

A comparison of different depth ablations in the treatment of painful bullous keratopathy with phototherapeutic keratectomy

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Abstract

Aim—To study the efficacy of phototherapeutic keratectomy (PTK) for pain relief for patients with painful bullous keratopathy and poor visual potential.

Methods—Patients with painful bullous keratopathy and poor visual potential were treated with superficial PTK (8–25 µm), intermediate (50–100 µm) or deep PTK (25% stromal thickness) using the Nidek EC5000 excimer laser after manual epithelial debridement. Follow up ranged from 1 to 24 months (mean 6.5 months). Outcome measures included symptomatic relief and need for further treatment.

Results—In the superficial PTK group five of eight (62%) patients improved symptomatically after treatment. The three (38%) who did not improve went on to have penetrating keratoplasty for pain relief. In the intermediate depth group only two of five (40%) patients had symptom alleviation. The three others (60%) required further procedures. 20 of 24 (83%) patients treated with deep PTK had significant or total alleviation of symptoms. Of these, one developed acute anterior uveitis 9 months after PTK and two required botulinum ptosis for persistent corneal epithelial defects, one of whom had three consecutive episodes of microbial keratitis. Three of 24 suffered occasional discomfort and one patient required a penetrating keratoplasty for continued pain.

Conclusion—PTK can be a useful therapeutic measure in painful bullous keratopathy with poor visual potential. Deep PTK appears to be more successful in pain management than superficial treatment.

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Bullous keratopathy is the painful end stage of a number of ocular conditions. Eyes with bullous keratopathy usually have an unstable epithelium and are at increased risk of developing microbial keratitis.^{1–3} Apart from a penetrating keratoplasty (PK), existing treatment modalities include lubricants, hyperosmotic agents, topical corticosteroid, and antibiotics,³ which typically have only a short term effect. Other options include the application of a bandage contact lens,^{3–6} covering the cornea with a conjunctival flap or amniotic membrane transplantation,⁷ diffuse anterior stromal puncture, and diamond burr polishing of Bowman's membrane. In an eye with low visual potential treatment of the pain by retrobulbar alcohol

injection, enucleation, or evisceration may even be appropriate. These treatments are not totally satisfactory for a variety of reasons: application of a bandage soft contact lens and the use of steroids may predispose to bacterial keratitis,^{2,3} conjunctival flaps may be cosmetically unsatisfactory; and the risk of rejection and lifelong care required with a corneal graft can pose a formidable problem to an elderly patient.

Thomann *et al*⁸ have reported phototherapeutic keratectomy (PTK) to be effective in the management of patients with bullous keratopathy from a variety of aetiologies; they report that the bullae resolve and pain is abolished in a large proportion of patients treated with a superficial ablation.

The preterminal neural plexus of the cornea is located just deep to Bowman's membrane. We hypothesised that a moderately deep ablation may have a superior effect on decreasing pain by the ablation of this neural plexus. It may also decrease swelling of the corneal stroma by decreasing the quantity of mucopolysaccharide and hence osmotic load. The increased scarring associated with a deeper ablation may also result in increased stability of the epithelium.

We report our experience in treating patients with painful bullous keratopathy and poor visual potential with both superficial and deep PTK.

Methods

Non-randomised consecutively presenting patients with painful bullous keratopathy and poor visual potential were included in the study. Patients were recruited through the corneal clinic at the Royal Victorian Eye and Ear Hospital or by corneal clinic consultants in their rooms.

Treatments were performed under topical anaesthesia using the Nidek EC5000 excimer laser following manual corneal epithelial debridement. A central 6.0–7.5 mm zone was treated with a surrounding 1 mm blend zone. Ablation zone diameter was determined by surgeon preference, the presence of pannus, and overall corneal diameter; maximum treatment zone was limited to 7.5 mm in order not prejudice future treatment options (penetrating keratoplasty).

