·Clinical Research·

General anesthesia versus local anesthesia for penetrating keratoplasty: a prospective study

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Abstract

• AIM: To examine which anesthesia general or local is more effective for penetrating keratoplasty (PKP).

• METHODS: Patients with indications for PKP (n=141) were enrolled in a prospective study and randomly divided into general anesthesia group (group A, 70 eyes) and local anesthesia group (group B, 71 eyes). Patients received optical PKP (group A1, 30 eyes; group B1, 30 eyes) or therapeutic PKP (group A2, 40 eyes; group B2, 41 eyes). Measurement of anterior chamber treatment time (T) for PKP patients and the ratio (R) of the area of the pupils to that of recipient graft region. T and R values, as well as perioperative and postoperative complications, were compared between groups A and B using t-test or χ^2 test.

• RESULTS: Patients were followed for 2wk after PKP. T was (13.45±8.64)min for group A and (7.36±5.24)min for group B, a statistically significant difference (P<0.001). The R value for group A was stable during the operation, while for PKP patients in group B the value initially increased then gradually decreased to normal after suturing. In group B, extrusion of intraocular contents occurred in 5 eyes, and iridal prolapse occured in 11 cases; no perioperative complications occurred in group A. Relapse rate for fungal keratitis was 13.04% in group B and 0% in group A.

• CONCLUSION: Under general anesthesia, pupils remaine stable during PKP and perioperative complications are averted. General anesthesia gives more time to treat pathological changes in the anterior chamber and treatment success rate is higher.

• KEYWORDS: penetrating keratoplasty; general anesthesia; local anesthesia
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INTRODUCTION

Penetrating keratoplasty (PKP), a mature micro-surgical technique, is often the first choice for patients with severe corneal disease and full-thickness corneal involvement[1-3]. However, PKP performed with the potential for serious complications [4-6]. Non-cooperation of patient and surgical error can both lead to serious consequences, such as extrusion of the intraocular contents. PKP is routinely performed under local anesthesia [7-10]. Although local anesthesia has some advantages, such as simplicity, no preoperative fasting requirement, and lower cost, it is usually hard to obtain full cooperation from patients, especially with extended operation times. Therefore, surgeons have to perform PKP quickly, which is highly stressful and also limits the time available to treat pathological changes in the anterior chamber, which increases the risk and decreases the success rate of PKP [11,12]. General anesthesia is used less frequently in PKP than local anesthesia due to its higher cost and greater complexity; however, full cooperation can be obtained from patients who undergo general anesthesia and surgeons then have more time to treat pathological changes in the anterior chamber, possibly reducing risks and increasing the success rate for PKP. In order to determine which anesthesia method is better for PKP, we carried out a prospective study to compare general anesthesia with local anesthesia in patients receiving PKP.

SUBJECTS AND METHODS

Subjects One hundred forty-one patients (141 eyes) receiving PKP between June 2008 to July 2011 in our department were recruited in this study. The average age was 43.71 ±20.35y. The study protocol was reviewed and approved by the Ethics Committee of the Medical School of Shandong University, and informed consent were obtained from all patients. The study was conducted in accordance with the tenets of the Declaration of Helsinki. The patients were randomly divided into 2 groups: general anesthesia group (group A, 70 eyes) and local anesthesia group (group B, 71 eyes). Each group was further divided into 2 subgroups: optical PKP (A1, 30 eyes and B1, 30 eyes) and

Table 1 Clinical characteristics for penetrating keratoplasty

PKP type	Preoperative diagnosis	Group A		Group B		Total
		Diameter of the graft ≤8 mm	Diameter of the graft >8 mm	Diameter of the graft ≤8 mm	Diameter of the graft >8 mm	
Optical	Keratoconus	11		17		
	Leucoma	8		6		
	Bullous keratopathy	6		4		60
	Corneal dystrophy	3		2		
	Corneal degeneration	2		1		
Therapeutic	Fungal keratitis	5	20	8	15	
	Adherent leucoma	4	3	4	4	
	Viral keratitis	3	3		6	81
	Bacterial keratitis		2		4	
Total		70		71		141

