening effect), phakic lenses and pseudophakic lenses.

The combined procedures are those that are utilized in a sequential manner to obtain optical and refractive results and they include a wide array of possible combinations of the procedures previously described to obtain these objectives (Figure 2).

One of the main criteria to consider the more suitable technique or treatment for our patient is refraction, age, the thinning degree and the irregular astigmatism. If it is possible to obtain a correct subjective and objective refraction and the patient shows an improvement in their visual acuity with optical correction, then the options of treatment will have as an objective to correct the refrac-

Table 1 Clinical classification of keratoconus^[3]

Stage	Characteristics
Stage I	Eccentric bulging Induced myopia and/or astigmatism of 5 D Average central keratometry of 48 D
Stage II	Induced myopia and/or astigmatism of 5 to 8 D Average central keratometry > 48 D but < 53 D Absent scarring Minimum corneal thickness of 400 microns
Stage III	Induced myopia and/or astigmatism of 8 to 10 D Average central keratometry > 53 D Absent scarring Central corneal thickness of 300 to 400 microns
Stage IV	Invaluable refraction Average central keratometry > 55 D Central corneal scar Corneal thickness < 200 microns

tive error more so than to stabilize the keratoconus. According to this, we present an algorithm suggested for decision making in respect to surgical criteria in patients with keratoconus (Figure 3). Evidently, every patient needs to be individualized.

SPECTACLES

These represent the best option for treatment of fruste keratoconus and keratoconus with small irregular astigmatism that are refractable and have a visual capacity > 20/40 or do not wish surgery to treat the ectasia or the slight ametropia. The recommendation in these cases is to have topographic follow ups every 6 mo to evaluate progression.

CONTACT LENSES

Contact lenses are treatment of choice for 90% of the patients with keratoconus. The degree of keratoconus influences the selection of the type of contact lens and also many of the patients that have been treated with penetrating keratoplasty use contact lenses^[6].

The most commonly used contact lens design in patients with keratoconus is the unique base curve in rigid gas permeable material. Lenses with multiple base curves can also be used. In patients with highly advanced keratoconus, hybrid or scleral lenses have been used^[6].

In recent studies, it's been identified that 79% of patients with keratoconus use contact lenses; of which, 21.3% have already had at least one penetrating keratoplasty. Sixty-seven point seven percent of the patients use the hybrid gas permeable lens, 13% soft contact lens, 4.2% scleral gas permeable lens and 15.1% use other types of contact lenses^[7].

Presently, new personalized lens models have been designed for the treatment of keratoconus for those with intolerance of the conventional contact lens. Examples of these include the PROSE lens (Prosthetic replacement

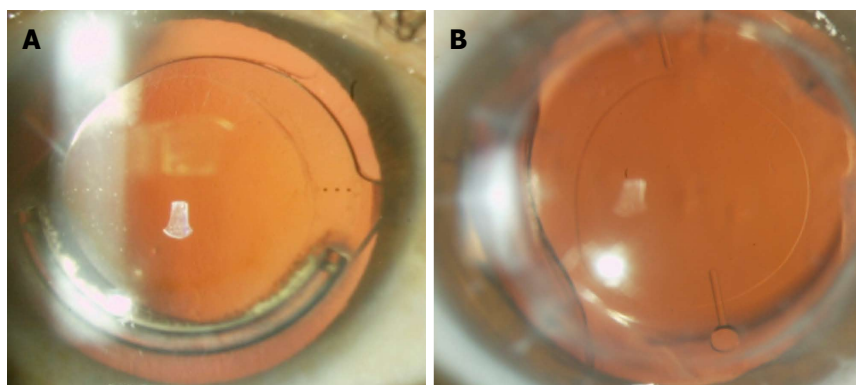


Figure 2 Combined procedures. A: Combination of intrastromal ring segments and pseudophakic toric intraocular lens; B: Pseudophakic plate toric intraocular lens following penetrating keratoplasty.

Table 2 Paraclinic criteria for diagnosis of keratoconus^[4]

Criteria	Values in keratoconus
Curvature	> 46 to 47 D
Asymmetry I-S	> 1.4 D
Irregularity	> 20 or 30 degrees with respect to the vertical meridian
Keratometric difference between the 2 eyes	> 1 D
Anterior elevation	< 15 m in Placido rings images and < 12 m in Scheimpflug images
Posterior elevation	< 35 m in Placido rings images and < 18 m in Scheimpflug images
Pachymetry	Thinnest, decentered point, difference of 100 m between center and periphery
Aphericity (Q)	Between -0.5 and < -1
Eccentricity	Approaching 1
Form factor	Approaching 0
Corneal irregularity	> 1.1-5
Medium toric keratometry	47.3-60 D
Surface irregularity index	> 1.55
Predicted corneal acuity (Holladay Report)	> 0
Keratoconus index (Maeda)	> 0
Keratoconus % index	> 100
Keratoconus prediction index	> 0.38
Surface variation index	> 41
Vertical asymmetry index	0.32
Keratoconus index	> 1.07
Central keratoconus index	> 1.03
Smallest curvature radius	> 6.71
Largest asymmetry index	> 21
Height decentration index	> 0.016
Aberration coefficient	> 1
Aberration	Vertical Coma and Coma-like RMS (> 1.5 m)
Corneal volume analysis	> 57.98 ± 2.65 mm ³
Corneal hysteresis	> 9.64 mmHg
Corneal resistance factor	> 9.6 mmHg

of the ocular surface ecosystem; BFS, Needham, MA); a device manufactured from a gas permeable polymer of fluorosilicone-acrylate with a Dk index of 85×10^{-12} mL O₂/s mL mmHg, which currently has reported 88% use success with 93% of the patients with AV > 20/40^[8].

The SynergEyes lens (SynergEyes, Inc, Carsbd, CA) is a third generation hybrid lens with a rigid gas permeable center and a “skirt” of hydrophilic material; it has the highest coefficient of oxygen diffusion of previous generations.

The use of these lenses is associated with a corrected distance visual acuity (CDVA) improvement of 85.2% of the keratoconus cases treated and a usage success rate of 86.9% of the keratoconus cases in which it was fitted^[9].

Another lens design is the personalized rigid gas permeable lens (Rose K Lens, Con-Cise Contact Lens Company, San Leandro, CA), with a 76% success rate in lens fitting^[10] and aberrometry guided scleral lens fitting, which recently have been tested for the treatment of high order aberrations in keratoconus. These lenses have proven to be effective in the correction of corneal aberrations such as vertical coma and secondary astigmatism, achieving an CDVA of 20/30 in average and corneal aberrations compatible with a corneal pattern of healthy population and low reduction of contrast sensitivity compared to conventional rigid gas permeable contact lenses^[11].

PHAKIC INTRAOCULAR LENSES

From 2003 to date, there have been increasing reports published of the use of phakic lenses as a sole or sequential procedure for the treatment of stable keratoconus. One of the firsts reports in literature was made by Lecisotti *et al.*^[12], when he reports for the first time the use of an anterior chamber phakic lens with angular support for the treatment of keratoconus. Following this, multiple studies with different types of phakic lenses (anterior and posterior chamber, toric and spherical) have been employed for the treatment of keratoconus and even for the management of residual ametropia following penetrating keratoplasty^[13].

The safety, efficacy and predictability indexes of all of the studies have demonstrated to be very suitable in cases in which the patient has been selected appropriately, in particular, adequately identifying progression and refractability; and given the case where the keratoconus is not stable, it is useful to utilize strengthening techniques such as cross-linking and placement of intrastromal rings in a simultaneous or sequential manner (Table 3).

