Combined penetrating keratoplasty and pars plana vitrectomy with the use of temporary keratoprosthesis

Kombinirana operacija presaditve roženice in pars plana vitrektomije z uporabo začasne keratoproteze

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Abstract

Background: Severe ocular trauma is surgically challenging and prognostically questionable due to injury of anterior and posterior segment. We evaluated the outcome of combined penetrating keratoplasty and pars plana vitrectomy with the use of temporary keratoprosthesis (PKP+PPV/TK) for such cases.

Methods: In a retrospective study records of 7 patients (7 eyes) with severe ocular trauma, who underwent PKP+PPV/TK in 2002–2007 at the Eye Hospital Univesity Clinical Centre Ljubljana, were evaluated. Final follow-up was done in 2008.

Results: The length of follow-up was 1–6 years (mean 3.3). All patients were male, 20 to 61-years-old. The mechanisms of injury were explosion, assault or injury with an object. There were 6 open globe injuries, of them one with IOFB, and one contusion with partial thickness corneal laceration and posttraumatic fungal keratitis and endophthalmitis. Retinal detachment occurred in 5 patients. Visual acuity at presentation was light perception (LP) in 6 patients, one patient was sedated. The PKP+PPV/TK was performed within two days (2), 10–15 days later (3) and more than 1 month later (2).

The visual outcome at the final follow-up was 0.9–1.0 cc in 2 patients, satisfactory (0.1 cc) in one, and bad (LP) in 3 patients. One painful blind eye was enucleated.

Complications included corneal graft failure, retinal detachment with proliferative vitreoretinopathy, secondary glaucoma and phthysis.

Conclusions: In two of seven eyes (28.6 %) excellent visual outcome after PKP+PPV/TK was achieved. Both were operated within 2 days after occurrence of pathological changes at posterior segment. Technically difficult PKP+PPV/TK

is a useful method in eyes, which could not be treated otherwise. The success depends on timing of the surgery and severity of the injury. It is necessary to have urgent corneal tissue access to perform the procedure in time.

Izvleček

Izhodišča: Hude poškodbe očesa so kirurško zahtevne in prognostično težko napovedljive zaradi hkratne poškodbe več očesnih struktur ali sekundarnih sprememb težko poškodovanega očesa. V raziskavi smo analizirali izhod kombinirane operacije presaditve roženice (PKP) in pars plana vitrektomije (PPV) z uporabo začasne keratoproteze pri poškodovanih očeh.

Metode: Raziskava je retrospektivna. Pregledali smo hospitalno dokumentacijo sedmih bolnikov – sedem oči z okvaro roženice in zadnjega segmenta, pri katerih je bila napravljena penetrantna keratoplastika v kombinaciji s pars plana vitrektomijo v letih 2002 do 2007 na Očesni kliniki UKC Ljubljana. Vse bolnike smo ponovno pregledali v letu 2008. Analizirali smo vzrok poškodbe, klinični potek, anatomski izhod in končno vidno funkcijo.

Rezultati: Bolnike smo sledili 1 do 6 let (povprečno 3,3 leta). Vsi bolniki so bili moški, stari 20 do 61 let (povprečno 42 let). Mehanizem poškodbe je bil eksplozija (2 bolnika), udarec z roko ali predmetom (5 bolnikov). Tri poškodbe so bile penetrantne z laceracijo roženice, dve rupturi, ena poškodba z intraokularnimi tujki in ena kontuzijska poškodba s posttravmatskim gljivičnim keratitisom in endoftalmitisom. Neposredno po poškodbi je bil odstop mrežnice prisoten pri 5 bolnikih. Vidna ostrina po poškodbi je bila dojem svetlobe pri 6 bolnikih; pri enem pa zaradi sedacije ni bila določljiva. PKP+VP je bila napravljena v 1-2 dneh pri 2 bolnikih, 10-15 dni kasneje pri 3 bolnikih in več kot 1 mesec kasneje pri 2 bolnikih.

