



Sevoflurane Insufflation Technique in Retinopathy of Prematurity Patients Underwent Intraocular Laser Photocoagulation: A Serial Case Report

Muhamad Adli^{1*}, Dian Irawati¹, Dedi Fitri Yadi²

1. National Eye Center Cicendo Eye Hospital - Padjadjaran University, Bandung, Indonesia
2. dr. Hasan Sadikin General Hospital - Padjadjaran University, Bandung, Indonesia

*corresponding author

DOI: 10.55497/majanestricar.v42i1.313

ABSTRACT

Introduction: Retinopathy of Prematurity (ROP) is a developmental abnormality of the retina and vitreous due to abnormal angiogenesis. The anaesthetic considerations in the preterm neonate were based on the physiological immaturity of the various organ systems associated congenital disorders, which may result in poor tolerance to anaesthetic drugs, and also considerations regarding the use of high oxygen concentrations.

Case illustration: We are reporting six cases of ROP patients who underwent intraocular laser photocoagulation under Volatile Induction and Maintenance Anaesthesia (VIMA) using a nasal cannula. The youngest patient at the time of the procedure was 32 weeks postmenstrual age, and the oldest patient was 36 weeks postmenstrual age, with the lowest weight of 1480 grams and the highest weight of 2770 grams. A gas mixture of oxygen, nitrous oxide, and 3-5 vol% sevoflurane was delivered through a nasal cannula delivered from an anaesthesia machine for anaesthesia induction and maintenance throughout the procedure. The anaesthesia effect was achieved less than five minutes after gas mixture delivery in all patients. Five of six patients showed satisfactory results without any serious adverse effects during and after the procedures, and one of the patients was intubated due to repeated apnoea and conversion of the surgical procedure from intraocular laser photocoagulation to vitrectomy. There was no adverse event observed after the procedure.

Conclusion: The effective induction and maintenance of anesthesia achieved through sevoflurane insufflation via nasal cannula suggest its viability as a practical and opioid-free alternative for volatile induction and maintenance anesthesia in pediatric procedures.

Keywords: laser photocoagulation; retinopathy of prematurity; sevoflurane; volatile induction and maintenance of anesthesia



Laporan Kasus Serial: Teknik Insuflasi Sevoflurane pada Pasien Retinopati Prematuritas yang Menjalani Fotokoagulasi Laser Intraokular

Muhamad Adli^{1*}, Dian Irawati¹, Dedi Fitri Yadi²

1. Pusat Mata Nasional RS Mata Cicendo - Universitas Padjadjaran, Bandung, Indonesia
2. Rumah Sakit Umum Pusat dr. Hasan Sadikin - Universitas Padjadjaran, Bandung, Indonesia

*penulis korespondensi

DOI: 10.55497/majanestscricar.v42i1.313

ABSTRAK

Pendahuluan: Retinopati prematuritas (ROP) adalah suatu kelainan dari pembentukan retina dan vitreus akibat suatu angiogenesis yang abnormal. Anestesi pada pasien neonatus prematur harus mempertimbangkan adanya imaturitas fisiologis pada berbagai sistem tubuh, kelainan kongenital, toleransi yang buruk terhadap obat-obatan anestesi, dan juga risiko akibat pemberian oksigen konsentrasi tinggi.

Ilustrasi Kasus: Kami melaporkan enam kasus pasien ROP yang dilakukan laser fotokoagulasi intraokuler (LIO) dalam teknik Induksi dan Rumatan Anestesi Volatil (VIMA) melalui insuflasi kanul hidung. Pasien termuda berusia 32 minggu postmestrual age, dan pasien tertua berusia 36 minggu postmestrual age dengan berat badan terendah 1480 gram dan terberat 2770 gram. Prosedur anestesi dilakukan dengan memberikan campuran gas O₂, N₂O, dan sevoflurane 3-5 vol% sebagai agen induksi dan rumatan. Efek anestesi dicapai kurang dari lima menit. Lima dari enam pasien menunjukkan hasil yang baik tanpa adanya komplikasi atau efek samping serius. Pada satu orang pasien dilakukan intubasi dikarenakan adanya apnea periodik dan perubahan prosedur pembedahan dari LIO menjadi vitrektomi, namun demikian tidak ditemukan adanya komplikasi maupun efek samping pasca pembedahan.

