Case Report

Anaesthetic Options during Laser Photocoagulation for Retinopathy of Prematurity – Case Series and Review of Literature

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Abstract

Background

Anaesthesia for retinopathy of prematurity (ROP) is one of the most challenging in all of ophthalmic anaesthesia. A series of premature or ex-premature babies who underwent laser photocoagulation for ROP in a stand-alone ophthalmic centre between 2017 and 2020 were audited and the various risk factors, anaesthetic concerns and their management are reviewed.

Methods

A standard protocol was followed for perioperative care. A totally inhalational technique anaesthesia was used with oxygen, air and sevoflurane via a supraglottic airway (SAD). Intravenous anaesthetic drugs were totally avoided. Enhanced recovery after surgery (ERAS), principles were followed, minimizing preoperative as well as postoperative fasting.

Babies were fed in the recovery area when fully awake and transferred to the referring NICU for monitoring after 2-3 hours.

Results

A total of 71 babies were studied with age ranging from 13 to 120 days (mean 38.7 + 22 days, median 30 days). Duration of the procedures ranged from 30 to 150 minutes (mean 84.5 + 30.3). Complete datasets were available for 51 babies, who comprised 31 males and 20 females. The median (range) post-conceptional age was 36 weeks (range 29-45) and the mean weight (+ standard deviation) was 1.37 + 0.43. Out of 71, 2 (3%) babies had apnoeic episodes with bradycardia, and 1 baby needed intubation (1.4%).

Conclusion

For laser photocoagulation, it is possible to avoid endotracheal intubation with a carefully selected anaesthetic plan, avoiding all agents which may have a residual effect and predispose to post-operative apnoea and ventilatory support.

Keywords: Retinopathy, prematurity, anaesthesia

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Article History
Received: 20th November 2021
Revision: 1st December 2021
Accepted: 28th December 2021
Published: 17th January 2022

How to cite this article: Gita Nath. Anaesthetic Options during Laser Photocoagulation for Retinopathy of Prematurity – Case Series and Review of Literature. Ind J Ophthal Anaesth 2022;2(1): 26-34

Introduction

Anaesthesia for retinopathy of prematurity (ROP) is one of the most challenging in all of ophthalmic anaesthesia. In this article, the various risk factors, anaesthetic concerns and their management are summarized. We also present our experience in managing this procedure.

With the improved survival rates of extremely premature and low birth weight infants due to advances in neonatal care, greater numbers of these babies are presenting with ROP in addition to other co-morbidities related to prematurity. Worldwide, almost 10% of all babies are born prematurely, defined as born before 37 weeks' gestation.[1] The main risk factors for ROP include gestational age, low birth weight, the APGAR score, pulmonary complications such as hyaline membrane disease, administration of supplemental oxygen and prolonged mechanical ventilation. Other factors are anaemia, blood transfusions, multiple gestations, intraventricular haemorrhage, sepsis and necrotizing enterocolitis. The incidence of ROP was found to be 33.9% in a series of 602 preterm infants.[2]

Materials And Methods

We have audited 71 premature or ex-premature babies who underwent laser photocoagulation for ROP from 2017 to 2020. The procedures were performed in Pushpagiri Vitreo-Retinal Institute, Hyderabad, a stand-alone eye hospital. Babies are referred here from neonatal centres in private and government hospitals.

In the pre-operative assessment, special note was made of the history in the neonatal intensive care unit (NICU) including intubation, nasal CPAP and history of apnoea.

Standard fasting instructions were given, namely breast milk 4 hours and formula feed 6 hours before the procedure. We make it a point to give clear oral fluids till 2 hours prior, by instructing the mother to give 5% dextrose solution with a syringe as tolerated.

The protocol followed was general anaesthesia (GA) with oxygen, air and sevoflurane via a supraglottic airway (SAD). Intravenous (IV) access was present for fluids and emergency drugs but no IV anaesthetic drugs were given at all. Induction and maintenance were with O_2/air/Sevoflurane (FiO_2 0.25) and the SAD was inserted when anaesthetic depth was adequate. 5% dextrose-normal saline was given, as it is an isotonic fluid and also contains glucose to avoid hypoglycaemia. This was given at 10 ml/kg/hr through a dial-a-flow flow controller so that excess fluid administration. Babies were well wrapped to prevent heat loss and skin temperature was monitored throughout (Figure 1). At the end of the procedure, the SAD was removed deep and baby was allowed to wake up. The baby was fed in the recovery area when fully awake and transferred to the referring NICU for monitoring after 2-3 hours.