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Ključne besede:

keratoplastika, keratoproteza, poškodba očesa, vitrektomija, roženica

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Prispelo: 6. apr. 2009, Sprejeto: 9. avg. 2009 Izhod vidne funkcije je bil odličen (0.8–1.0cc) pri 2 bolnikih, zadovoljiv (0.1cc) pri enem bolniku in slab (dojem svetlobe) pri 3 bolnikih. Pri enem bolniku iz zadnje skupine je bila zaradi bolečega sekundarnega glavkoma potrebna enukleacija. Komplikacije po večletnem sledenju so bile odpoved roženičnega presadka, odstop mrežnice s PVR, težko vodljiv sekundarni glavkom ter atrofija zrkla.

Zaključki: Pri dveh od sedmih (28,6%) oči je bil izhod po kombiniranem posegu PKP+PPV

Introduction

In severe ocular trauma the anterior and the posterior segment can be directly injured or secondarily decompensated. The pull on the retina due to vitreous prolapse or proliferative vitreoretinopathy may lead to retinal detachment. Intraocular foreign bodies need to be removed and more so, if they cause intraocular inflammation. Corneal opacity prevents vitreoretinal surgery, which is the key to visual preservation in such cases.1 If the penetrating keratoplasty is preformed as a preparatory procedure, the delay of the vitreoretinal surgery could worsen the outcome.² The use of temporary keratoprosthesis (Eckardt temporary keratoprosthesis, Landers wide-field temporary keratoprosthesis) allows early vitreoretinal surgery with clear view of the posterior segment and a closed-pressure system. The Eckardt temporary keratoprosthesis, which is used at our institution (Figure 1), is manufactured in two different sizes (\$\phi_7\$ mm and 8 mm) for phakic or aphakic eyes.³ It is squeezed in the trepanned cornea and secured to it. It allows wide field pars plana vitrectomy and also preserves the peripheral cornea for penetrating keratoplasty, which is done subsequently.⁴ Surgical outcome depends on the extension of the posterior segment pathology.



z uporabo začasne keratoproteze odličen. Obe očesi sta bili operirani v 2 dneh po nastopu patoloških sprememb zadnjega segmenta.

Tehnično zahtevni kombinirani poseg presaditve roženice s pars plana vitrektomijo in uporabo začasne keratoproteze je uporabna metoda pri očeh, ki jih sicer drugače ne bi mogli zdraviti. Uspešnost je odvisna predvsem od pravočasnosti posega in od teže poškodbe. Da bi poseg pravočasno izvedli je potrebno zagotoviti možnost takojšnje pridobitve roženičnega presadka.

In this retrospective study we reviewed and analyzed the anatomic and visual outcome after penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis.

Methods

Study design

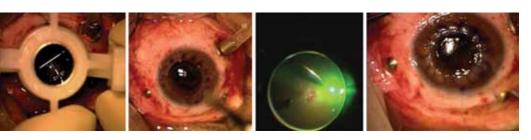
A retrospective study was designed. The hospital records, surgical reports and outpatient clinic follow up documentation of seven patients (seven eyes), who underwent the penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis between years 2002 and 2007 at the Eye Hospital, University Clinical Centre Ljubljana, were reviewed. All patients were invited for additional follow-up in the year 2008. For the patients who were unable or unwilling to attend it, the last documented follow-up from the outpatient clinic records was considered the final outcome.

Inclusion criteria

The eyes had to have a history of severe trauma with injury of the anterior and posterior segment or the complications involving anterior or posterior segments after ocular trauma. The penetrating keratoplasty combined with pars plana vitrectomy were performed by the same surgeons (MGP, VP), and the use of the Eckardt temporary keratoprosthesis had to be documented. The follow-up of at least one year was mandatory.

Figure 1: The Eckardt tempo

Eckardt temporary keratoprosthesis is made of silicone, 7 mm or 8 mm in diameter and is secured to the cornea with sutures. Figure 2: The technique of penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis.



Surgery

The technique of penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis is illustrated in Figure 2.

Infusion cannula is first secured to the sclera, 3.5 mm posterior to the limbus (first picture from the left in Figure 2). A vacuum trephine is then centred on the cornea, even in the presence of freshly closed lacerations (first picture from the right in Figure 2). Further, the recipient bed is made for the Eckardt keratoprosthesis-TKP (\u03c6 7 mm, silicone), which is then secured to the cornea (second picture from the left in Figure 2). Pars plana vitrectomy is performed next using various vitreoretinal techniques for retinal alignment (perfluorocarbon, laser photocoagulation, etc) and when needed IOFB removed (third picture from the left in Figure 2). The surgery is preceeded with corneal transplantation, silicone oil tamponade and closure of sclerotomies (fourth picture from the left in Figure 2).