Simpulan: Pencapaian induksi dan pemeliharaan anestesi yang efektif melalui teknik insuflasi sevoflurane melalui kanula hidung mengindikasikan potensi sebagai opsi praktis dan bebas opioid untuk induksi dan pemeliharaan anestesi volatile pada prosedur pediatrik.

Kata Kunci: laser fotokoagulasi; retinopati prematuritas; sevofluran; volatile induction and maintenance of anesthesia

INTRODUCTION

Retinopathy of prematurity (ROP) is a developmental abnormality of the retina and vitreous due to abnormal angiogenesis. Retinal blood vessels fail to grow and develop normally in premature infants, sometimes resulting in visual impairment and blindness.¹ Due to the immature physiology inherent in preterm and ex-preterm neonates, anesthesiologists face a substantial challenge when providing care to these patients. The considerations for anesthesia in preterm neonates revolve around the physiological immaturity of their diverse organ systems, associated congenital disorders further complicates matters (potentially leading to a diminished tolerance for anesthetic drugs), and carefully contemplate the utilization of high oxygen concentrations in the anesthesia management of these neonates.²

An ideal anesthesia for preterm and ex-preterm infants would be 'fast track anesthesia,' which minimizes cardiac and respiratory depression. Respiratory complications in ex-preterm infants can still occur until 60 weeks post-conceptual age.³ A meticulous dose and chosen anesthesia regimens should be considered thoroughly based on the patient's condition. The availability of an Intensive Care Unit (PICU/NICU) as a postoperative care should be considered in anesthetic planning, especially for patients with a high risk of postoperative respiratory and cardiac events.

As an induction and maintenance volatile anesthesia agent, sevoflurane provides rapid induction and emergence from anesthesia in pediatric patients.⁴ In this serial case report, we performed a volatile induction and maintenance anesthesia (VIMA) technique using a nasal cannula on six patients who underwent laser photocoagulation using a laser indirect ophthalmoscope (LIO) by delivering a gas mixture of O₂ 0.4 – 0.7 L/m, N₂O 0.3 – 0.5 L/m, and sevoflurane 3 – 3.5 volume % through a nasal cannula. All patients experienced the anesthesia effect within five minutes of receiving the gas mixture. Emergence from anesthesia occurred in less than five minutes after discontinuing N₂O and sevoflurane administration. Additionally, none of these patients required admission to the PICU.

CASE ILLUSTRATION

Case 1

The first patient was a male infant born at 30 weeks gestational age weighing 1450 grams and was treated in NICU for 25 days before being sent to the perinatology ward and scheduled for laser photocoagulation. The laser photocoagulation procedure was performed at 36 weeks postmenstrual age/PMA (gestational age plus chronological age), weighing 2100 grams. A gas mixture of O₂ 0.5 L/m, N₂O 0.5 L/m, and sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia and continued for anesthesia maintenance until the end of the procedure.

Case 2

The second patient was a female infant born at 26 weeks gestational age, weighing 800 grams with nasal septum anomaly, a large Patent Ductus Arteriosus, and was treated in NICU for eight weeks before being sent to the perinatology ward and scheduled for laser photocoagulation. The laser photocoagulation procedure was performed at 34 weeks PMA, weighing 1480 grams. A gas mixture of O₂ 0.4 L/m, N₂O 0.4 L/m, and sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia and continued for anesthesia maintenance. Anesthesia emergence was achieved in less than five minutes.

Case 3

The third patient was a female infant born at 28 weeks gestational age weighing 1300 grams and was treated in NICU for four weeks before being scheduled for laser photocoagulation. The laser photocoagulation procedure was performed at 32 weeks PMA, weighing 1800 grams. A gas mixture of O₂ 0.4 L/m, N₂O 0.4 L/m, and sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia and continued for anesthesia maintenance. There was a respiratory event recorded during the procedure, which was apnea and oxygen desaturation from 99% to 75%. During the apnea event, the heart rate dropped from 144 to 110. After positive pressure ventilation supplementation using a face mask for about 30 seconds, respiration went back to normal, and oxygen saturation

went back to 99%, then the maintenance of anesthesia continued through a nasal cannula until the end of the procedure. At the end of the procedure, N₂O and sevoflurane were stopped. Anesthesia emergence was achieved in less than five minutes.

