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Anesthesia during corneal transplantation in children

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Summary : The anesthesiological management of 17 children (age range: 1 - 16 years) having keratoplasty from 2008 to 2015 is described here. The risk of intraoperative surgical complications is higher than in adults. Especially increased intraocular pressure resulting in expulsive hemorrhage associated with an irreversible reduction of visual acuity has to be avoided. All children received intravenous fentanyl (0.1 µg Kg^{-1}), propofol (3-5 mg Kg^{-1}), and atracurium (0.5 mg Kg^{-1}) before an endotracheal tube was inserted. Anesthesia was maintained with desflurane (0.5 MAC) and remifentanil (0.25 µg Kg^{-1} min^{-1}). All children received acetazolamide (1 mg Kg^{-1}), and mannitol 10% (1 g Kg^{-1}). The upper part of the body was elevated by 30°, and positive end expiratory pressure was 0 mbar. Before surgical opening of the eye, intravenous atracurium (0.1 mg Kg^{-1}) was administrated if the train-of-four was not zero. Expulsive hemorrhage was not observed in this survey. In all patients, corneal transplantation was successful. Measures to reduce intraocular pressure and to provide full relaxation are efficient methods to ensure successful keratoplasty in children.

Abbreviations: VAT: vis a tergo

Key words : ocular pressure ; ophthalmology ; pediatric ; surgery ; keratoplasty.

INTRODUCTION

Corneal transplantation in children is a great challenge for the microsurgeon as well as for the anesthesiologist and requires a high degree of cooperation. Typical indications for corneal transplantation in children include corneal dystrophy and corneal scars, as well as traumatic and non-traumatic corneal lesions (1). Successful corneal transplantation needs reduced intraocular pressure, and expulsive hemorrhage associated with an irreversible reduction of visual acuity has to be avoided (2). A warning sign for expulsive hemorrhage during the corneal transplantation is a positive vitreous pressure (vis a tergo, VAT) (3). It is defined as pulsations of the iris-lens-diaphragm with propulsive movement of intraocular tissue. These are divided into grades 0 – 4 VAT. None pulsation corresponds to grade 0, minor pulsation to grade 1, iris prolapse until the level of corneal trepanation to grade 2, iris prolapse beyond the level of corneal incision to grade 3, and expulsive hemorrhage to grade 4 (4). A full neuromuscular blockade using non-polarizing neuromuscular blocking agent and the administration of acetazolamide and mannitol has been used in order to reduce the intraocular pressure and avoid VAT. In this single-center retrospective study, we performed a detailed analysis of the anesthesia record of all children who underwent general anesthesia for primary corneal transplantation beween 2008 and 2015 in Homburg/Saar, Germany. The objective was to present relevant aspects that should be considered for anesthesia in these young patients in order to avoid complications when the eye is open.

Case description

This retrospective case analysis was approved by the local ethics committee (Landesärztekammer des Saarlandes, Ethikkommission, Faktoreistrasse 4, 66111 Saarbruecken, Germany, current trial registration number 206/16). We report on 17 patients (age ≤ 16 years) undergoing primary elective corneal transplantation between January 2008 and December 2015 at the Saarland University Medical Center in Homburg/Saar, Germany.

Data Source and Measurements

We retrospectively reviewed the medical records. Medical records of 17 patients (Table 1) had been collected concurrently with patient care

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Table 1
Patients' characteristics. Continuous variables are expressed as mean with minimum and maximum. Categorical variables are presented as numbers (percentages).
ASA score = Society of Anesthesiologists physical status score.

Population characteristics		
(n=17)		
Male	15	(88)
Age (years)	9.4	(1-16)
Body weight (Kg)	41	(10-85)
Size (cm)	139	(76-185)
ASA score 1	15	(88)
ASA score 2	2	(12)
Asthma	2	(12)
Inhaled fenoterol	2	(12)

by nurses or treating physicians (ophthalmologist, anesthesiologist, and pediatrician) and included detailed information about the medical conditions of the children undergoing corneal transplantation along with the procedure and postoperative course. Data were reviewed in particular for patients' characteristics, indications for corneal transplantation and comorbidities as well as intra- and post-operative course (raised blood pressure, bradycardia, decreased oxygen saturation, allergy, vis a tergo, surgical complications, and early post-keratoplasty outcome).

