Results of viscobubble deep anterior lamellar keratoplasty after failure of pneumatic dissection

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ABSTRACT

Aim To report the outcomes of bubble formation obtained by means of intrastromal injection of ophthalmic viscoelastic device (OVD) after failure of pneumatic dissection for deep anterior lamellar keratoplasty (DALK).

Methods DALK was performed in 140 keratoconic eyes of 130 patients by injecting air and OVD only secondarily, after pneumatic dissection had failed; the bubble formation rates after air and OVD injection were recorded; complications, best spectacle-corrected visual acuity (BSCVA) and corneal tomographic parameters were evaluated 3 months, 6 months and 12 months postoperatively, as well as after complete suture removal.

Results Air injection created a big bubble in 106/140 eyes (75.71%); OVD injection was not attempted in 4 eyes (perforation during cannula insertion n=2; air bubble burst n=2) and created a big bubble in 28 of the remaining 30 eyes (93.33%, 20% of the total). Manual dissection was required in 2/30 eyes (6.66%, 1.42% of the total) after failed OVD-assisted dissection. Deep folds, interface opacity and reduced BSCVA were noted in both eyes after failed OVD-assisted dissection. BSCVA was statistically better after pneumatic-assisted than after OVD-assisted dissection (P 0.01) only up to 3 months postoperatively; no statistically significant differences were recorded between the two techniques at later examinations.

Conclusion Intrastromal injection of OVD after failed pneumatic dissection increases considerably the success rate of bubble formation (from 75.71% to 95.71% in our series); however, when bubble formation fails, infiltration of OVD into the residual stroma makes manual dissection particularly challenging and causes severe interface haze resulting in poor visual outcomes.

INTRODUCTION

Deep anterior lamellar keratoplasty (DALK) is gaining popularity for the treatment of keratoconus and other corneal stromal diseases mainly because it spares the healthy recipient endothelium, thus eliminating the risk of its immunological rejection. 1,2

Among the surgical techniques proposed to achieve complete stromal removal, the big bubble (BB-DALK) technique, described by Anwar and Teichmann, is the most popular; 3 it foresees pneumatic dissection to cleave the stroma from the underlying Descemet membrane (DM) or more precisely, as recently described, in most cases from a very thin, predescemetic stromal layer (PDL). 4

However, even for experienced surgeons the success rates of bubble formation rarely exceed 70%–80%, thus usually forcing corneal surgeons to complete the procedure by means of manual dissection in a relatively high number of eyes. 5–7

However, manual layer-by-layer dissection of the emphysematous tissue is time-consuming, is associated with a relatively high risk of perforation, and even if carried out as deep as possible, never achieves bearing of DM, thus resulting in a stromal surface of variable smoothness and optical quality. 8

More recently, the injection of ophthalmic viscoelastic device (OVD) has gained popularity as a secondary procedure to be able to obtain a visco-bubble (VB-DALK) after the failure of pneumatic dissection. 3,9–11 The aim of this study is to compare the success rate, type of cleavage obtained, visual results and complications of this approach.

This study reports the cumulative outcomes of DALK in eyes with keratoconus operated on with a sequential approach foreseeing primarily pneumatic dissection and only when air injection had failed to create the BB, a subsequent OVD injection for the same purpose.

METHODS

In this prospective interventional case series, we evaluated the outcomes of all consecutive keratoconic eyes that underwent DALK between March 2014 and June 2016 at the ophthalmology department of the University of ‘Magna Graecia’, Catanzaro, (Italy).

All patients were spectacle-intolerant and contact lens-intolerant; eyes with scars reaching DM, as evaluated by anterior segment optical coherence tomography (AS-OCT), or history of previous corneal hydrops were excluded. The study followed the tenets of the 1964 Declaration of Helsinki and was approved by the local ethics committee; detailed informed consent was provided to all patients undergoing surgery.