Group A: Optical PKP with general anesthesia; Group B: Optical PKP with general anesthesia.

therapeutic PKP (A2, 40 eyes and B2, 41 eyes). If the patient's condition can allow elective surgery and waiting time for fresh corneal material, the purpose of the PKP is to improve vision and they were included in the optical PKP group. If the patient's disease is in active state, the patient's condition is stable after drug treatment, and the patient is very painful because the lesion cannot be eliminated, the purpose of the PKP is to preserve the eye and relieve the pain. For those patients, recovery of visual acuity will be considered at a later stage. Those patients were included in the therapeutic PKP group. Patients with the following conditions were excluded from the study: patients with specific diseases such as severe heart disease and mental illness, patients with intraocular content extrusion, patients taking long-term medications, and patients with systemic application of corticosteroids. Patients' diagnoses are listed in Table 1. All patients' lens and scleral elasticity were normal.

Methods

General anesthesia procedures General anesthesia with endotracheal intubation was induced by intravenous drugs. Patients fasted for at least 8h and intramuscular atropine 0.5 mg was given 30min before the surgery. While lying prostrate, patients were given midazolam 3-5 mg/kg, fentanyl 5 μg/kg, vecuronium bromide 4 mg/kg, and propofol 2 mg/kg. Blood pressure, ECG, SPO_2, and $PETCO_2$ were monitored continuously. General anesthesia was maintained by a micro pump with propofol (5-6 mg/kg/h) and remifentanil (6-8 μg/kg/h) during the operation. Ten minutes before the graft transplantation, 2 mg of vecuronium bromide was used, and three minutes before graft transplantation, 20-40 mg of propofol was given. After all sutures were complete, the micro pump for propofol was stopped, and the instillation speed of remifentanil was reduced. After the surgery was finished, the micro pump for remifentanil was stopped. Patients were expected to regain spontaneous breathing and consciousness within 3-10min after the operation; if they did not, they were given flumazenil. Once patients recovered spontaneous breathing, myodynamia, and consciousness, the endotracheal tube was removed. When vital signs were stable, the patients were transported to the recovery ward on a stretcher.

Local anesthesia procedures Peribulbar anesthesia was applied using a 5 gauge local anesthesia needle along the supraorbital incisure and the infraorbital notch and 4 mL of 2% lidocaine was injected behind the eyeball at each site. Two milliliters of 2% lidocaine was injected into the upper and lower musculus orbicularis oculi, respectively. The eye was then pressed to lower the intraorbital pressure and to facilitate diffusion of the lidocaine until the intraocular pressure was lower than normal. When eye movements were completely still, orbicularis muscle function disappeared or was significantly reduced and local pain and temperature sensations ceased, surgery was performed.

Recording pupil changes during the operation All PKPs were done under the same operating microscope and were videotaped under the same magnification. The images of the procedure were processed and analyzed by the anterior Segment Digital Imaging System XP (Beijing KangRongHua company, Beijing, China) to measure the area of the pupils during the surgery and calculate the ratio (R) of the area of the pupil to that of the recipient graft bed. When the corneal pathological changes in the anterior chamber ceased and the recipient bed was viable, 2 sutures, 4 sutures and 16 sutures were performed. The area of the pupil and that of the recipient graft site were measured three times, and the average value was used to calculate R. The time (T) to treat the anterior chamber, *i.e.* the time from finishing the recipient graft site to beginning the first suture, was also recorded. For patients receiving optical PKP, T was negligible because sutures began immediately after corneal pathological changes were removed. Thus we just recorded and analyzed T values for patients receiving therapeutic PKP.