Documentation

Patient's demographic data, mechanism of the eye injury and presenting visual function and clinical exam of the eye was documented first. Details of the surgery timing, any additional surgery(ies) and/or complications were collected. The anatomic and the visual outcome, and any late complication were evaluated from the documentation or from the additional follow-up visit in the 2008.

Results

Demographic data, mechanism of injury and clinical exam at presentation are shown in Table 1. All patients were male, ranged from 20 to 61-year-old-mean 42 years. The mechanism of injury was explosion – 2 eyes, assault or injury with an object – 4 eyes. There were 3 penetrating injuries with corneal laceration, 2 ruptures, one injury with intrabulbar foreign body, and one contusion with partial thickness corneal laceration and subsequent posttraumatic fungal keratitis and endophthalmitis. The most frequent posterior segment pathology was retinal de-

	Sex, Age yr	RE/LE	Trauma type	BCVA	Anterior segment pathology	Posterior segment pathology
1	M, 45	RE	Penetrating	LP	Corneal laceration	Retinal detachment, vitreous haemorrhage
2	M, 31	LE	Penetrating	LP	Corneal laceration	Retinal detachment
3	M, 36	RE	Penetrating	LP	Corneal laceration	Retinal detachment
4	M, 61	LE	Contusion	LP	Fungal corneal ulcer	Endophthalmitis
5	M, 51	LE	Rupture	LP	Corneal laceration	Retinal detachment, vitreous haemorrhage
6	M, 51	LE	Rupture	LP	Corneal laceration	Retinal detachment
7	M, 20	RE	IOFB	UKN	Corneal laceration	Vitreous haemorrhage, IOFB

Table 1: Patient data.

IOFB – intraocular foreign body, LE – left eye, LP – light perception, RE – right eye, UKN – unknown, yr – years

Figure 3: Case 1 – 61-year-old male patient with non-penetrating injury of the left eye with a tree branch.

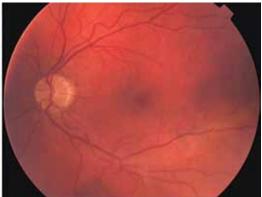


tachment in 5 eyes, followed by intraretinal foreign bodies in 1 eye, and endophthalmitis in 1 eye. Visual acuity at presentation was light perception in 6 eyes; in one patient the visual acuity could not be obtained due to conscious sedation in the intensive care unit.

The combined PK and PPV was done within two days in 2 eyes, 10 to 15 days later in 3 eyes and more than 1 month later in 1 eye. Table 2 shows all surgeries performed.

The follow up was 1 to 6 years (mean 3.3 years), Table 3. The visual outcome was excellent (0.9–1.0 cc) in 2 eyes, satisfactory (0.1 cc) in one eye and bad (light perception) in 3 eyes. One eye from the last group was enucleated due to painful secondary glaucoma.

At the final follow-up visit two corneal grafts were clear, one was partially and 3 were completely opaque with neovascularisation. 2 of the eyes with transparent corneas were aphakic and one pseudophakic. In all 3 of these eyes with transparent cornea, the retina was attached. In the other 3 eyes with opaque corneal graft, the ultrasonic ex-



amination revealed retinal detachment with PVR, combined with glaucoma and with completely excavated disc in one eye and with ocular atrophy in one eye. One eye had been enucleated because of painful absolute glaucoma without any complications of the socket.