Preoperatively, demographic data were collected and every patient underwent a complete ophthalmological evaluation including refraction, slit-lamp examination, tonometry, funduscopy, endothelial specular microscopy (EM-3000; Tomey, Erlangen, Germany), as well as AS-OCT (Casia; Tomey, Tokyo, Japan). Best spectacle-corrected visual acuity (BSCVA) was recorded and converted from Snellen values into the logarithm of the minimum angle of resolution (logMAR) units.

Intraoperatively, success or failure of pneumatic and OVD-assisted dissection, type of the bubble obtained (according to Dua’s classification), 12 as well as complications were noted.
Postoperative examinations were scheduled and performed in all patients 3 months and 6 months postoperatively, when all sutures were still in place, as well as 12 months after surgery, that is, after complete suture removal. Postoperative complications occurring during the follow-up period were also recorded.

Statistical analyses were performed using SPSS Statistics V.20 (IBM, Armonk, New York, USA). Results of descriptive analyses were expressed as means±SD for quantitative variables, and as counts and percentages for categorical variables. For the analysis of quantitative measures we used the Student’s t-test for normally distributed variables; P values <0.05 were considered to be statistically significant.

Surgical technique
Local anaesthesia with peribulbar injection of a mixture of 10 mL 10% ropivacaine hydrochloride and 150 IU of hyaluronidase was obtained for all but three procedures that required general anaesthesia because the patient’s age was less than 18 years.

All DALK surgeries were performed by the same surgeon (VS) according to a standardised surgical technique described previously in detail, using pupil dilatation as an effective reference to judge the depth of dissection and guide the cannula insertion; all steps of the surgical procedure are shown in the supplementary video.

When pneumatic dissection failed, the procedure was continued, attempting at creating BB with the injection of OVD (VIVACY sodium hyaluronate 1.55%, I-SPACE Laboratoires, La Ravoire, France) according to the following surgical steps (figure 1): removal of about 80% of the anterior emphysematous tissue by means of hand dissection; insertion of a 27-gauge anterior chamber cannula connected to a syringe containing OVD into the same track previously used for the air injection; slow injection of OVD into the deep stroma until a bubble was achieved, extending up to the trephination edge (8.00–8.25 mm in diameter); usually a small bubble was formed starting from the site of injection and its presence was easily recognised, without requiring any additional test for confirmation. Once the bubble was obtained, all the remaining surgical steps did not differ substantially from those of BB-DALK including removal of all sutures within 12 months from surgery.

Starting the following morning, betamethasone 0.2% and chloramphenicol 0.5% eye drops were administered every 2 hours, then tapered off to a single daily steroidal administration 1 month after partial suture removal and finally discontinued at month 6 after surgery.

RESULTS
A total of 140 consecutive eyes of 130 patients with keratoconus underwent DALK in the period mentioned above and were included in the study. Forty-nine patients were women (37.69%) and 81 were men (62.31%); the age ranged from 17 years to 73 years (average ±SD was 39.83±14.79 years).

Preoperatively, the mean preoperative keratometric value was 65.25±8.27 dioptres (D), ranging from 51.30 D to 84.00 D and the average thinnest point measured by AS-OCT was 348.21±71.10 µm (range 112–481 µm). The BB-DALK and the VB-DALK eyes did not differ significantly preoperatively with regard to mean preoperative keratometric values (65.44±8.54 D vs 63.55±7.17 D; P=0.27) and mean thinnest point (350.55±74.24 µm vs 364.07±27.34 µm; P=0.34); these data are summarised in table 1.

Table 1: Preoperative and postoperative mean keratometric values.

In two cases (1.42%), corneal perforation occurred during cannula insertion and manual dissection was used to complete the procedure.

Pneumatic dissection succeeded in forming BB in 106 of 140 eyes (75.71%); however, in 2 of these cases the bubble burst while trying to enlarge it up to the trephination edge, necessitating conversion into penetrating keratoplasty (PK). Periphereral microperforations of DM occurred in four cases during completion of the stromal excision; all of them were managed conservatively.