The current criteria for the placement of a phakic lens in keratoconus takes into account a stable keratoconus, correctable refractive error due to the types of phakic lenses available, endothelial count greater than 2500 cel/mm², anterior chamber depth > 2.8 mm in cases of

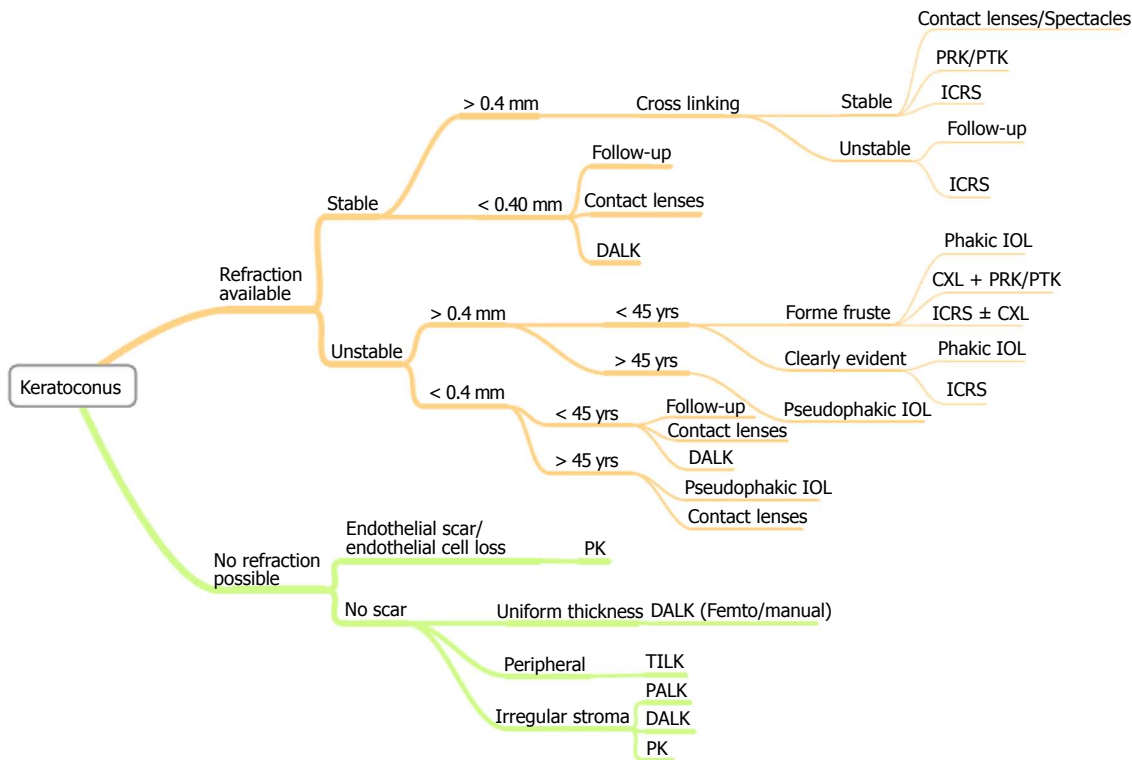


Figure 3 Proposed algorithm for keratoconus treatment. PRK: Photorefractive keratectomy; PTK: Phototherapeutic keratectomy; ICRS: Intrastromal corneal ring segments; DALK: Deep anterior lamellar keratoplasty; CXL: Corneal collagen cross-linking; IOL: Intraocular lenses; PK: Penetrating keratoplasty; TILK: "Tuck-In" lamellar keratoplasty; PALK: DALK assisted by pachymetry.

posterior chamber lenses (Figure 4), absence of uveal pathology or glaucoma.

PSEUDOPHAKIC INTRAOCULAR LENSES

The current trend for management of large ametropias in patients over 45 years old with keratoconus is the use of replacement of the crystalline lens with pseudophakic^[26] intraocular lenses (Figure 5). These options are considered specifically in this age group given the tendency for arrested progression of the keratoconus starting the fourth decade of life^[27].

Previous reports have been published by our group in 2011^[28] about this treatment option. Our experience consists of the treatment of 19 eyes of patients with keratoconus which underwent refractive lens exchange for the correction of ametropia of the compound myopic astigmatism type in stable keratoconus. The preoperative and postoperative sphere was of -5.25 ± 6.4 D and 0.22 ± 1.01 D respectively. The preoperative and postoperative cylinder was of -3.95 ± 1.3 and 1.36 ± 1.17 , with preoperative spherical equivalent of -7.10 ± 6.41 D and postoperatively of -0.46 ± 1.12 D. The preoperative UDVA was 1.35 ± 0.36 (logMAR) and postoperative of 0.29 ± 0.23 (logMAR). The procedure was safe, predictable, effective and subjectively gratifying for all of the patients^[28].

Recently, Nanavaty *et al*^[29] reported a series of 12 cases of keratoconus patients treated with a plate toric pseu-

dophakic lens implant for the management of ametropia. Their results report a UDVA of 20/40 or better in 75% of the patients and CDVA of 20/40 or better in 83.3% of the treated cases. The preoperative sphere of -4.8 ± 5.6 D was reduced to 0.3 ± 0.5 D and the cylinder decreased from 3 ± 1 D to 0.7 ± 0.8 D. None of the cases reported in both series had keratoconus progression^[29].

There are also a few reports of combined intraocular lens treatment (piggyback) for the management of residual ametropia in keratoconus patients who underwent cataract surgery either at the same time or considering sequential implant^[30].

The great advantage of this technique over the others is that it allows for the appropriate ametropia correction, caused by the keratoconus, to be made in just one procedure without the need of additional treatments and, with current techniques such as biometry through interferometry and corneal topography/tomography, the lens calculation tends to be more accurate every time^[28].

CORNEAL COLLAGEN CROSS-LINKING

The collagen crosslinking technique was first described in the 70's; however, it wasn't until 2003 that ultraviolet light A (370 nm) combined with riboflavin for the strengthening of the corneal collagen fibers in human eyes was used to stop keratoconus progression^[31].

Since then, numerous studies have been published

Table 3 Phakic intraocular lenses for keratoconus studies

Ref.	Criteria	Lens	Preoperative	Postoperative	P-value
Leccisotti <i>et al</i> ^[12]	12 eyes. KC I y II	Angular supported, spherical	Sphere -10.23 ± 2.85 D Cyl -2.79 ± 1.11 D CDVA 0.13 ± 0.17	Sph 0.46 ± 0.45 D Cyl -2.35 ± 1 D UCVA 0.44 ± 0.8 CDVA 0.03 ± 0.05	0.002
Alfonso <i>et al</i> ^[14]	25 eyes	Posterior chamber, spherical	Sph -8.54 ± 4.15 D Cyl -1.24 ± 1.19 D CDVA 0.13 ± 0.15	Sph 0.0 ± 0.25 D Cyl -0.45 ± 0.73 D SE -0.32 ± 0.55 D UCVA 0.17 ± 0.19 CDVA 0.12±0.12	< 0.05
Venter <i>et al</i> ^[15]	18 eyes	Iris supported, toric/spherical	Sph -4.64 ± 2.74 D Cyl -3.07 ± 2.04 D CDVA ≥0.5	SE -0.46 ± 0.6 D UDVA ≥ 0.2 en 94%	< 0.05
Alfonso <i>et al</i> ^[16]	30 eyes	Posterior chamber, toric	SE -5.38 ± 3.26 D Cyl -3.48 ± 1.24 D UDVA 0.8 logMar CDVA 0.10	SE -0.08 ± 0.37 D Cyl 0.41 ± 0.61 D UDVA 0.10 logMar CDVA 0.10	
Kamiya <i>et al</i> ^[17]	27 eyes, mild KC	Posterior chamber, toric	SE -10.11 ± 2.46 D Cyl -3.03 ± 1.58 D UCVA 1.51 ± 0.2 CDVA -0.11 ± 0.08	SE 0.00 ± 0.35 D UCVA -0.09 ± 0.16 CDVA -0.15 ± 0.09	
Sedaghat <i>et al</i> ^[18]	16 eyes,	Anterior chamber, iris supported	Sph -12.5 ± 4.61 D Cyl 2.95 ± 4.06 D SE -13.9 ± 4.61 D UDVA CF CDVA 0.21 ± 0.14	Sph -0.03±1.81 D Cyl 2.08 ± 1.04 D UDVA 0.15 ± 0.13 CDVA 0.11 ± 0.1	< 0.0001
Kato <i>et al</i> ^[19]	36 eyes	Iris supported, toric, spherical	SE -8.38 ± 3.42 D Cyl 2.44 ± 2.25 D UDVA 1.39 ± 0.42	SE -0.42 ± 0.89 D Cyl 0.62 ± 0.69 D UDVA 0.02 ± 0.21	
Hashemian <i>et al</i> ^[20]	22 eyes	ICL toric	SE -4.98 ± 2.63 D Cyl -2.77 ± 0.99 D UDVA 0.63 ± 0.2 dec.	SE -0.33 ± 0.51 D Cyl -1.23 ± 0.65 D UDVA 0.85 ± 0.21 dec.	
Combined procedures Moshirfar <i>et al</i> ^[21]	19 eyes	Intacs/verisyse, sequential vs simultaneous	SE -12.38 ± 4.2 D Cyl 3.3 ± 1.8 D UCVA 2.025 ± 0.32 CDVA 0.34 ± 0.22	SE -1.2 ± 1.15 D Cyl 2.06 ± 1.1 D UCVA 0.465 ± 0.18 CDVA 0.15 ± 0.09	No difference regarding sequential vs simultaneous
Izquierdo <i>et al</i> ^[22]	11 eyes Progressive KC I and II	Crosslinking/verisyse	Sph -5.7 D Cyl -1.45 D SE -6.42 D UDVA 1.4 ± 0.4 CDVA 0.14 ± 0.06	Sph -0.27 D Cyl -0.9 D SE -0.72 D UDVA 0.16 ± 0.06 CDVA 0.04 ± 0.05	< 0.05
Alfonso <i>et al</i> ^[23]	40 eyes	Keraring/ICL	SE -9.65 ± 6.9 D UDVA 1.0 CDVA 0.3	SE -1.2 ± 1.3 D UDVA 0.3 CDVA 0.18	
Güell <i>et al</i> ^[24]	17 eyes Progressive KC I and II	Crosslinking and toric artiflex/artisan	SE -6.99 ± 3.2 D Cyl -3.54 ± 1.38 D UDVA < 1 CDVA 0.1 ± 0.09	SE -0.22 ± 0.33 D Cyl -0.62 ± 0.39 D 0.17 ± 0.13 CDVA 0.10 ± 0.09	
Navas <i>et al</i> ^[25]	11 eyes KC I -IV	ICRS and toric and spherical ICL	Sph -9.04 ± 6.03 D Cyl -2.95 ± 1.35 D SE -10.52 ± 5.88 D UDVA 1.31 ± 0.37 CDVA 0.289 ± 0.14	Sph -0.06 ± 0.46 D Cyl -1.22 ± 0.65 D SE -0.68 ± 0.45 D UDVA 0.14 ± 0.04 CDVA 0.16 ± 0.08	< 0.01