Case illustrations

Case 1

61-year-old male patient presented with a non-penetrating injury of the left eye with a tree branch. Two months later fungal corneal ulcer and endophthalmitis developed. The patient was immediately transferred to our institution, with visual acuity of LP and severe inflammation in the left eye (Figure 3, left picture). Penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis was performed immediately. A subsequent secondary IOL implantation, viscocanalostomy and pupiloplasty were done two years later. The visual outcome

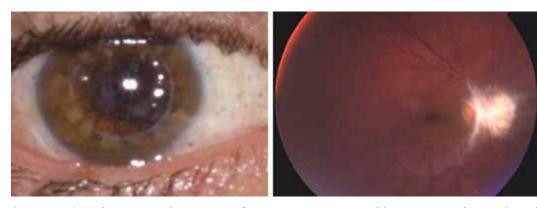
	Sex, Age yr	RE/LE	Combined procedure delay	Surgical procedure(s)	Subsequent surgical procedure(s)
1	M, 45	RE	Intermediate	1.Lx 2.PPV, Sil, PK	SOR
2	M, 31	LE	Late	1.PPV, Sil, PK	
3	M, 36	RE	Intermediate	1.PPV, Sil, PK	
4	M, 61	LE	Early	1.PPV, Lx, PK, Amfo+Vanko	IOL
5	M, 51	LE	Intermediate	1.PPV, Sil, SelfPK 2.PK	
6	M, 51	LE	Late	1.PPV, Sil 2.SOR, Sil, PK	Enucleation
7	M, 20	RE	Early	1.PPV, IOFB removal, Lx, Sil, PK	SOR

Table 2: Surgery data.

EARLY...1-2 days, INTERMED...3-14 days; LATE...more than two weeks;

IOFB-intraocular foreign body, IOL-secondary intraocular lens implantation, Lx-lensektomy, PK-penetrating keratoplasty, PPV-pars plana vitrectomy, SelfPK-keratoplasty with own cornea, Sil-silicone oil tamponade, SOR-silicone oil removal,

Figure 4: Case 2 – 20-year-old male patient with explosive-related injury and IOFB of the right eye and severe eye damage of the left eye.



(BCVA 1.0) and anatomical outcome of anterior and posterior segment (Figure 3, right picture) five years later are excellent.

Case 2

20-year-old male patient had explosive injury and IOFB of the right eye and severe eye damage of the left eye. The patient was seen by an ophthalmologist in the intensive care unit immediately after trauma. Primary surgical intervention was done. On the very next day the penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis was performed on the better right eye. The right eye was left aphakic with excellent visual (BCVA 0.9) and anatomical outcome (Figure 4) 1 year later.

Discussion

The anatomic and visual success rate after severe injured eyes managed with combined penetrating keratoplasty and pars plana vitrectomy depends on the extent of pre-existing injury of the anterior and the posterior segment and on timing of the surgery.⁵

In our study the visual acuity on the final follow-up visit improved compared to the preoperative value in three eyes of seven operated eyes (42.3%). An excellent visual outcome (BCVA 0.9–1.0) was achieved in two eyes. In one eye with multiple IOFBs (patient No. 7 in Table 1 and Table 2), operated one day after injury. It was also achieved in an eye with fungal corneal ulcer and endophthalmitis after eye contusion (patient No. 4 in Table 1 and Table 2), operated on the same day as transferred to our institution. In one eye satisfactory ambulatory vision (BCVA 0.1) was attained. This eye had a penetrating stab injury with primary surgical intervention and lensectomy. The combined procedure was done within 2 weeks. In the rest of the eyes the VA remained the same as after trauma or deteriorated. Our 2 patients, who were operated immediately after eye injury or appearance of endophthalmitis despite bad preoperative visual function (in one patient VA was LP, in one patient the VA could not be tested due to general sedation), performed the best on the final follow up visit with the VA of 0.9–1.0.

Proper timing of vitrectomy is very important in functional and anatomic prognosis after severe eye injury or related endophthalmitis. Early vitrectomy can lower the probability of proliferative vitreoretinopathy and retinal detachment, which are frequent in severe trauma and associated with poor anatomic and visual prognosis.5,6,7 With early vitrectomy performed in the first days after trauma retinal tears and detachment can be treated, and fibrocellular proliferation can be prevented, we can remove infection, growth factors, and blood from vitreous cavity. The disadvantages are higher risk of bleeding, wound leakage, increased difficulty to detach the posterior hyaloid and control suprachoroidal haemorrhage. In spite of possible complications of early vitrectomy for severe trauma with extensive damage to the eye, early vitrectomy can alter the prognosis.