Complications during penetrating keratoplasty and primary infectious disease relapse Complications during PKP and primary corneal infectious disease relapse rate were

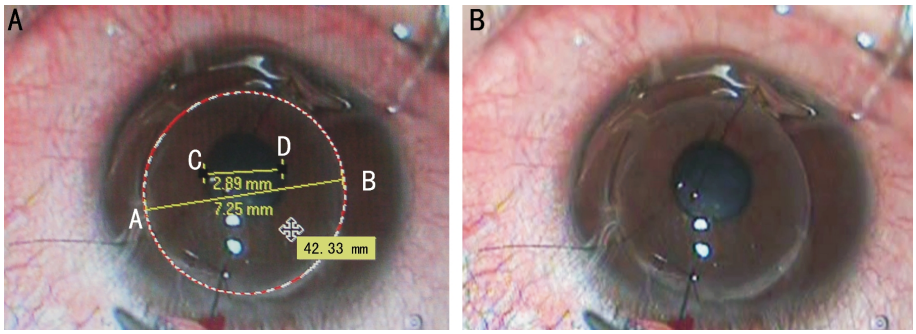

Figure 1 Diameters of the pupil and the recipient hole or graft A: The diameter of the pupil and the graft measured by the digital imaging system; AB is the diameter of the graft and CD is the diameter of the pupil; The dashed line circle is the graft; B: The original picture captured after two sutures were finished.

recorded. Reasons for the complications during PKP were also recorded.

Surgical procedures All PKP were performed conventionally with 16 interrupted sutures by the same surgeon. After the graft was fixed to the recipient bed by 8 sutures, an iris restorer was placed in the anterior chamber to probe and separate the anterior synechiae. A viscoelastic agent was used in reconstructing the anterior chamber if needed. Then, 2 or 3 drops of compound tropicamide were used to dilate the pupil and another 8 sutures were made.

Statistical Analysis Statistical analyses were performed using SPSS version (Chicago, USA). *T* values are shown as mean± SD and were compared between the two groups using *t*-test. For various groups, R values during PKP were plotted and the changing tendency was observed. Incidences of complications during PKP and the primary infectious disease relapse rate were compared between groups using χ^2 test. The significance level α was set at 0.05.

RESULTS

T was (13.45±8.64)min for patients under general anesthesia (group A2) and (7.36 ±5.24)min under local anesthesia (group B2). The difference between the 2 groups was statistically significant (P<0.001).

The diameter of the pupil and the recipient graft site at different time points during PKP was measured by the anterior segment digital imaging system XP to calculate the area of the pupil and that of the recipient graft site (Figure 1). The R of the area of the pupil to that of the recipient site at different time points during PKP is shown in Figure 2. R values in the general anesthesia group (A1 and A2) were stable with only a slight change during PKP (also see Figure 3 for representative pictures). In the local anesthesia group, the R values clearly changed during PKP, especially for patients receiving therapeutic PKP (B2). For the B2 patients, the R value increased when the recipient site was viable and remained elevated until the anterior chamber treatment was finished, after which it then remained stable until all sutures were complete (Figures 2, 3). For patients receiving optical PKP under local anesthesia (B1), R was generally stable during PKP; however, it increased dramatically after the first four sutures and remained high until all 16 sutures were complete (Figure 2).

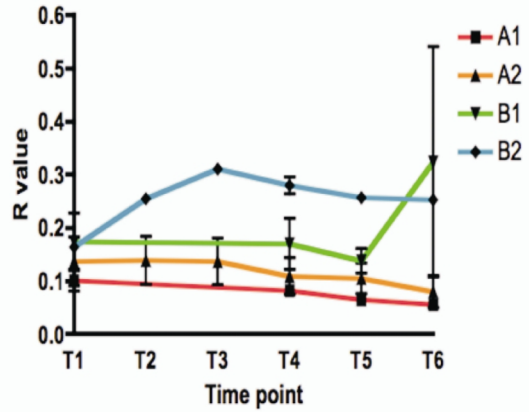

Figure 2 Change of R value during PKP A1 patients received optical PKP under general anesthesia. A2 patients received therapeutic PKP under general anesthesia. B1 patients received optical PKP under local anesthesia. B2 patients received therapeutic PKP under local anesthesia. Time point T1 was when the recipient hole was ready; T2 was when treatment of anterior chamber was begun; T3 was when treatment of anterior chamber was finished; T4 was when 2 sutures were finished; T5 was when four sutures were finished; T6 was when 16 sutures were finished.

