

Clinical Results of Deep Anterior Lamellar Keratoplasty in Treatment of Advanced Keratoconus; Big Bubble Technique

Bushra Akbar, Rana Intisar-ul-Haq, Mazhar Ishaq, Paree Chera, Kashif Siddique

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See end of article for authors affiliations

Correspondence to:
Bushra Akbar
Post graduate trainee
ophthalmology
Department of Ophthalmology,
Armed Forces Institute Of
Ophthalmology,
Rawalpindi, Pakistan
Email:
dr.bushra.akbar@gmail.com

Purpose: To evaluate refractive results and complications of deep anterior lamellar keratoplasty (DALK) using Anwar's big bubble technique in advanced keratoconus.

Study Design: Quasi experimental study.

Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi from November 2015 to December 2016.

Material and Methods: Seventeen eyes of seventeen patients with advanced keratoconus who underwent DALK using Anwar's big bubble technique with 1 year postoperative follow up were included in study. Uncorrected and corrected distant visual acuities (UDVA, CDVA, snellen acuity converted to logMAR notation), spherical equivalent SE (Diopters D)], refractive astigmatism [(Ast, D)], slit lamp biomicroscopy and endothelial cell count (ECD) were recorded at baseline and at 1, 6 and 12 months postoperatively. Intra and postoperative complications were documented.

Results: The mean patient age was 26.29 ± 10.403 years including 12 males (76.47%) and 4 (23.53%) females. The mean baseline logMAR UDVA and CDVA were 1.376 ± 0.286 and 1.211 ± 0.228 , which significantly improved at all test points to final logMAR UDVA and CDVA of 0.964 ± 0.183 and 0.647 ± 0.279 at 1 year ($p = 0.000, 0.000$ respectively). Improvement in Ast was only significant at 1 year ($p = .0.0$) while changes in SE were not significant ($p = .0.330$). No significant ECD loss (p) or rejection was recorded at any postoperative exam.

Conclusion: DALK using Anwar's big bubble technique has shown lesser complications in terms of endothelial rejection and endothelial cell loss with satisfactory refractive results in young keratoconus patients and we recommend it to be a preferred surgical technique over penetrating keratoplasty, despite its technical challenges and steep surgical learning curve.

Key words: Deep anterior lamellar keratoplasty, Anwar's big bubble, refractive outcome, advanced keratoconus.

Keratoconus is a degenerative, non-inflammatory corneal ectatic disorder characterized by progressive central, paracentral stromal thinning, protrusion and visual deterioration due to myopia, myopic astigmatism and irregular astigmatism. Early to moderate cases of keratoconus are managed with spectacles, rigid gas

permeable contact lenses, providing satisfactory visual rehabilitation and the disease progression can be effectively halted by corneal collagen cross linking. However, keratoconus affects mainly young working population, advanced cases requires surgical intervention due to non satisfactory and intolerant fitting of contact lens, extreme corneal thinning

restricting the corneal cross linking or intracorneal ring segments, and apical scarring in the visual axis, with a resultant very poor or unacceptable vision¹. Common surgical options include PKP and DALK. DALK is a selective form of layered keratoplasty, which involves the removal and replacement of diseased layers of cornea while retaining the recipient healthy endothelium^{1,2,3}. This preservation of endothelium minimized the incidence of endothelial allograft rejection and concomitantly the dose and duration of postoperative steroids administration and the complications associated with its use^{2,3}. PKP remained procedure of choice for all keratoplasty indications for decades, despite its draw backs, largely due to its superior visual outcomes and a longer surgical experience^{2,3,4}. Visual outcome is predominantly influenced by corneal transparency both in PKP and DALK, however the visual recovery was significantly compromised in DALK by scattering of light at donor host interface irregularity owing to residual stroma adherent to descemet's membrane^{5,6}. Many surgical methodologies has been described for separation of stroma from descemet's membrane and endothelium in DALK to achieve optimal interface, starting with Barraquer microkeratome and Malbran "peeling off technique" based on deep stromal dissections^{7,8}.