To perform pars plana vitrectomy using the temporary keratoprosthesis and corneal grafting successfully, it is necessary to have the possibility of urgent corneal tissue access. Alternative suturing of own corneal button at the end of the combined procedure is the choice for temporary postponing corneal grafting. But because of opaque cor-

	Sex, Age yr	RE/LE	Follow up yr	Final BCVA	Corneal graft	Retina	Complications
1	M, 45	RE	6	0.1	Clear	Attached, normal	
2	M, 31	LE	3	LP	Opaque, NV	Detached, anterior PVR	Atrophy
3	M, 36	RE	3	LP	Opaque, oedema	Detached, PVR	
4	M, 61	LE	5	1.0	Clear	Attached, normal	
5	M, 51	LE	2	LP	Opaque, oedema	Detached, PVR	Absolute glaucoma
6	M, 51	LE	3	/	Opaque, NV	/	Absolute glaucoma
7	M, 20	RE	1	0.9	Clear	Attached, retinal scar	

Table 3: Outcome.

LP -light perception, NV-neovascularisation, PVR-proliferative vitreoretinopathy

nea the postoperative control of the posterior segment is impossible. Secondary donor grafting in patient No. 5 (Table 1, 2, 3) was performed in 4 days after primary combined procedure and resulted in opaque cornea and absolute glaucoma.

Visual and anatomic success also depends on the extent of the injury and retinal detachment.7,8,9,10 Both two patients with excellent final visual acuity were without retinal detachment after injury. Retinal detachment occurring immediately after the eye trauma is a serious complication of eye injury and has a poor prognosis for successful outcome.⁸ For those eyes early vitrectomy is mandatory for obtaining al least some anatomic and visual prognosis. In all 5 of our patients with retinal detachment occurring after trauma, the combined procedure was done as soon as corneal graft was assessable; but more than 10 days after injury. Four of these patients had opaque cornea, silicone oil tamponade, retinal detachment with PVR and visual acuity deteriorated at the final follow-up examination; one eye was enucleated. The most common complication and reason for failure in managing of severe ocular trauma is proliferative vitreoretinopathy,¹¹ which was also the case in our study (Table 3).

Long-term improvement in visual acuity after combined procedure was reported in as little as $16 \% - 21 \%^{2, 11}$ and in as high as $82 \%^{12}$ of operated eyes. Our results fall in-between the above mentioned extremes with 42.8 % (3 of 7 eyes) improvement of visual acuity and 28.6 %(2 of 7 eyes) excellent visual acuity achievement. The authors in the literature claim the worse visual outcome to be the result of performing surgery even in the most severely injured eyes.¹¹ Should a more selective approach towards the most severely injured eyes bring better visual outcome, is a matter of debate. However, in a patient with extensive and often bilateral eye injury or other pathology, the motivation for surgery, expectation and realistic goal may only be to salvage the eye and not to improve the visual acuity.¹¹ Besides patient selection issue, our data show that the delay of repair of the posterior segment pathology plays an important part in visual outcome.

According to the literature, the corneal graft survival depends on the delay of the keratoplasty more than 2 months after injury, usage of the silicone oil tamponade, attachment of the retina, preoperative visual acuity of at least hand motions and any further surgeries.¹¹ The reports of immune graft rejection are varying, ranging from 4 % to 28.6 %,^{12,13,14} and there is most probably an underestimation of it due to the problem of detection. Namely, in an eye with low acuity slight haziness or blurring can easily be missed by the patient. From the retrospective review, we were not able to detect possible immune rejections of the 4 finally opaque corneal grafts. Anyhow, in patient No. 2 most probable cause of corneal graft opacification was phthisis, in patients No. 5 and 6 the cause could be the glaucoma. There is no obvious cause in patient No. 4; the patient had had permanent silicone tamponade, which is considered a risk factor for graft failure.11,14,15

Uncontrolled glaucoma is according to the literature not a major problem after the penetrating keratoplasty combined with pars plana vitrectomy temporary keratoprosthesis.^{11,12} One of the patients (patient No. 6) developed uncontrolled glaucoma, painful blind eye after two pars plana vitrectomies with silicone oil tamponade due to complicated retinal reablation. The eye needed to be enucleated. Another patient (patient No. 5) presented with advanced glaucoma with total disc excavation at the final follow up. According to unwilling for further actions, a possibility of low compliance for medical pressure control exists.

