Original Article

Comparison of the Endosaver with noninjector techniques in Descemet's stripping endothelial keratoplasty

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Purpose: Minimal loss of corneal endothelial cells during corneal transplantation is a major target but remains a point of controversy among specialists. Hence, the available method to best achieve this continues to stir progress in the field. The aim of this study is to evaluate the use of the Endosaver injector device for graft insertion in Descemet's stripping endothelial keratoplasty (DSEK) and compare the visual outcomes and endothelial cell survival between the Endosaver injector and Goosey grasping forceps insertion techniques. **Methods:** This was a retrospective, interventional, consecutive case series undertaken at the University of Southampton Eye Department to assess outcomes of DSEK using the Endosaver injector device compared to noninjector DSEK insertion. Postoperative specular microscopy alongside manifest refraction at 6 and 12 months was evaluated and compared. Mann–Whitney U-test was employed for the statistical analysis of data. **Results:** Both the Endosaver and Goosey forceps groups showed an improvement in best corrected visual acuity. No significant statistical difference was found in preoperative and postoperative best-corrected visual acuity between the Endosaver and non-Endosaver insertion groups. Mean preoperative endothelial cell count was 2660 (±130) for the Endosaver group and 2608 (±66) for the non-Endosaver group. Postoperative endothelial counts at 6 and 12 months showed a significant difference between the Endosaver: 2104 (±199)–1896 (±226) and the non-Endosaver: 1492 (±207)–1314 (±224) ($P < 0.005$) groups, respectively. **Conclusion:** The Endosaver injection device is associated with less trauma to endothelium during graft insertion due to the minimal touch technique employed. A smaller insertion wound of 4.0 mm compared to noninjector cases enabled a more stable system during surgery with no or minimal anterior chamber shallowing. The combination of a stable host with minimal endothelial graft handling and subsequent trauma potentially leads to higher endothelial cell counts when the Endosaver injection device is used compared to forceps insertion.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_360_17

Quick Response Code:

Key words: Endothelium, keratoplasty, refraction, injector

Descemet's stripping endothelial keratoplasty (DSEK) has largely replaced full thickness penetrating keratoplasty as the procedure of choice for endothelial pathology.[1] Donor lenticule preparation can be achieved either manually after placement of the corneal tissue in an artificial anterior chamber (AC) or mechanically with the use of a microkeratome (DSAEK).[2]

Benefits of DSEK over traditional penetrating keratoplasty include early visual recovery, refractive stability, postoperative astigmatism, wound and suture-related complications, and intraoperative and late postoperative risks, whereas DSEK maintains similar final visual outcome, complication rate, and endothelial loss.[3] Complete anatomical correction as in the case of Descemet's membrane endothelial keratoplasty provides a number of advantages as almost immediate visual rehabilitation, but it has yet to be taken up by the majority of corneal transplant surgeons as it is a lot more technically challenging and has been initially associated with controversially high complication rates.[4]

Both DSEK and DSAEK completely eliminate surface corneal incisions or sutures, maintain much of the structural integrity of the cornea, and induce minimal refractive change, inflicting distinct advantages over traditional penetrating keratoplasty.[5]

Several studies in the past have raised concerns about a greater endothelial loss during DSEK and DSAEK due to severe donor tissue manipulation and the steep initial learning curve. Terry *et al*. reported a mean donor endothelial cell loss of 34% at the 6-month postoperative examination and Price and Price reported cell loss at 6 months and 1 year after DSEK that was higher than penetrating keratoplasty.[6,7]

Several techniques have been described for the insertion of the graft in the AC. The most common techniques involve tissue folding and insertion with forceps[4] or the use of a

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Manuscript received: 19.05.17; Revision accepted: 01.09.17

Cite this article as: Tsatsos M, Athanasiadis I, Kopsachilis N, Krishnan R, Hossain P, Anderson D. Comparison of the Endosaver with noninjector techniques in Descemet's stripping endothelial keratoplasty. Indian J Ophthalmol 2017;65:1133-7.

disposable DSAEK glide (Tan EndoGlide; AngioTech, Reading, PA/Network Medical Products, North Yorkshire, UK).[8] The purpose of this study is to describe and evaluate the use of the Endosaver (Ocular Systems, Inc USA) for inserting the graft in thin manually dissected DSEK (TMDSEK) and compare it with noninjector insertion techniques.