Figure 1. A 1.1 Kg premature baby anaesthetized with size 1 LMA

Results

A total of 71 babies underwent laser photocoagulation for ROP under anaesthesia during this period. Their age ranged from 13 to 120 days (mean 38.7 + 22 days, median 30 days). Complete datasets were available for 51 babies, of whom there were 31 males and 20 females. The gestational age, post-conceptional age (PCA), weight at birth and at the time of the procedure are detailed in Table 1. Duration of the procedures ranged from 30 to 150 minutes (mean 84.5 + 30.3).

Table 1. Patient characteristics

	Mean + SD	Range	Median
Gestational age (weeks)	31.1 + 2.8	21 - 36	32
Post-conceptional age (weeks)	35.6 + 3.1	29 - 45	36
Weight at birth (kg)	1.37 + 0.43	0.73 – 3.45	1.3
Weight at time of procedure (kg)	1.61 + 0.50	0.95 – 3.22	1.5

Outcome: All babies were monitored in the recovery area under the direct supervision of the anaesthetist. Once they were awake and alert, usually within 30 minutes, they were given fed with breast milk / formula feed. Since they were given only volatile anaesthesia, there was no residual drowsiness. After they were fed, the babies were calm and did not need further analgesics such as paracetamol. Out of 71, 3 babies had apnoeic episodes with bradycardia, and 1 of them needed intubation. All 3 were shifted back to the NICUs from which they were referred.

Review Of Literature And Discussion

Pathophysiology: The intrauterine development of the retina occurs in a hypoxic environment which stimulates angiogenesis through the action of vasoactive factors, such as insulin-like growth factor (IGF-1), vascular endothelial growth factor (VEGF) and erythropoietin. These factors, along with maternally derived factors, stimulate new vessel formation. After a premature birth, the higher oxygen levels resulting from oxygen administration along with loss of placental and maternal vascular growth factors lead to vaso-obliteration. Subsequently, there is a retinal neovascularization phase which is driven by hypoxia as well as fluctuating oxygen levels as may be seen in babies with apnoeic episodes. The upregulation of VEGF and IGF-I causes abnormal vascular overgrowth into the vitreous and retina ultimately leading to haemorrhages and retinal detachment. Despite the recognition of ROP in 1942, it is a balancing act between the oxygen requirement from the pulmonary point of view versus prevention of ROP, and there is still no consensus as to the optimum oxygenation target.[3]

Anaesthetic concerns

These are summarized in Table 2.

1.Prematurity

Anaesthesia in the premature baby is associated with all the problems presented by term neonates, but these are further exaggerated. These include rate dependent cardiac output, increased tendency to airway closure, exaggerated hormonal response to pain and propensity to hypothermia and hypoglycaemia. The increased body water as well as the immature excretory mechanisms alter the pharmacokinetics of anaesthetic drugs. Adverse events such as hypoxia, hypotension and acidosis may reopen the

ductus arteriosus, since the circulation is still transitional[4]

Table 2. Anaesthetic concerns in neonates and preterm babies

Cardiovascular	Rate dependent cardiac output Increased parasympathetic tone Reopening of PDA
Respiratory	Increased tendency to airway closure Oxygen toxicity Respiratory distress syndrome, bronchopulmonary dysplasia Propensity to apnoea
Nervous system	Possible neurotoxicity of anaesthetic agents
Pain response	Exaggerated hormonal response to pain
General	Propensity to hypothermia, hypoglycaemia and hypocalcemia
Pharmacokinetic	Increased loading dose but prolonged action of anaesthetic drugs
Apnoea of prematurity	Hypoglycaemia Hypoxia Hypothermia Pain and stress Low gestational age Comorbidities: bronchopulmonary dysplasia necrotizing enterocolitis Apnoea at home

In addition, the premature infant is prone to ***apnoea of prematurity***, defined as apnoea of >15 sec duration which may be accompanied by bradycardia. PCA of 60 weeks or more minimizes the likelihood of apnoea; but for ROP surgery, there is no option but to proceed in order to preserve the baby's vision. Other risk factors for post-operative apnoea include the history of apnoea at home, CNS morbidity and lung disease. Anaemia has been found to increase the likelihood of apnoea, but there is no evidence that pre-operative transfusion reduces the incidence. Another modifiable factor is intraoperative hypothermia. The choice of anaesthetic drugs is important and respiratory depressant drugs such as opiates increase the chances of apnoea.[4]

2. Effects of pain and stress:

It is now accepted that pain causes immediate stress response as well as long term neurological and psychological effects on the neonate.5 These effects are even more pronounced in preterm babies due to inadequate maturation of the descending inhibitory pathways.[6-8] Painful stimuli may also lead to apnoea, and hence all efforts must be made to minimize pain in these babies.