CDVA: Corrected distance visual acuity; UDVA: Uncorrected distance visual acuity; ICRS: Intrastromal corneal ring segments.

about the effect of UVA light on keratoconus. It is known that the more meaningful effects are the progression halt of the keratoconus and in some reports there's also mention of its regression on an average of 2 D (from 1 to 4)^[32,33].

At this moment, the long term effects of the imple-

mentation of this procedure are still unknown, with minimal or inexistent adverse effects being described in many of the cases with longer follow ups^[32,33]. Some publications report a central haze, which tends to resolve itself with time, as the main complication and that it is more evident when performing a corneal^[34] densitometry,

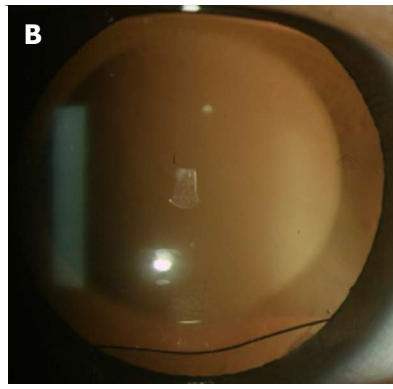
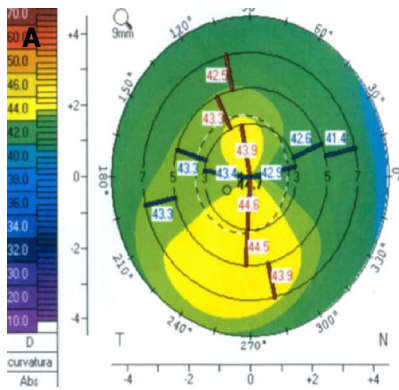


Figure 4 Phakic toric intraocular lens implantation in (A) forme fruste keratoconus case, (B) notice the rhomboidal marks of the lens toricity axis.

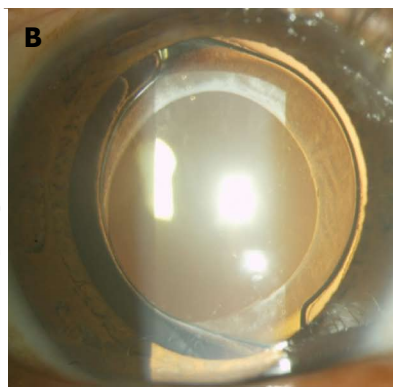
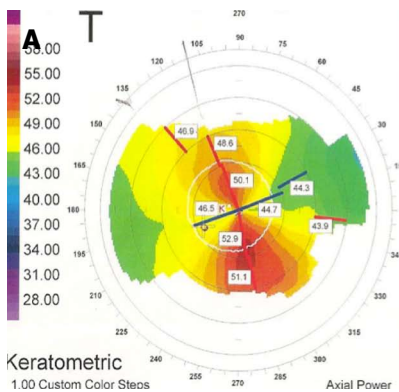


Figure 5 Pseudophakic toric intraocular lens in (A) frank keratoconus, (B) notice the three dot marks for toric intraocular lenses alignment.

remaining in up to 8.6%^[35]. Up to now, in the majority of the studies done, no significant endothelial cell loss has been reported^[36], but recently it has been identified that the pre-operative corneal thickness > 400 microns is an important factor which determines the absence of CXL effects on the endothelium^[37]. Through confocal microscopy it has been identified that during early phases of the scarring process some changes occurs such as a hyper-reflective phenomenon in the collagen fibers of the medial to posterior stroma^[36], as well as epithelial thinning, stromal edema and keratocytes apoptosis in the first 4 to 6 wk. Subsequently, an epithelial thickness and collagen compaction occurs^[38].

Today, the more widely accepted criteria to perform a corneal crosslinking include patients with topographic evidence of keratoconus progression, corneal thickness > 400 microns and keratoconus without deep stromal scarring or history of corneal hydrops. Numerous modifications have been developed to the technique, amongst which we have the transepithelial crosslinking and accelerated cross-linking (Figure 6) for the optimized effect on experimental models^[39-41].

EXCIMER LASER

Until a few years ago, the keratoconus or its fruste form was considered a total contraindication to keratorefractive surgery with excimer laser. Recently, these techniques have been utilized in the treatment of patients with fruste keratoconus or its mild forms with satisfactory visual results. Currently, there have been results of photorefrac-

tive keratectomy with and without being combined with crosslinking as an adjunctive treatment in the management of ametropia secondary to keratoconus.

The advantage of this technique is that it does not need the creation of an epithelial/stromal flap; this way, performing the ablation immediate to the ocular surface, the structural loss associated to LASIK is prevented, which has proven to be a factor related to ectasia progression in keratoconus. This technique is ideal for the treatment of small ametropias, such that it is not recommended for large ablations (ideally, less than 50 microns) given the possibility of postoperative haze. It is important to be cautious considering that there are reports of ectasia even when employing this technique^[42]. In regards to this technique, Bilgihan *et al*^[43] and Bahar *et al*^[44] have reported an improvement UDVA in fruste keratoconus patients treated with PRK. During the follow up period they don't report keratoconus progression. Based on these results, the authors conclude that photorefractive keratectomy seems to be a safe strategy on eyes suspected of having frank keratoconus. Recently, Guedj *et al*^[45] have reported follow up of keratoconus suspects treated with PRK, where they demonstrate lack of ectasia progression in any of their 62 eyes at 5 year follow up, considering an average refractive sphere error of -3.48 ± 3.14 D and cylinder -0.97 ± 0.92 D.

The combination of PRK with crosslinking has been a most utilized strategy and, in these cases, the criteria for its application has to do with the residual stromal bed posterior to ablation, which ideally should be greater than 400 microns. The techniques that combine these proce-

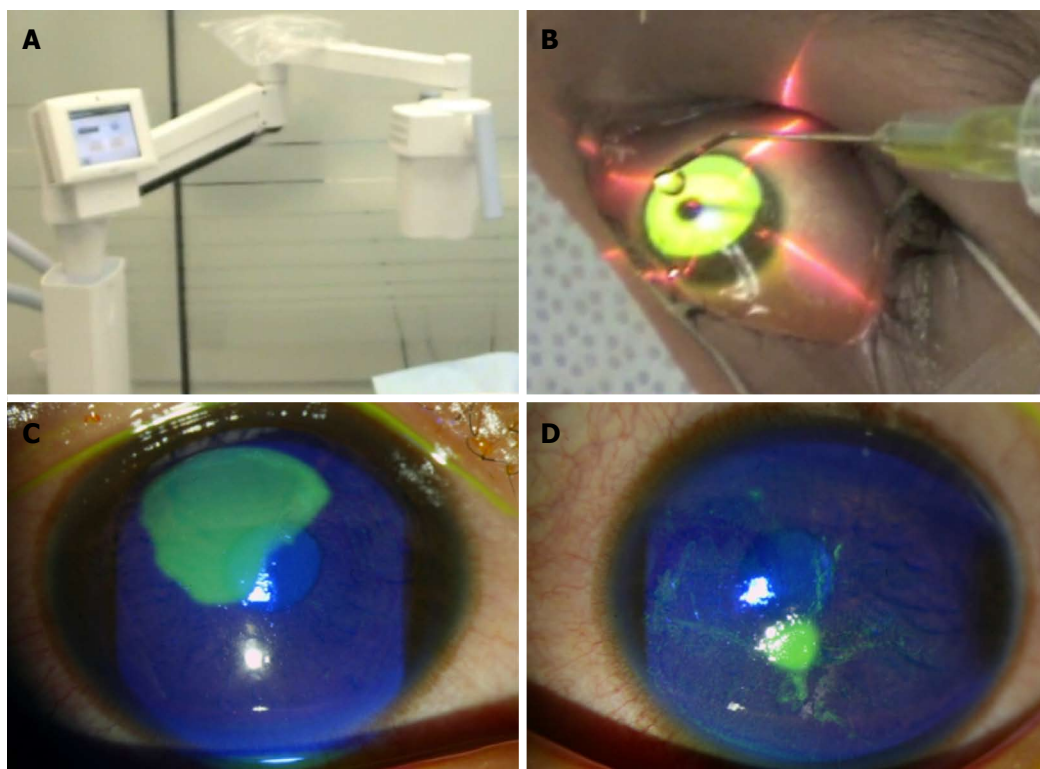


Figure 6 Collagen cross-linking. A, B: Accelerated corneal collagen cross-linking (A) equipment (B) and riboflavin instillation, collagen cross-linking (CXL) treatment could be decreased to 3 min with Ultraviolet-light intensity of 30 mW/cm^2 achieving the same energy on cornea of conventional CXL of 5 J/cm^2 ; C: Right eye three days after accelerated cross-linking showing corneal epithelium recovery; D: Left eye also after three days following accelerated CXL.