Injection of OVD succeeded in creating BB in 28 eyes of the remaining 30 eyes (93.33%, ie, 21.43% of the total 140 eyes). In 2 of 30 cases (6.66%, ie, 1.42% of the total 140 eyes) injection of OVD resulted in a diffuse stromal infiltration without bubble formation, and the procedure was continued using layer-by-layer manual dissection. Adding together BBs obtained with air injection and those obtained with OVD injection, a bubble

Figure 1 Intraoperative images illustrating viscoelastic-assisted big bubble formation for deep anterior lamellar keratoplasty. (Top left) after failed pneumatic dissection, 70%–80% of the anterior emphysematous tissue is removed by means of hand dissection; (top right) the viscoelastic substance is injected through the same track used for the air injection and a bubble is slowly formed; (middle left) A 30° blade is used to open the ceiling of the bubble; (middle right) blunt-tipped corneal scissors are employed to divide the residual stroma into four quadrants, which are then excised (bottom left), baring the pectodermic donor layer; (bottom right) surgery is completed with two running 10–0 nylon sutures.
was created in 134 of 140 eyes with a cumulative success rate of 95.71%.

When pneumatic dissection succeeded, a type 1 bubble was formed in 100 of 106 eyes (94.34%) and a type 2 bubble in the remaining 6 cases (5.66%); no bubbles of the mixed type were obtained. Instead, all the bubbles obtained by means of OVD injection were of the type 1.

Three months after surgery mean BSCVA was significantly better (P<0.01) in the eyes with successful pneumatic dissection (0.38±0.22 logMAR) than in the eyes with successful OVD-assisted dissection (0.66±0.23 logMAR), but 6 months and 12 months after surgery the difference was not statistically significant (table 1).

In the two eyes that underwent manual dissection after failure of bubble formation with OVD-assisted dissection, slit-lamp examination and AS-OCT showed the presence of extensive deep folds and interface opacity (figure 2) clearing up very slowly during the follow-up period, but still persisting at the time of this review (12 months after surgery) with consequent BSCVA limited to 20/50 and 20/60, respectively.

Postoperative endothelial cell density averaged 2235±353 cells/mm² in BB-DALK and 2198±253 cells/mm² in VB-DALK with a mean cell loss of, respectively, 9.6% and 10.1% from the preoperative value.

Epithelial and stromal rejection were recorded respectively in 2 and 4 of the 106 BB-DALK eyes (1.89% and 3.77%) and in 1 and 2 of the 30 VB-DALK eyes (3.33% and 6.66%), percentages similar to those reported in the past.7 14 15 All immunological episodes resolved with topical steroidal treatment.

**DISCUSSION**

Over the last few decades, DALK has been developed for the surgical treatment of eyes with corneal stromal disease and healthy endothelium;1 2 BB-DALK has emerged as the most popular among several techniques mainly because it allows complete removal of the stroma, baring DM or PDL, thus avoiding the creation of a new, optically significant stromal interface.2 5 14

However, despite continuous refinement and improvement, pneumatic dissection fails in a variable, but relatively high number (up to 36%) of cases even in the hands of experienced corneal surgeons.5 15 For eyes with failed bubble formation, various surgical approaches have been proposed, in an attempt at completing the lamellar procedure without resorting to conversion into PK.