Case 4

The fourth patient was a female infant born at 27 weeks gestational age weighing 1035 grams and was treated in NICU for 48 days before being scheduled for laser photocoagulation. The laser photocoagulation procedure was performed at 39 weeks PMA weighing 2770 grams. A gas mixture of O₂ 0.5 L/m, N₂O 0.5 L/m, and sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia and continued for anesthesia maintenance. At the time of insertion of the intravenous line, the patient woke up so that sevoflurane was increased to 4 vol%. Once the intravenous line was in place, sevoflurane was reduced to 3.5 vol% as the patient's respiration and pulse rate decreased from 35 to 20 and 125 - 135 to 90 - 105, respectively. After respiration and heart rate were back to the baseline, the procedure continued. At the end of the procedure, N₂O and sevoflurane were stopped, and anesthesia emergence was achieved in less than three minutes.

Case 5

The fifth patient was a female infant born at 33 weeks gestational age weighing 2200 grams and was treated in NICU for seven days before being scheduled for laser photocoagulation at 36 weeks gestational age weighing 2500 grams. A gas mixture of O₂ 0.5 L/m, N₂O 0.5 L/m, and

sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia. After 3 minutes, the patient was still awake, so the sevoflurane was increased to 5 vol% until the patient was asleep at 4 minutes 20 seconds. Periodic apnea was observed during the procedure, so the sevoflurane was decreased to 4 vol%. During periodic apnea, O₂ was increased to 0.7 L/m, and N₂O was decreased to 0.3 L/m. The lowest heart rate observed during periodic apnea was 90 bpm. At the end of the procedure, N₂O and sevoflurane were stopped, and anesthesia emergence was achieved in less than 2 minutes.

Case 6

The sixth patient was a male infant born at 30 weeks gestational age weighing 1580 grams and was scheduled for laser photocoagulation at 34 weeks gestational age weighing 2000 grams. A gas mixture of O₂ 0.5 L/m, N₂O 0.5 L/m, and sevoflurane 3 vol% was delivered through a nasal cannula to induce anesthesia and continued for anesthesia maintenance. Periodic apnea was observed several times during the examination. After the ophthalmologist did the retinal examination, they decided to do a vitrectomy procedure; therefore, we decided to do the endotracheal intubation to secure the airway and ventilation during the procedure. Endotracheal tube insertion was facilitated by increasing the depth of anesthesia using sevoflurane 8 vol% with no addition of opioids or muscle relaxants. Tetracaine 0.5% eye drop was given to the patients as an analgesic before the insertion of the vitrectomy trocar. No adverse events were observed during the postoperative period.

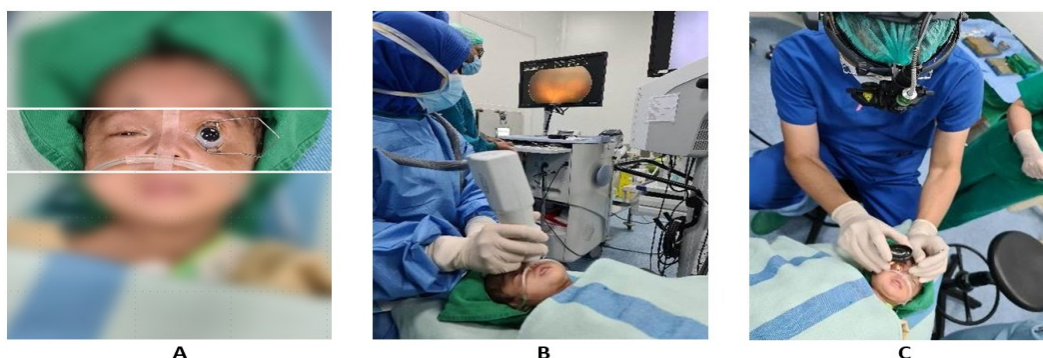


Figure 1. (A) Insufflation using a nasal cannula; (B) Diagnostic retinal camera; (C) Laser procedure