dures can be sequential or be applied in the same surgical time and, in the majority of the reports, the combination of these techniques are associated with a significant improvement in respect to UDVA, improvement in keratometries and ceasement of keratoconus progression^[46-48].

However, laser treatment experiences in keratoconus must be taken with caution because of the few reports and short term follow-up reported until now in the literature. Our knowledge about the progression in this kind of cases is still poor and the risk-benefit ratio in low ametropia treatment must be taken in consideration.

INTRASTROMAL RING SEGMENTS

Intrastromal segments are manufactured of polymethyl methacrylate (PMMA) and were initially utilized for the treatment of myopia and astigmatism^[5] (Figure 7). Recent studies have reported the effective use in the treatment of keratoconus and currently its stabilizing effect on ectasia is still controversial^[49-51]. There are 5 models available, each with variations in their curvature radius, thickness and arc longitude, according to the effect to be achieved: (1) Ferrara rings (Mediphacos Inc, Belo Horizonte, Brazil); (2) Bisantis segments (Opticon 2000 SpA and Soleko SpA, Rome, Italy); (3) Intrastromal rings, Intacs (Addition Technology, Fremont, California, United States); (4) Myoring (Dioptex, GmbH, Austria); and (5) Cornealring (Visiontech Medical Optics, Belo Horizonte, Brazil). This technology is ideal for use in patients with central

corneal thickness over 400 microns and clear central cornea^[49]. For their placement it is important to consider the algorithm designed for each one of the manufacturing companies to obtain the optimum effect given that such effect tends to be somewhat unpredictable^[52]. In 1991, the first intrastromal segment implant on human eyes was done^[53] and, through time, numerous studies have been published about the refractive results of this technology^[49-56]. The majority of the authors concur that the refractive result that is obtained with the rings is better in patients with keratoconus of I and II Amsler Krumeich degree and refraction with a low spherical equivalent in which myopia is less than the astigmatism; additionally, the refractive effect tends to remain in time but not the case of the corneal curvature effect, which tends to present regression^[50].

Alió *et al*^[56] has described that in keratometries $> 53 \text{ D}$ an optimal visual effect was not observed. In the treatment of fruste keratoconus, with spherical equivalent of -4.5 D , Güell *et al*^[57] report at 4 year follow up, UDVA and CDVA improvement with 82.05% of eyes within a $\pm 1 \text{ D}$ refraction in range of emmetropia without showing progression of keratoconus during the follow up period.

The channels for the insertion of the segments can be created mechanically or with a femtosecond laser. The most common complications associated with the mechanical dissection are: epithelial defects on the insertion site, anterior and posterior perforations, inadequate depth placement of the ring, extrusion, infectious keratitis, stro-

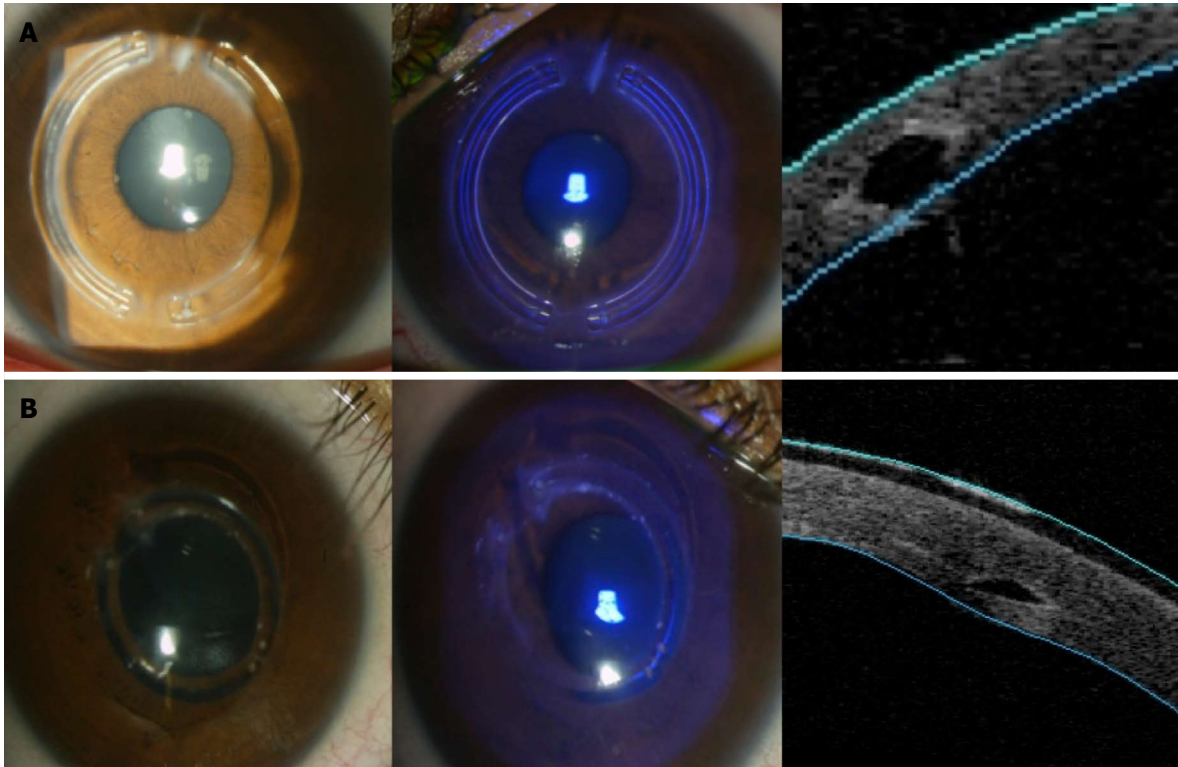


Figure 7 Different intrastromal ring segments models (A) clinical and optical coherence tomography showing hexagonal shape and (B) another design with triangular shape.

mal thinning, stromal edema, intraepithelial growth in the tunnel, corneal melting and tunnel vascularization^[58-61]. The use of the femtosecond laser reduces the risk of complications in the creation of the tunnels, however it has been reported that the main complication with this technique is the incomplete formation of the tunnel (up to 2.7% of the cases), among those cited previously for the manual technique^[62]. Recently, the combined technique of intrastromal segments and crosslinking has been used sequentially with the purpose of attaining stability in cases of progressive keratoconus, nevertheless, no long term favorable results have been reported for this trend^[63,64].

KERATOPLASTY

The first keratoplasty reports in history were in 1840 by Franz Mùhlbauer, who described a technique of triangular grafts to perform the first anterior lamellar keratoplasty. However, these early efforts to perform corneal grafts were not successful. The penetrating transplant was considered the treatment of choice for keratoconus for many decades; nevertheless, one of the principal disadvantages has to do with the risk of immunological rejection which can occur in up to 20% of the patients with good prognosis, such as the case of keratoconus^[65]. This technique continues to be the treatment of choice when there are endothelial scars (secondary scars to hydrops) or low receptor endothelial cell count.

The current tendency in keratoplasty is to preserve the receptor's endothelium with the objective of avoid-

ing the risk of endothelial rejection, which is normally a conditional for graft failure^[66]. The advantages of the lamellar techniques over the penetrating keratoplasty are that these techniques have lower recuperative time periods, earlier management of astigmatism and sutures and lower incidence of post-operative glaucoma and graft rejection^[67].

In recent years, multiple more advanced and reproducible surgical techniques have been developed to achieve this objective. Currently there are techniques based on manual and automated dissection of the donor and receptor graft (microkeratome, femtosecond laser and excimer laser) to obtain lamellar transplants at different depths depending on the treatment expected outcome^[68-70].