The easiest and ‘most instinctive’ approach consists of trying to inject air again either through the same track or through a new one; however, re-injecting through the same track, even large quantities of air, usually fails to succeed, as the air keeps on escaping following the same path as in the first injection, that is, usually into the peripheral cornea, the trabecular meshwork and then into the anterior chamber. Instead, inserting the cannula again through a new track, deep enough to allow successful bubble formation, is often made particularly difficult by the presence of stromal emphysema resulting from the initial injection. For these reasons, this approach, although often attempted, has been found unsatisfactory.11 16

More often a failed BB-DALK is converted into a manual DALK, by means of careful and painstaking hand dissection of the emphysematous tissue, with the purpose of leaving a recipient bed as thin and smooth as possible. This time-consuming step also bears a relatively high risk of perforation and, if haze results from the stromal interface and/or the recipient bed are irregular, vision may be affected in both quantity and quality with possible lack or delay of full recovery.8

In recent years, VB-DALK has been proposed as a surgical technique to bare DM, usually, as a second choice to be considered after failure of pneumatic dissection.11 17–19

The rationale of attempting OVD-assisted dissection after unsuccessful air injection is based on the evidence of small air bubbles and DM microdetachments also forming in those eyes in which BB could not be created.9 The loss of pressure, caused by the leakage of air through the corneal stroma; trephination edge, and/or trabecular meshwork and anterior chamber, may be responsible for stopping these microbubbles from merging and forming BB; for the same reason additional air injections through the same track fail to build intrastromal pressure high enough to create BB. Instead, when OVD is injected through the same track that was used unsuccessfully for air injection, the higher viscosity and surface tension of this substance makes it advance very slowly, even against reduced resistance, thus infiltrating the corneal tissue and probably sealing the interlamellar and intralamellar spaces created by the air previously injected. As a result, OVD may find its way into the spaces of small air-induced detachments, promoting their coalescence into a single bubble, which then extends up to the trephination edge size.

The amount of viscoelastic substance used in the procedures was neither fixed nor exactly measured; however, the volume of OVD sufficient to form the bubble and extend it up to the trephination edge usually ranged from 0.5 mL to 1.0 mL. According

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**Table 1** Baseline characteristics and postoperative measurements after big-bubble and viscobubble deep anterior lamellar keratoplasty (DALK)

<table>
<thead>
<tr>
<th>Measures</th>
<th>Big-bubble DALK</th>
<th>Viscobubble DALK</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative corneal curvature (D)</td>
<td>65.4±8.54</td>
<td>63.5±7.17</td>
<td>0.27</td>
</tr>
<tr>
<td>Preoperative thinnest point (μm)</td>
<td>350.5±74.24</td>
<td>364.0±27.34</td>
<td>0.34</td>
</tr>
<tr>
<td>Bubble formation</td>
<td>106/140 (75.71%)</td>
<td>28/30 (93.33%)</td>
<td>NA</td>
</tr>
<tr>
<td>Type 1 bubble</td>
<td>100/106 (94.34%)</td>
<td>28/28 (100%)</td>
<td>NA</td>
</tr>
<tr>
<td>Type 2 bubble</td>
<td>6/106 (5.66%)</td>
<td>0/28 (0%)</td>
<td>NA</td>
</tr>
<tr>
<td>BSCVA 3 months (logMAR)*</td>
<td>0.38±0.22</td>
<td>0.66±0.23</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BSCVA 6 months (logMAR)</td>
<td>0.17±0.12</td>
<td>0.18±0.10</td>
<td>0.67</td>
</tr>
<tr>
<td>BSCVA 12 months (logMAR)</td>
<td>0.11±0.08</td>
<td>0.13±0.07</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Data are expressed as mean ±SD.

*BSCVA, best spectacle-corrected visual acuity; D, dipters; logMAR, logarithm of the minimum angle of resolution; NA, not applicable.

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**Figure 2** Postoperative (6 months) slit-lamp appearance (left) and anterior segment optical coherence tomography (right) of one of the two eyes in which injection of both air and viscoelastic substance failed to create a big bubble. Central interface opacity and extensive deep stromal folds seen at the slit-lamp substantiate as high reflexivity and irregular profile of the interface in the tomogram.
to Dua, the risk of a bubble burst may be increased by extending the bubble size beyond 8.25 mm rather than by the amount of OVD injected; for this reason we limited, in all cases, the extension of viscodissection to that size.