To the best of our knowledge, this is the first study in Pakistan on clinical outcomes of DALK using Anwar's big bubble technique in advanced keratoconus. We aim to share our initial clinical experience in terms of refractive outcomes and complications at 1 year after DALK using Anwar's big bubble technique in Pakistani eyes with advanced keratoconus to generate local data and pave a way for guidelines regarding surgical interventions in treatment of advanced keratoconus in Pakistan.

METHODS AND MATERIALS

This quasi experimental study enrolled consecutive patients of advanced keratoconus who underwent successful DALK using Anwar's big bubble technique at Armed forces institute of ophthalmology from November 2015 to Nov 2016 after approval of local ethical committee. An informed consent was obtained from all the participants of study. Inclusion criteria included patients with advanced keratoconus between 18 and 30 years of age. Advanced keratoconus was defined as grade 4 disease according to the RETICS classification¹ (Insufficient corneal thickness for ICRS

implantation or CXL with persistent contact/scleral lenses intolerance and poor CDVA of 0.6). Exclusion criteria included eyes with corneal scarring and opacity involving descemet's membrane and endothelium (healed hydrops) other ocular comorbidity (amblyopic, strabismus, posterior segment pathology), systemic diseases, neurological problems, or any topical or systemic medications that may affect visual acuity, intraoperative complications meriting a conversion to penetrating keratoplasty or failure to achieve big bubble, requiring completion of DALK by lamellar dissection. Preoperative and postoperative ocular examinations at 1, 6 and 12 months included UDVA, CDVA (measured on Snellen visual acuity chart, converted to logMAR notation), SE, Ast, slit lamp biomicroscopy and dilated fundus examination. Ocular investigations included corneal topography (dual scheimpflug based corneal topography, Galilei G4), specular microscopy (Topcon sp-3000, USA) for endothelial cell density analysis and Anterior Segment Optical Coherence Tomography (ASOCT, Topcon Maestro 2000, Japan) for assessment of trephination depth in superficial corneal opacities.

DALK using Anwar's Big Bubble technique was done by a single corneal surgeon in all patients under general anaesthesia. The geometric center of the recipient cornea was marked after draping and eye lid speculum insertion as per standard clinical techniques. A partial thickness trephination of 8.0 mm (range 8.0 - 8.50 mm) diameter at predicated depth in corneal stroma (350 to 500 microns) was achieved via MORIA suction trephine with Guard (MORIA, France) making sure centration at all times. A 30-gauge needle, bent at 60 degrees 5 mm from the tip with bevel facing down, attached to a 3 ml syringe was used to inject the air, 3 to 4 cm from the entry site, into deep stroma to achieve big bubble, that separates the stroma and the descemet's membrane, evidenced as a semi opaque central disk with a sudden ease on resistance of the plunger. Deepest stromal layers were gently dissected from center to periphery into 4 quarters by angled blunt tipped Holland DALK scissors (DALK Set, Katena USA). These dissected deep stromal layers were then excised with Holland DALK right and left scissors (DALK Set, Katena, USA) to expose the clear and shiny descemet's membrane. The wound edges were then trimmed as vertically as possible to minimize post-operative astigmatism.

Donor corneas were procured by hospital corneal and retrieval program and transported in McCarey-Kaufmann medium. Donor corneas deemed fit based

on negative infectious serology (HIV, hepatitis) and optical clarity, were only used for DALK in our study. Donor graft of 0.25 mm larger than recipient bed was trephined with endothelial side up on Teflon block. The endothelium was stained with trypan blue and peeled off with methylcellulose sponge. The donor graft was then sutured onto the recipient bed with sixteen 10-0 nylon interrupted sutures (ALCON laboratories USA).