Methods

This was a retrospective, interventional, consecutive case series performed at the University of Southampton by two surgeons (PH and DFA) between 2012 and 2014. Local Ethics Committee and National Health Service Research and Development approval were obtained (Research Ethics Committee number: 07/H0512/39).

All corneal graft material was supplied by United Kingdom National Health Service Blood and Transplant (UK NHSBT).

A total of 46 eyes of 44 patients (21 men, 13 women; mean age 62 ± 6.8 years) with Fuchs endothelial dystrophy and postphacoemulsification bullous keratopathy were enrolled in this study. A percentage of 26% of the cohort was diagnosed as bullous keratopathy and 74% as Fuchs endothelial dystrophy. The patients were divided in two groups. Group A consisted of 23 eyes undergoing TMDSEK with the use of the Endosaver device (the Endosaver, Ocular Systems Inc., Winston-Salem, North Carolina, USA) while Group B consisted of 23 eyes undergoing TMDSEK with the use of a Goosey type grasping forceps (Ambler Surgical, USA). Outcome measures included best-corrected visual acuity (BCVA) after 6 and 12 months and central endothelial cell density (ECD) before and after 12 months after surgery. Central ECD was measured with noncontact specular microscopy (EM-3000, Tomey, Japan). Postoperative cell loss was calculated as the percentage of the preoperative donor ECD. Two patients were excluded due to co-pathology affecting the visual outcome (age-related macular degeneration and anterior ischemic optic neuropathy-related optic nerve atrophy).

Surgical technique

The donor corneoscleral rim was mounted on the artificial AC (Baron, Katena products USA), which (AC) was then filled with balanced salt solution. BSS was used to maintain AC pressure throughout the procedure. TMDSEK was performed, and donor lenticule was harvested as described previously.[9]

A small temporal clear corneal or scleral tunnel incision (approximately 5.5 mm for the forceps group and 4.0 mm for the Endosaver group) was marked on the host with calipers and made with a keratome blade. A circle was marked on the recipient corneal epithelium with an 8.75 mm disc marker densely coated with gentian violet. A reverse Sinskey hook was then used to score the Descemet's membrane on the posterior side of the host cornea. This was performed under continuous BSS flow using an AC maintainer and along a circle marked on the anterior cornea. The Descemet's membrane and endothelium were subsequently stripped using a Melles Descemet's stripper/scraper.

The DSEK graft was then mounted on the Endosaver injection device endothelial side up, and viscoelastic material was then applied to the endothelial surface of the donor button. In the forceps group, the button was folded so that the endothelium is on the inside, with 60% of the button on one side of the fold and 40% on the other. The folded graft was grasped gently with a Goosey type forceps and introduced into the recipient AC through the 5.5-mm incision.

In the Endosaver group, the graft was placed on the graft carrier with the stromal side down under the operating microscope. Viscoelastic was then placed on the endothelial surface of the donor disc [Fig. 1]. The thumb screw dial on the Endosaver was rotated to retract the carrier along with the allograft into the insertion sheath.

The Endosaver device was rolled 180° so that the donor graft would deploy endothelial side down within the recipient AC. The sheath was introduced into the incision while simultaneously starting low-pressure irrigation to stabilize and deepen the AC. The tip of the sheath was advanced to the far edge of the Descemetorhexis, and the graft was delivered in the AC.

The graft was unfolded by gently sliding the Simcoe into its fold and introducing BSS. It was centered using peripheral pressure from the flow of BSS into the chamber. The wound was closed with 10-0 nylon suture.