There were three patient groups:

- (1) patients treated with superficial PTK—up to 25 µm central zone ablations
- (2) intermediate depth ablations varying from 50 to 100 µm in depth

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Table 1 Superficial phototherapeutic keratectomy treatment group

Patient	Age (years)	Sex	Indication (cause of BK)	Depth of ablation (μm)	Diameter of ablation (mm)	Follow up (months)	Outcome	Complications /further procedure
1	48	F	Penetrating injury Painful pseudophakia	25	9.0	1*	Persistent pain	Recurrent bullae PK at 1 month
2	81	M	Painful pseudophakia	25	9.0	6	Symptomatic relief	nil
3	83	F	Painful pseudophakia	25	9.0	11	Symptomatic relief	nil
4	86	F	Painful aphakia	8	9.0	13	Symptomatic relief	nil
5	80	M	Painful pseudophakia	25	7.5	3*	Persistent pain	PK at 3 months
6	42	M	Painful pseudophakia	25	7.5	5*	Persistent pain	PK at 5 months
7	86	F	Painful pseudophakia	25	9.0	12	Symptomatic relief	nil
8	79	F	Painful pseudophakia	25	9.0	11	Symptomatic relief	nil

BK = bullous keratopathy, PK = penetrating keratoplasty, *time at initiation of further (different) treatment.

(3) deep PTK—25% of central corneal thickness as assessed by ultrasound pachymetry before epithelial debridement.

Treatment depth varied between groups 1 and 2 as it became apparent that deeper ablations were feasible and could be more efficacious.

All patients were treated postoperatively with topical antibiotic (chloramphenicol) and corticosteroid (fluorometholone) one drop four times a day; both were stopped within 2 weeks of corneal epithelial healing. Patients were assessed for symptomatic relief during the postoperative period. In particular, the presence of persistent corneal epithelial defects (PED), recurrence of epithelial bullae, microbial keratitis, and requirement for further treatment were documented.

Results

The majority of patients had pseudophakic bullous keratopathy with no associated ocular or systemic disorder, patients with a different aetiology for their bullous keratopathy or associated systemic disorder are outlined in Tables 1–3.

SUPERFICIAL PTK

Eight consecutive patients with PBK were treated with superficial PTK (Table 1). Depth of treatment varied from 8 to 25 μm . Three patients (38%) required penetrating keratoplasty for pain relief at 2, 3, and 5 months after PTK. Follow up on the other five (62%) ranged from 6 to 13 months (mean 9.8 months); these five patients reported their eyes

were either markedly improved or completely comfortable after the procedure.

INTERMEDIATE DEPTH PTK

Five consecutive patients were treated with intermediate depth PTK (Table 2). Three (60%) required a penetrating keratoplasty or conjunctival flap for pain relief, only two (40%) had alleviation of symptoms following laser.

DEEP PTK

Twenty four consecutive patients were treated with a deep PTK (Table 3). Mean preoperative pachymetry was 762 μm (range 588–969 μm). In three patients pachymetry was not assessable preoperatively (because of the marked degree of stromal oedema). These three patients were treated empirically with 250 μm ablations. Mean ablation depth was 206 μm (range 147–290 μm). Follow up ranged from 1–18 months (mean 6.1 months).

Two patients continued to have pain from recurrent bullae: one went on to have a penetrating keratoplasty (Table 3, patient 19), the other had an amniotic membrane graft (Table 3, patient 2), both performed 3 months after PTK. Both patients are now symptom free.

A further two patients had intermittent discomfort and were retreated with PTK. One of these patients (Table 3, patient 20) had had an initial treatment zone of diameter 6.5 mm with a 250 μm ablation, 1 month after treatment he presented with a large recurrent crescent shaped bulla outside the treatment zone from 4 to 7 o'clock. He was re-treated in

Table 2 Intermediate depth phototherapeutic keratectomy (PTK) group

Patient	Age (years)	Sex	Indication	Pachymetry (pre-PTK, μm)	Depth of ablation (μm)	Diameter of ablation (mm)	Follow up (months)	Epithelial stability post PTK	Complications/further treatment
1	86	F	Pseudophakia, pain	N/R	50	9.0	2*	recurrent bullae	PK at 2 months
2	86	F	Painful pseudophakia	N/R	80	8.0	24	stable	nil
3	59	F	Failed PK, pain	N/R	100	6.5	1	recurrent bullae	deep PTK at 1 month
4	83	M	Pain, pseudophakia	620	100	8.0	1*	recurrent bullae	conjunctival (Gunderson) flap
5	75	F	Pain, band keratopathy, microbial keratitis, PED	828	100	7.5	4	microcyst s	nil

PK = penetrating keratoplasty, PED = persistent epithelial defect, *time at initiation of further (different) of treatment.

this area with a localised 150 µm ablation with the previously treated area masked by a cyclodialysis spatula. One month later he had a further bulla, again outside the treatment zone between 2 and 4 o'clock. One month later the bulla had resolved and no further excimer ablation was required. The second of these patients (Table 3, patient 14) was re-treated 8 months after the first ablation and was pain free at 1 month.