The most frequently used techniques are the techniques of manual dissection, due to the little additional material required in terms of that used in a penetrating keratoplasty^[66]; within this category we have Melles'^[71] water and air dissection technique, the big-bubble dissection technique^[72], divide and conquer technique and Anwar's^[73] visco-dissection technique. Unfortunately, the great majority of these techniques require specially advanced surgical skills, given that the conversion rate to penetrating keratoplasty can be up to 40% in inexperienced hands and 2% to 6% in experienced surgeons^[74].

Perhaps the most important limitations of the lamellar techniques continue to be the irregular borders of the corneal surface dissection that are obtained through manual technique, also the endothelial folds that are con-



Figure 8 Femtosecond anterior lamellar keratoplasty, upper image showing the clinical photograph and lower image optical coherence tomography showing the residual stromal and endothelial tissue of around 50 microns.

ditioned by structural alterations of the receptor cornea in its posterior or more internal section (determined by the anterior and posterior curvature of the treated patient). Another of the limitations is the CDVA that patients reach that, although it's true that have lower post-surgical astigmatism than the PKP patients, CDVA, high order aberrations and contrast sensibility are similar to the penetrating technique^[75].

One of the new trends is to use the femtosecond laser (Figure 8) to perform a tissular disruption at predetermined depths by the surgeon and this way can be more precise in the graft dissection to be placed as well as the receptor with the aim of achieving better visual results. However, the reported short term results have not been able to overcome the penetrating technique^[76].

The deep anterior lamellar transplant assisted by pachymetry (PALK) was described by Carriazo *et al.*^[77] in 2007. The purpose of this technique is to perform a photoblation with an excimer laser guided by topography and pachymetry of 95% of the stromal surface in a way that more regular cuts can be made at specific diameters without observing adverse perforation effects of the Descemet membrane. The initial visual results are similar to the reported by other techniques of lamellar keratoplasty and not superior in visual quantity or quality to the penetrating keratoplasty; nevertheless, showing improvement in terms of recuperation periods, post-surgical astigmatism and the use of pharmaceuticals and the suture management in the post-operative period. This same technique has recently been reported by Spadea *et al.*^[78], obtaining 20/40 CDVA at 2 years in 89% of the patients in that series.

CONCLUSION

Keratoconus continues to be one of the most frequent corneal pathologies worldwide, being one of the primary causes of corneal blindness. Its early detection is essential and each day there are more complex and improved resources/equipment for its detection. The historic

evolution, in terms of treatments, has currently supplied us with many resources for its management, which can provide gratifying visual results for the patient and are ideal in terms of surgical techniques and lower complication rates. In order to be able to choose one of the treatments previously set out, it's important to consider the main outcome objectives for the desired treatment and the patient expectations regarding their visual rehabilitation. In the future, surely new treatment techniques will have scientific foundations in molecular mechanisms which can halt the initial onset of ectasia.

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Volume End





Contents

Quarterly Volume 3 Number 4 November 12, 2013

MINIREVIEWS

- 32 Melatonin and derivatives as promising tools for glaucoma treatment
Alkozi HA, Pintor J

CASE REPORT

- 38 Multifocal granulomata in presumed *Toxocara canis* infection in adult
Kuniyal L, Biswas J

Contents

World Journal of Ophthalmology
Volume 3 Number 4 November 12, 2013

APPENDIX I-V Instructions to authors

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Melatonin and derivatives as promising tools for glaucoma treatment

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Core tip: This mini review depicts the main features of melatonin and derivatives as interesting agents for the treatment of the ocular hypertension associated with glaucoma.

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Abstract

Neurohormones melatonin and its analogues are present with an important physiological and pharmacological ability to reduce intraocular pressure (IOP); thus, they are suitable for the treatment of ocular hypertension often associated with glaucoma. It is demonstrated that two of its analogues, 5-MCA-NAT and IIK7, are more effective than melatonin to reduce IOP for a longer period of time. The research for the discovery of better compounds resulted in the development of newer and improved analogues compared to 5-MCA-NAT and IIK7. Furthermore, already commercially available drugs currently used as treatment for other pathologies, presenting a resemblance to the melatonin structure, are being tested as potential glaucoma drugs. In this sense, agomelatine, which is already used as an anti-depressant medicine, is recognized as a worthy candidate since it reduces IOP, even under hypertensive conditions. To sum up, the use of melatonin and its analogues as promising anti-glaucomatous substances is of great importance and should be given serious consideration.

INTRODUCTION

There is a general interest in searching for novel compounds capable of reducing intraocular pressure (IOP) as an improved alternative to the existing drugs. IOP can be lowered through the reduction of aqueous humor production or by increasing its outflow through the trabecular meshwork or uveoscleral pathways. The interest for searching for new compounds relies on the fact that most of the existing drugs produce important side effects, hampering the treatment of certain patients. Side effects are a common issue in glaucoma medications. β -blockers such as timolol can cause bradycardia and hypotension and they are unsuitable for patients suffering from cardiovascular problems^[1], asthma, obstructive pulmonary disease or corneal dystrophy^[2]. Cholinergic agonists such as pilocarpine produce fixed pupils and induce myopia and cataracts^[1], whereas prostaglandins (*e.g.*, latanoprost) cause eyelash growth, iris pigmentation^[3], muscle and joint pain^[2]. Frequently, ocular redness and ocular surface discomfort obligates patients to abandon the treatment.

Several new compounds and approaches are under development in companies' pipelines or in academic institutions. Among the plethora of substances, the naturally occurring are more attractive as its administration is expected to result in fewer side effects^[4]. Among these, the neurohormone melatonin emerges as a promising substance with interesting hypotensive properties^[5]. The use of 5-MCA-NAT (a melatonin analogue, see below) when applied to the eye does not produce severe side effects. It does not affect corneal and lens transparency nor cause redness or corneal edema. No negative effects were noticed in general ocular examinations^[5]. It is important to bear in mind that most of melatonin intake is not by prescription as it is considered a dietetic supplement. In this case, high dosages and an elevated number of intakes could produce some minor side effects. The Mayo Clinic indicates that the most common side effects are drowsiness, headache and dizziness. Moreover, large doses of melatonin can interfere with some medications, such as anticoagulants, immunosuppressants, diabetes medications and birth control pills.

There are two interesting works describing the melatonin effect and its analogues on reducing IOP. Serle *et al.*^[6] demonstrated that a melatonin analogue was able to reduce IOP in glaucomatous monkeys, suggesting these molecules as a possible treatment of ocular hypertension related to glaucoma. Additionally, a group of ophthalmologists started to use melatonin during cataract surgery because it reduces IOP substantially, which is recommendable during phacoemulsification^[7].

From these two relevant works, the question arises as why these groups decided to use melatonin and its analogues for clinical purposes and mainly for reducing IOP. The present mini review introduces the reader to the basis of why melatonin is an attractive molecule to reduce IOP and why it should be considered in the future as a respectable alternative to the current ocular hypertension and glaucoma therapies.

MELATONIN, MORE THAN A PINEAL GLAND HORMONE

Melatonin is a molecule known by its chemical name N-acetyl-5-methoxytryptamine (Figure 1). It has been traditionally related to a particular area of brain, termed the pineal gland, where it is synthesized in low illumination conditions like during the night^[8] and it regulates many day-night processes, called circadian rhythms^[9]. It is necessary to emphasize that this substance is also synthesized in other tissues and ocular structures such as the retina, the ciliary body or the lens. This clearly suggests that melatonin can exert some local actions on the tissues where it is synthesized or in surrounding areas. Keeping in mind that melatonin is released by the lens or the ciliary body, its presence in the aqueous humor, modifying the physiology of these structures being bathed in the fluid, can be speculated about. Interestingly, one of the possible physiological processes to be modified is IOP.

It is documented that in many animal models there are changes in IOP during the day (high IOP) and night (low IOP). It is possible that both processes are associated considering the circadian pattern of melatonin production. Consequently, we should study what happens if we topically apply melatonin during the day when IOP is high.

MELATONIN REGULATES INTRAOCULAR PRESSURE

When melatonin is topically applied at a single dose of 100 $\mu\text{mol/L}$ in a volume of 10 μL , there is a transient reduction in IOP and values return quickly to initial figures in about 2 h^[10]. This effect is similar to that of endogenous melatonin at night which reduces IOP. Despite the acquired hypotensive effect, the rapid return to normal pressure values suggests that either it is necessary to regulate the doses or to look for an alternative compound to produce a more sustained effect^[11].

There are several commercially available melatonin analogues depicting similar behavior to melatonin. Two compounds present sharper and long lasting effects on reducing the IOP compared to melatonin. In particular, the compound N-butanoyl-2-2-methoxy-6H-isindolo ([2,1-a]indol-11-yl) ethanamine (abbreviated as IIK7) has a hypotensive effect that lasts up to 7 hours and the compound 5-methylcarboxyamino-N-acetyltryptamine (also known as 5-MCA-NAT), which can reduce IOP for up to 9 h (Figure 1)^[12]. Consequently, 5-MCA-NAT is more interesting since it presents a longer term effect with a significant reduction of IOP for up to 96 h. This remarkable effect has been taken into consideration as we indicate below^[11] (Table 1).