3. Type of surgery

The procedures done for ROP range from examination and photocoagulation to invasive vitreoretinal surgery, and this naturally determines the type of anaesthesia required.

4. Effects of various anaesthetic agents:

Opiates and muscle relaxants are associated with the risk of post-operative apnoea and hypoventilation. Another issue is that of the neurodevelopmental effects of both inhalational as well as intravenous agents on the developing brain, which have been well-demonstrated in

animal studies. According to recent results from the GAS, PANDA and MASK studies, a single exposure to anaesthesia is not associated with behavioural or neurocognitive deficits, but more research is needed regarding multiple exposures or prolonged anaesthesia.[9]

5. Post-operative monitoring and discharge

Retrospective studies have reported that the first episode of post-operative apnoea occurred within 4 hours after surgery, implying that if there has been no apnoeic event during this period, it may be safe to discharge the patient.[10] However, 3 and 4 out of 5 apnoeic events were missed by either nursing observation or pulse oximetry alone respectively; hence a combination of these modes with electrocardiography may be necessary to detect all apnoeic episodes.[11] Younger preterm infants of <46 weeks PCA or those with other risk factors should be monitored for at least 12 h post-operatively. Infants of 46 and 60 weeks PCA may be monitored for a minimum of 6 hours.[12]

Anaesthetic options

The possible options for anaesthetic care include the following:

- Topical anaesthesia alone
- Sedation (enteral or intravenous)
- Sedation + topical anaesthesia
- GA – supraglottic airway device
- GA – endotracheal intubation

Early studies done in the 1980's reported a number of systemic complications during cryotherapy for ROP. These included worsening cyanosis, haemodynamic disturbances like arrhythmias, bradycardia, hypertension and hypotension, seizures and even respiratory or cardiorespiratory arrest.[13] Hence, endotracheal intubation and monitoring was advocated by Sullivan et al, who safely treated 20 eyes in 13 babies.[14]

Haigh et al compared the systemic complications with 3 different anaesthetic techniques for cryotherapy for ROP. Of 30 premature infants, 12 babies were done under topical anaesthesia alone, 6 babies had GA with endotracheal intubation and the remaining 12 had GA combined with topical anaesthesia. They found more severe and protracted cardiorespiratory complications when topical anaesthesia was used alone.[15]

Coming to the 21st century, a postal survey of 46 ophthalmologists in the UK done in 2007 found that there was considerable variation among them, not only regarding the anaesthetic methods they used, but also in their beliefs about the severity and effect of neonatal stress during treatment.[16] The various methods used included the following:

- IV sedation
- Sedation + paralysis + ventilation
- Morphine + pancuronium
- Oral sedation
- Rectal chloral hydrate
- Topical in combination with above
- Topical alone was not used by any of the respondents

An editorial in the same issue discusses the various concerns regarding this procedure. First of all, they acknowledge the immense levels of stress surrounding the procedure, both for the neonate as well as for the parents. Considering this, they suggest that minimal/conscious sedation is not enough for these babies – they need deep sedation and analgesia. This in turn is associated with respiratory depression and airway obstruction, which is difficult to observe and monitor under the drapes. Hence, they suggest that neonates should be electively intubated and ventilated before laser treatment.[17]

Table 3 lists the different anaesthetic options which have been used for ROP surgery.[18-24] A comparison of intubation with long nasal prongs in 54 babies found that the 23 of 30 intubated babies were still intubated on the 3rd postoperative day.[18] Conscious sedation with fentanyl and midazolam was used in 15 babies, but 6 of them needed to be intubated.[19] Even with intravenous ketamine sedation, 2 out of 11 needed postoperative ventilatory support.[21] In a recent study on 61 infants who underwent 72 procedures; sevoflurane, opiates and neuromuscular blockers were used and all babies were intubated. Only 14 (19.4%) were extubated at the end of the procedure and 29 (40.3%) of them were still ventilated 24 hours later.[24]

Table 3. Anaesthetic options and outcome in ROP surgery and comparison with present series