Postoperatively, patients were advised topical antibiotics moxifloxacin (vigamox, Alcon) 4 hourly and topical steroids prednisolone acetate 1% (Predforte, Allergan) eye drops 6 hourly gradually tapered over a period of 6 weeks. Suture removal and manipulation was done between 24 to 27 weeks after 2nd postoperative exam at 6 months and suture removal was completed till 12 months, one week prior to the last follow up exam in all patients. Meanwhile, only loose or infected sutures were removed or replaced if required.

Data analysis was done using SPSS version 20. Quantitative data was described as mean \pm standard deviation and nominal data as frequencies. Paired sample t- test was used to analyze change in the parameters over baseline at post-operative test points of 1, 6 and 12 months. p value of <0.05 with 95% confidence interval was considered statistically significant.

RESULTS

Seventeen eyes of 17 patients were included in this study who underwent DALK using big bubble

technique and completed a minimum follow up of 12 months. Big bubble was achieved in (94.11%) 17/18 of eyes. Two eyes were excluded from the study due to failed big bubble (5.88%) 1/18 with subsequent manual stromal lamellar dissection in one eye and an intraoperative macro perforation requiring conversion to PKP in the other eye. No other intraoperative or postoperative complication was recorded.

The mean age was 26.29 ± 10.40 years. There were 13 (76.47%) males and 4 (23.53%) females. Suture manipulation was done in 3 eyes and mean suture manipulation time was 25.588 ± 1.325 (range 24 - 28) weeks. The mean suture removal time was 11.555 ± 0.472 . Mean baseline logMAR UDVA was 1.376 ± 0.286 which significantly improved over all postoperative test points of 1, 6 and 12 months with a final UDVA of 0.964 ± 0.183 at 1 year. ($p = 0.001, 0.000, 0.000$ respectively) **Table 1**. Mean baseline logMAR CDVA 1.211 ± 0.228 improved significantly at all predetermined test points to a mean logMAR CDVA of 0.647 ± 0.279 ($p = 0.000, 0.000, 0.000$ respectively) at 12 months **Table 1**. The mean pre op SE -3.806 ± 1.358 and Ast -3.205 ± 2.653 although showed a reduction over post-operative test points but it was not significant ($p > 0.05$) except for a postoperative astigmatism at 1 year ($p = 0.010$). **Table 1**. ECD evaluated by specular microcopy did not show any significant loss over the postoperative follow up ($p = 0.082$) **Table 1**. No signs of endothelial decompensation or rejection were reported in any eye over 1 year follow up in our study.

Table 1: Refractive Results after deep Anterior Lamellar Keratoplasty using ANWAR'S big bubble technique.

Study Parameters	PREOPERATIVE	POST OPERATIVE		
		1 MONTH	6 MONTHS	12 MONTHS
Mean \pm SD				
UDVA (logMAR)	1.376 ± 0.286	1.079 ± 0.331	1.061 ± 0.263	0.964 ± 0.183
<i>p</i> Value		0.001*	0.000*	0.000*
CDVA(logMAR)	1.211 ± 0.228	0.982 ± 0.174	0.782 ± 0.237	0.647 ± 0.279
<i>p</i> Value		0.000*	0.000*	0.000*
SE(D)	-3.806 ± 1.358	-4.741 ± 1.150	-4.080 ± 2.432	-3.092 ± 2.420
<i>p</i> Value		0.325	0.864	0.330
AST(D)	-3.205 ± 2.653	-3.455 ± 0.806	-3.161 ± 0.905	-2.088 ± 1.441
<i>p</i> Value		0.869	0.836	0.010*

(* p Value <0.05 , Paired sample t test)



Fig. 1A: Anterior segment photograph after big bubble DALK in Advance d Keratoconus 1 week follow up.



Fig. 1B: Post Big Bubble DALK anterior segment photograph in advance keratoconus.