5-MCA-NAT was tested in normotensive models as well as under hypertensive conditions, including glaucomatous monkeys (Table 1). Interestingly, the effects on the monkeys, a model closer to the human glaucomatous pathology, were extremely interesting. Compared to vehicle treatment, twice daily administration of 5-MCA-NAT for 5 d reduced IOP from 1 to 5 h after the first dose and the IOP-lowering effects were shown to last at least 18 h following administration, based on IOP measurements made after the fourth and eighth doses^[6].

One interesting characteristic to take into account was that the ocular hypotensive effect of 5-MCA-NAT was enhanced by repeated dosing. The maximum reduction of IOP was acquired 3 h after each morning dose and was 10% on day 1, 15% on day 3, and 19% on day 5 (control = 100%). No adverse ocular or systemic side effects were observed during the 5 treatment days, suggesting that this compound could be used perfectly as ocular hypertension treatment^[6] (Table 1).

IIK7 reduced intraocular pressure by acting through MT₂ melatonin receptors, presumably decreasing aqueous humor formation. Its effect is concentration dependent and it can reduce IOP 38.5% \pm 3.2% when compared to controls (Table 1). It is important to notice that these

Table 1 Hypotensive effects of melatonin analogues: animal models, conditions and receptors involved

Compound species	IOP reduction	Receptor involved	Ref.
Melatonin			
Human	32.0% ± 3.2%	Unknown	[7]
Rabbit	22.0% ± 1.6%	MT ₂ , MT ₃	[10,11]
Mouse (glaucomatous)	33.4% ± 2.5%	MT ₂	UD
5-MCA-NAT			
Monkey (hypertensive)	19.2% ± 2.1%	MT ₃	[6]
Rabbit	42.5% ± 1.6%	MT ₃	[10,11]
IIK7			
Rabbit	38.5% ± 3.2%	MT ₂	[12]
INS48848			
Rabbit	36.0% ± 2.0%	MT ₃	[22]
INS48852			
Rabbit	33.1% ± 1.4%	MT ₂	[22]
INS48862			
Rabbit	26.0 V ± 1.3 V	MT ₂	[22]
Agomelatine			
Rabbit			
Normotensive	20.8% ± 1.4%	MT ₂	[25]
Hypertensive	68.8% ± 5.7%	MT ₂	[25]

The values represent the mean ± SEM for the indicated compounds in the respective animal model. IOP: Intraocular pressure; UD: Unpublished data.

experiments have not been performed in glaucomatous monkeys yet but only in rabbits^[12].

In summary, it seems that some compounds, such as melatonin, 5-MCA-NAT and IIK7, clearly reduce IOP. But what is the mechanism for this IOP reduction? What receptors activate these substances in order to produce the observed effects?

MELATONIN AND ITS ANALOGUES ACTIVATE MELATONIN RECEPTORS

Melatonin exerts its effect *via* membrane and nuclear receptors. The protein membrane receptors are better understood and until recently three proteins have been cloned. Two of these membrane receptors, termed MT₁ and MT₂, are melatonin receptors belonging to the 7-transmembrane G protein-coupled receptor family (GPCR). There have been claims that a third receptor exists, the MT₃ melatonin receptor, although it has not been cloned yet. Some authors have identified it as quinone reductase 2 (QR2), demonstrating features of a melatonin receptor in some animal models (for a review see^[9]).

MT₁, MT₂ and the probable MT₃ melatonin receptors are present in several ocular structures, according to pharmacological, biochemical and immunological studies^[13,14]. This evidence suggests that melatonin plays a role in physiological processes in ocular tissues, such as the modulation of IOP, and it has been documented that MT₂ and MT₃ are responsible for IOP reduction.

When melatonin, 5-MCA-NAT and IIK7 are applied to normotensive or hypertensive eyes, they produce a dissimilar IOP reduction, depending on the compound

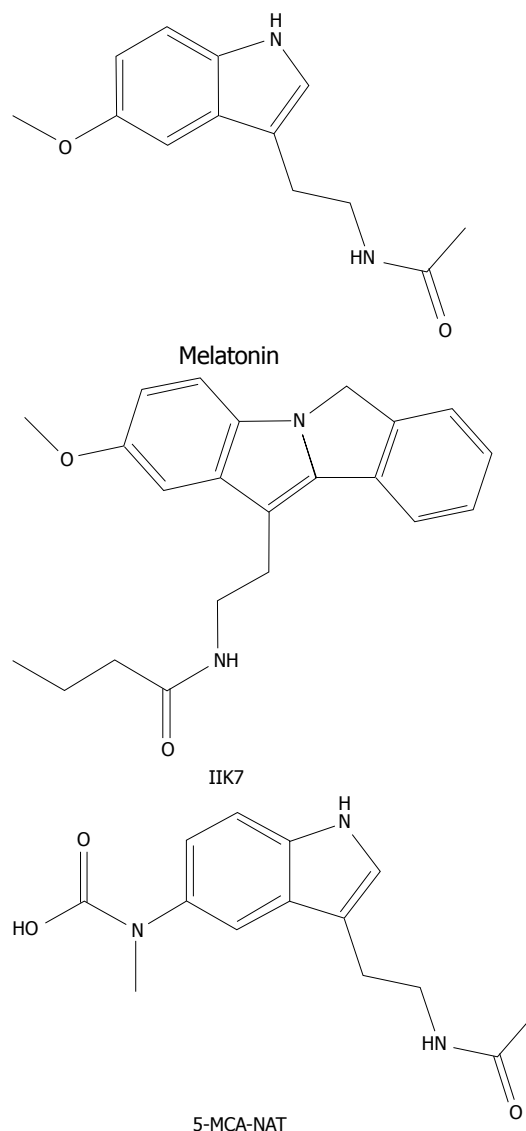


Figure 1 Chemical structure of melatonin and analogues. Melatonin (N-acetyl-5-methoxytryptamine), IIK7 (N-butanoyl-2-(2-methoxy-6H-isoindolo[2,1-a]indol-11-yl)ethanamine) and 5-MCA-NAT (5-methylcarboxyamino-N-acetyltryptamine).

under study. The use of selective antagonists for melatonin receptors has allowed identification of the presence of MT₂ melatonin receptors in the ciliary body of experimental animals, such as New Zealand white rabbits. This has been confirmed through immunohistochemical studies. In these studies it has been possible to verify the presence of MT₂ melatonin receptors on pigmented and non-pigmented ciliary epithelia. Accordingly, the application of melatonin or IIK7, which is a selective MT₂ agonist, results in a reduction in the production of the aqueous humor^[12] (Figure 2).

5-MCA-NAT has been suggested as an MT₃ melatonin receptor agonist that reduces IOP. To date, the location of the receptor is unknown. As there is a controversy with the possible identification of the MT₃ receptor which is tentatively identified in some animal models as QR2, some sophisticated experiments were performed to

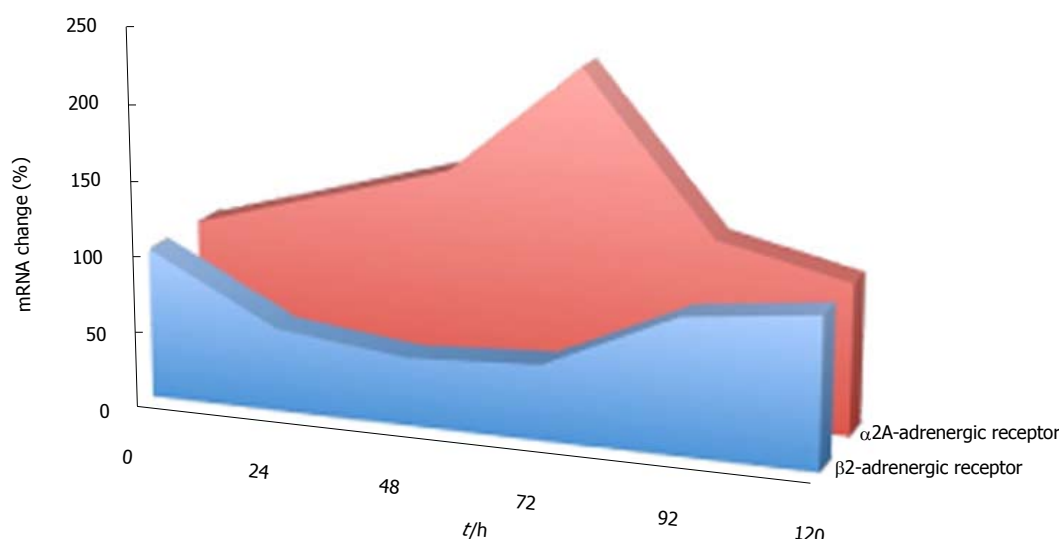


Figure 2 Expression of mRNA levels in ciliary body cells. The amounts of mRNA and concomitant adrenoceptors were changed after the application of 5-MCA-NAT. While there was an increase of α 2A-adrenoreceptors (in red), there was a decrease in the levels of β 2-adrenoreceptors (in blue).

clarify the issue^[15-17]. In New Zealand rabbits, the use of a siRNA silencing QR₂ (therefore avoiding the expression of this enzyme) did not abolish the hypotensive effect of 5-MCA-NAT, clearly indicating that, in this animal model, MT₃ \neq QR₂, opening the possibility of speculating about the existence of a receptor that needs to be cloned to fully understand its functioning and location^[18].