In our series, all VBs originated from the central cornea, at the site of OVD injection and were classified as type 1, according to Dua’s classification. Although previous authors reported that VB-DALK exposes DM, they did not mention the morphology or other characteristics of the bubbles obtained and it is therefore quite possible that their judgement was flawed because Dua’s study had not been published till then. The absence of type 2 bubbles could be explained by the fact that the cohesive substance encounters much more resistance than air to diffuse between the stromal lamellae and does not migrate into the peripheral cornea where bubbles of type 2 form, thus eliminating this possibility.

As OVD must be injected at a pressure relatively higher than air, the fact that bubbles obtained this way are all of type 1 increases the safety of the procedure, as the residual PDL reduces the risk of bubble bursting and macroperforations.

As for air injection, for OVD injection several variables may play a role in facilitating the dissection by this substance (stage of keratoconus, and therefore tissue thickness and consistency, depth of injection, concentration and molecular composition of OVD, etc).

In order to standardise some of these possible variables, we included in our study only patients with keratoconus who underwent the same BB-DALK technique, which foresees creating an intrastromal track reaching a deep predescemetic plane (less than 65 µm from DM) in a reproducible fashion. In addition, for all VB-DALK the same track created for pneumatic dissection was used also to inject OVD; in this way we avoided preparation of another deep track through whitish, emphysematous and softened tissue, which would have been poorly reproducible and at high risk of perforation.

In our series, mean BSCVA was significantly better after BB-DALK than after VB-DALK only up to 3 months postoperatively, while at later examinations BSCVA did not differ significantly between the two surgical techniques and was similar to that reported in previous papers. We hypothesised that this result may be related to a minimal persistence of OVD in PDL (a 10 µm acellular layer composed of collagen type-I lamellae), inducing a temporary modification of its reflectivity (figure 3); we are presently undertaking a densitometric analysis of the stromal interface to verify this theory.

In the two VB-DALK procedures with failed bubble formation, completion of lamellar stromal dissection by hand was very challenging: it was difficult to judge the depth reached by the hand dissection as well as the smoothness of the surface created, as tissue infiltration of OVD changes substantially its characteristics, reducing its transparency and increasing its roughness. However, the poor visual result obtained and the presence of interface haze do not depend on the final thickness of the residual bed, which was below 50 µm in both cases. Probably it was the poor optical quality of the interface obtained by dissecting through tissue modified by OVD infiltration that affected the outcome, suggesting that failure of bubble formation at the time of VB-DALK should be treated by conversion to PK or mushroom PK rather than resorting to manual dissection.

Although our study only included eyes with transparent keratoconic corneas, the VB-DALK technique could also be used for eyes with other types of stromal diseases, even though we cannot anticipate whether the injection of OVD into stroma with different characteristics (presence of extensive scars, vessels, dystrophic and/or degenerative deposits) will result in outcomes similar to those obtained in keratoconic eyes.

In conclusion, our series confirms that a standardised sequential approach including an initial attempt with air injection followed secondarily by an OVD injection through the same track may succeed in BB formation in almost all cases (in our series 97.10%; ref. 11) final visual outcomes are similar, independently of the type of dissection, but in the first postoperative months OVD-assisted dissection negatively affects the interface transparency and reduces visual acuity significantly. Further studies are required to confirm the reproducibility of our results and eventually improve the technique, testing different types and concentrations of OVD or different depths of stromal injection.

Collaborators Domenico Ceravolo and Bruzzichessi Donatella.

Contributors VS was the guarantor of integrity for the entire study. VS and MB were involved in study design and manuscript revision/review. VDL, AL, AC, CB, GCS were involved in data acquisition. All authors were involved in statistical analysis. VS, VDL, AL, AC were involved in manuscript preparation.

Competing interests MB receives travel expenses reimbursement and royalties from Moria (Antony, France).

Patient consent Obtained.

Ethics approval Local ethics committee.

Provenance and peer review Not commissioned; externally peer reviewed.

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Clinical science