Reference	N	Anaesthesia method	Post-operative ventilation	Post-operative apnoea and other issues
Woodhead et al, 200718	54	30 intubated 24 Long nasal prongs	23/30 (77%); 50% for > 2 days 1/24 (4%)	
Spector et al, 200719	15	Conscious sedation with fentanyl and midazolam without mechanical ventilation	6/15 (40%)	Baseline activities, feeding 17 hours after
Parulekar et al, 200820	10	Oral sedation + sub-tenon block		3 (30%) – Excessive movement 2 (20%) – Bradycardia 2 (20%) – Apnoea
Lyon et al, 200821	11	Ketamine sedation IV	2/11 (18%)	
Jiang et al, 201622	97 31 47 19	 Topical anaesthesia Fentanyl sedation, intubation, IPPV GA, intubation	 3 (9%) 2 (4%) for > 2 days 2 (11%) for > 1 days	 8 (26%) - apnoea More post-op cardiorespiratory instability
Sinha et al, 201423	56	GA with intubation – 46 GA with SAD – 10	 2 (3.5%)	 3 (5%) – apnoea IV paracetamol and topical anesthetics reduced intra-operative opioid requirement
Kaur et al, 202024	72	GA with intubation Sevoflurane, opiates, NMB	 58 (81%) 29 (40%) for > 24 hours	
Present study	71	Volatile inhalation and maintenance, LMA	1 (1.4%)	2 (3%) – apnoea

Many of the above case series report small numbers with a significant proportion of babies needing post-operative ventilation. Prolonged or repeated invasive mechanical ventilation in premature and low birth weight babies is known to increase morbidity and can also contribute to mortality.[25] If the baby already requires ventilatory support for the pulmonary problems of prematurity, continuation of this support is inevitable. But if the child is currently self-ventilating, it is preferable to avoid anaesthetic techniques which may tip the balance, putting them back on the ventilator. Hence choosing an anaesthetic technique which reduces the need for post-operative ventilatory support is definitely preferable. Another issue is the upper airway problems which may be present in these babies because of previous intubation and ventilation resulting in laryngo-tracheomalacia or tracheal stenosis. Avoiding intubation if at all possible is likely to reduce the chances of airway oedema and further compromise.

The results of the present study compare favourably with previously published studies, since only 1 of our 71 patients needed post-operative ventilation (an incidence of 1.4%) and 2 out of 71 (2.8%) had apnoea and bradycardia. These are similar to the results of a study by Sinha et al, but those were a much healthier cohort of babies, with a median PCA of 56 weeks (range 36-60) and over 87% of them weighing more than 3 Kg.[23] In contrast, the median PCA in our series was 36 weeks (range 29-45) and the mean weight was 1.37 + 0.43. In our series, we deliberately avoided any intravenous sedatives, opioids or neuromuscular blockers and opted for a totally inhalational technique. Thus, there were absolutely no residual effects of anaesthetic drugs which could increase the likelihood of apnoea.We also followed the principles of enhanced recovery after surgery (ERAS), by minimizing preoperative as well as postoperative fasting. Other precautions that were taken included limiting the FiO2 to 25%, ensuring continuous infusion of glucose containing fluid to avoid hypoglycaemia and keeping the baby as warm as possible by wrapping.

Conclusion

Anaesthesia for ROP surgery is one of the most challenging situations for the neonatal anaesthesiologist, especially when conducted in a stand-alone high quality ophthalmic centre rather than a multispecialty hospital. The very fact that so many modalities are being used implies that there is no single ideal technique. The choice of anaesthetic technique depends on several factors including the set-up i.e., whether the procedure is being done in a stand-alone eye hospital or multispecialty centre; in the NICU or operation theatre. The surgical procedure is also an important deciding factor, as vitreo-retinal surgery mandates GA with endotracheal intubation.

Close monitoring of the baby is required, be it by the anaesthesiologist or neonatologist. If topical anaesthesia alone is chosen, the procedure is more challenging for the ophthalmologist, it takes longer and may be less complete. Several studies have found increased cardiorespiratory problems with solely topical anaesthesia.

Many studies recommend GA with endotracheal intubation, but for laser photocoagulation alone, it is possible to avoid this with a carefully selected anaesthetic plan, avoiding all agents which may have a residual effect and predispose to post-operative apnoea and ventilatory support.

Acknowledgement: My sincere thanks to the administration and staff of Pushpagiri Vitreo-Retinal Institute, Hyderabad. Special thanks to Dr Sai Kiranmayee who performed the majority of the photocoagulation

procedures in this series and also helped with data collection.

Financial support: Nil

Conflicts of interest: Nil

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