Table 1. Respondents characteristic

Gestational Age (weeks)	Birth Weight (grams)	Age at Procedure (weeks)	Body Weight at Procedure (grams)	Congenital Anomaly	Periodic Apnea	Total Gas Flow (L/min)	Vol %	Duration of Induction (minutes)	Duration of Anesthesia Emergence (minutes)
26	800	34	1480	Large PDA, nasal septum anomaly	None	0.8 - 1	3	< 3	< 5
27	1035	39	2770	None	None	1	3 - 4	< 5	< 3
28	1300	32	1800	None	Yes	0.8 - 1	3	< 3	< 5
30	1450	36	2160	None	None	1	3	< 3	< 3
33	2200	36	2500	None	Yes	1	3 - 5	< 5	< 2
30*	1580	34	2000	None	Yes	1	3	< 2	< 10

*Intubated due to surgical procedure conversion

DISCUSSION

ROP is a retinal vascular disease in premature infants. All babies less than 32 weeks gestational age or less than 1501 grams birth weight should be screened for ROP. Though it is well established through many studies that premature infants perceive painful stimuli and that ROP screening is a necessary but recognizably painful procedure, there are still no specific guidelines as to which type of anesthesia is preferable to others.⁵ This may cause a further problem in low and middle-income (developing) countries with limited health resources, where even normative ROP screening is still a big challenge to perform. These populations have higher threshold ROP morbidity.⁶⁻⁸

ROP remains among the leading causes of childhood blindness. It affects mainly premature infants who tend to be systematically and clinically unstable and are more prone to complications and anesthesia related adverse effects when undergoing examination or treatment. Premature infants requiring an ophthalmic examination or even surgery for ROP have a high prevalence of co-existing bronchopulmonary dysplasia (BPD). The reactive airway is one of the clinical presentations of BPD.⁹ Preterm and former preterm children had higher adverse event rates (14.7% vs 8.5%) compared with children born at term. Airway and respiratory adverse events were most commonly reported.¹⁰ General anesthesia using fentanyl and endotracheal tube has shown instability in

cardiorespiratory and difficulty in extubating in premature patients.¹¹

Short anesthesia induction time, stability and controllability of anesthesia during the procedure, rapid recovery from anesthesia, and no residual anesthesia before discharge should be ideal for ROP patients. A better comprehension of different analgesic and anesthetic methods used during screening and treatment may help in choosing a suitable option for ROP screening and treatment. The available anesthetic methods include sedoanalgesia, general anesthesia, peribulbar, and sub-tenon block. General anesthesia using a laryngeal mask airway (LMA) was found to be the most common type during LIO.¹² In this case report, we use only VIMA using sevoflurane insufflation technique delivered via a nasal cannula, and tetracaine drops as a local anesthetic without any intraoperative intravenous analgesic.

To fulfill the ideal anesthesia criteria for these patients, we decided to choose insufflation VIMA with spontaneous respiration technique using sevoflurane delivered through a nasal cannula. Given the nature of physiological obligate nasal breathers in infants, the proper size of the nasal cannula is vital to ensure gas exchange in the inspiration and expiration process. During NICU care, all of the patients already received oxygen supplementation using a nasal cannula without any other airway devices. On the day of the procedure, all patients were brought to the operating room using an incubator and oxygen supplementation using a nasal cannula.

The nasal cannula source was switched to an anesthesia machine in order to be able to deliver oxygen, nitrous oxide, and sevoflurane. After all the monitors were attached to the patient and baseline vital signs were read on the monitor, then oxygen, nitrous oxide, and 3 vol% sevoflurane started to be given to the patients. Since all of the gases were delivered via nasal cannula, the onset of induction was expected to be longer than face mask induction. We were not able to measure the inspired gas delivered to all patients. All patients were able to maintain spontaneous ventilation throughout the procedures. To prevent hypothermia, we used a circulated water mattress warmer for all these patients. The temperature for all the patients ranges between 36.5 – 37.5 °C throughout the LIO procedure.