Finally, filtered air was delivered to the eye through a cannula through one of the sideport incisions to make an air bubble with borders extending past the edges of the graft. No inferior or superior iridotomy were performed, but the

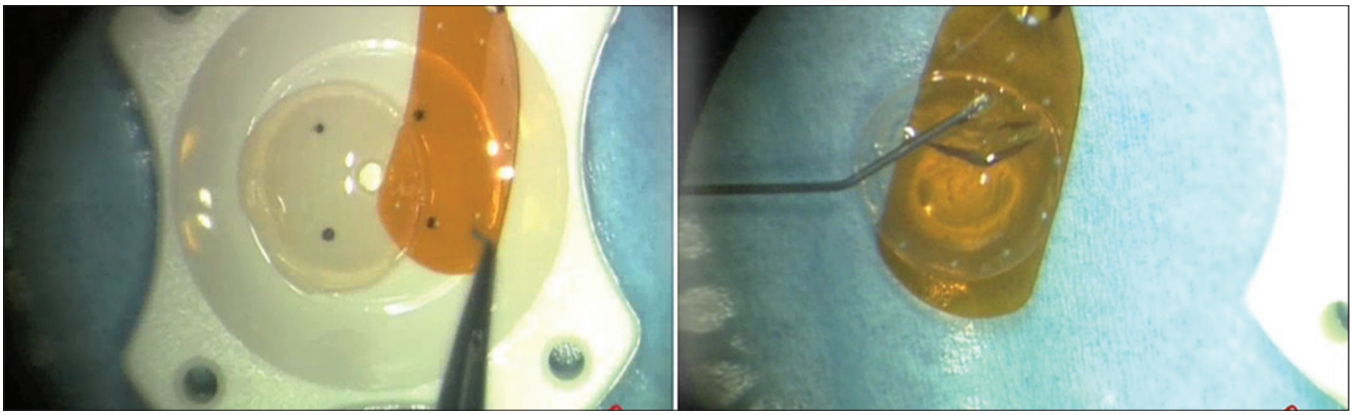

Figure 1: Endosaver group: The lamellar graft is placed on the graft carrier with the endothelial side up. Viscoelastic is then placed on the endothelial surface

transplanted eyes were kept on cyclopentolate 1% drops three times a day for 2 days.

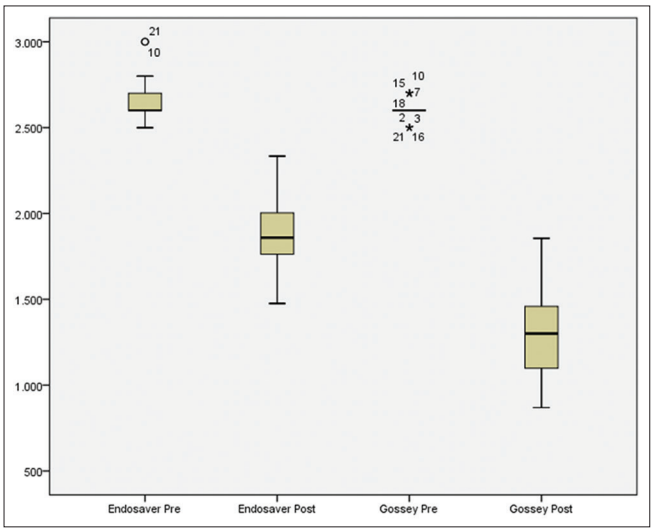

Figure 2: Graphic depicting box plots of endothelial cell count number between Endosaver and non-Endosaver group preoperative and at 12 months after Descemet stripping endothelial keratoplasty. The mean postoperative cell loss rate was 29% at 12 months for the Endosaver and 50% at 12 months for the forceps group. The result was statistically significant ($P \leq 0.050$)

Statistics

Mann–Whitney U-test was employed for the statistical analysis of data as not all values were normally distributed.

Results

Tables 1, 2 and Fig. 2 summarize the clinical outcomes of the patients.

No significant statistical difference was found in preoperative and postoperative BCVA between the Endosaver and non-Endosaver insertion groups [Table 1]. At 6 months, the Z-score was −1.8915 and the $P = 0.05876$. At 12 months, the Z-Score was −1.6095 and the $P = 0.1074$.

In the Endosaver group, all 23 patients (100%) had a clear graft at 6 and 12 months with improved BCVA; in this cohort, no complications such as primary graft failure or rejection were noted. 82.6% reached a BCVA of 6/12 or better within 6 months. Twelve patients (52.1%) achieved visual acuity better than 6/9 at 6 months and 4.3% achieved 6/6 within 6 months and 17.3% at 12.