Apart from melatonin and its derivatives, some other compounds, like 5-MCA-NAT, can keep IOP below normal values for up to 5 d. This long-term effect is mediated by the action of melatonin receptors on the expression of genes expressing proteins important for the homeostasis of the aqueous humor.

To date, it has been possible to demonstrate that the 5-MCA-NAT long-term effect is in part the result of the expression inhibition of carbonic anhydrases. This down-regulation means that 24 h after 5-MCA-NAT application there is a reduction in IOP because the amounts of carbonic anhydrases are severely reduced. In particular, when 5-MCA-NAT is applied, carbonic anhydrase 2 is reduced 32% (protein levels), while carbonic anhydrase 12 is reduced 39% (protein levels). This reduction in protein expression mimics the carbonic anhydrase inhibitor action, such as dorzolamide or acetazolamide^[19].

Likewise, the expression of adrenergic receptors is modified by the application of 5-MCA-NAT. Interestingly, this melatonin analogue is able to produce a sequential process consisting of an initial reduction in the β 2-adrenoreceptors expression, followed by an increase in α 2A-adrenoreceptors^[20]. Altogether, these consecutive effects produce a sustained reduction in IOP lasting for at least 96 h^[21].

In summary, 5-MCA-NAT, apart from a sharp hypotensive effect, exerts a long term effect, maintaining low IOP for 4 d.

SO, WHAT IS NEXT NOW?

Several aspects need to be studied, taking into account that melatonin and analogues can significantly reduce IOP.

It is clear that it is necessary to research and design new melatonin analogues with more profound and long lasting effects^[5]. Inspire Pharmaceuticals Inc. (now absorbed by Merck) has designed several melatonin analogues with interesting hypotensive properties to reduce IOP. In recent studies, melatonin analogues, termed INS48848, INS48852 and INS48862, demonstrated similar behavior to melatonin, 5-MCA-NAT and IIK7^[22]. Indeed, these three compounds decreased IOP in a dose-dependent manner similar to melatonin, 5-MCA-NAT and IIK7, confirming their efficiency in decreasing IOP (Table 1). Concerning their selectivity on melatonin receptors, the effects of INS48848 were completely blocked by prazosin, an antagonist of MT₃ melatonin receptors, and were potently inhibited by luzindole, a non-selective antagonist of melatonin receptors. However, DH97, a selective MT₂ receptor antagonist, had a limited effect against INS48848 and the results obtained from INS48862 and INS48852 were contradictory. Luzindole and prazosin had no significant effects against those two compounds, whereas DH97 blocked them completely. These results strongly suggest that INS48848 could be acting through the MT₃ melatonin receptors and that INS48862 and INS48852 could be acting preferentially through MT₂ melatonin receptors. In any case, all these compounds are worthy candidates to reduce IOP, especially when it is abnormally elevated^[22].

Another alternative to the development of newly synthesized compounds is to search for melatonergic compounds already used for other medical purposes. Compounds such as ramelteon ((S)-N-[2-(1,6,7,8-tetrahyd-

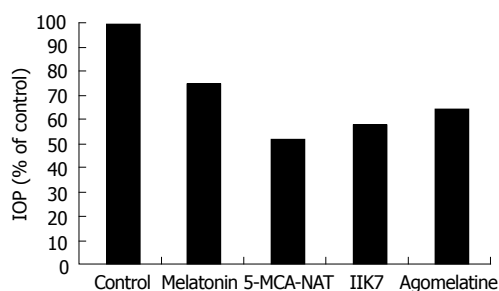


Figure 3 Comparative effects of melatonin and analogues in an animal model. Equal doses of melatonin or the corresponding analogues (100 μ mol/L, 10 μ L), reduced intraocular pressure in New Zealand white rabbits. Differences among the compounds rely on the activation of different receptors in each case (see text).

ro-2H-indeno-[5,4-b]furan-8-yl)ethyl]propionamide), also known as *Rozzerem*, used for sleep disorders^[23] or agomelatine (N-[2-(7-methoxynaphthalen-1-yl)ethyl]acetamide), known also by the names *Valdoxan*, *Melitor*, *Thymanax*^[24], used for the treatment of depression, could be candidates to reduce IOP since their structure is similar to melatonin.

There is a lack of information regarding the use of ramelteon in IOP studies. Agomelatine significantly reduces IOP when topically applied on rabbit eyes. Agomelatine (10 μ L, 100 μ mol/L) reduced IOP by $20.8\% \pm 1.4\%$ and its maximal IOP reduction was 180 minutes after the compound application. Interestingly, this compound exhibited an ability to reduce IOP in hypertensive conditions. It is noteworthy to stress that under high IOP the ability of this melatonin analogue to reduce IOP was $68.8\% \pm 5.7\%$ (Figure 3, Table 1)^[25].

There is a clear advantage in using compounds already commercialised for other conditions as the timeline for testing and clinical trials is significantly reduced.

CONCLUSION

It is necessary to perform an exhaustive study on the role of melatonin and its analogues in the different ocular structures since it is very probable that this knowledge will contribute to the discovery of more effective treatments for pathologies like glaucoma, corneal wound healing, cataracts or retinal pathology^[26].

Taking into account the importance of the role of melatonin and its analogues in hypertension, often associated with glaucoma, it is quite evident that these compounds should be used as treatment to reduce IOP. Melatonin or agomelatine can simply and rapidly reduce IOP, although further research is required to prove that they can be safely used as treatment for ocular hypertension.

Most of the presented data resulted from experiments assaying melatonin or its analogues on animal models. We still have a long way to go to test these compounds on human beings. Nevertheless, there are a lot of positive points regarding the efficacy of certain melatonin-ergic compounds. For instance, melatonin itself is able to reduce IOP in normotensive humans, as previously described^[7]. These authors reported an approximate

30% reduction in IOP during cataract surgery compared to the initial patient's pressures. This is quite interesting because the IOP reduction has been obtained in normotensive patients and it could be even more substantial in hypertensive (glaucomatous) patients. Several experiments in animal models demonstrated that melatonin and analogues are able to reduce IOP equally in normotensive and hypertensive animals, being more effective in hypertensive than in normotensive animals (Table 1). Also, experiments performed with 5-MCA-NAT on hypertensive monkeys, a step before human clinical trials, have proved that this melatonin analogue reduced IOP.

In conclusion, agomelatine is the compound that we strongly believe should be tested in glaucomatous patients for its ability to reduce IOP. Agomelatine is already used as a depression treatment drug under the commercial name Valdoxan^[24]. Since many of the pre-clinical tests have already been completed, we should not be surprised if agomelatine clinical trials start and it becomes the first melatonin-ergic compound to join the group of glaucoma treatment substances.

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Multifocal granulomata in presumed *Toxocara canis* infection in adult

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study is to focus on the diagnosis of case where presence of multifocal granuloma and absence of larvae in granuloma makes the diagnosis atypical. A combination of history, clinical examination, laboratory tests and histopathological analysis is important before reaching any diagnosis.

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Abstract

Human infection of *Toxocara canis* in eye is usually an outcome of accidental ingestion of the embryonated eggs. The average age at diagnosis of ocular Toxocariasis is 7.5 years, ranging from 2 to 31 years. It constitutes 1%-2% of uveitis in children. Diagnosis is based upon the clinical features observed in a young patient and confirmed by the presence of specific IgG in the serum or aqueous humor by Enzyme-linked immunosorbent assay test. We report a case of Presumed *Toxocara* infection in 45-year-old male which is unique in presentation with multifocal granulomata in retina. Our PubMed search could not produce case with similar presentation. Probably this is the first reported case of multifocal granulomata in presumed ocular *Toxocara* in any age group

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Key words: Presumed; *Toxocara canis*; Ocular; Multifocal; Granulomata

Core tip: *Toxocara* infection is one of the causes of posterior uveitis. Diagnosis is often made by presence of larvae in the choroidal granuloma. The aim of this

INTRODUCTION

The larva of the nematode *Toxocara canis* was first identified as a cause of intraocular disease by Nichols (1956). Human infection is usually an outcome of accidental ingestion of the embryonated eggs^[1]. The average age at diagnosis of ocular Toxocariasis is 7.5 years (ranging from 2 to 31 years). It constitutes about 1%-2% of uveitis in children^[2]. *Toxocara* should be considered as a possible causative agent of posterior uveitis. Diagnosis is based upon clinical features observed in a young patient and should be confirmed at least by the presence of specific IgG in the serum (ELISA test, 90% specificity and 91% sensitivity)^[3]. We present here presumed ocular *Toxocara* infection in a 45 year adult. The case is unique for its presentation at this age and multifocal granulomata on retinal evaluation. PubMed search could not reveal presence of multifocal granulomata in ocular *Toxocara* infection before.