Three other patients reported significant improvement in symptoms but still have occasional discomfort. The follow up on these three patients ranged from 2 to 7 months. The 17 other patients (71%) describe their eyes as comfortable and pain free. Thus, symptoms were significantly or completely alleviated in a total of 20 of 24 patients (83%).

COMPLICATIONS (DEEP PTK)

In addition there were three other patients who had complications, despite symptom alleviation, after PTK.

One patient (Table 3, patient 22) had delayed corneal epithelial healing following a deep PTK—he retained a 2.0 by 1.5 mm epithelial defect at 6 weeks. He was treated with botulinum toxin ptosis and his epithelium healed within a month.

Another patient (Table 3, patient 12) developed microbial keratitis 2 months after PTK. This healed rapidly, but he re-presented with a further episode of microbial keratitis 3 months later; this again resolved but recurred within a month. On resolution of his third episode of microbial keratitis he was left with a 1.5 by 3.0 mm persistent corneal epithelial defect and

Table 3 Deep phototherapeutic keratectomy group

Patient	Age (years)	Sex	Indication	Pachymetry (pre-PTK, µm)	Depth of ablation (µm)	Ablation diameter (mm)	Follow up (months)	Epithelial stability post PTK	Complications /further treatment
1	81	F	Painful aphakia	N/R	250	7.5	18	stable epithelium	nil
2	59	F	Failed corneal graft	969	290	7.5	12	recurrent pain, no large bullae	nil amniotic membrane graft at 3 months
3	84	M	Painful pseudophakia	588	147	7.5	11	microcysts	nil
4	84	F	Painful pseudophakia	708	175	7.5	11	microcysts	nil
5	84	M	Painful pseudophakia	900	250	7.5	9	few small recurrent bullae	nil
6	89	M	Painful aphakia	892	160	9.0	10	few small recurrent bullae	nil
7	49	M	Failed corneal graft pain	831	195	7.0	7	recurrent bullae Symptomatic improvement	occasional discomfort
8	50	M	Birth (forceps) trauma, pain	800	200	7.5	5	microcysts Symptomatic improvement	occasional discomfort
9	59	F	Buphthalmos Painful pseudophakia	913	228	7.5	9	microcysts	acute anterior uveitis at 8 months
10	72	F	Painful pseudophakia	694	173	7.0	1	microcysts	nil
11	70	F	Painful pseudophakia	817	204	7.5	6	microcysts	nil
12	84	M	Painful pseudophakia	675	160	7.5	8	PED	microbial keratitis ×3, subsequent PED requiring Botox ptosis
13	86	F	Painful pseudophakia	785	195	7.5	6	microcysts	nil
14	81	M	Painful pseudophakia	825	200	7.5	9	recurrent bullae	retreatment at 8 months, now pain free
15	75	F	Painful pseudophakia	834	209	7.5	3	microcysts	nil
16	80	M	Painful pseudophakia	964	240	7.0	4	microcysts	nil
17	73	F	Painful Pseudophakia	764	191	7.5	3	microcysts	nil
18	71	F	Painful pseudophakia	810	190	7.5	3	microcysts	nil
19	76	F	Painful pseudophakia	620	155	7.5	3*	recurrent bullae + pain	PK at 3 months
20	81	M	Pseudophakia	N/R	250	6.0	2	microcysts	required retreatment at 1 month
21	27	F	Diabetic PVR Painful pseudophakia	N/R	250	7.5	2	microcysts Symptomatic improvement	occasional discomfort
22	60	M	Aphakia, pain, microbial keratitis	800	200	7.5	3	PED	Incomplete epithelial healing. Botox ptosis at 1 month
23	83	F	Painful pseudophakia	710	177	7.5	1	microcysts	nil
24	81	F	Failed corneal graft, pain	855	214	7.5	2	microcysts	nil

PK = penetrating keratoplasty, PVR = proliferative vitreoretinopathy, PED = persistent epithelial defect, Botox = botulinum toxin, *time at initiation of further (different) treatment.

underwent a botulinum toxin ptosis. A month later his epithelium was healed and stable.