As is known, sevoflurane as an inhalation anesthetic does not have any irritation in the respiratory tract, and it has a small distribution coefficient, short induction and recovery times due to its low blood-gas partition coefficient, short equilibrium time, and quick induction, making sevoflurane a good choice for day surgery.¹³ The Minimum Alveolar Concentration (MAC) of sevoflurane remained constant for neonates and infants < 6 months of age, 3.2 - 3.3 vol%, and then decreased to 2.5 vol% in infants > 6 - 12 months of age, where it remained unchanged in children up to 12 years.¹⁴ Another consideration in preterm infants is the impact of hypothermia on mortality and morbidity rate.

Nitrous oxide (N₂O) has been used for well over 150 years in clinical dentistry for its analgesic and anxiolytic properties. This small and simple inorganic chemical molecule has indisputable effects of analgesia, anxiolysis, and anesthesia that are of great clinical interest.¹⁵ At present there is insufficient evidence to support or refute its continued usage in pediatric practice. Though several new anesthetic agents have been developed, an alternative as flexible and cost-effective as nitrous oxide is yet to be discovered. Its use at clinically used concentrations and duration does not appear to be related to hematologic complications and neurobehavioral effects on the developing brain.¹⁶ In these cases, the use of N₂O showed an excellent analgesia effect. Opioid-free anesthesia

techniques allow rapid emergence, lower the risk of cardiorespiratory events during surgical procedures, and lower the risk of postoperative nausea and vomiting.¹⁷

There is a lack of clinical research regarding pain scores in laser procedures for ROP patients, but in comparison with adult patients, most adult patients describe it as a mild to moderate pain (Visual Analogue Scale 1 – 5) after the procedure.¹⁸ All patients in this case report were given 10 mg/kg BW intravenous paracetamol after the procedure. Paracetamol (acetaminophen) has been one option for neonatal pain therapy, and recently, it has been suggested as a novel treatment for patent ductus arteriosus of preterm infants.^{19, 20} As in FLACC (face, legs, activity, cry, and consolability) observational pain scoring in pediatrics patients, we observe the ease to console of these patients as an indicator of pain level, and all of them were easy to console by feeding breast milk or formula milk.

Although a postoperative PICU was prepared for these patients, as no respiratory or cardiac events were identified postoperatively, none of them were discharged to the PICU. All these patients were observed and discharged from the hospital the day after the procedure.

CONCLUSION

The sevoflurane insufflation technique via nasal cannula successfully induced and maintained anesthesia during the procedure. Volatile induction and maintenance anesthesia using sevoflurane insufflation, without the use of opioids, may serve as a practical alternative method in pediatric procedures. However, additional experience may be necessary to determine its clinical usefulness.

CONFLICT OF INTEREST

We have no conflicts of interest to disclose.

REFERENCES

1. Sola A, Chow L, Rogido M. Retinopathy of prematurity and oxygentherapy: A changing relationship. *An Pediatr.* 2005;62(1):48-61.
2. Taneja B, Srivastava V, Saxena KN. Physiological and anaesthetic considerations