DISCUSSION

Archila, in 1985, performed stromal dissection with aid of 1 cc air injection above the descemet's membrane, with subsequent spatula dissection of overlying recipient stroma⁹. Sugito and Kundo introduced hydro delamination of residual stromal fibers followed by delamination of hydrated stromal fibers from the descemet's membrane¹⁰. Melles et al conceptualized the technique of lamellar dissection depth by exchanging aqueous with air and creating an optical air endothelium interface, that acts as convex mirror and reflects the depth of instrument in stroma coupled with viscodissection of lamellar plane to bare descemet's membrane^{11,12}. Anwar and Teichmann described the famous big bubble technique, where a large air bubble facilitates the separation of descemet's membrane from stroma after initial partial stromal trephination with resultant optimal interface, totally baring descemet's membrane¹³. This limited post-operative interface haze, provided excellent visual results, early visual rehabilitation in keratoconus¹⁴. Despite its steep learning curve and technical challenges, clinically significant advantages of Anwar's big bubble DALK has shifted the paradigm from PKP to DALK amongst corneal surgeons across the globe for endothelium and descemet's membrane sparing corneal disorders¹³⁻¹⁷. However very few tertiary care centers in Pakistan are offering selective layered keratoplasties at present in contrast to other developing countries of south east Asia^{15,16}.

Keratoconus has been the leading indication for keratoplasty in many populations and geographical

zones in the last few decades. This paradigm shift in indications has been probably the outcome of developmental state and socioeconomic profile of population, clinical significant advantages of DALK and improvement of eye banks and surgical sophistication^{18,19,20}. We performed DALK in seventeen eyes of advanced keratoconus using big bubble technique with a 1-year post-operative follow up. Big bubble was achieved in 17 (94.1%) eyes out of 18 eyes and only one eye 5.88% required layer by layer stromal dissection that was comparable to or better than similar studies¹³⁻¹⁷. Only one eye (5.88%) required conversion to PKP due to intraoperative macro perforation. Anwar in his study reported perforation in 16 (9%) eyes out of 181 eyes and conversion to PKP in one eye, Feizi et al reported a conversion rate of 2.3% in 103 eyes. This success rate of big bubble formation and conversion rate in our study can be considered acceptable for a being beginners in challenging surgical learning curve^{13,14}.

The mean gain in UDVA and CDVA from 1.1376 ± 0.286 to 0.964 ± 0.18 and 1.211 ± 0.228 to 0.647 ± 0.279 one year in our study is comparable to results reported by Feizi et al¹⁴. Gain of more than 3 Snellen lines in CDVA was achieved in 94.44% of eyes similar to gain of more than 2 lines in 91% of eyes reported by Danosoury²³. A CDVA of 20/70 in 40% and 20 /40 in 30% of eyes was achieved as compared to 20 /40 or better achieved in 77.8% of eyes in similar clinical trials of DALK using big bubble technique¹⁴. Similarly the SE and Ast showed reductions over the follow up test points¹⁴. In current study, astigmatism of more

than 4 D in 17% of eyes was documented in accordance with high post DALK Ast in 26% of eyes in previous similar trials at 1 year that was managed with relaxing incisions and adjustment sutures¹⁴. These differences in refractive results and post DALK refractive error in our study compared to previous similar clinical studies in international studies may be explained by variations in factors affecting post DALK refractive status like suturing techniques, mean time of suture removal, suture manipulation for high cylindrical errors, refraction at variable duration after suture removal and our limited surgical expertise^{21,24}. Moreover the quality of vision can also be negatively affected by interface haze even if stroma fully excised and no interface haze is detectable on slit lamp²². This can be seen as selective stromal reflectivity on confocal microscopy and decreased contrast sensitivity⁶. The reason being not completely understood and speculated to be excessive healing response²². No case of subepithelial or stromal graft rejection or endothelial cell was reported in this study which was less than reported immunologic rejection of 3 to 8% after DALK, and 14.3% reported by Feizi et al^{6,24,25}. This may be attributed to our careful patient selection excluding allergic co-morbidities, explained by Feizi et al in his study, that led us to an obvious advantage of early tapering of steroids and no complications post operatively of raised intraocular pressures. Lu et al²⁶ have shown that DALK with big bubble technique using femto laser is a new safe, effective and accurate technique for treating patients having keratoconus.