In the forceps group, all 23 patients (100%) had a clear graft at 6 and 12 months with improved BCVA. Again no graft failures or graft rejections were observed; 61.9% reached a BCVA of 6/12 or better within 6 months. Five patients (23.8%) achieved visual acuity better than 6/9 at 6 months and 4.7% achieved 6/6 at 12 months.

Table 1: Preoperative and postoperative best-corrected visual acuity between the Endosaver and non-Endosaver groups LogMAR BCVA

Group A Endosaver				Group B Non-Endosaver			
Patients	Pre-op	6 months	12 months	Patients	Pre-op	6 months	12 months
1	0.76	0.4	0.4	1	0.71	0.34	0.28
2	1.2	0.3	0.3	2	0.71	0.12	0.12
3	0.76	0.19	0.02	3	0.71	0.22	0.2
4	0.76	0.38	0.34	4	0.65	0.34	0.32
5	0.76	0.12	0.1	5	0.71	0.32	0.32
6	0.76	0.22	0.12	6	0.71	0.44	0.44
7	0.62	0.2	0.12	7	0.71	0.18	0.18
8	0.76	0.14	0.12	8	0.62	0.32	0.18
9	0.76	0.22	0.14	9	0.71	0.44	0.26
10	0.76	0.46	0.32	10	0.71	0.34	0.34
11	0.3	0.26	0.04	11	0.71	0.42	0.2
12	0.76	0.32	0.2	12	0.71	0.28	0.28
13	0.76	0.22	0.22	13	1	0.32	0.32
14	0.76	0.22	0.22	14	1.17	0.72	0.45
15	0.76	0.46	0.26	15	0.42	0.32	0.1
16	0.76	0.36	0.36	16	0.62	0.44	0.18
17	1.4	0.2	0.2	17	0.22	0.3	-0.08
18	0.83	0.44	0.43	18	1.36	0.44	0.38
19	0.22	0.30	0.08	19	0.54	0.2	0.34
20	0.52	0.34	0.18	20	1.3	0.52	0.2
21	0.22	0.14	0.08	21	0.97	0.68	0.29
22	0.34	0.34	0.1	22			
23	1.2	0.02	0.2	23			
Mean	0.72	0.27	0.19		0.76	0.36	0.25
SD	0.28	0.11	0.11		0.26	0.14	0.12

Table 2: Preoperative and postoperative endothelial cell density between the study groups

Patients	Group A			Group B		
	Preoperative	6 months	12 months	Preoperative	6 months	12 months
1	2600	1892	1763	2600	1650	1468
2	2600	1792	1476	2500	1667	1508
3	2600	2010	1985	2500	1350	1098
4	2600	2200	2003	2700	1900	1855
5	2600	1993	1839	2600	1510	1300
6	2600	2100	1789	2600	1490	1300
7	2800	2200	1859	2700	1260	1076
8	2500	1978	1839	2600	1680	1459
9	2700	2182	2000	2600	1540	1300
10	3000	2319	1695	2700	1695	1300
11	2700	1989	1763	2600	1440	1300
12	2600	1720	1633	2600	1450	1300
13	2600	1915	1843	2600	1220	985
14	2600	2450	2334	2600	1680	1468
15	2600	2400	2322	2700	1220	1021
16	2600	2370	2273	2500	1590	1483
17	2600	2322	2180	2600	1310	1198
18	2800	2320	2003	2700	1010	869
19	2500	2000	1892	2600	1480	1340
20	2700	2100	2024	2600	1280	1086
21	3000	2280	1691	2500	1650	1459
22	2700	2000	1623	2600	1580	1486
23	2600	1910	1792	2700	1680	1580
Mean±SD	2660±130	2104±199	1896±226	2608±66	1492±207	1314±224

SD: Standard deviation

Two patients (both in Group B) had limited vision at 12 months due to retinal pathology (AION and AMD, and were excluded from the study).