- for the preterm neonate undergoing surgery. *J Neonatal Surg.* 2012;1(1):14.
3. Macrae J, Ng E, Whyte H. Anaesthesia for premature infants. *BJA Educ.* 2021;21(9):355-63. doi: 10.1016/j.bjae.2021.03.007.
 4. Goa KL, Noble S, Spencer CM. Sevoflurane in paediatric anaesthesia: a review. *Paediatr Drugs.* 1999 ;1(2):127-53. doi: 10.2165/00128072-199901020-00005.
 5. O'Sullivan A, O'Connor M, Brosnahan D, McCreery K, Dempsey EM. Sweeten, soother and swaddle for retinopathy of prematurity screening: a randomised placebo controlled trial. *Arch Dis Child Fetal Neonatal Ed.* 2010;95(6):F419-22. doi: 10.1136/adc.2009.180943.
 6. Chen Y, Feng J, Li F, Yin H, Liang J, Li X. Analysis of changes in characteristics of severe retinopathy of prematurity patients after screening guidelines were issued in China. *Retina.* 2015;35(8):1674-9. doi: 10.1097/IAE.0000000000000512.
 7. Roohipour R, Karkhaneh R, Farahani A, Ebrahimiadib N, Modjtahedi B, Fotouhi A, et al. Retinopathy of prematurity screening criteria in Iran: new screening guidelines. *Arch Dis Child Fetal Neonatal Ed.* 2016 ;101(4):F288-93. doi: 10.1136/archdischild-2015-309137.
 8. Weaver DT, Murdock TJ. Telemedicine detection of type 1 ROP in a distant neonatal intensive care unit. *J AAPOS.* 2012;16(3):229-33. doi: 10.1016/j.jaapos.2012.01.007.
 9. Kim HJ, Choi JG, Kwak KH. Bronchoconstriction following instillation of phenylephrine eye drops in premature infants with bronchopulmonary dysplasia: two cases report. *Korean J Anesthesiol.* 2015;68(6):613-6. doi: 10.4097/kjae.2015.68.6.613.
 10. Havidich JE, Beach M, Dierdorf SF, Onega T, Suresh G, Cravero JP. Preterm Versus Term Children: Analysis of Sedation/Anesthesia Adverse Events and Longitudinal Risk. *Pediatrics.* 2016 ;137(3):e20150463. doi: 10.1542/peds.2015-0463.
 11. Jiang JB, Strauss R, Luo XQ, Nie C, Wang YL, Zhang JW, et al. Anaesthesia modalities during laser photocoagulation for retinopathy of prematurity: a retrospective, longitudinal study. *BMJ Open.* 2017;7(1):e013344. doi: 10.1136/bmjopen-2016-013344.
 12. Alselaimy R, Al Tawil L, Abouammoh MA. Anesthesia in retinopathy of prematurity. *Saudi J Ophthalmol.* 2022;36(3):251-259. doi: 10.4103/sjopt.sjopt_229_21..
 13. Eger EI 2nd. New inhaled anesthetics. *Anesthesiology.* 1994;80(4):906-22. doi: 10.1097/00000542-199404000-00024.
 14. Lerman J, Sikich N, Kleinman S, Yentis S. The pharmacology of sevoflurane in infants and children. *Anesthesiology.* 1994;80(4):814-24. doi: 10.1097/00000542-199404000-00014.
 15. Emmanouil DE, Quock RM. Advances in understanding the actions of nitrous oxide. *Anesth Prog.* 2007 ;54(1):9-18. doi: 10.2344/0003-3006(2007)54[9:AIUTAO]2.0.CO;2.
 16. Gupta S, Mehta A. Open eye injury with full stomach. *The Internet Journal of Anesthesiology.* 2009;22(2):1-7.
 17. Franz AM, Martin LD, Liston DE, Latham GJ, Richards MJ, Low DK. In Pursuit of an Opioid-Free Pediatric Ambulatory Surgery Center: A Quality Improvement Initiative. *Anesth Analg.* 2021;132(3):788-97. doi: 10.1213/ANE.0000000000004774.
 18. Al-Hussainy S, Dodson PM, Gibson JM. Pain response and follow-up of patients undergoing panretinal laser photocoagulation with reduced exposure times. *Eye (Lond).* 2008;22(1):96-9. doi: 10.1038/sj.eye.6703026.
 19. Juujärvi S, Kallankari H, Pätsi P, Leskinen M, Saarela T, Hallman M, et al. Follow-up study of the early, randomised paracetamol trial to preterm infants, found no adverse reactions at the two-years corrected age. *Acta Paediatr.* 2019;108(3):452-8. doi: 10.1111/apa.14614.
 20. Balasubramanian H, Jain V, Bhalgat P, Parikh S, Kabra N, Mohan D, Sheth K. Low dose paracetamol for management of patent ductus arteriosus in very preterm infants: a randomised non-inferiority trial. *Arch Dis Child Fetal Neonatal Ed.* 2023;108(2):130-5. doi: 10.1136/archdischild-2022-323781.