The major limitations of this study is a small sample size, relatively shorter duration of follow. We strongly feel that large prospective multi center trials on big bubble DALK recruiting larger number of advanced keratoconus patients with a long term follow up to increase surgical experience and will help to generate standardized data on clinical results, recurrence of disease and factors predicting refractive outcomes in our population. DALK using Anwar's big bubble technique has shown lesser complications in terms of endothelial rejection and endothelial cell loss, with satisfactory refractive results in young keratoconus patients, and we recommend it to be a preferred surgical technique over penetrating keratoplasty, despite its technical challenges and steep surgical learning curve.

CONCLUSION

DALK using Anwar's big bubble technique has shown lesser complications in terms of endothelial rejection

and endothelial cell loss with satisfactory refractive results in young keratoconus patients and we recommend it to be a preferred surgical technique over penetrating keratoplasty, despite its technical challenges and steep surgical learning curve.

Author's Affiliation

Dr. Bushra Akbar
Department of Ophthalmology, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan

Dr. Rana Intisar-ul-Haq
Department of Ophthalmology, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan

Dr. Mazhar Ishaq
Department of Ophthalmology, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan

Dr. Parea Chera
Department of Ophthalmology, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan

Dr. Kashif Siddique
Statistician, Research (Academic Affairs), King Salman Armed Forces Hospital, KSA

Role of Authors

Dr. Bushra Akbar
Study design, Data acquisition, interpretation, and analysis of data, manuscript drafting.

Dr. Intisar-ul-Haq
Study design, critical review.

Dr. Mazhar Ishaq
Critical review.

Dr. Parea Chera
Data collection, interpretation and manuscript drafting

Dr. Kashif Siddique
Study design, interpretation, analysis of data and critical review

REFERENCES

1. Arnalich-Montiel F, Alió del Barrio JL, Alió JL. Corneal surgery in keratoconus: which type, which technique, which outcomes? Eye and Vision. 2016; 3(2): 1-14.
2. Terry M. The Evolution of Lamellar Grafting Techniques Over Twenty-five Years. Cornea, 2000; 19 (5): 611-616.
3. Funnell C, Ball J, Noble B. Comparative cohort study of the outcomes of deep lamellar keratoplasty and