Patient Description

The characteristics of 17 children (21 eyes) are reported in Table 1. Indications for corneal transplantation were : congenital hereditary endothelial dystrophy (n = 4), keratoconus (n = 3), traumatic lesion (n = 4), corneal decompensation due to congenital glaucoma (n = 2), corneal hereditary stromal dystrophy (n = 2), aniridia (n = 1), mucolipidosis (n = 1), and corneal ulcer (due to herpes n = 2, acanthamoeba n = 1, and pseudomonas n = 1).

Anesthesia

Children were allowed to drink clear fluids up to two hours before surgery. After fasting, all children were pre-medicated successfully with a midazolam juice (0.5 mg Kg^{-1}; maximum body weight = 24 Kg) or a midazolam pill (3.75 mg; for body weight ≥ 24 Kg), both given one hour before induction of anesthesia. For intravenous cannulation, an EMLA patch was placed at the back of the hand 30 minutes before entering the operating room. Intravenous cannulation was possible for all patients before or after induction of anesthesia. Monitoring included electrocardiogram, pulse oximetry, body temperature, and non-invasive blood pressure.

The anesthesia induction was performed either with inhaled sevoflurane (3 children) or intravenous fentanyl (0.1 µg Kg^{-1}) and propofol (3-5 mg Kg^{-1}). All patients received intravenous atracurium (0.5 mg Kg^{-1}) to facilitate endotracheal tube insertion. Patients were normoventilated with an FiO_2 of 0.3 (pressure controlled).

For maintenance of anesthesia, desflurane (0.5 MAC) in oxygen and air and remifentanil (0.25-0.5 µg Kg^{-1} min^{-1}) were administered in order to achieve an adequate depth of anesthesia. Fluid replacement by full electrolyte solution at a rate of 4 ml Kg^{-1} h^{-1} was given. Body temperature was maintained at 36 °C by raising the temperature in the operating room and by applying an electrically heated blanket. All patients received cefuroxime (50 mg Kg^{-1}) as a single dose antibiotic prophylaxis.

Specific treatment to reduce intraocular pressure

Before surgery, specific treatment to reduce the intraocular pressure included acetazolamide (1 mg Kg^{-1}), mannitol 10% (1 g Kg^{-1}), 0 mbar positive end expiratory pressure, and 30° proclive position of the body. All those measures were applied to all children. Before opening the eye, additional atracurium (0.1 mg Kg^{-1}) was needed to reduce the train-of-four to zero in four patients. Moreover, deep sedation was required, and high blood pressure had to be avoided. After opening the eye, only two cases were observed with iris prolapse until the level of corneal incision (vis a tergo grade 1), 13 with strong pulsations (vis a tergo grade 2), and two with iris prolapse beyond the level of corneal incision (vis a tergo grade 3). There were no cases with expulsive hemorrhage (vis a tergo grade 4). Prophylaxis against postoperative nausea and vomiting was achieved with intravenous ondansetron (0.1 mg Kg^{-1}, maximum of 4 mg).

End of anesthesia and recovery room

Postoperative pain therapy started intra-operatively using intravenous metamizole (30 mg Kg^{-1}). At completion of surgery, maintenance agents were tapered down. The trachea was extubated when the children were fully awake with intact airway reflexes. No patient needed prolonged mechanical ventilation assistance. An antagonist for drug-induced neuromuscular blockade was not needed.

In the post anesthesia recovery room, five patients needed additional piritramide (0.1 mg Kg^{-1}) to reduce pain. One patient was treated with clonidine (1 µg Kg^{-1}) against shivering. No emergence delirium or postoperative nausea and vomiting were observed. All patients were monitored in the post anesthesia recovery room until Aldrete Score reached > 8 points (5). After discharge from the recovery room, no patients needed further monitoring. Intraoperative unexpected awareness was not reported.

Drug-induced allergic reaction or negative side effects were not seen. In case anaphylactoid responses were observed, ß2-agonists (Berotec®-spray or IV reproterol), antihistaminic medications (Tavegil® and Ranitic®), corticosteroids (Urbason®), and, in case of persisting bronchospasm, adrenaline (Suprarenin®) would have been administered. A residual neuromuscular blockade could have been treated with acetylcholinesterase inhibitors (neostigmine) and atropine.