The third patient (Table 3, patient 9) had a previous history of buphthalmos and anterior uveitis and presented with a further episode of uveitis 8 months after PTK, her corneal epithelium was stable.

Discussion

Our experience suggests that PTK may be an effective treatment for the resolution of pain and discomfort in symptomatic painful bullous keratopathy. Deep PTK appears to be more successful and associated with a lower requirement for further treatment in comparison with superficial PTK.

Pires *et al*⁷ found that amniotic membrane transplantation resulted in alleviation of symptoms in 90% of patients with mean follow up period of 34 weeks; our results for deep PTK are comparable with this. Anterior stromal puncture, also commonly used for symptomatic BK, has been shown to decrease corneal sensitivity and area covered by bullae⁹ and increased the proportion of pain-free patients from 40% pretreatment to 70% post-treatment; however, this treatment may be associated with a risk of corneal perforation.

Two patients who developed persistent epithelial defects after PTK had had the routine post-PTK topical medication; it is unlikely that this treatment is implicated in the delayed epithelial healing in these patients. Those on topical antihypertensive therapy did not manifest delayed healing or further epithelial breakdown. The three patients with concomitant intraocular disease (buphthalmos glaucoma, insulin dependent diabetes, and idiopathic anterior uveitis) showed no delayed healing and had stable epithelium at last review, examination of the influence of other disorders on the outcome of PTK would require a larger study.

The main sensory nerve plexus in the cornea (derived from the nasociliary branch of the ophthalmic division of the trigeminal nerve) is located in the stroma in the immediately subepithelial region, with a lower density plexus deeper in the stroma.¹⁰ Peak sensitivity, neural density, and occurrence of bullae are maximal in the central cornea.^{11 12}

One rationale for this treatment is ablation of these nerve plexuses thereby reducing corneal sensation. Deep PTK would be expected to ablate the subepithelial plexus more completely than superficial PTK and in addition partially ablate the deeper plexus. The lack of discomfort in the two patients who had persistent epithelial defects following deep PTK supports this theory. This resultant neurotrophin theoretically increases the risk of epithelial breakdown and microbial keratitis; we saw little evidence of this with a stable epithelium present in the majority of patients post PTK. Indeed the excimer ablation may stabilise epithelial adhesion to the underlying stroma making the formation of large bullae less likely.¹³ Anterior stromal puncture has been shown to increase expression of extracellular

proteins (type IV collagen, fibronectin and laminin) in bullous keratopathy.¹⁴ These substances are important in epithelial adhesion to the underlying stroma¹⁵; a similar process may occur following photoablation. Furthermore, the reduced thickness of the cornea could also reduce the extent of epithelial oedema by reducing the osmotic load of the stroma thereby increasing the efficacy of "dehydration" of the cornea by the remaining endothelium.

This treatment modality has several other advantages: it is a quick procedure, easy to perform, relatively cheap, and conserves donor corneal material for cases where visual rehabilitation is possible. Additionally hospital admission is not required and importantly the treatment does not prejudice other treatment options—such as penetrating keratoplasty—should they be required at a later time.

The two patients requiring retreatment (deep PTK) illustrate that the treatment zone should be large enough to prevent symptom recurrence from bullae reforming outside the ablation area. We now believe that at least an 8 mm central zone with a 1 mm blend zone and 25% stromal depth ablation may be appropriate to limit potential recurrence; these parameters are easily adjusted for with the Nidek EC 5000 laser used in this study.

Patients in our study were not randomised and were treated consecutively with increasing ablation depth; this introduced the possibility of selection bias, a standard ablation zone size would also increase comparability between patients. A prospective, randomised masked trial with a standardised treatment zone and depth is required to assess the efficacy of this treatment.

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