- penetrating keratoplasty for keratoconus. *Eye*. 2005; 20 (5): 527-532.
4. **Jones M, Armitage W, Ayliffe W, Larkin D, Kaye S.** Penetrating and Deep Anterior Lamellar Keratoplasty for Keratoconus: A Comparison of Graft Outcomes in the United Kingdom. *Investigative Ophthalmology & Visual Science*, 2009; 50 (12): 5625-9.
 5. **Fontana L, Parente G, Sincich A, Tassinari G.** Influence of Graft-Host Interface on the Quality of Vision After Deep Anterior Lamellar Keratoplasty in Patients with Keratoconus. *Cornea*, 2011; 30 (5): 497-502.
 6. **Feizi S, Javadi M, Rastegarpour A.** Visual Acuity and Refraction after Deep Anterior Lamellar Keratoplasty with and Without Successful Big-Bubble Formation. *Cornea*, 2010; 29 (11): 1252-1255.
 7. **Barraquer J.** Lamellar keratoplasty (special techniques). *Ann Ophthalmol*. 1972; 4: 437-469.
 8. **Polack F.** Lamellar keratoplasty: Malbran's "peeling off" technique. *Arch Ophthalmol*. 1971; 86: 293-296.
 9. **Archila E.** Deep lamellar keratoplasty dissection of host tissue with intrastromal air injection. *Cornea*, 1985; 3: 217-218.
 10. **Sugita J, Kondo J.** Deep lamellar keratoplasty with complete removal of pathological stroma for vision improvement. *Br J Ophthalmol*. 1997; 81: 184-188.
 11. **Melles G, Rietveld F, Beekhuis W, Binder P.** A Technique to Visualize Corneal Incision and Lamellar Dissection Depth During Surgery. *Cornea*, 1999; 18 (1): 80-86.
 12. **Melles G, Lander F, Rietveld F, Remeijer L, Beekhuis W, Binder P.** A new surgical technique for deep stromal, anterior lamellar keratoplasty. *The British Journal of Ophthalmology*, 1999; 83 (3): 327-333.
 13. **Anwar M, Teichmann KD.** Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. *J Cataract Refract Surg*. 2002; 28: 398-403.
 14. **Feizi S, Javadi M, Jamali H, Mirbabae F.** Deep Anterior Lamellar Keratoplasty in Patients with Keratoconus: Big-Bubble Technique. *Cornea*, 2010; 29 (2): 177-182.
 15. **Tan DTH, Mehta JS.** Future of lamellar corneal transplantation. *Cornea*, 2007; 26: S21-S28.
 16. **Fogla R.** Deep anterior lamellar keratoplasty in the management of keratoconus. *Indian Journal of Ophthalmology*, 2013; 61 (8): 465-8.
 17. **Söğütlü Sarı E, Kubaloğlu A, Ünal M, Piñero Llorens D, Koytak A, Ofluoğlu A et al.** Penetrating keratoplasty versus deep anterior lamellar keratoplasty: comparison of optical and visual quality outcomes. *British Journal of Ophthalmology*, 2012; 96 (8): 1063-1067.
 18. **de Sanctis U, Alovisi C, Baucheiro L, Caramello G et al.** Changing trends in corneal graft surgery: a ten-year review. *Int J Ophthalmol*. 2016; 9 (1): 48-52.
 19. **Rezaei Kanavi M, Javadi M, Motevasseli T, Chamani T, Rezaei Kanavi M, Kheiri B et al.** Trends in indications and techniques of corneal transplantation in Iran from 2006 to 2013; an 8-year review. *J Ophthalmic Vis Res*. 2016; 11 (2): 146.
 20. **Altay Y, Burcu A, Aksoy G, Singar Ozdemir E, Ornek F.** Changing indications and techniques for corneal transplantations at a tertiary referral center in Turkey, from 1995 to 2014. *Clinical Ophthalmology*, 2016; 10: 1007-1013.
 21. **Javadi M, Feizi S, Mirbabae F, Rastegarpour A.** Relaxing Incisions Combined With Adjustment Sutures for Post-Deep Anterior Lamellar Keratoplasty Astigmatism in Keratoconus. *Cornea*, 2009; 28 (10): 1130-1134.
 22. **Feizi S, Javadi M, Mohammad-Rabei H.** An Analysis of Factors Influencing Quality of Vision after Big-Bubble Deep Anterior Lamellar Keratoplasty in Keratoconus. *American Journal of Ophthalmology*, 2016; 162: 66-73.
 23. **Cheng Y, Visser N, Schouten J, Wijdh R, Pels E, van Cleynenbreugel H et al.** Endothelial Cell Loss and Visual Outcome of Deep Anterior Lamellar Keratoplasty versus Penetrating Keratoplasty: A Randomized Multicenter Clinical Trial. *Ophthalmology*, 2011; 118 (2): 302-309.
 24. **El-Danasoury A.** Big Bubble Deep Anterior Lamellar Keratoplasty (BB-DALK). *International Ophthalmology Clinics*, 2013; 53 (1): 41-53.
 25. **Feizi SJavadi M.** Factors Predicting Refractive Outcomes after Deep Anterior Lamellar Keratoplasty in Keratoconus. *American Journal of Ophthalmology*, 2015; 160 (4): 648-653.
 26. **Lu Y, Chen X, Yang L, Xue C, Huang Z.** Femtosecond laser assisted deep anterior lamellar keratoplasty with big-bubble technique for keratoconus. *Indian J Ophthalmol* 2016; 64(9): 639-642.