Complications during PKP and reasons for complications are shown in Table 2. Local complications during PKP included extrusion of intraocular contents and iris prolapse. Extrusion of intraocular contents comprised the lens only in some cases (10 eyes) and the lens and part of the vitreous body in others (4 eyes). There was no extrusion of intraocular contents in the general anesthesia group (0/70), but there were 14 cases in local anesthesia group (14/71), and the difference between the 2 groups was statistically significant (χ^2=210.9997, P< 0.001). Extrusion of intraocular contents was caused either by patient actions such as coughing, head or limb movement, or breath-holding leading to an increase of the intraorbital pressure (5 cases among the therapeutic PKP patients under local anesthesia) or by insufficient local anesthesia, leading to inadequate anesthesia of the orbicularis muscle and inadequate myosis (9 cases in the local anesthesia group).

Iris prolapse occurred in 11 patients in the local anesthesia groups, which resulted from high intraorbital pressure which disrupted the suture. A viscoelastic agent had to be used in these patients. No iris prolapse occurred in the general

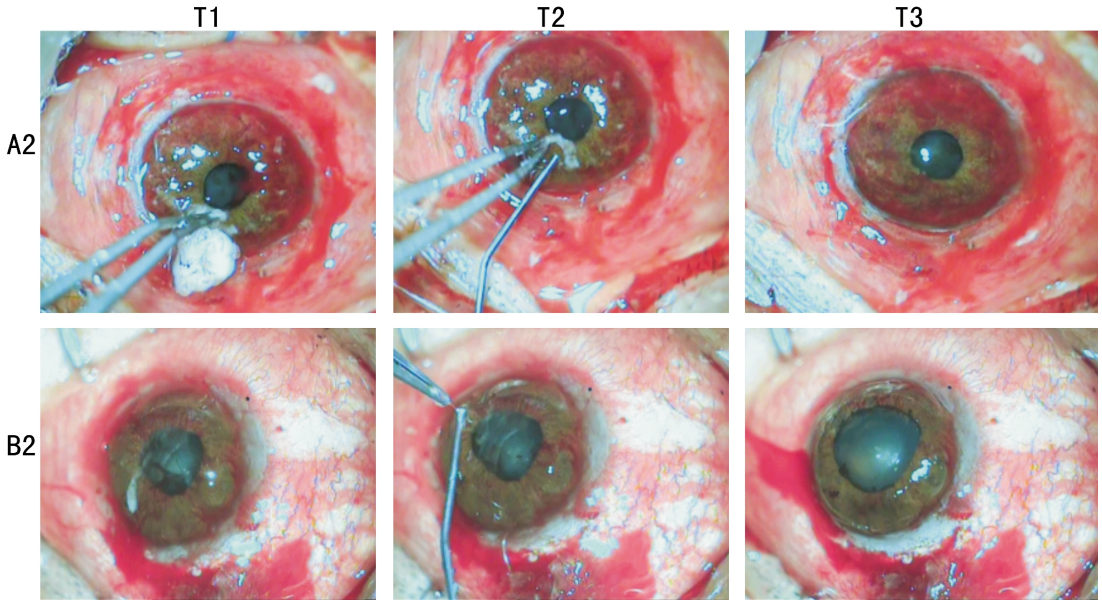

Figure 3 Pupil changes during PKP Changes of pupils of two representative patients receiving therapeutic PKP under general anesthesia (A2) and local anesthesia (B2), respectively, at different time points during PKP are shown. T1 signifies when the recipient hole was ready; T2 shows when treatment of anterior chamber was begun; with T3 representing when treatment of anterior chamber was finished.

Table 2 Causes of intraocular content extrusion and iris prolapsed during penetrating keratoplasty procedure

Groups	*n*	Patient factors				Operative factors				Total
		Coughing	Breath holding	Closing eye	Subtotal	Insufficient anesthesia	Inadequate myosis	Operation stimulation	Subtotal	
A1	30	0	0	0	0	0	0	0	0	0
A2	40	0	0	0	0	0	0	0	0	0
B1	30	0	0	0	0	1	0	0	1	1
B2	41	1	1	3	5	3	2	1	6	11

A1: Optical PKP with general anesthesia; A2: Therapeutic PKP with general anesthesia; B1: Optical PKP with local anesthesia; B2: Therapeutic PKP with local anesthesia.

anesthesia group, and the occurrence of iris prolapse was statistically different between the 2 groups (χ^2=11.763, P=0.001).