Corneal Microsurgery

Immediately before corneal trepanation by the microsurgeon (B.S.), another time-out was initiated to check neuromuscular block and anesthetic depth. The transplantation diameter ranged from 4.6 to 8.3 mm. Trephination was performed using the 193 nm excimer laser (n = 14) described in detail elsewhere to obtain horizontal and vertical alignment of the graft in the host opening (6), otherwise manual trephination was performed (n = 3). One or more iridotomies were performed so that the expected fibrin reaction would not lead to extended adhesion of the iris to the intraocular lens with secondary angle-closure glaucoma. In order to achieve an optical rehabilitation in central perforated cornea and lens lacerations, a simultaneous artificial lens implantation was performed in two patients after suturing a Flieringa-ring before opening the eye in an amblyopia-risk age < 7 years. After temporary fixation of the donor button in the recipient bed with 8 interrupted sutures, a permanent wound closure was achieved by a 16-bite double-running diagonal cross-stitch suture (10–0 nylon) in 19 patients. Single-knot sutures were preferred in case of defects of the Bowman's layer (n = 2). The surgical procedure lasted 45 minutes and the entire period of narcosis was 75 minutes.

In all patients, corneal transplantation was successful during short-term follow-up (Fig. 1).

Discussion

The major problem during keratoplasty concerns the control of intraocular pressure during the open eye situation to avoid expulsive hemorrhage associated with an irreversible reduction of visual acuity.

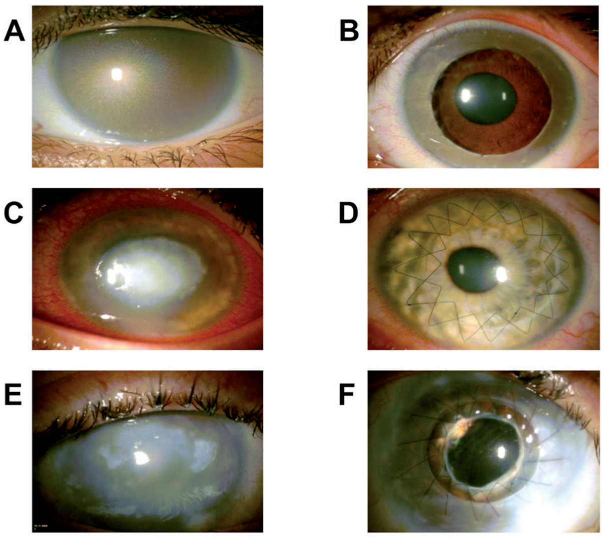

Fig. 1 — A: Congenital hereditary stromal dystrophy in a 2-year-old boy (left). B: After penetrating keratoplasty and "all sutures out", visual acuity reached 0.8 (right). C: Acanthamoeba keratitis in a 14-year-old boy with history of wearing contact lenses with a well-defined central ulceration and infiltration before (left). D: After penetrating keratoplasty (right, sutures still in place). E: 4-year-old boy with congenital glaucoma. It took several years and over 10 operations to stabilize the glaucoma. Because of this prolonged treatment period and because of chronic damage to the corneal endothelium, swelling of the cornea with concomitant deposition of calcifications developed (left). F: clear corneal graft with all sutures in after penetrating keratoplasty (right).

In previous studies, several anesthetic techniques during keratoplasty are described. Peribulbar anesthesia was previously compared with general anesthesia in a prospective study in adults with keratoplasty. Expulsive hemorrhage was described during peribulbar anesthesia in 14/71 patients, whereas with full neuromuscular block and deep anesthesia, 0/70 patients had expulsive hemorrhage. Moreover, general anesthesia was associated with decreased time stress during the treatment of the anterior chamber, stabilized pupils, and decreased surgical complications (7). In contrast to adults, peribulbar anesthesia in children is no option during keratoplasty (8). The pressure of childrens' vitreous body is higher than in adults, and the risk of expulsive hemorrhage increases (9).

Therefore, treatments to reduce the intraocular pressure during general anesthesia are needed. The most favorable muscle relaxants to avoid a vis a tergo are atracurium, rocuronium (10) or vecuronium (7).

In a randomized clinical trial in adults undergoing keratoplasty, the use of laryngeal mask without neuromuscular blockade was compared to the use of endotracheal intubation with neuromuscular blockade. The authors observed less cough with laryngeal mask and no surgical complications in both groups. However, information about intraocular pressure was missing (11). Similar to previous observations, cough was no problem in our study (7, 8, 12, 13). Since the corneal sutures leave the globe water-tight at the end of surgery, the influence of cough after eye surgery seems of less importance (14). In contrast, the influence of expulsive hemorrhage that is associated with an irreversible reduction of visual acuity is high (12, 13, 15). An open eye situation needs stable airway management. If the laryngeal mask needs to be replaced by an endotracheal tube during open eye surgery, the risk of irreversible reduction of visual acuity is high. Especially in children with an increased risk of respiratory problems (16), we prefer endotracheal tube during open eye surgery.