Postoperative ECD at 6 months ranged from 1720 to 2450 cells/mm^2 for Group A (mean: 2104 ± 199 cells/mm^2) and from 1010 to 1900 cells/mm^2 (mean: 1492 ± 207 cells/mm^2) for Group B. At 12 months, ECD ranged from 1476 to 2334 cells/mm^2 for Group A (mean: 1896 ± 226 cells/mm^2) and from 869 to 1855 cells/mm^2 (mean: 1314 ± 224 cells/mm^2) at for Group B [Table 2 and Fig. 2]. The results at 6 and 12 months were statistically significant using Mann–Whitney U-test. The *Z*-Score at 6 months was 5.73396, the $P < 0.0001$ and the result was significant at $P \leq 0.05$. The value of U was 3. At 12 months, the Z-Score was 5.3338. The $P = 0.001$ at a level of significance at $P \leq 0.05$. The U-value was 14.

The mean postoperative cell loss rate was 21% and 29% at 6 and 12 months, respectively, for the Endosaver group, whereas in the forceps group and for the same period, it was 43% and 50%, respectively. The rate of cell loss between the two groups was statistically significant at 6 months but not at 12 months. The *Z*-Score at 6 months was-5.701, the $P < 0.0001$ and the result was significant at $P \leq 0.05$. The value of U was 4,5. At 12 months, the Z-Score was 0.45037. The $P = 0.65272$ at a level of significance at $P \leq 0.05$. The results were not statistically significant and the U-value was 243.5.

Discussion

Mechanical trauma to the donor endothelium is caused by tissue manipulation during DSEK/DSAEK surgery and remains a serious concern during endothelial surgery.[7]

Several donor insertion techniques have been developed up to date. Busin *et al*. reported 20.0% endothelial cell loss after 6 months and 23.5% after 12 after DSAEK using the Busin glide pull-through technique.[10] The IOL sheet-glide–assisted pull-through technique was found to have 25% cell loss after 6 months.[11] A double-glide technique (IOL sheet-glide–assisted Busin glide technique) has reported low endothelial cell damage rates 25.8% cell loss after 6 months).[12] Endothelial cell loss using the Tan EndoGlide has been reported as low as 25.76%.[13]

The size of the incision has been proven to play an important role in endothelial cell loss as well. Terry *et al*. suggested that incision width has a significant effect on endothelial cell loss regardless of donor graft insertion technique or device.[14] With a 5-mm wide incision, 18.0% endothelial cell damage by forceps insertion and 20.0% damage by Busin's glide were noted. In contrast, with a 3-mm wide incision, 30.0% endothelial cell damage was noted by forceps insertion and 28.0% damage by Busin's glide.[14]

Endothelial cell counts showed a statistically significant difference between the Endosaver and forceps group at both 6 and 12 months intervals indicating the less invasive, aggressive-traumatic nature of Endosaver insertion system. Most of the endothelial compromise appears to have occurred at the early postoperative period as suggested by other researchers[10] since the endothelial cell loss rate between the two groups showed statistically significant difference in the first 6 months but no significant difference between 6 and 12 months.

The large endothelial loss seen in the 6-month period in the forceps group (42%) further indicates the more traumatic nature of this type of DSEK graft insertion compared to the injector method (21%). At the 12-month interval, the endothelial counts remained significantly different between the two groups, but the additional reduction of endothelial cell count appears to be large but not as dramatic (29% to 50%, respectively).

The mean postoperative donor endothelial cell counts were higher in the Endosaver group suggestive of less trauma during insertion. The Endosaver device caused less trauma during graft insertion possibly due to the no or minimal touch technique employed. Furthermore, a smaller insertion wound of 4 mm compared to noninjector cases enabled a more stable system during surgery.

Postoperative mean visual acuities were slightly better in the Endosaver group although not statistically significant compared to the forceps group.

To the best of our knowledge, this is the first study comparing Endosaver and forceps graft insertion techniques in terms of damage to the corneal endothelium and visual outcome 6 and 12 months after DSEK.

Additional studies using a large number of patients are required to fully evaluate the usefulness and potential advantages of this new donor inserter.

Conclusion

The Endosaver injection device is associated with significantly less endothelial trauma compared to the forceps technique for the insertion of the donor endothelial lenticule. The difference in endothelial cell loss between the Endosaver and forceps groups is more pronounced at 6 months compared to 1 year, further elucidating the significantly more traumatic nature of the forceps endothelial graft insertion. As endothelial graft surgery becomes smoother and is performed more routinely the quest for the least traumatic graft delivery is bound to continue.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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