We also compared the relapse of primary corneal infectious diseases after PKP in the 2 groups. All cases of relapse were due to fungal keratitis. Among 23 patients with fungal keratitis in the local anesthesia group, 3 relapsed within 2wk after PKP (13.40%), while none of the 25 patients with fungal keratitis in the general anesthesia group suffered a relapse. The rate of relapse was statistically different between the 2 groups (χ^2=9.0144, P<0.01).

DISCUSSION

In this prospective study, we compared the effects of general and local anesthesia on PKP outcomes. Our results showed that compared with local anesthesia, general anesthesia prolonged treatment time of the anterior chamber (in therapeutic PKP), stabilized pupils, decreased the occurrence of complications during the operation, and prevented the relapse of fungal keratitis after operation.

The process of treating the anterior chamber is the most important step in therapeutic PKP, during which pathological tissue of the cornea is removed and an "open sky" recipient bed is made [13]. Surgeons need enough time during this period to treat the anterior chamber thoroughly [14]. However, this step represents the part of PKP with the highest risk since most of the extrusion of intraocular contents occurs at this point[11,12,15]. To reduce the risk of extrusion of intraocular contents, all muscles associated with PKP, including the musculus orbicularis oculi, levator palpebrae superioris muscle, sphincter pupillae, and dilator pupillae, must remain completely relaxed to keep intraocular and intraorbital pressure low and stable, a task which is difficult to achieve under local anesthesia [16-21]. Further, voluntary movements of patients under local anesthesia, such as coughing, can also lead to extrusion of intraocular contents. Therefore, when surgeons perform therapeutic PKP on patients under local anesthesia, they must treat the anterior chamber as quickly as possible. In contrast, general anesthesia can relax all ocular muscles, maintaining a low and stable intraocular and intraorbital pressure, and patients have no movements under general anesthesia, which greatly reduces the risk of extruding of intraocular contents and gives the surgeon enough time to treat the anterior chamber thoroughly. This is supported by our results, which show that the time to treat the anterior chamber (T) was significantly longer in the general anesthesia group than in the local anesthesia group and the incidence of intraocular content extrusion was significantly lower (Table 2).

The size of pupils also changed a little in the general anesthesia group compared with the local anesthesia group (Figures 2, 3), showing that general anesthesia could maintain low and stable intraocular and intraorbital pressures. We calculated the required sample size for detecting difference in relapse rate of patients with primary infectious corneal diseases after PKP between the two groups. With 80% of power and a significant level α at 0.05, Z_{α} is 1.96 (for a two-tailed test) and $Z_{1-\beta}$ is 0.8416. We used a σ of 0.15 based on published paper [22]. Based on published data, the relapse rate of patients with infectious corneal diseases after PKP ranged from 12% to 15%[22,23]. We set the Δ (difference in relapse rate) between two groups to be 0.15. The calculated required sample size is 16 patients per arm. Our actual sample size was greater than the required sample size. Our study showed that patients with fungal keratitis who received therapeutic PKP under general anesthesia had a much lower relapse rate than those in the local anesthesia group. This suggests that more thorough treatment of the anterior chamber in the general anesthesia patients leads to a better prognosis. Taken together, these results indicate that for patients receiving therapeutic PKP, general anesthesia has a better outcome than local anesthesia and therefore should be the option of choice for anesthesia.

For patients receiving optical PKP, our results showed that there was no difference between general anesthesia and local anesthesia with respect to the incidence of extrusion of intraocular contents (0% for both groups, Table 2). Compared with local anesthesia, general anesthesia is more complex and requires fasting and a longer recovery time; therefore, local anesthesia should be chosen for patients receiving optical PKP[8,9].

However, our study has some limitations. The sample size of this study was small, and only patients who underwent PKP at our hospital were included. The nature of patients treated at our hospital may not necessarily be representative of those seen in other settings. Therefore, cautions should be used when generalizing our findings.

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Conflicts of Interest: Wang X, None; **Dang GF,** None; **Li YM,** None; **Li WF,** None; **Wu XY,** None.

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