Also, during an open eye situation, we try to avoid positive end expiratory pressure, high peak pressure, and succinylcholine, because these measures tend to increase intraocular pressure (12, 17). A similar increase is observed in patients in the Trendelenburg position or in the prone position (18, 19). In contrast, when patients are in the prone position with the head rotated 45º laterally, intraocular pressure in the upper positioned eye decreases significantly (mean ± standard deviation : 14.95 ± 4.64 mmHg, n = 22) compared to the lower positioned eye (20.40 ± 5.15, n = 22) and prone position without head rotation (18.21 ± 5.73, n = 23) (19).

Reduced intraocular pressure has been observed after the intravenous administration of mannitol (8, 20). Mannitol has been used for a long time to reduce intracranial pressure. The recommended dose of mannitol (mannitol 20%; 0.25 g Kg^{-1}) for intracranial pressure reduction is higher than the dose needed to reduce intraocular pressure (mannitol 10%; 0.1 g Kg^{-1}) (21). The effect of mannitol on intracranial cerebral pressure is based on two mechanisms. On the one hand, it decreases blood viscosity, leading to reflex vasoconstriction, and, therefore, to lower intracranial blood volume. On the other hand, the reduction of the intracranial pressure can be ascribed to an osmotic effect (22). Contraindication to the application of mannitol such as symptoms of cardiac decompensation and anuria did not exist in any of our young patients of less than 16 years of age. Adverse drug reactions such as nausea/vomiting, epigastric pain, headaches, states of confusion, cramps, and tachycardias were not observed (23). Indeed, the administration of mannitol to reduce intraocular pressure is a well-known method that has been used for more than 50 years (23, 24).

Typically, acetazolamide is applied to reduce intraocular pressure in children with glaucoma (24). Acetazolamide is a reversible carbonic anhydrase inhibitor that reduces the intraocular production of intraocular fluid in the non-pigmented epithelium and thus reduces the intraocular pressure (25). The successful use of carbonic anhydrase inhibitors for intraocular pressure lowering in children has already been reported in previous studies (26). Contraindications to acetazolamide such as hypersensitivity, electrolyte shift, kidney-, adrenal glands, and liver insufficiency, as well as hypochloremic acidosis did not exist in any of our patients. Adverse drug reactions such as hypersensitivity, gastrointestinal complaints (nausea, vomiting, and diarrhea), and paresthesia were not observed (27).

In all children, balanced anesthesia with desflurane and remifentanil was performed. This was chosen due to the advantages of better controllability and bronchodilating effect of high concentrations of desflurane (28). Controllability is needed during corneal transplantation in order to have no adverse effects on the intraocular pressure. Contraindications to the use of volatile anesthetics such as neuromuscular diseases or predisposition for malignant hyperthermia did not exist in any of our cases (29). Combining remifentanil and volatile anesthetic agents in our study allowed appreciable mutual potentiation and sparing of both drugs (30, 31). Concerns about remifentanil causing high pain-discomfort scores in the recovery period could not be confirmed in our observation, because postoperative pain therapy started intraoperatively using intravenous metamizole (32). Alternatives to a balanced anesthesia would have been a total intravenous anesthesia.

Anesthesia induction by means of sevoflurane was implemented in non-cooperative patients, despite premedication with midazolam. Complications such as bronchospasm and cardiac depression were not observed (33). Because of the known adverse drug reactions to a remifentanil bolus administration, such as thorax rigidity and bradycardia, fentanyl was used as the opioid for anesthesia induction (34, 35). There were no adverse drug reactions observed. Contraindications to the use of propofol for anesthesia, such as soy allergies, did not exist in any of our patients. Cardiodepressive side effects were also not observed (36).

Our major limitation is that we report a small patient population in a single center, without a control group. However, corneal transplantation in small children is very rarely necessary and is typically only performed in highly specialized centers. It requires excellent cooperation between the ophthalmologist and the anesthesiologist. Confirmation of our findings in other distinct populations is required. Similarly, in terms of success and safety, it would be of considerable interest to evaluate the ability of the hereby reported management technique in a large multicenter randomized trial.

Conclusions

The decision of the best anesthetic treatment regarding risk and benefit for children undergoing keratoplasty has to be discussed between the surgeon and the anesthesiologist. We here report a case series of 17 children, where deep neuromuscular blockade, as well as use of mannitol, acetazolamide, and elevated upper body for reducing intraocular pressure were successful for their management during keratoplasty.

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