Technically difficult penetrating keratoplasty combined with pars plana vitrectomy using the temporary keratoprosthesis enables surgical rehabilitation of otherwise inoperable eyes. It allows comprehensive anatomical reconstruction of the injured eye with opaque cornea, so that the best possible visual outcome can be achieved. The success rate depends on the extent of pre-existing injury of the anterior and the posterior segment and on the timing of the surgery. If operated early, better VA could be attained. However, when severe bilateral injury occurs, the motivation for extensive ocular surgery (even if delayed) can be different, aiming at ambulatory vision or even ocular salvage.

Abbreviations

- IOFB intraocular foreign body
- IOL secondary intraocular lens implantation
- LP light perception
- NV neovascularisation
- PK penetrating keratoplasty
- PKP+PPV/TK combined penetrating keratoplasty and pars plana vitrectomy with the use of temporary keratoprosthesis
- PPV pars plana vitrectomy
- PVR proliferative vitreoretinopathy
- SelfPK keratoplasty with own cornea
- Sil silicone oil tamponade
- SOR silicone oil removal
- UKN unknown
- Yr years

References

- Skorpik C, Menapace R, Gnad HD, Paroussis P. Silicone oil implantation in penetrating injuries complicated by PVR. Results from 1982 to 1986. Retina 1989; 9: 8–14.
- 2. Garcia-Valenzuela E, Blair NP, Shapio MJ, Gieser JP, Resnick KI, Solomon MJ, et al. Outcome of vitreoretinal surgery and penetrating keratoplasty using temporary keratoprosthesis. Retina 1999; 19: 424–9.
- D.O.R.C. International b.v. Focus on highlights. http://www.dorc.nl/literature/highlights_upgrade_05-2009.pdf
- 4. Eckardt C. A new temporary keratoprosthesis for pars plana vitrectomy. Retina 1987; 7: 34–7.
- Dong X, Wang W, Wie L, Chiu AM. Long-term outcome of combined penetrating keratoplasty and vitreoretinal surgery using temporary keratoprosthesis. Eye 2006; 20: 59–63.
- Rahman I, Maino A, Devadason D, Leatherbarrow B. Open globe injuries: factors predictive of poor outcome. Eye 2006; 20: 1336–41.
- Tseng W, Cortez RT, Ramirez G, Stinnett S, Jaffe GJ. Prevalence and risk factors for proliferative vitreoretinopathy in eyes with rhegmatogenous retinal detachment but no previous vitreoretinal surgery. Am J Ophthalmol 2004; 137: 1105–15.
- Globocnik Petrovic M, Lumi X, Drnovsek Olup B. Prognostic factors in open eye injury managed with vitrectomy: retrospective study. Croat Med J 2004; 45: 299–303.
- Cruvinel Isaac DL,Ghanem VC, Nascimento MA, Torigoe M, Kara-Jose N. Prognostic factors in open globe injuries. Ophthalmologica 2003; 21: 431–5.
- Yan H, Cui J, Zhang J, Chn S, Xu Y. Penetrating keratoplasty combined with vitreoretinal surgery for severe ocular injury with blood-stained cornea and no light perception. Ophthalmologica 2006; 220: 186–9.
- Roters S, Szurman P, Hermes S, Thumann G, Bartz-Schmidt KU, Kirchhof B. Outcome of combined penetrating keratoplasty with vitreoretinal surgery for management of severe ocular injuries. Retina 2003; 23: 48–65.
- Gallemore RP, Bokosky JE. Penetrating keratoplasty with vireoretinal surgery using the Eckardt temporary keratoprosthesis: modified technique allowing use of larger corneal grafts. Cornea 1995; 14: 33–8.
- Gelender H, Vaiser A, Snyder WB, Fuller DG, Hutton WL. Temporary keratoprosthesis for combined penetrating keratoplasty, pars plana vitrectomy, and repair of retinal detachment. Ophthalmology 1988; 95: 897–901.
- Noorily SW, Foulks GN, McCuen BW. Results of penetrating keratoplasty associated with silicone oil tamponade. Ophthalmology 1991; 98: 1186–9.
- Karel I, Kalvodova B, Kuthan P. Results of penetrating keratoplasty in bullous silicone oil keratoplathy. Graefes Arch Clin Exp ophthalmol 1998; 236: 255–8.