CASE REPORT

A 45-year-old male presented with complaints of gradually progressive diminution of vision since one and half years in the left eye. There were no pets in the house. Patient was a known diabetic controlled on oral hypogly-

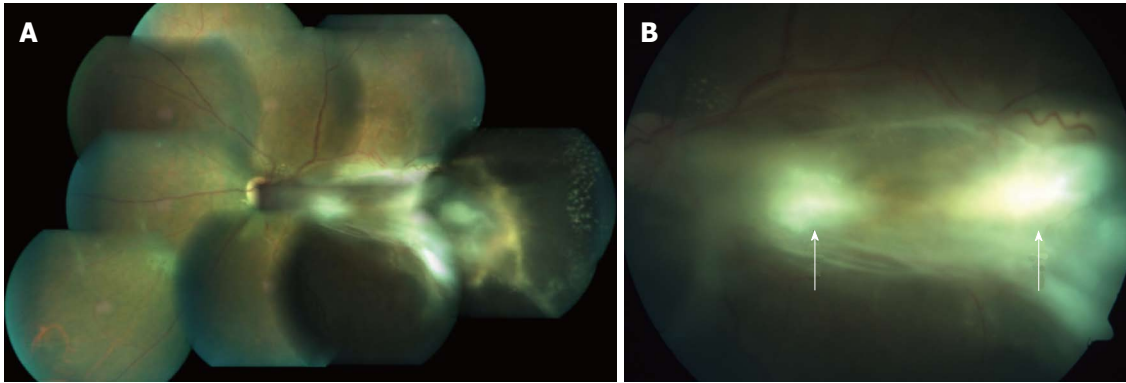


Figure 1 Fundus photo of patient' right eye. A: Montage colour fundus photo of patient showing extent of lesion with multifocal granulomata and temporal exudative retinal detachment; B: Fundus photo showing granulomata.

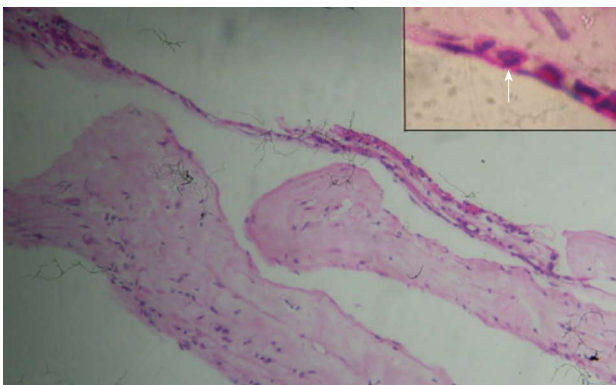


Figure 2 Haematoxylin and Eosin staining X 200: Micro photograph showing an epiretinal membrane with chronic inflammatory cells comprising of lymphocytes Inset: Shows few eosinophils (arrow). No larva seen.



Figure 3 Post operative fundus photograph showing scar extending from disc to temporal periphery.

cemic agents. At presentation his corrected visual acuity in right eye was 6/5 for distance with near vision N6 and left eye had counting finger for distance with near vision < N36 on snellens chart. Anterior segment findings were within normal limits. Right eye fundus was within normal limits whereas left eye fundus showed fibrous membranous band extending from optic nerve head to temporal periphery with subretinal exudation and exudative retinal detachment temporally (Figure 1). The unique thing about this lesion was that it covered area from posterior pole to far temporal periphery and showed multifocal choroidal granulomata which are very unusual of *Toxocara* granuloma (Figure 1). Investigation revealed positive IgE titer of *Toxocara* in anterior chamber tap (16.93NTU). Optical coherence tomography showed macular traction with increased retinal thickness. Patient was started on oral steroids and planned for surgery. Vitrectomy with membrane peeling was done. Silicone oil was injected when break occurred while removing adherent membrane. Histopathological analysis of the membrane showed fibrous tissue with chronic inflammatory cells. No *Toxocara* parasite was seen. On careful examination few eosinophils were seen (Figure 2). After 6 wk of surgery retina was attached with scarring extending from disc to temporal periphery. Patient had vision

of counting finger which was due to scarring (Figure 3). Patient was doing well on ten weeks of follow up.

DISCUSSION

Ocular Toxocariasis usually occurs in young healthy children. It is usually limited to one eye and infected by one larva (Schlaegel, 1978)^[4]. There are few clinical reports of retinal lesions in adults due to *Toxocara* infection. Larva is rarely identified from the lesions. Definitive histopathological diagnosis is possible only after enucleation. Because of the absence of larva on histopathology, we refer our case as Presumed Ocular Toxocariasis.

Ocular involvement can occur in form of chronic endophthalmitis, papillitis, posterior pole granuloma and peripheral granuloma^[1]. Patients with posterior pole granuloma may initially present with relatively hazy vitreous body and sign of acute inflammation, in which the posterior pole granuloma is observed as an ill-defined hazy mass with surrounding vitreous inflammation. These lesions are usually very well-defined and relatively small, ranging from 0.75 to 6.0 mm in diameter in size. In peripheral granuloma, a dense white peripheral inflammatory granulomatous mass is localized. Alternatively, the inflammation may be diffuse and appears as a “snowbank” as seen in pars planitis. Fibrocellular bands may run from

a peripheral inflammatory mass to posterior retina or the optic nerve leading to both traction and rhegmatogenous retinal detachment^[5].

Our patient presented with combined picture of posterior and peripheral granuloma with multifocal granulomata. The presence of multifocal granulomata in our patient was unusual and probably the first time reported.

The major causes of visual acuity loss are: severe vitritis (52.6% of the cases), cystoid macular edema (47.4%) and tractional retinal detachment (36.8%)^[6]. It is possible that the lesions are due to a toxic or immunoallergic reaction towards larval antigens, mainly associated with larval death. The disruption occurring after larval death may determine an inflammatory reaction and granuloma formation. We also found the presence of chronic inflammatory cells along with eosinophils confirming the inflammatory nature of the membrane.

Treatment therapy should be guided according to: visual acuity, severity of inflammation, irreversible ocular damage^[1]. Generally peripheral granulomata are silent or show minimal inflammatory reaction and do not require therapy. Corticosteroid therapy helps to reduce the inflammatory process without permitting the overgrowth of the infectious agent. Anthelmintic therapy is not worldwide accepted because of the possibility that larvae death may increase the inflammatory reaction. Pars plana vitrectomy is useful and indicated to remove vitreous opacities and epiretinal membranes, to relieve the vitreoretinal traction, to prevent and treat retinal detachment^[7,8].

In our patient we successfully removed the membranes despite its firm adherence to underlying tissue. The vision was counting finger because of scarring over posterior pole caused by the membrane.

A study with longer follow up is required to see how multifocal granulomata differ in prognosis from usual focal granuloma of Toxocara.

COMMENTS

Case characteristics

A 45-year-old male presented with complaints of gradually progressive diminution of vision since one and half years in the left eye.

Clinical diagnosis

Right eye fundus was within normal limits whereas left eye fundus showed

fibrous membranous band extending from optic nerve head to temporal periphery with subretinal exudation and exudative retinal detachment temporally.

Treatment

Patient was started on oral steroids and planned for surgery. Vitrectomy with membrane peeling was done. Silicone oil was injected when break occurred while removing adherent membrane. Histopathological analysis of the membrane showed fibrous tissue with chronic inflammatory cells. No Toxocara parasite was seen.

Related reports

Ocular Toxocariasis usually occurs in young healthy children. It is usually limited to one eye and infected by one larva (Schlaegel, 1978). There are few clinical reports of retinal lesions in adults due to Toxocara infection. Larva is rarely identified from the lesions.

Peer review

This manuscript entitled "Multifocal Granulomata in Presumed Toxocara Canis Infection in Adult" to report a 45 years old case with fibrous membranous band extending from optic disc to temporal periphery with subretinal exudation and exudative retinal detachment temporally. A positive IgE titer of Toxocara was also found in AC tapping. This is an interesting paper and well written.

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